

Title	OPTICAL ACTIVITY OF SPIRO [4.4] NONANE AND BICYCLO[3.3.0] OCTANE DERIVATIVES : PROPOSAL OF A SYMMETRY RULE FOR β , γ -UNSATURATED KETONES
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OPTICAL ACTIVITY OF SPIRO [4.4] NONANE AND BICYCLO [3.3.0] OCTANE DERIVATIVES

---- PROPOSAL OF A SYMMETRY RULE FOR β, γ –UNSATURATED KETONES

> by HIROKO KURITANI

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- Optically Active Spiro[4.4]nonane Derivatives: Syntheses and Circular Dichroism of βγ-Unsaturated Ketones. Hiroko Kuritani, Fumio Iwata, Munenori Sumiyoshi, and Keiji Shingu, J. C. S. Chem. Comm., 542 (1977).
- 2) Optically Active Spiro[4.4]nonane Derivatives: Syntheses and Circular Dichroism of Homoconjugated Dienes and Diketimine Derivatives. Hiroko Kuritani, Munenori Sumiyoshi, Fumio Iwata, and Keiji Shingu, J. C. S. Chem. Comm., 543 (1977).
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ABSTRACTS

Optically active spiro[4.4]nonane and cis-bicyclo[3.3.0]octane derivatives were prepared and their absolute configurations were determined by chemical correlation.

Their chiroptical properties were reasonably explained theoretically and the symmetry rule for β,γ -unsaturated ketones was proposed based on μ -m coupling mechanism.

I. Introduction

The fundamental principles of the chiroptical phenomena had been discovered more than 160 years ago¹⁾ and far before the great progress of stereochemical concept and classical theory of optical activity in last century.²⁾ Rosenfeld was the first to explain the physical origin of optical activity in homogeneous isotopic media by classical quantum mechanical terms (in 1928).³⁾ Later in 1937, Condon, Alter and Eyring established the so-called one-electron theory based on helical path of electron.⁴⁾ In the same year, on the basis of the classical quantum theory, Kirkwood⁵⁾ reformulated Kuhn's coupled oscilator model⁶⁾ and gave an expression for the monochromatic rotation of a dissymmetric molecule in terms of its geometrical configuration and the polarizability tensors of its constituent groups.

In spite of the beautiful developments in theory, the studies undertaken in the early 1930's on the applications of optical rotatory dispersion⁷⁾ and circular dichroism to organic chemical problems were often hampered by technical difficulties. But in the middle of the 1950's optical rotatory dispersion measurements, and shortly thereafter, the circular dichroism measurements were facilitated when a photoelectric spectropolarimeter becomes available,^{8,9)} and the assignment of absolute cofiguration of an optically active compounds based on their chiroptical phenomena has now become an intriguing problem for organic chemists. Mason¹⁰⁾ successfully applied the coupled oscilator model to the compounds of C₂ symmetry and since then the exciton coupling model has become one of the most attractive model of optical activity for organic chemists.¹¹⁾

On the other hand there have been proposed a number of semiempirical rules based on the one-electron model; octant rule for ketones (Djerassi), helicity rule for skewed diens (Charney), sector rule for mono-olefins (Scott) and so on.¹²⁾

Above all, the octant rule for saturated carbonyl compounds¹³⁾ has been one of the symmetry rules most extensively studied by both the experimentalists and theorists in connection with its applicability and validity. In its simplest form, the rule states that "the sign of the contribution which a given perturbing atom at point P(x,y,z) makes to

anomalous rotatory dispersion (of the ketone) will vary as (the sign of) the simple product, $X \cdot Y \cdot Z$ of its coordinates".¹⁴

However, increasing accumulated experimental data containing awkward doubts and exceptions to the rule has gradually obscured the strict meaning of the original 'octant' rule, though the rule has been and still now is of great value in assignments of structure and conformation.¹⁵⁾ Recently, Kirk and his co-workers have summarized and analysed a large number of experimental data of c.d. of saturated carbonyl compounds and estimated the sign and magnitude of the contribution from various position of perturber.¹⁶⁾ From their result, it is recognized that what governs the contribution to the c.d. of $n + \pi^*$ transition is not the product (xyz) but the form of sequense of bonds connecting the carbonyl group and the Today, the application of the so-called 'octant rule' for perturber. determining the configuration and conformation has become limited to the case which are essentially identical with those where the octant rule is already known to work.¹⁷⁾

On the other hand, the basic study of the chiroptical property of β,γ -unsaturated ketones has been performed by some groups mainly in the 1960's.^{18,19)} Of these studies, Mislow^{19d)} concluded from his analyses that a double bond of β,γ -unsaturated ketone is one of the important substituent groups whose geometric disposition in a particular far octant is sufficient for the determination of the sign of the long wavelength Cotton effect and that an enhanced Cotton effect accompanying an enhanced intensity in absorption is typical of conformations approximating the array in Figure 1A (or its antipode according to the sign of the Cotton effect).





The apparent agreement between the observed sign of c.d. and that expected from the octant rule when applied to double bond as a perturber permitted a generalization of the octant rule^{19d)} to include β ,Y-unsaturated ketones, although the theoretical principles involved are somewhat different from the case of the saturated alkyl ketones.¹⁹⁾ This extended octant rule has been effectively utilized for the determination of absolute configuration^{18,20)} and, in some cases, for the assignment of rotomeric conformations in situation where free rotation may occur.^{18,21,22)} However, as Mislow has already pointed out, the above generalization was inferred





CH₂

9



10

8



<u>11</u>



13

CH₂

14

3

CH₂

from the results of only three special cases (Figure 1 A, B, C).^{19d)} Hence it is instructive to consult another types of arrays for further generalization of the rule and thereupon for the conformational analyses.

Spiro[4.4] nonane derivatives $^{23\sim35)}$ have been useful substrates for chiroptical studies and offered the opportunity to investigate the interactions between functional groups in a certain mutual disposition because of their relatively rigid geometry. While the introduction of carbonyl group to one 5-membered ring of spiro[4.4] nonane does not cause any dissymmetric character, further introduction of double bond in the other ring makes the whole system dissymmetric, that is, the introduced double bond can be taken as the only perturber to the carbonyl group for the first order analyses and this makes the analyses of c.d. simple.

Meanwhile, cis-bicyclo[3.3.0]octane derivatives seem to have another type of skeleton appropriate for the study of the interaction between chromophores in β, γ -unsaturated ketones. These have been found in natural products and proved to be a useful precursor for the syntheses of some monoterpenes,³⁶⁾ yet the absolute configuration of its simplest asymmetric derivatives has not been established.37) Thus, as the model of some types of β , γ -unsaturated ketones, it has become neccessary to synthesize optically active β , γ -unsaturated ketones $1 \sim 4$ and their related compounds $5 \sim 14$ with spiro[4.4] nonane and bicyclo[3.3.0] octane skeletons, and to determine their absolute configurations by chemical corelations to the known compounds. These β, γ -unsaturated ketones $1 \sim 4$ have different types of mutual array of carbonyl and double bond and will surely offer an useful information about the effect of the relative orientation of two chromophores to their chiroptical properties.

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 0]octan-3-one has already been established.

II. Syntheses and absolute configurations of spiro[4.4] nonane derivatives.

1. Syntheses and optical resolution of spiro-alcohols.

There have been reported four methods of syntheses of the starting material, spiro[4.4]nonane-1,6-dione (5) (Scheme 1~3). These methods adopted different courses of cyclization to five-membered ring for the production of spiro-compound; thermal decarboxylation of anhydride^{1,2)} (Scheme 1), acid-catalyzed rearrangement of α,β -epoxyketone³⁾ (Scheme 2), intramolecular Claisen condensation^{3,4)} and acyloin condensation²⁾ (Scheme 3). The method in Scheme 1 was adopted for the benefit of large-scale synthesis.



Scheme 1



Scheme 2



Scheme 3

The treatment of Υ -butyrolactone⁵⁾ with hydrogen bromide in ethanol gave ethyl 4-bromobutyrate (<u>15</u>), which was emplyed twice for ethyl malonate synthesis to give tetraethyl 1,1,4,7-heptanetetracarboxylate (<u>17</u>) via trietyl 1,1,4-butanetricarboxylate (<u>16</u>). Alkaline hydrolysis afforded tetracarboxylic acid (<u>18</u>) which was treated with acetic anhydride to yield the bisanhydride. Thermal decomposition gave the desired spiro-dione 5 in 22% yield from diethyl malonate.

The course of preparation of racemic spiro-alcohols $\underline{19} \sim \underline{23}$ is outlined in Scheme 4.

According to Gerlach's procedure,⁶⁾ reduction of the diketone 5 with lithium aluminum hydride gave a mixture of three isomeric diols, cis-cis, cis-trans, and trans-trans.* The most minor product, (\pm) -trans, transspiro[4.4]nonane-1,6-diol (<u>19</u>), eluted last by column chromatography on silica gel to give diastereomerically pure crystals in 6.7% yield after recrystallization. A mixture of other two diols were oxidized with Jones' reagent** to give diketone <u>5</u>, reduced and separated repeatedly.

According to Cram's method⁸⁾ the partial hydrogenation*** of <u>5</u> over Adams catalyst in ethanol gave a mixture of cia- and trans-6-hydroxyspiro[4.4]nonan-1-one (<u>20</u> and <u>21</u>),**** which was nicely separated by column chromatography on silica gel in the isolated ratio 25:1.*****

- * 'Cis, cis','cis, trans', and 'trans, trans' correspond to rel-(lR, 5R, 6R), rel-(lR, 5S, 6S), and rel-(lR, 5S, 6R),⁷⁾ respectively.
- ** a solution of $CrO_3(100 \text{ g})$ and **c**. H_2SO_4 (100 ml) in $H_2O(250 \text{ ml})$. Oxidation of 1 mol alcohol needs 0.2895 mol of the solution.
- *** Recently, more effective method of reduction of <u>5</u> into ketol <u>20</u> and <u>21</u> using lithium hydridotri-t-butoxyaluminate at -30°C in tetrahydrofuran was reported; 94% yield, largely (95%) one product (g.l.c.).⁴⁾
- **** 'Cis' and 'trans' correspond to rel-(5R, 6R) and rel-(5R, 6S), respectively.
- ***** The ratio of 'cis' and 'trans' was reported by Cram⁸⁾ as 6:1 by the reduction in 95% ethanol and 1:2 in glacial acetic acid.



Scheme 4

The Wittig reaction of cis-ketol $\underline{20}$ with triphenylmethylphosphonium bromide and potassium t-butoxide in benzene gave cis-6-methylenespiro[4. 4]nonan-1-ol ($\underline{22}$)* in 18% yield without the recovery of $\underline{20}$, while the reaction with other solvent or base resulted in much lower yields. The protection of the hydroxyl group by the use of dihydropyrane before the introduction of exo-double bond made the carbonyl group less reactive to result in the complete recovery of the starting ether $\underline{24}$.**

In case of the synthesis of endo-olefinic alcohol $\underline{23}$, on the contrary, tetrahydropyranyl group functioned effectively as a protective group toward base. Cis-(tetrahydropyranyloxy)spiro[4.4]nonan-l-one $(\underline{24})$ *** with tosyl hydrazine in ethanol containing a small amount of pyridine gave the hydrazone $\underline{25}$ which was easily converted to the olefin $\underline{26}$ by the action of n-butyllithium.⁹⁾ The removal of the protecting group using hydrochloric acid in methanol proceeded smoothly to yield cis-spiro[4.4]non-6-en-l-ol ($\underline{23}$).****

Efficient optical resolution of the alcohols $\underline{19} \sim \underline{23}$ was readily achieved by converting them into diastereomeric mixture of camphanates $\underline{19'} \sim \underline{23'}$, respectively, by treatment with (-)-camphanyl chloride⁶ (derived from (-)-camphoric acid)¹⁰) in pyridine. (Scheme 5). The mixture of $\underline{19'}$ was chormatographically separated into (-)- $\underline{19'a}$ and (+)- $\underline{19'b}$ according to Gerlach's procedure.⁶) The mixture of $\underline{20'}$ was separated through column chromatography with benzene-ethyl acetate followed by recrystallization from cyclohexane, giving the more polar part (-)- $\underline{20'a}$ and the less polar part (+)- $\underline{20'b}$. The mixture of $\underline{22'}$ was separated in a similar manner to give (-)- $\underline{22'a}$ and (+)- $\underline{22'b}$. The employment of fractional crystallization alone could afford only diastereomerically pure (-)- $\underline{22'a}$. As both $\underline{21'}$ and $\underline{23'}$ did not give separated spots on thin layer chromatogram (silica gel), the separation of each mixture was

- * 'Cis' means rel-(lR, 5R).
- ** In contrast, tetrahydropyranylether of trans-ketol <u>21</u> reacted very smoothly with the Wittig reagent to give the corresponding olefin.

*** 'Cis' means rel-(1R, 5R).

**** 'Cis' means rel-(lR, 5S).





successfully achieved only by the use of fractional crystallization. The less soluble part of <u>21'</u> gave diastereomerically homogeneous (-)-21'a. <u>23'</u> was separated successively from n-hexane and methanol to yield (-)-23'a and (+)-23'b both in diastereomerically pure form.

The physical data of these diastereomeric camphanates are listed in Table 1 together with their absolute configurations determined in the following section.

Compound	Absolute Configuration	TLC	Solubility (solvent)	МР (°С)	[d] ₅₈₉ (solvent)
<u>19'a</u> <u>19'b</u>	1R,5S,6R 1S,5R,6S	more polar less polar	· · · · ·	220 174	-72° (CH ₂ Cl ₂) +51°
<u>20'a</u> 20'b	5R,6R 5S,6S	more polar less polar		115	-69° (EtOH) +40°
<u>21'a</u> <u>21'b</u>	55,6R 5R,6S	l spot	less soluble (cyclohex.) more soluble	108	-90° (EtOH)
<u>22'a</u> 22'b	1R,5R 18,5S	more polar less polar	less soluble (n-hex.) more soluble	132 90	-2.8° (EtOH) 0.0°
<u>23'a</u> 23'b	1R,5S 1S,5R	l spot	less soluble (n-hex.) more soluble	131 84	-132° (MeOH) +125°

Table 1. The absolute configuration and physical properties of diastereomeric camphanates.

2. Determination of absolute configurations

The absolute configuration of (-)-trans, trans-diol (<u>19</u>), obtained by alkaline hydrolysis of (-)-<u>19'a</u>, has been (etermined by kinetic resolution method (Horeau's method)¹¹⁾ as (1R, 5S, 6R). (Scheme 6)⁶⁾



Scheme 6

In addition, cis, trans-diol from (-)-dione 5 has recently been assigned as (5S) from the circular dichroism spectra of its bis-p-dimethylaminobenzoate based on the exciton coupling theory.* (Scheme 7, Figure 2)¹²) Therefore, (-)-diketone 5 from these (5S)-alcohols has been unambiguously determined as (S).

* The racemic diketone <u>5</u> was resolved by condensation with the oxamohydrazide, (-)-H₂NNHCOCONHCH(CH₃)Ph. The hydrazone was recrystallized and hydrolysed by refluxing in acetone-water in the presence of iodine to give (-)-5.



Scheme 7

Since diketone 5 is the starting material of other four spiro-alcohols $20 \sim 23$, the preparative course starting with the optically active diketone 5 via the same steps as racemic series seemed appropriate to establish the configuration in entire series. However, such a course was soon found unprofitable because of the instability of free ketols 20 and 21, which, under acidic or alkaline conditions, underwent cis-trans isomerization accompanied by considerable amount of decomposition,

(-)-5



Figure 2. The u.v., and calculated (....) and observed (----) c.d. of (-)-bis-p-dimethylaminobenzoate of cis,trans-spiro[4.4]nonan-1,6-diol in ethanol.

probably by retroaldol-aldol reaction (opening and reclosing of the ring).* Thus, it could not safely be expected that the further conversion of these ketols under various reaction conditions would necessarily proceed with no racemization.

As it was also found that the resolution via camphanic ester was more conveniently achieved with cis- and trans-ketols $\underline{20}$ and $\underline{21}$, we turn our attention to the pathways which correlate the configuration in each compound with that of diketone $\underline{5}$ not through the free ketol $\underline{20}$ but by employing the camphanates $\underline{20}'$ as the key compound. The correlation sequence finally employed is outlined in Scheme 8.

The reduction of (-)-20'a with excess lithium aluminum hydride in absolute ether afforded an epimeric mixture of diol 27, which was oxidized with Jones' reagent to give the known (R)-(+)-diketone 5, $[\alpha]_{589}^{20}$ +135° $(c \ 0.457, cyclohexane)(lit.,^{6)}(S)$ -diketone, $[\alpha]_D^{20}$ -135° (c 0.5, cyclohexane), in 93% yield from (-)-20'a. Thus, the configuration of 27 at the spiro atom was unambiuously established as (R), completing the assignment of (5R, 6R)-configuration to cis-ketoester (-)-20'a.

(-)-21 was related to (S)-(-)-diketone 5 in a similar manner, its absolute configuration being determined as (5S, 6R).

The Wittig reaction of (-)-20'a under the same condition as $(\pm)-$

* Elimination and rearrangement of the tosylate of cis-ketol 20 has been reported.⁴⁾





cis-ketol <u>20</u> gave a small amount of exo-olefin, which was found identical with (-)-22'a by TLC, IR and NMR examination. As <u>22'b</u> and other diastereomeric esters could not be detected in the reaction product, the possibility of isomerization between diastereomeric esters during the reaction was denied, though the yield was rather poor (18%).

The keystep for the correlation between 20' and 23' was the preparation of optically active ketol ether 24 from 20'a. The sequence employed, though lengthy, offered a sure method for the functional interconversion between carbonyl and hydroxyl groups of β -hydroxy ketone without affecting the asymmetric center. The catalytic reduction of (-)-20'a over Adams catalyst gave epimeric mixture of diol monocamphanates, which was separated by fractional recrystallization from cyclohexanebenzene to afford the more soluble epimer (-)-28, $[d]_{589}$ -24.3° (ethanol) and the less soluble one $(-)-\underline{29}$, [d] $_{589}$ -139.9° (ethanol) in the ratio (-)-28, after converted into its tetrahydropyranyl ether, was 4:1. reduced with lithium aluminum hydride to eliminate the camphanyl group and oxidized with Collin's reagent 13 to afford the ketol ether 24 in 35% yield from (-)-28. The cis-configuration of 24 was established by its IR spectrum which was identical with that of the racemic one obtained directly from the cis-ketol 20.* This fact was conclusive evidence that the configurations of the hydroxyl groups of 28 and 29 are cis and trans,** respectively. The assignment is also consistent with that deduced from the stereochemical consideration that the hydrogen addition to 20'a should

Treatment of optically active ether <u>24</u> with methanol-hydrochloric acid gave initially the spot of cis-ketol <u>20</u> on TLC, and two spots corresponding to cis- and trans-ketol (<u>20</u> and <u>21</u>) appeared after several minutes. Similar behavior was also observed in the conversion of racemic <u>24</u> into <u>20</u>. Tetrahydropyranyl ether from trans-ketol <u>21</u> gave, on treatment with hydrochloric acid, the spot of trans-ketol in the biginning. Mutual interconversion between cis- and trans-ketol was observed under either acidic or basic conditions.
** The absolute configuration of <u>28</u> and <u>29</u> are (1R, 5R, 6R) and (1R, 5R, 6S).

occur preferentially from the less hindered side of the carbonyl group.

The conversion of $\underline{24}$ into the unsaturated alcohol $(-)-\underline{23}$ was achieved smoothly by the same course as the racemate. Since optically active $\underline{23}$ was found much more unstable than the racemic one, especially in neat state, it was immediately converted to the camphanate, which was found diastereomerically pure after removing resinous contaminants and identical with $(-)-\underline{23'a}$ previously obtained by resolution of $(\pm)-\underline{23}$. Thus, it was proved, that the configuration at the spiro atom was little affected during the conversion of $(-)-\underline{20'a}$ into $(-)-\underline{23'a}$, the configuration of the latter being established as (1R, 5S).

In this manner the assignment of configuration to all the camphanates was placed on a firm footing. In addition, an interesting relationsphip was found between the configuration and physical properties of each pair of diastereomeric camphanates resulting from the resolution with (-)camphanyl chloride (Table 1). The diastereomer having R-configuration as

Compound	Absolute Configuration	TLC	Solubility (solvent)	MP (°C)	^[α] 589 (solvent)
I'a ¹⁵⁾ I'b	lR,2R,5R ls,2s,5s		less soluble (ether) more soluble	128 134	-42.9° (CHCl ₃) +20.3°
II'a ¹⁶⁾ II'b	1R,5S 1S,5R	2 spots	less soluble (ether-pent.) more soluble	159 135	-27° (CHCl ₃) +12.6°
III'a ¹⁶⁾ III'b	5R,6R 5S,6S	2 spots		152 133	-18.5° (CHCl ₃) +5.8°

Table 2. The absolute configurations and physical properties of diastereomeric camphanates reported in the literatures.

to the carbon atom to which the camphanyloxy group is attached showed more polarity on chromatography, less solubility and higher melting point than the corresponding isomer. These trends are also found in other cyclic secondary alcohols resolved with (-)-camphanyl chloride (see Table 2). The alcohols listed in Table 1 and 2 have a similar spacial arrangement, viz., bonds to methylene and branched chain around the methine carbon to which the hydroxyl group is attached (Figure 3). From these data it can be concluded that the camphanyl chloride is not only an effective resolving agent for secondary alcohols similar to those in Table 1 and 2 but a useful tool to predict the absolute configuration by camparison of the physical properties of the diastereomeric pair.



Figure 3. The spacial arrangement of secondary alcohol whose diastereomer obtained with (-)-camphanyl chloride shows more polarity on chromatography, less solubility and/or higher melting point than its corresponding isomer.

3. Syntheses of optically active $\beta,\gamma\text{-unsaturated}$ ketones and other related compounds

Synthetic courses of two β,γ -unsaturated ketones <u>1</u> and <u>2</u>, and other related compounds are shown in scheme 9, 10 and 11.



Scheme 9

The final step of syntheses of <u>1</u> and <u>2</u> was the hydrolyses and oxidation of <u>22'a</u> and <u>23'a</u>, which was easily achieved by usual methods though the yield of the desired unsaturated ketones decreased in the optically active series compared with the racemic one. The decrease was possibly due to the instability and/or sluggish reactivity of optically active alcohols.

The treatment of (1R, 5R) - (-) - 22'a with alkaline in aqueous methanol generated (1R, 5R) - (-) - cis-6-methylenespiro[4.4]nonan-1-ol (22), $[\alpha]_{589}$ -51.8° (methylene chloride), which was oxidized with Collins' reagent to give (R) - (+) - 6-methylenespiro[4.4]nonan-1-one $(\underline{1})$, $[\alpha]_{589} + 140°$ (methanol). Ketone $\underline{1}$ was also obtained by the partial Wittig reaction of (R) - (+) diketone $\underline{5}$ with triphenylmethylphosphonium bromide and potassium tbutoxide in pentane in 17% yield $([\alpha]_{589} + 135°, methanol)$. The almost concordant specific rotation of $\underline{1}$ prepared via the two route denied the possibility of the racemization of diketone $\underline{5}$ during the reaction,* also placing the assignment of configuration to $\underline{1}$ on a firm footing.

Wittig reaction of unsaturated ketone <u>1</u> under the same reaction conditions as above gave (R)-(+)-1,6-dimethylenespiro[4.4]nonane (<u>9</u>), $[<math>\alpha$]₅₈₉ +190° (isooctane).

(1R, 5S)-(-)-<u>23'a</u> was converted in a similar manner to (S)-(-)spiro[4.4]non-6-en-1-one (<u>2</u>), [α]₅₈₉ -317° (isooctane), in 13% yield, via (-)-cis-spiro[4.4]non-6-en-1-ol (<u>23</u>), [α]₅₈₉ -86.9° (pentane).

(R)-(+)-ketone $\underline{2}$ was also converted by Wittig reaction to (R)-(+)-6-methylenespiro[4.4]non-l-ene ($\underline{10}$), [d]₅₈₉ +109° (isooctane) in 44% yield.

* The photolytic racemization of spiro[4,5]octan-1,6-dione has been reported.¹⁶⁾







Scheme 10

(S)-(+)-Spiro[4.4]nonan-1,6-diene (8) was synthesized according to Cram's procedure.¹⁴⁾ (S)-(-)-Diketone <u>5</u> was treated with hydroxyamine bydrochloric acid in dry pyridine and ethanol to give dioxime <u>30</u>, which was hydrogenated over Adams catalyst in acetic acid to afford diamine <u>31</u>. Dimethylation of <u>31</u> with formaldehyde and formic acid gave bis-tertiary amine <u>32</u>, which was converted to (S)-(+)-quaternaryammonium salt <u>33</u>, $[\alpha]_D + 28^\circ$ (methanol), with methyl iodide. Treatment of (+)-33 with freshly prepared silver oxide and thermal pyrolysis gave (S)-(+)-diene <u>8</u> $[\alpha]_D + 119.3^\circ$ (n-pentane).

(S)-(-)-Disemicarbazone <u>6</u>, $[\alpha]_D$ -134.6° (methanol), was easily prepared from (S)-(-)-diketone <u>5</u> with semicarbazide hydrochloric acid by usual manner.

 $(S)-(-)-Bis-2,4-dinitrophenylhydrazone 7, [$\mathcal{O}]_D -231.8° (methanol), was derived from <math>(S)-(-)-5$, by the use of acetic acid in anhydrons ethanol as catalyst, because of instabilitly of diketone 5 toward mineral acids.

(1S, 5R, 6S)-(+)-Diol <u>19</u> was converted to (1S, 5R, 6S)-(+)-dibenzoate <u>34</u>, $[\mathcal{A}]_{D}$ +129.2° (methanol), by the use of benzoyl chloride in pyridine.



(+)- 8

(-)- <u>33</u>

<u>32</u>

Scheme 11

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- III. Syntheses and absolute configurations of bicyclo[3.3.0]octane derivatives.
- Syntheses, optical resolution and absolute configurations of cis-bicyclo-[3.3.0]oct-7-en-2-one and some related compounds.

The courses for the synthesis and resolution of endo-cis-bicyclo-[3.3.0]oct-7-en-2-ol (37)* are summarized in Scheme 12.**



Scheme 12

The alcohol $\underline{37}$ was prepared according to Crandall's procedure.²⁾ Commercially available 1,3-cyclooctadiene ($\underline{35}$) was oxidized with an equimolar amount of perbenzoic acid in benzene to give the monoepoxide $\underline{36}$,

- * 'endo-cis' corresponds to rel-(1R,2R,5R).
- ** A great number of methods for preparation of functionalized cis-bicyclo-[3.3.0]octane have been reported.¹⁾

which was rearranged by the action of lithium diethylamide* to yield the unsaturated alcohol 37 in 48% yield from the diene 35. The relative configuration of this alcohol has already been established as 'endo-cis' by Crandall.² **

Optical resolution of the alcohol <u>37</u> was nicely achieved by converting it to the diastereomeric mixture of camphanates <u>37'</u>, which was obtained in quantitative yield by treating <u>37</u> with (-)-camphanyl chloride in pyridine. The diastereomeric mixture <u>37'</u> was separated by fractional crysta lization, or by chromatography on silica gel, to give the more polar and less soluble part <u>37'a</u>, $[\alpha]_{589}$ +129.0° (ethanol), and the less polar and more soluble part <u>37'b</u>, $[\alpha]_{589}$ -139.8° (ethanol), each in pure form.***

Absolute configuration of <u>37'a</u> was determined by the course shown in Scheme 13. Oxidation of <u>37'a</u> with sodium metaperiodate in the presence of ruthenium dioxide⁴⁾ gave the diacid <u>38</u>, $[\&]_{589}$ +3.2° (ethanol). Solvolysis of <u>38</u> with sulfuric acid in methanol proceeded only partially, affoding the desired alcohl <u>39</u>, $[\&]_{589}$ -11.8° (ethanol), and methyl camphanate (<u>42</u>), $[\&]_{589}$ -124.4° (ethanol), as well as the esterification product <u>40</u>, $[\&]_{589}$ -4.87° (ethanol), and a small amount of the olefinic product <u>41</u>, $[\&]_{589}$ +54.1° (carbon tetrachloride). Methanolysis of <u>42</u> with hydrogen chloride gave (-)-<u>39</u> and (-)-<u>42</u> in 80% yield. (-)-<u>39</u> was oxidized with Jones' reagent to yield the ketone <u>43</u>, $[\&]_{589}$ -66.8° (methanol). Hydrolytic decarboxylation of (-)-<u>43</u> with concentrated hydrochloric acid gave 3-oxocyclopentaneacetic acid (<u>44</u>), which was purified via the methyl ester <u>45</u>, $[\&]_{589}$ -121.0° (chloroform). The optical rotation of the regenerated acid <u>44</u>, $[\&]_{589}$ -115.5° (chloroform), was nearly the same as that of the crude product.

- * Lithium diisopropylamide, potassium t-butoxide or lithium phosphate has been reported more effective than lithium diethylamide for the rearrangement of epoxide.³⁾
- ** IR spectra of <u>37</u> showed a strong internal OH-π hydrogen bond, establishing the endo-configuration of hydroxyl group (see Experimental Section).

*** Diastereomeric purity was ascertained by HPLC.



Scheme 13


R-(+) [x]_D+22°,CHCl₃







S-(-) [∞]_D-53.1°,CHCl₃

R-(-)-<u>47</u>

Scheme 14

The absolute configuration of <u>44</u> has already been determined by two routes of chemical correlations by Hill (Scheme 14).⁵⁾ One is correlated with norcamphor (<u>46</u>), and the other with 2-cyclopenteneacetic acid <u>47</u>, both establishing (S)-(-)-configuration of <u>44</u>. Since every reaction used for the degradation of <u>37'a</u> cannot affect the asymmetric center in <u>44</u>, the (1R,2R,5R) absolute configuration has now been assigned to (+)-<u>37'a</u> from the known (S)-configuration of (-)-<u>44</u> and from the established relative configuration of 37.²)

However, it should be noted that considerable discrepancy from the reported data was found concerning the optical rotation of 3-oxocyclo-pentaneacetic acid (<u>44</u>). Thus, according to Hill's work,⁵) a maximum rotation of -63° can be estimated for <u>44</u> from a route of chemical correlation in which (R)-(-)-2-cyclopenteneacetic acid (<u>47</u>) (84.3% optically pure, based on Mislow's work⁶) was converted to $(-)-\underline{44}$, $[d]_{589}$ -53.1° (chloroform). In the present work, the observed rotation for $(-)-\underline{44}$ (116°) should be regarded as the maximum value since the diastereomeric purity of (+)-37'a was ascertained by HPLC.

Syntheses of several optically active compounds from the camphanates 37'a and 37'b thus configurationally established are summarized in Scheme Hydrolysis of (+)-camphanate 37'a gave optically pure (+)-alcohol 15.



(+)-13









(-)-<u>37'b</u>



KOH



(-)- <u>49</u>

Jones' ox







<u>37</u>, $[\alpha]_{589}$ +210.6° (methanol),* which was oxidized with Collins' reagent to give (lR,2R)-(+)-cis-bicyclo[3.3.0]oct-7-en-2-one (<u>3</u>), $[\alpha]_{589}$ +619° (isooctane), in 50% yield. Wittig reaction of (+)-<u>3</u> in pentane yielded (lR,2R)-(+)-cis-8-methylenebicyclo[3.3.0]oct-2-ene (<u>14</u>). (+)-Alcohol <u>37</u> was treated with to\$yl chloride in pyridine to afford the tosylate <u>48</u>, $[\alpha]_{589}$ +520° (carbon tetrachloride), which was reduced with lithium aluminum hydride to give (lR,5R)-(+)-cis-bicyclo[3.3.0]oct-2-ene (<u>13</u>), $[\alpha]_{589}$ +88.9° (isooctane), in 24% yield.

Catalytic hydrogenation of (-)-camphanate <u>37'a</u> over Adams catalyst in ethanol afforded the camphanate (-)-<u>49</u>, $[\alpha]_{589}$ -22.4° (ethanol), which was hydrolyzed to give (lR,2S,5R)-endo-cis-bicyclo[3.3.0]octan-2-ol (<u>50</u>), $[\alpha]_{589}$ -30.6° (ethanol). Oxidation of (-)-50 with Jones' reagent gave (lR,5R)-(-)-cis-bicyclo[3.3.0]octan-2-one (<u>11</u>), $[\alpha]_{589}$ -176.3° (isooctane), in 78% yield. Wittig reaction of (-)-<u>11</u> with triphenylmethylphosphonium bromide and n-butyllithium in pentane afforded (lR,5R)-(-)-cis-2-methylenebicyclo[3.3.0]octane (<u>12</u>) in 10% yield.

* [\$\alpha]_{589}\$ +156.7° (chloroform). This value is higher than that obtained by resolving 37 via \$\alpha\$-methylbenzylurethane ([\$\alpha]_{589}^{23}\$ -123.7°, chloroform). This data was informed us by one of the referees of J. Org. Chem.

 Synthesis, Optical resolution and absolute configuration of cis-8methylenebicyclo[3.3.0]octan-2-one.

All reaction courses are summarized in Scheme 16 and 17. After some preparative experiments, tetrahydropyranyl group was found superior to methoxymethyl⁷⁾ and methoxyethoxymethyl⁸⁾ as the protective group of the alcohol,* though it introduces another asymmetric center, complicating the analyses of NMR spectra.

Tetrahydropyranyl ether 51^{**} was prepared in 93% yield from (±)alcohol <u>37</u> by the action of dihydropyran in the presence of catalytic amount of phosphorousoxychloride. The ether 51 was oxidized with mchloroperbenzoic acid under alkaline condition⁹⁾ to give a diastereomeric mixture of epoxides <u>52</u>.*** Reduction of <u>52</u> with lithium aluminum hydride gave a mixture of alcohols <u>53</u>, which showed four spots on TLC over silica gel, suggesting the presence of two isomers of epoxide <u>52</u> (endo and exo) and the attack of lithium aluminum hydride at 2- and 3-positions of each isomer of the epoxide <u>52</u>. Consideration about the stereochemistry of the reactions indicates, however, that the configuration of the main product is exo-2-ol, since the epoxidation of <u>51</u> would occur preferentially from exo-side to give mainly exo-epoxide, which would then be attacked by lithium aluminum hydride at 3-position predominantly.

Oxidation of the mixture of alcohols 53 with Collins' reagent gave a mixture of ketones 54, which was treated with triphenylmethylenephosphorane in benzene to afford the olefin 55. HPLC of 55 showed the presence

- * Methoxymethyl ether from <u>37</u> was very volatile and methoxyethoxymethyl ether was not appropriate because of the instability of the resulting alcohol under the deprotecting conditions.
- ** HPLC of <u>51</u> showed two peaks of the same strength, which originate from two diastereomers caused by the newly introduced asymmetric center.
- *** Presence of two isomers (endo and exo) of <u>52</u> could not be detected by HPLC which showed two peaks of almost the same strength. In the case that the protective group is methoxyethoxymethyl, product ratio was about 7:1 by NMR examination.



 $R = \int_{0}^{\infty}$



ÒR





0









Scheme 16

of two isomers in the ratio 7:2. Acidic hydrolysis of <u>55</u> yielded a mixture of unsaturated alcohols, which was separated by column chromatography over silica gel to give the less polar alcohol <u>56</u> and the more polar one <u>57</u>. The structure of <u>56</u> was ascertained by its IR spectrum which showed a very strong intramolecular $OH \rightarrow \pi$ hydrogen bond, whilst no intramolecular hydrogen bond was observed for <u>57</u>.



(±)- <u>56</u>



ĊΗ2

(+) - 4

Ó

COCI Pyr.



(-)- <u>56'a</u>

CH2 OR (+)- <u>56'b</u>

кон



(+)-<u>56</u>



ÔН







The alcohol <u>56</u> was resolved via camphanate ester as in the case of <u>37</u>. The mixture of camphanates <u>56'</u> was separated by column chromatography over silica gel to give, after recrystallization from methanol, the more polar part 56'a, $[\alpha]_{589}$ -99.4° (ethanol), and the less polar part <u>56'b</u>, $[\alpha]_{589}$ +86.7° (ethanol). The absolute configuration of <u>56'</u> was determined by converting it to <u>12</u>. Thus alkaline hydrolysis of (+)-<u>56'b</u> regenerated (+)-<u>56</u>, $[\alpha]_{589}$ +103.9° (pentane), which was treated with tosyl chloride in pyridine to give (+)-tosylate <u>58</u>, $[\alpha]_{589}$ +97.6° (carbon tetrachloride). Reduction of (+)-<u>58</u> with lithium aluminum hydride gave (+)-olefin <u>12</u>, which has (15, 55)-configuration. Hence the absolute configuration of (+)-<u>56</u> was established as (15, 25, 5R).

Oxidation of (+)-alcohol <u>56</u> with pyridinium chlorochromate in the presence of sodium acetate gave (1S, 5R)-(+)-cis-8-methylenebicyclo[3.3.0]oct-2-one (<u>4</u>), $[\alpha]_{589}$ +80.3° (isooctane). Facile rearrangement of (<u>t</u>)-<u>4</u> to α,β -unsaturated ketone <u>59</u> was observed on treatment with alumina, also confirming the homoconjugated structure of <u>4</u>. (Scheme 18)



Scheme 18

Catalytic reduction of $(+)-\underline{4}$ over Pd-C gave a mixture of endo- and exo-methyl ketone <u>60</u>, the separation of which has not yet been achieved. The negative sign of c.d. of <u>60</u> in the $n \rightarrow \pi^*$ region also confirms the (1S, 5R)-configuration of $(+)-\underline{4}$. Absolute configurations and physical properties of diastereomeric camphanates <u>37'</u> and <u>56'</u>

The absolute configuration and physical properties of diastereomeric camphanates <u>37'</u> and <u>56'</u> are summarized in Table 3. Here again, the camphanates from (-)-camphanyl chloride and the secondary alcohols having the configuration shown in Figure 3 exhibit more polarity on chromatography, less solubility and higher melting point than the corresponding diastereoisomer, in accord with the trend of the compounds previously studied (Table 1 and 2). These results shows that camphnate is also useful for the optical resolution and the determination of absolute configuration of these endo-cis-bicyclo[3.3.0]octan-2-ol derivatives.

Compound	Absolute Condiguration	TLC	Solubility (solvent)	мр (°С)	<pre>[α] 589 (solvent)</pre>
<u>37'a</u> <u>37'b</u>	1R,2R,5R 1S,2S,5S	more polar less polar	less soluble (n-hex.) more soluble	111 79	+129° (EtOH) -140°
<u>56'a</u> 56'b	1R,2R,5S 1S,2S,5R	more polar less polar	less soluble more soluble	122 95	-99.4° (EtOH) +86.7°

Table 3. The absolute configuration and physical properties of diastereomeric camphanates.

 Bicyclo[3.3.0]octenol as an effective tool for the determination of absolute configuration of chiral acids.

----- The absolute configuration of aryl-t-butylacetic acid.

Horeau's method has found the greatest use in the assignment of the absolute configuration of chiral secondary alcohls.¹⁰⁾ Since this method is based on the kinetic resolution of a racemic acid anhydride by an optically active alcohol, the absolute configuration of a chiral acid can also be determined, in principle, by the use of an active alcohol of known configuration.¹¹⁾ This possibility has preliminarily been tested by Horeau¹⁰⁾ using (-)-menthol (<u>65</u>) with some acids which have an asymmeric tertiary carbon atom attached by an alkyl and a phenyl group (<u>61</u>; R = methyl,ethyl n-propyl, and isopropyl).

One prerequisite for the success of this empirical method is the clearcut decision of the sequence of "size" of the substituents in the chiral acid. Hence, the kinetic resolution of t-butylphenylacetic acid $(\underline{63})$ of known configuration¹²) seems interesting in testing the defference in "size" between a t-butyl and a phenyl group which cannot a priori be decided.



Another is the selection of effective alcohols which give satisfactory optical yields in the kinetic resolution. endo-cis-Bicyclo[3.3.0]octanol $\underline{37}$ and $\underline{50}$ are expected to be more effective than $\underline{66}$ for the chiral descrimination (consequently, for the assignment of the absolute configuration) of acids, since, because of their endo-cis structure, the differences in the steric requirement between the substituents around the hydroxy methylene carbon in them are larger than that in $\underline{66}$.

Table 4. Kinetic resolution of acid anhydrides with optically active alcohols.

Entry	Anhydride of the Acid	Alcohol	Reaction Time	Recov- ered Alcohol	Esterifi- cation Yield	Observed Rotation of the Residual Acid	Optical Yield
(NO)	(mg)	(mg)	(hr) [·]	(mg)	(%)	(degree)	(8)
	62					•	
1	160.4	(+)- <u>37</u> 34.	5 4	_ b)	67 ^{e)}	+0.201 ^{g)}	69
2	162.4	(+)-50 34.	1 4	_ b)	81 ^{e)}	+0.156 ^{g)}	45
3	167.2	$(-)-\underline{66}^{a}$ 44.	2 4	_ b)	81 ^{e)}	+0.145 ^{g)}	40
	<u>63</u>			•			
4	162.9	(+)- <u>37</u> 27.	0 19	16.2 ^{C)}	40 ^{f)}	+0.068 ^{h)}	33
5	212.9	(+)- <u>37</u> 35.	8 237	_ d)	100 ^{f)}	+0.215 ^{h)}	32
6	215.3	$(-) - \underline{66}^{a}$ 45.	7 236	d)	100 ^{f)}	+0.012 ^{h)}	2
	<u>64</u>				<u> </u>		
7	253.3	(+)- <u>37</u> 35.	0 237	7.9 ^{C)}	77 ^{f)}	+0.377 ^h)	22
8	193.5	$(-) - \frac{66}{66}^{a}$ 28.	8 236	_ d)	100 ^{f)}	+0.045 ^{h)}	3

a) [α]₅₈₉ -50.34° (*c* 4.07, ethanol)

b) not isolated

c) isolated by column chromatography on silica gel

d) alcohol was not detected by TLC on silica gel

e) calculated from the titrated volume according to Horeau's procedure¹⁾

f) calculated from the recovered alcohol

g) measured at 589 nm in benzene (10 ml, l = 1 dm)

h) measured at 405 nm in ethanol (10 ml, l = 1 dm)

From these points of view, the kinetic resolution of the anhydride of (\pm) -2-phenylbutanoec acid $(\underline{69})^*$ and that of (\pm) -t-butylphenylacetic acid $(\underline{63})$ are examined by the use of the alcohols $\underline{37}$, $\underline{50}$, and $\underline{66}$. In addition, the anhydride of (\pm) -t-butyl- α -naphthylacetic acid $(\underline{64})$ was examined as the application of this method to the configuration assignment of aryl-t-butylacetic acid. Each acid anhydride was prepared from the sodium salt of acid with oxalyl chloride.¹⁰⁾ Kinetic resolution was carried out according to Horeau's procedure,¹⁰⁾ using a small amount of the active alcohol and about double the molar quantity of the anhydride. The results are listed in the table 4.

In entry $1 \sim 3$ with 2-phenylbutanoic anhydride, all three alcohls, (+)-<u>37</u>, (+)-<u>50</u>, and (-)-<u>66</u>, gave the same enantiomer of residual acid, (+)-<u>62</u> (<u>65a</u>, R = ethyl). Therefore, it turned out that the steric arrangement around the hydroxy methylene group in (+)-<u>37</u> and (+)-<u>50</u> is the same as that in (-)-<u>66</u> which has the configuration shown by <u>67</u>,¹⁰⁾ where L (large) and M (medium) indicate the relative "size" of the substituent groups. This is consistent with the expectation from the established absolute configuration of (+)-<u>37</u> and (+)-<u>50</u>.** In particular, (+)-<u>37</u> gave extremely high optical yield, demonstrating its powerful ability in the determination of absolute configuration of chiral acids.

Furthermore, these experimental results make it reasonable to postulate that the configuration of the residual acid obtained by the reaction with the alcohl <u>67</u> is shown by <u>65b</u>, since the phenyl and ethyl groups in <u>65a</u> (R = ethyl) are considered to be L and M, respectively.***,***

- * 2-Phenylbutanoic acid (<u>61</u>), which is the standard acid for Horeau's method, is commercially available.
- ** Bridged five membered rings correspond to L group and methylenes to M group.
- ** In Horeau's method, the relative sizes of phenyl and alkyl groups in active secondary alcohols are established as L and M, respectively.
- *** Horeau reported a striking illustration of the concept of steric size in alkylphenylcarbinols with 2-phenylbutanoic anhydride;¹⁰⁾ the phenyl group always appears to be the "largest" - even though alkyl group is t-butyl or triphenylmethyl.

In entry 4, 5 and 6, the effect of an increase in "size" of the alkyl substituents in acids was examined by use of the anhydride of $(\pm)-\underline{63}$ of known absolute configuration.¹²⁾ Both $(+)-\underline{37}$ and $(-)-\underline{66}$ gave the dextro residual acid $\underline{63}$ whose configuration is shown as $\underline{68}$.¹²⁾ Since this residual acid also is expected to have the arrangement of $\underline{65b}$, the phenyl and t-butyl groups can be decided as L and M, respectively. This result is in harmony with the order of "size" of the groups found in benzylic alcohols by Horeau.¹⁰⁾

However, the optical yield was very poor by the use of $\underline{66}$, showing that $\underline{66}$ is unsuitable for the kinetic resolution of this type of acid, whilst $\underline{37}$ gave the relatively high optical yield. This indicates the great usefulness of $\underline{37}$ for the determination of the absolute configuration of aryl-t-butylacetic acid, which seems troublesome by means of chemical method.*

Next, the determination of the hitherto unknown absolute configuration of t-butyl- α -naphthylacetic acid (<u>64</u>) was undertaken (entry 7 and 8). (+)-<u>37</u> gave much higher optical yield than (-)-<u>66</u>, affording the dextro residual acid <u>64</u>. If naphthyl group is assumed to be "larger" than t-butyl group as is the case with phenyl group in <u>68</u>, the absolute configuration of (+)-<u>64</u> is expected to be (S), that is, <u>69</u>. This was confirmed by its chemical correlation with (S)-(+)-<u>63</u>,** and bicycloalcohol <u>37</u> has proved to be useful for the kinetic resolution to determine the absolute configuration of aryl-t-butylacetic acid.

- * The configurational assingment of 2-naphthylpropionic acid was achieved by the method of quasi-racemate.
- ** Both (+)-<u>63</u> and (+)-<u>64</u> were prepared according to Mosher's procedure and converted to (+)-dimethyl t-butylsuccinate, [α]₅₈₉ +12.4° (c 1.123, ethanol), via several steps.¹⁴)

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1. β, γ -Unsaturated ketones 1 and 2.

The u.v. and c.d. spectra of two β,γ -unsaturated ketones <u>1</u> and <u>2</u> are shown in Figure 4 and 5, respectively. The data are summarized in Table 5. The u.v. absorption of <u>1</u> and <u>2</u> at ca. 300 nm are assigned to the $n + \pi^*$ transition of carbonyl. Since the absorp-





(-) - 2





tion intensity for the reference compounds (see Table 6) ranges from 19 to 24 in the region of 300 nm, the intensities of two β,γ -unsaturated ketones <u>1</u> and <u>2</u> (and also diketone <u>5</u>) are evidently enhanced ones, showing the existence of interaction between a carbonyl and other chromophores.¹⁾

The interaction between a carbonyl group and a C=C double bond has so far been widely studied (Figure 6).¹⁾ Hyperchromic effect was not observed in the case that carbonyl group and C=C double bond are coplanar and parallel, or perpendicular to each other ($\underline{70}$ $\underline{72}$). But when the two groups are not coplanar and located at an appropriate position, an increase of absorption coefficient of $n + \pi *$ transition was observed, and this behavior is well known as 'homoconjugation' ($\underline{73}$, $\underline{74}$. compare $\underline{75}$). Hence the





	isooctane				meth	anol		
	u.	v.	с.	đ.	u.,	7.	с.	đ.
Compound	λ_{max}	ε	λ_{\max}	Δε	$\lambda_{\texttt{max}}$	ε	λ_{\max}	Δε
(R)-1	322sh	29.2	319sh	+0.90				
-	310	56.9	309	+1.50				
	301	66.1	301	+1.47	298.5	65.2	302	+0.91
	294sh	59.2	293sh	+1.16				
	286sh	45.9	285sh	+0.79				
	204	5630	207	+11.95			231	-0.081
					199.5	5930	202	+11.4
	182.5	10000		. · ·				
(0) 2	22605	42.0	227-b					
(S) - <u>2</u>	3265N	42.0	32/SN	-1./8				
	314Sh	/8.8	312	-3.07				
	306	86.8	306	-3.14	303.5	87.9	305	-2.53
	298sh	76.4	298sh	2.52				•
	197	4760	205	-11.7				
	1							

Tavle 5. U.v. and c.d. spectra of (R) - (+) - 6-methylenespiro[4.4]nonanl-one (<u>1</u>) and (S)-(-)-spiro[4.4]non-6-en-l-one (<u>2</u>).

Table 6. U.v. data of cyclic ketones.^{2,3)}

Compounds	solvent	λ _{max} (ε)
spiro[4.4]nonan-1-one a mixture of cis- and trans- spiro[4.4]nonan-1-one (<u>20</u> and <u>21</u>)	95% EtOH 95% EtOH	300 (21) 300 (24)
cyclopentanone	EtOH n-hexane	300 (16) 299 (20)
camphor	n-hexane	293 (20)
cyclobutanone	n-hexane	280 (18)
menthone	n-hexane	295 (20)



1500





72

70 λ_{max} 214

ε

λ_{max} 209.5 298.4 ε 3110 32

<u>71</u>

no enhancement of $n \rightarrow \pi^*$ transition



284

30

75

 λ_{max}

295



74 308 $^{\lambda}$ max 266

266 ε 27

Figure 6. U.v. of some β,γ -unsaturated ketones and reference ketone.

enhancement of absorption observed for $\underline{1}$ and $\underline{2}$ in 300 nm region can be attributed to the homoconjugation (interaction between a carbonyl and a double bond), though the relative array of two chromophores in $\underline{2}$ is entirely different from the types ever studied.

In the region of 200 nm, both ketones show two main absorption bands. The absorption of carbonyl has been assigned, in general, as $n + \pi^*$, $n + \sigma^*$, $\sigma + \pi^*$ and $\pi + \pi^*$ from longer to shorter wavelength, respectively, though a clear-cut conclution has not yet been drawn for $\sigma + \pi^*$ and $\pi + \pi^*$ transition.⁴⁾ Therefore, the lower frequency band in <u>1</u> and <u>2</u> was attributed to the $n + \sigma^*$ transition of carbonyl group in agreement with the fact that it underwent blue shift when the solvent was changed from isooctane to methanol. The fact that the dione, but not the corresponding dienes (see following

section), shows the absorption in this region also supports this assignment. The absorption in the higher frequency side was then assigned to $\pi + \pi^*$ transition of C=C double bond.

In c.d. spectra, the signs in the $n \rightarrow \pi^*$ region are negative and positive for <u>2</u> and <u>1</u>, respectively. From the generalized octant rule proposed by Mislow and his coworkers,⁵⁾ the enhanced absoption together with enhanced c.d. must correspond to the conformation and absolute configuration as depicted in Figure 1A, or, (-)-A or (+)-A in Figure 7 according to the c.d. sign. As can easily be seen from molecular models, the olefinic double bond of both compounds is always placed in the upper left (or lower right rear) octant with respect to the carbonyl group, irrespective of the relatively mobile conformation of 5-membered rings. If the extension of generalized octant rule as proposed by Mislow is valid, <u>2</u> as well as <u>1</u> must show the positive c.d. sign in the $n + \pi^*$ region. Hence the observed positive c.d. for exo-olefinic ketone <u>1</u> is consistent with the prediction from the generalized octant rule. However, the endo-olefinic ketone <u>2</u>



(+)-A

(-)-A



Figure 7. Mutual disposition of the carbonyl group and double bond.

shows a negative c.d., that is, dissignate behavior, though it shows enhanced u.v. and c.d. absorption in this region compared to the exoolefinic ketone 1.

The generalized octant rule was proposed originally for the case in which the carbonyl group and olefinic double bond are arranged as A in Figure 7. But it has often been applied to the assignment of conformation or even of configuration in the case in which rotomers can exist, stressing the contribution of A conformation. $^{6 \sim 9)}$

Endo-olefinic ketone 2 cannot assume A conformation. Instead, the arrangement of its chromophore can be shown by B in Figure 7. Hence, it is now proved that in such a conformation the c.d. sign in the $n \rightarrow \pi^*$ region is opposite to expectations from the generalized octant rule. The inapplicability of the generalized octant rule to the ketone 2 exhibits that the sign of $n \rightarrow \pi^*$ region is dependent upon the direction of the double bond as well as its position in the carbonyl octant. In other words, the octant rule for β , γ -unsaturated ketone (generalized octant rule) is not true octant rule, but is restricted to the only one inherently dissymmetric system as in Figure 7A, that is, the c.d. sign in the $n \rightarrow \pi^*$ region is predicted to be negative or positive only for the type of array (-)-A or (+)-A, respectively. Thus the results found for $\underline{2}$ illustrates another rule for the inherently dissymmetric β , γ -unsaturated ketones; the sign of c.d. is negative or positive for the type of array (-)-B or (+)-B, respectively.

This conception can be further illustrated in some reinvestigated compounds. Figure 8 shows the epimers of A-norcholestanones studied by Zeeh⁸⁾ and Ziffer.¹⁰⁾ These compounds have vinyl group at C(5) position and show opposite c.d. sign to each other in the $n \rightarrow \pi^*$ region. Zeeh assigned β -configuration to one isomer that showed negative c.d. sign, and α -configuration to the other on the basis of generalized octant rule, whereupon the double bond was considered to be rotated towards the steroid skeleton (Figure 9). But Silverton and Ziffer established the reverse assignment as depicted in Figure 8 and 9 by X-ray study.¹⁰⁾ The double bond was found to be orientated towards outside of the steroid skeleton. The conformation is also likely to be that preferred in solution, and it is similar to the conformation of endo-olefinic ketone <u>2</u>, that is, B configuration in Figure 7. If the chiroptical contribution from each asymmetric



^{∆ε}300

-4.06





^{∆ε}295



-1.27





Zeeh (1968)

Ziffer (1975)

Figure 9. Conformation of A-norcholestanone 76 and 77; assumed from generalized octant rule (left) and determined by X-ray analysis (right).

perturber can be additional, the effect of double bond can be estimated by comparison of c.d. data between <u>76</u> and <u>78</u>, and between <u>77</u> and <u>79</u>. The contribution from carbon skeleton (octant contribution) thoroughly appears in the saturated ketones <u>78</u> and <u>79</u>, and therefore, the contribution from vinyl group ($\delta \Delta \epsilon$) is roughly estimated as -2.79 (1.27-4.06) and +2.24 (3.03-0.79) for <u>76</u> and <u>77</u>, respectively. These values are antipodal to each other and compatible with that of the endo-olefinic ketone <u>2</u> ($\Delta \epsilon = -2.53$ in methanol), in which the olefinic group is the only dissymmetric perturber.

Another example is the 16,17-fused cyclobutane adduct of 3-acetoxypregna-5, 16-dien-20-one <u>80</u> and <u>81</u> (Figure 10).^{6d, 9)} Negative c.d. sign of <u>80</u> was reasonably explained on the basis of A-arrangement in Figure 7, whilst in <u>81</u> the acetyl group was supposed to be rotated so that the methyl group is directed towards the steroid skeleton, in order to explain the positive c.d. sign on the basis of the same A-arrangement. However, the c.d. sign of <u>81</u> can be reasonably explained on the basis of B-arrangement which allows the acetyl group to assume a sterically preferred position as in case of <u>80</u>.







80

[0]₂₉₅

-18,180



81

[0]₃₀₀ +15,380

Figure 10. C.d. of 16,17-fused cyclobutane adduct of 3-acetoxypregna-5,16-dien-20-one.

2. Spiro[4.4] nonane-1,6-dione (5).

The u.v. and c.d. spectra of (S)-(-)-spiro[4.4] nonane-1,6-dione $(\underline{5})$ are shown in Figure 11. The data are summarized in Table 7 and 10. Similarly to β,γ -unsaturated ketones $\underline{1}$ and $\underline{2}$, the absorption in the $n + \pi^*$ region is much enhanced compared to the non-conjugated cyclopentanones (see Table 6). In the diketone $\underline{5}$, there must surely exist the overlap integral (hence the interaction) between the two carbonyl groups, though it may not be so large as in **d**-dicarbonyl compounds. Therefore, the $n + \pi^*$ transition in one carbonyl group would interact with the next lower tran-









cyclo	ohexane	meth	anol
$\lambda_{\texttt{max}}$	ε	λ_{\max}	E
326.5sh 316.5sh 311.5 305.5sh 301.0 295.0sh 285.5sh 273.5sh 259.0sh	53.4 88.2 98.4 98.2 100.3 89.0 75.5 51.0 22.3	320.0sh 314.0sh 307.0sh 299.0 293.0sh 282 0sh 270.0sh	44.3 64.2 78.5 87.0 83.9 69.7 45.6
217.5sh 205.0sh 202.0	1210 3670 3800	219.5 203.3 196.0sh	1150 3040 2100

Table 7. U.v. spectra of spiro[4.4]nonane-1,6-dione (5).

Table 8. C.d. spectra of (S)-(-)-spiro[4.4] nonane-1,6dione (5) in EPA at different temperatures.

+23°C		-68°C		-190	-190°C	
λ_{max}	Δε	λ_{max}	Δε 	^λ max	Δε	
326 sh 323 313 305 303.5 295 287 282 sh 226	-0.67 -0.78 -1.17 +0.04 -0.03 +1.56 +1.66 +1.27 -8.00	327sh 322sh 313 306sh 295 287 280sh 225.5	-0.74 -1.07 -1.49 -0.71 +0.95 +1.27 +0.94 -5.87	318sh 314 308sh 294sh 287 224.5	-1.67 -1.84 -1.53 +0.24 +0.69 -4.72	
$R^{n-\pi^*}$ -22.4 x 10 ⁻⁴⁰		$R^{n-\pi*}$ -0.38 x 10 ⁻⁴⁰		R ⁿ⁻ +1.84	π* x 10 ⁻⁴⁰	

sition in the other carbonyl, which presumably corresponds to the absorption observed at 203 and 219 nm. These two absorptions are assigned to $n \rightarrow \sigma^*$, since they does not show bathochromic shift when the solvent is changed from nonpolar to polar one.

The c.d. in 300nm region shows two oppositely signed bands.* For investigation of the origin of these two bands, the c.d. of (S) - (-) - 5 was measured in EPA (ether-petane-ethenol, 5:5:2) solution at different







Figure 13. C.d. of (R) - (+) - 5 in iso-pentane-methylcyclohexane

Figure 12. C.d. spectra of (S)-(-)-spiro-[4.4]nonane-1,6-dione (5) in EPA (5:5:2) at different temperatures. 5:1 (upper) and EPA 5: 5:2 (lower) given by Lightner.¹¹⁾

The theoretical explanation for u.v. and c.d. of 5 hitherto reported are reviewed in Section VI.

temperatures. The results are shown in Figure 12 and Table 8. The correction factors for the density change of EPA are given in Table 9.^{12,14}) The temperature dependent c.d. of <u>5</u> in hydrocarbon solvent given by Lightner^{11,12}) are also shown in Figure 13 together with the c.d. in EPA. Since the temperature dependence of c.d. spectra shows the existence of more than two optically active species, thermodynamical treatment was made in the following way.¹⁵)

Suppose there are only two species participating in the equilibrium, the next relationship holds for the observed rotational strength R_0^T * at 300 nm region, according to Boltzmann's distribution.

$$R_{0}^{T} = (R_{S} - R_{U}) \frac{1}{1 + \exp(-\Delta G^{0}/NkT)} + R_{U}$$
(1)

where R_S and R_U are the rotational strength of the nore and the less stable species, respectively, and ΔG^0 is the difference of Gibb's free energy between two species. When an appropriate value of ΔG^0 is chosen, a plot of R_0^T against $1/\{1 + \exp(-\Delta G^0/NkT)\}$ should become linear. Various plots are shown in Figure 14 for different values of ΔG^0 . A straight line was obtained in only the case of $\Delta G^0 = +1.1$ Kcal. From this value the following results could be obtained.

Table 9. Correction factors, v_{25}^{T} , for EPA contraction at different temperatures.^{12,14})

		Tempera	ature, °C		
25	-25	-75	-125	-160	-165
1.000	0.922	0.852	0.787	0.744	0.737

* The rotational strength of k-th transition R_k can be written¹³⁾ as

 $R_{k} \approx 0.696 \times 10^{-42} \int_{0}^{\infty} [\theta_{k}(\lambda)] \frac{d\lambda}{\lambda} = 0.299 \times 10^{-38} \int_{0}^{\infty} \Delta \varepsilon_{k}(\lambda) \frac{d\lambda}{\lambda}$



Figure 14. A plot of R_0^T against $1/\{1+\exp(-\Delta G^0/NkT)\}$ with different ΔG^0 values.

Molar fraction of the energetically preferred species in EPA is 1.0 at -190°C and 0.87 at room temperature.

and

$$R_{S} = +1.92 \times 10^{-40} \text{ e.s.u.}$$

 $R_{II} = -29.3 \times 10^{-40} \text{ e.s.u.}$

Therefore, the observed c.d. at -190°C corresponds to the c.d. spectra of the more stable species. This spectra exhibit a negative couplet as shown in Figure 12. Then the spectra of the less stable species can be obtained from the two spectra at -190°C and room temperature, using the molar fraction of the more stable species at room temperature (0.87). The result is depicted in Figure 15, which shows only one negative Cotton effect for the less stable species.

According to the X-ray analysis and the valence-force calculation of the diketone 5, the conformation supposed for stable speceies is that depicted in Figure 16.¹⁶⁾ This conformation is the intermediate between the half-chair and envelope form, which is unfavorable with respect to dipole-dipole repulsion between neighboring carbonyl groups. But this disadvantage can be overcome by the release of the steric repulsion between two methylene groups at C-4 and C-6. Hence the conformation of the



Figure 15. Synthesized c.d. spectra of the less stable conformer of (S)-spiro[4.4]nonane-1,6-dione (5) in EPA.



Figure 16. The molelar structure of spiro[4.4]nonane-1,6-dione (5) by X-ray analyses (upper) and Valence-Force calculation (lower).



Figure 17. Octant projection of <u>5</u> determined by X-ray analyses. energetically unpreferred species can be assumed as the intermediate between half-chair and envelope form, which is disadvantageous with respect to the steric repulsion between two methylene groups, i.e., the 5-membered rings are puckered to the opposite direction to that of the stable species, releasing the dipole-dipole repulsion.

The observed couplet for the stable species can be presumed to result from the interaction of two neiboring chromophores, whereas the single c.d. sign of the less stable species possibly results from the reduced interaction between them.

There are several factors affecting the stability of these two species, e.g., steric repulsion, steric strain, etc. Of these, the dipole-dipole interaction would considerably contribute to the stability of two conformers of diketone 5. Then the c.d. of 5 is expected to be solvent dependent (dielectric constant dependent). In fact, large changes in c.d. spectra were observed depending upon the used solvents (Figure 18 and Table 10). These changes are not considered to result only from solvation, since similar rotational strengths were observed for the solvents with close values of dielectric constant irrespective of their solvating nature. Solvation effect, however, cannot completely be neglected because some solvents with large solvation effect (such as chloroform) do not show linear relationship of rotational strength with dielectric constant. But, as a whole, the observed rotational strengths roughly correlate with the dielectric constants, indicating that the more and the less stable species have different dipole-dipole interaction energies. Similarly to the case of the temperature dependent spectra, the difference in Gibb's free energy between the supposed two species are shown as

$$\Delta G^{0} = \Delta E_{S} + \Delta V/D \qquad (2)$$

where ΔE_S is the term of steric repulsion, which is independent upon the kind of solvent in the case where solvation does not concern. D is the dielectric constant of solvent, and ΔV is the difference in dipole-dipole interaction energy when D = 1.0. From equation 1 and 2,

$$\Delta E_{S} + \Delta V/D = 2.303 \text{NkTlog} \frac{R_{0}^{T} - R_{U}}{R_{S} - R_{0}^{T}}$$
(3)

Ī	cyclohexane dioxane		ane	di-n-butylether		chloroform		
	D =	2.02	D = 2.21		D = 3.06		D = 4.70	
	λ nm	Δε	λnm	Δε	λnm	Δε	λnm	Δε
	328sh 322sh 317 308sh 288 258 222 208	-1.36 -2.01 -2.53 -1.93 +0.58 -0.05 -5.05 -6.18	318sh 311 304sh 290sh 286 253 224 208	-1.72 -2.75 -1.46 +0.54 +0.75 -0.028 -6.69 -7.38	321sh 312.5 305sh 293sh 286.5 264 252	-1.41 -1.86 -1.39 +0.17 +0.54 +0.026 -0.047	319sh 311 302sh 285 252sh	-1.95 -2.37 -1.47 +0.78 -0.046
	-5.69 x	10-40	-3.69	$\times 10^{-40}$	-3.85 :	$\times 10^{-40}$	-4.42	k 10 ⁻⁴⁰
	methyle chlo	ene oride	methanol		acetonitrile			
Ī	D =	D = 8.9 D = 32.6		D = 37.5				
	λnm	΄Δε	λ nm	Δε	λ nm	Δε		
	318sh	-1.53	318sh	-1.13	317sh	-1.16		

Table 10. Solvent dependent c.d. of (S)-(-)-spiro[4.4] nonane-1,6-dione (5).

58

-1.38

-1.49

-1.24

+0.97

-5.61

-7.75

 -1.06×10^{-40}

314sh

310.5

306sh

221.5

285

205

309

302sh

291sh

284

222

206.5

-1.43

-0.83

+0.74

+0.99

-7.13

-10.01

 -0.82×10^{-40}

309.5

301sh

290sh

284

-1.89

-1.09

+0.56

+0.79

 -2.87×10^{-40}



Figure 18. Solvent dependent c.d. of (S)-(-)-spiro[4.4]nonane-1,6-dione (5).



Figure 19. A plot of $\log\{(R_0^T - R_U)/(R_S - R_0^T)\}$ against 1/D using R_0^T in different solvents.

Figure 19 shows the plot of log $(R_0^T - R_U)/(R_S - R_0^T)$ against 1/D using the observed values of R_0^T in different solvents. Except for the case of chloro-form the plots gave a straight line. From the intercept and the slope of the line the following values were obtained.

 $\Delta E_{S} = 1.28 \text{ Kcal/mol}$ $\Delta V = -0.9 \text{ kcal/mol}$

The negative value of ΔV is consistent with the assumed two species; the conformer which is sterically stable but unstable in dipole-dipole interaction is the one depicted in Figure 16. Combined contributions of the two effect are considered to render it more stable.

Though, as was proposed by Lightner,¹¹⁾ the possibility that the equilibrium between solvated and non-solvated species contributes to the change of rotational strength has not yet been denied, further investigation on the conformationally more rigid dicarbonyl compounds will surely tell the truth about this problem.

3. Diketimine Derivatives <u>6</u> and <u>7</u> of (S) - (-) - diketone <u>5</u>

U.v. and c.d. spectra of (S)-(-)-bissemicarbazone <u>6</u> and (S)-(-)-bis-2,4-dinitrophenylhydrazone <u>7</u> are shown in Figure 20 and 21, and Table 11 and 12, respectively. In the u.v. spectra, <u>6</u> was not much different from the usual semicarbazone in the $\pi \rightarrow \pi^*$ region (cyclohexanone semicarbazone;¹⁷⁾ $\lambda_{\max} = 229.5$ nm, $\varepsilon = 11,200$), but the splitting of the band into two peaks (215 and 232.5 nm) clearly indicates the interaction of two chromophores. In fact, the c.d. spectra of <u>6</u> showed a negative couplet in this region. Suppose the direction of the transition moment of semicarbazone is nearly the same as that of C=N double bond, the sign of the couplet is in accord with that predicted from the exciton model.



Figure 20. U.v. and c.d. spectra of (S)-(-)- disemicarbazone <u>6</u> in methanol.



Figure 21. U.v. and c.d. spectra of (S)-(-)-bis-2,4-dinitrophenylhydrazone 7.

Table 11. U.v. and c.d. spectra of (S)-(-)-bissemicarbazone <u>6</u> in methanol Table 12. U.v. and c.d. spectra of (S)-(-)-bis-2,4-dinitrophenylhydrazone $\underline{7}$ in methanol.

λ_{max}	ε	^λ max	Δε
232.5	22800	240	-52.6
215sh	16500	210	+25.8

^λ max	£ ·	λ _{max} Δε
430sh	10800	432 +20
365	39100	372 -81
274sh	15800	333 +31.6
249sh	20500	250sh -8.4
230	26500	242 -9.72
194	27000	224 +15.8

The u.v. spectra of $\underline{7}$ also did nct show any large difference from that of the reference compound, cyclopentanone 2,4-dinitrophenylhydrazone;¹⁸⁾ λ_{\max} nm (£), 363 (22,500), 280 (8,000), 255 (14,000), 228 (17,000). Only slight differences are the inflection at 430 nm and the broadening of band at 365 nm in $\underline{7}$. Every absorption was accompanied by the Cotton effect, and, particularly, the band at 365 nm was splitted into a negative and a positive c.d., showing the presence of two transitions. Since this couplet resembles to that of semicarbazone <u>6</u>, a similar consideration based on the exciton model may be possible, though the character of this transition has not yet been fully understood.¹⁹ 4. Dienes <u>8</u>, <u>9</u>, and <u>10</u>.

The u.v. and c.d. spectra of (S)-(+)-spiro[4.4]nonane-1,6-diene ($\underline{8}$; endo-endo), (R)-(+)-1,6-dimethylenespiro[4.4]nonane ($\underline{9}$; exo-exo), and (R)-(+)-6-methylenespiro[4.4]non-1-ene ($\underline{10}$; exo-endo) are shown in Figure 22, 23, and 24, respectively. Data are summarized in Table 13. The dienes $\underline{9}$ and $\underline{10}$ show couplet patterns in this region, though the maxima in the shorter wavelength side could not be reached. But the endo-endo diene $\underline{8}$ shows no couplet pattern, and c.d. maximum of $\underline{8}$ in the longest wavelength is almost concordant with the u.v. maximum. By repeated measurements no small negative maximum at 220 nm region could be found, contrary to the report of Gerlach²⁰ and Wagnière.²¹⁾ Such a



(+) –<u>10</u>

Figure 22. U.v. and c.d. spectra of (S)-(+)-spiro[4.4]nonane-1,6-diene (8) in n-hexane.





Figure 23. U.v. and c.d. spectra of (R)-(+)-1,6-dimethylenespiro-[4.4]nonane (9) in isooctane.



small negative c.d. could be attributed to minute quantities of contaminants possibly caused by a difference in the synthetic method.*

* The diene <u>8</u> was prepared by the pyrolysis of bis-4-methylphenyl-thionocarbonate of trans, trans-diol <u>19</u>.²⁰⁾ The preparation of <u>8</u> from bistosylhydrazone of diketone <u>5</u> by treatment with n-butyllithium also resulted in contamination by impurities.¹²⁾
| | isooctane ^a | | | | methanol ^b | | | |
|-----------------|------------------------|---------------|------------------|-------|-----------------------|-------|------------------|-------|
| | u. | v. | c. | đ. | u. | v. | c. | đ. |
| Compound | λ_{max} | ε | λ _{max} | Δε | λ_{max} | ε | λ_{\max} | Δε |
| (S) – <u>8</u> | 198.5 | 14000 | 197.5 | +15.6 | 198.5 | 15000 | 199.5 | +14.5 |
| (R) – <u>9</u> | 205sh
187 | 7251
13300 | 211 | +29.6 | | | 212 | +28.0 |
| (R) - <u>10</u> | 186 | 15600 | 200 | +16.4 | | | 201 | +13.1 |

Table 13. U.v. and c.d. spectra of spiro-dienes 8, 9, and 10.

^a (S) -8 was measured in n-pentane ^b (S) -8 was measured in methanol-pentane (3:1).



Exciton model



A.B.P. model











Figure 25. The lower frequency ccupling mode (left) and allylic bond polarization model (right).

The exciton model²²⁾ was applied to these dienes using the pointdipole approximation of the $\pi \rightarrow \pi^*$ transition moment. The moment was placed at the midpoint of each double bond and directed along the bond axis. The lower frequency coupling mode calculated for each diene is shown by a set of arrows (Figure 25). The coupling modes for exo-exo <u>9</u> and exo-endo <u>10</u> are compatible with the observed positive signs of couplets for all the possible conformations examined with molecular models. But in the case of endo-endo diene <u>8</u>, the observed positive c.d. for (S)configuration was opposite to predictions for all conformations except for a rather unfavorable one, as already pointed out by Wynbery.

In contrast, when the allylic bond polarization model (A. B. P. model)* proposed by Andersen²³⁾ is employed as an alternative, the expected c.d. sign for the longest wavelength region was in agreement with that observed for endo-endo <u>8</u> as well as for exo-exo <u>9</u>. (See Figure 25) Also the c.d. of exo-endo <u>10</u> can be explained by this model, if the longer wavelength band is assinged to the endo-olefin as is well known. Thus the apparently anomalous c.d. of the endo-endo diene <u>8</u> might be attributed to the overriding effect of the allylic bond polarization.

The A. B. P. model was proposed for the elucidation of c.d. of chiral olefins stressing the effect of dissymmetrical substitution in allylic position.²³⁾ This model was applied successfully to spiro[4.5]decane-1,6-dienes, though the exciton model is also effective for some of them.



^{Δε}203 +11





Δε202 -22





Δε_{239.5} +24

5. (1S, 5R, 6S)-(+)-1,6-Dibenzoyloxyspiro[4.4]nonane (34).

U.v. and c.d. spectra of dibenzoate <u>34</u> are shown in Figure 26 and Table 16. Both α and p bands show positive Cotton effects and no coupling feature was observed. Molecular model examination indicated that in this case the two C-O bonds are parallel to each other and considerably far apart, making the application of the dibenzoate rule proposed by Nakanishi and Harada²⁴⁾ inappropriate.* In this case (the case in which the inter-



Figure 26. U.v. and c.d. spectra of (1S,5R,6S)-(+)-1,6-dibenzoyloxyspiro[4.4]nonane (<u>34</u>) in methanol.

* On the other hand, p-dimethylaminobenzoate of cis-trans glycohol showed a couplet pattern in the p band, making the application of dibenzoate rule possible. (See Scheme 7 and Figure 2). action between two benzene chromophores cannot be observed spectroscopically), the sector rule for isolated benzoate chromophore can be applied (Figure 27). The prediction from the supposed most stable conformer (Figure 28) is in accord with the experimental results.





Figure 27. Benzoate sector rule.





Figure 28. Assumed conformer of dibenzoate <u>34</u>.

Table 14. U.v. and c.d. spectra of (1S,5R,6S)-(+)-dibenzoate 34 in methanol

u.	v.	c.d.
λ_{max}	ε	λ_{max}
281	1500	
273.8	1850	277.5 +0.117
269sh	1620	273.5 +0.155
235sh	24600	
230.5	27300	230 +3.67
195.7	85700	

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V. U.v. and c.d. of cis-bicyclo[3.3.0]octane derivatives.

----- Results and discussion.

1. cis-Bicyclo[3.3.0]octan-2-one (11).

(-)-11

U.v. and c.d. spectra of (1R,5R)-(-)-cis-bicyclo[3.3.0]octan-2-one (<u>11</u>) are shown in Figure 29 and Table 15. The maximum absorption coefficient in the $n \rightarrow \pi^*$ region is nearly the same as that of the usual cyclopentanone systems.¹) Interestingly it is larger in methanol than in isooctane. This phenomenon was also found in the u.v. of other two β,γ -unsaturated bicyclo[3.3.0]octanones <u>3</u> and <u>4</u>, in which $\Delta \varepsilon_{max}$ is also enhanced in ethanol



Figure 29. U.v. and c.d. spectra of (1R,5R)-(-)bicyclo[3.3.0]octan-2-one (<u>11</u>) in isooctane (-----) and methanol (-----).

	isooc	tane			meth	anol	
u.v	•	c.đ.		u.v	•	c.d.	
λ_{max}	ε	λ_{max}	Δε	λ_{max}	ε.	λ_{max}	Δε
325sh	7.4	328.3	-0.732			322.5sh	-0.28
314.5	12.7	315.5	-1.46	310	11.8	308.0sh	-0.99
304.0	16.5	304.5	-1.52	298sh	18.5	300.5	-1.29
294.0	15.9	294.0	-1.10	292	19.5	295sh	-1.23
286sh	13.6	285.5sh	-0.65	280sh	17.4	285sh	-0.91
276sh	9.9	277.0sh	-0.35				
266sh	6.2						
191sh	739	191.5	+2.0	195.5*	230	195.0*	+0.163
190	770						

Table 15. U.v. and c.d. spectra of (1R, 5R) - (-) - bicyclo[3.3.0] - octan-2-one (<u>11</u>).

Shortest wavelength reached.

compared to that in isooctane.

The method of calculation of $\Delta \epsilon$ value for optically active cyclopentanone system has been well developed by Kirk and Klyne²⁾ though that for cis-bicyclo[3.3.0]octanone system has not yet been established. cis-Bicyclo[3.3.0]octanone somewhat resembles to cis-hexahydrindan-1-one, for which Kirk and Klyne proposed $\Delta \epsilon$ values in methanol (-2.4 and -1.8 for two conformations <u>82</u> and <u>83</u>, respectively). The observed value (-1.29 in methanol) for the ketone <u>11</u> is comparable to that for <u>83</u> in which C₁-CO bond assumes equatorial orientation with respect to the cyclohexane ring.



84

Hence the conformation of <u>11</u> is assumed to be <u>84</u>, though the puckering mode of cyclopentanone ring cannot be determined (half-chair or envelope). In this conformation, the contribution from the cyclopentanone ring to the c.d. sign is opposite to that from the cyclopentane ring though the sign is dominated by the octant contribution of cyclopentane ring. The structurally related compound. tricyclo[5.2.1.0^{4,10}]-



decan-2-one $(\underline{85})^{3}$ was reported to show smaller $\Delta \varepsilon$ value (+0.8 in ethanol) than <u>11</u>. This value is possibly due to the oppositely signed contribution of two cyclopentane rings.³⁾.

2. Olefins <u>12</u>, <u>13</u>, and <u>14</u>.

U.v. and c.d. spectra of olefins (1R,5R)-(-)-cis-2-methylenebicyclo-[3.3.0]octane $(\underline{12})$, (1R,5R)-(+)-cis-bicyclo[3.3.0]oct-2-ene $(\underline{13})$, and (1R,5R)-(+)-cis-7-methylenebicyclo[3.3.0]oct-2-ene $(\underline{14})$ are shown in Figure 30, 31, and 32, respectively. The data are summarized in Table 16. Since the olefin $\underline{12}$ and the diene $\underline{14}$ could not be purely isolated because of the low yield of Wittg reaction and their high volatility, only the qualitative spectra are given ($\Delta \varepsilon$ are tentatively calculated by assuming that ε s are equal to 10,000 and 20,00 for $\underline{12}$ and $\underline{14}$, respectively).



Figure 30. U.v. and c.d. spectra of (1R,5R)-(-)-cis-2-methylenebicyclo[3.3.0]octane (<u>12</u>) in pentane. ε_{max} is tentatively adjusted to 10,000. The investigation of the optical activity of monoolefins has been made by many groups,⁴⁻¹⁸⁾ but has always been encountering some difficulties because of the uncertainty in the origin of the transitions superimposed at 200 nm region. At present, it is well known that the shape of the c.d. spectrum of chiral olefin does not necessarily follow the shape of the u.v. absorption curve and that there is usually more than one Cotton effect within the region 220-185 nm. At the lower frequency side of the Cotton effect arising from the electric dipole allowed $\pi + \pi^*$ transition (the c.d. maximum should coincide with the u.v. maximum in wavelength) there is observed an electric dipole forbidden, magnetic dipole allowed c.d. band, usually referred to as a $\pi + 3s$ Rydberg transition.¹³)



Figure 31. U.v. and c.d. spectra of (1R,5R)-(+)-cis-bicyclo[3.3.0]oct-2-ene (<u>13</u>) in isooctane.



Figure 32. U.v. and c.d. spectra of (1R,5R)-(+)-cis-g-methylenebicyclo[3.3.0]oct-2-ene (<u>14</u>) in isooctane. ε_{max} is tentatively adjusted to 20,000.

Table 16	U.v.	and c.d.	spectra	of	olefins	12,	13,	and	14	in	isooctane.
----------	------	----------	---------	----	---------	-----	-----	-----	----	----	------------

	u.	.v.	c.	d.
Compound	$\lambda_{\texttt{max}}$	E	λ_{max}	Δε
(-)- <u>12</u> ^a	195sh 191.5	9100 10000 ^b	197	-3.56
(+) - <u>13</u>	190	10100	200 196.5 188 ^d	-2.00 0.0 +8.57
(+) - <u>14</u>	192	20000 ^C	198	+37.5

a 12 was measured in n-pentane.

b ϵ_{max} was tentatively adjusted to 10,000.

c ε_{\max}^{max} was tentatively adjusted to 20,000.

d Shortest wavelength measured.

Table 17. Characteristic wavelengths of c.d. maxima for

Table 17. Characteristic wavelengths of c.d. maxima for olegins.¹⁸⁾

	Olefin Class	λ ₀ (nm)	$\lambda_{l}(nm)$	$\lambda_2(nm)$
(A)]	,1-Disubstitured ethylenes (exocyclic methylene)		200 ± 2	189 ± 1
(B)]	L,2-Disubstituted ethylenes (cyclohexene)	_	200 ± 2	ca.185
•		2.		
(C) 1	Trisubstituted ethylenes (methyl-cyclohexane)		203.5 ± 1.5	192 ± 3
	$(\Delta^{1(9)} - octalin)$		210 ± 2	192 ± 3
. 3	Increment for alkyl substituen	t:-		
	'α'-guasi-equatorial	—	+2 to +3	?
	'α'-quasi-axial	· · ·	-7 to -10	?
(D) 1	Tetrasubstituted ethylenes	215-225	195-210	ca.185-19

At the higher frequency side of the $\pi + \pi^*$ Cotton effect there is observed another optically active transition, which is assigned as a $\pi + \sigma^*$ (CH) or $\pi + p_y$ transition and is not expected to contribute significantly to the isotropic absorption curve. At still the higher frequency region but falling into a rather narrow energy span, there may be observed a $\sigma_{(CH)} + \pi^*$ transition Cotton effect.¹⁴

Apart from the assignment of the transition, almost all chiral monoolefin show two Cotton effects in this region. Their c.d. signs are opposite in general, but the same in some cases. The Cotton effects at the shorter (ca. 190 nm) and longer (ca. 200 nm) wavelength are designated as λ_2 and λ_1 , respectively.

Recently, Hudec and Kirk¹⁸⁾ analysed c.d. data between 185 and 230 nm for 228 chiral olefins empirically in order to clarify the main features of the relationship between molecular structure and chiroptical properties, though the cyclopentene and methylenecyclopentane analogues are not discussed in detail and only included for comparison, because of their relatively limited number and less definite conformations. From their result, characteristic wavelengths of c.d. maxima for monoolefins are summarized in Table 17. If an analogy is allowed, the olefins <u>12</u> and <u>13</u> belong to the classes A and B in Table 17, respectively. The main conclusions given by Kirk¹⁸⁾ for the lowest energy c.d. bnad (200 nm), λ_1 , are as follows:

Class A

1,1-Disubstituted ethylenes. Exocyclic methylene compound r the most part follow a carbonyl-like "Octant Rule", the main point of difference being a large consignate (obedient to a carbonyl-like octant rule) contribution from a " β "-axial methyl group, which can outweigh effects of carbocyclic rings:

Class B

Cis-1,2-disubstituted ethylenes. Cyclohexene analogues give a c.d. band with sign corresponding to a consignate effect of allylic axial C-H bonds.

In Class A compounds, the wavelength λ_1 is generally 200 ± 2 nm and λ_2 is probably in the vicinity of 188-190 nm, although less clearly defined.

A few compounds exhibit only a broad c.d. band because of the overlap of two bands of the same sign, as has been shown by Yogev et al.⁸⁾ Each curve of this kind was successfully resolved int two Gaussian components with maxima in the expected regions. However, in the few methylene cyclopentane analogues (e.g. 16- and 17-methylenesteroids) the curve could not been resolved and only a single Cotton effect has been reported. Consignate behavior is shown also in these single c.d. of the methylene cyclopentane compounds.

The olefin <u>12</u>, here prepared, also shows only one Cotton effect at 196 nm. This is well in accord with the reported empirical rule by Kirk, though the quantitative analysis has not yet been undertaken.

In cyclopentene analogues of class B studied by Kirk, a single c.d. band was observed between 190 and 200 nm and it could not be determined whether it belongs to λ_1 or λ_2 . But the dissignate (opposite to a carbonyllike octant rule) contribution of the methyl group in 3-methylcyclobutene and 3-methylcyclopentene suggested that it is λ_1 . On the contrary, the cyclopentene analogue <u>13</u> showed two Cotton effects in this region, which can probably be assigned as λ_1 and λ_2 in order of decreasing wavelength. The appearance of two oppositely signed c.d.s is the usual feature of cyclohexene analogues, but it is the first illustration for cyclopentene analogues. The negative c.d. sign in λ_1 observed for <u>13</u> is consistent with predictions from the octant projection by Scott and Wrixon,⁷⁾ that is, the cyclopentane ring contribute to the dissignate character of the endo-olefin.

The c.d. of <u>14</u> cannot be expressed by the combined spectra of <u>12</u> and <u>13</u>, demonstrating the existence of interaction between two C=C double bonds. The prediction from the exciton theory¹⁹⁾ gives strongly positive or weakly negative c.d. sign in the longer wavelength side, depending upon the puckering mode of the five membered rings. However, the positive c.d. sign expected from A.B.P. model,¹¹⁾ whichever double bond is taken into account, is consistent with the observation.

3. β, γ -Unsaturated ketone 3 and 4.

U.v. and c.d. spectra of (1R,5R)-(+)-cis-bicyclo[3.3.0]oct-7-en-2one (<u>3</u>) and (1S,5R)-(+)-cis-8-methylenebicyclo[3.3.0]octan-2-one (<u>4</u>) are shown in Figure 33 and 34. The data are summarized in Table 18. As stated before, their ε and $\Delta \varepsilon$ are more pronounced in methanol than in isooctane; this behavior was not observed in spiro ketones. The u.v. absorption at ca. 300 nm are easily assigned to the $n + \pi^*$ transition of carbonyl group. The absorption intensities of <u>3</u> and <u>4</u> are enhanced compared to saturated ketones, as in the case of spiro-ketones <u>1</u> and <u>2</u>, the magnitudes of absorption coefficients of compounds of both series being comparable.



(+) - 4



Figure 33. U.v. and c.d. spectra of $(1R, 5R) - (+) - cis-bicyclo[3.3.0]oct-7-en-2-one (<math>\underline{3}$) in isooctane (-----) and methanol(-----).

In the c.d. spectra, the signs in the $n \rightarrow \pi^*$ region are positive for both <u>3</u> and <u>4</u>. The relative array of the carbonyl group and the double bond in the ketone <u>3</u> is similar to the arrangement (A in Figure 1) proposed by Moscowitz and his coworkers as the generalized octant rule.²⁰⁾ Hence the sign and relatively large magnitude of the Cotton effect observed for <u>3</u> are well consistent with the prediction from the generalized octant rule, though ε and $\Delta \varepsilon$ are not so much enhanced as in bicyclo[2.2.2]oct-5-en-2-one (<u>73</u>), dehydronorcamphor homologues (<u>74</u>) or bicyclo[3.2.0]hept-2-en-7-one derivatives (<u>86</u>), which have been regarded as a suitable model for A-arrangement in Figure 1 or 7. The magnitude of ε and $\Delta \varepsilon$ of <u>3</u> are



<u>73</u>



86a

Y

86b





<u>74a</u>

74b



<u>74c</u>

<u>74d</u>

rather comparable to those of 2,3-dihydrotriquinacen-2-one ($\underline{87}$, λ_{\max} 297 nm, ε 88; λ_{\max} 305 nm $\Delta\varepsilon$ ca+7.5 in ethanol),³⁾ exhibiting a similarity of <u>3</u> to <u>87</u> in the arrangement of two chromphores rather than to the compounds (<u>73</u>, <u>74</u> and <u>86</u>) stated above. The reason for the small difference in $\Delta\varepsilon$ between <u>3</u> and <u>87</u> is possibly due to minute difference in conformation between two ketones or to the effect of the double bond in γ -position of <u>87</u>.

The behavior of <u>4</u> in c.d. spectra is more interesting. The $\Delta \varepsilon$ of <u>4</u> is not so much large as that of <u>3</u> in spite of the comparable ε value to that of <u>3</u>, and in addition, the sign of the Cotton effect in the $n \rightarrow \pi^*$

		isooc	tane		methanol			
	u.	v.	c.d.	•	u.	v.	c.(1.
Compound	$\lambda_{\texttt{max}}$	ε	$\lambda_{\texttt{max}}$	Δε	λ _{max}	ε	λ_{max}	Δε
(+) - 3.	320sh	32.8	323	+2.62				
	313	62.8	212.5	+5.19	308sh	79.5	307sh	+5.14
	302.5	73.0	302.0	+5,64	299.5	99.4	299	+6.10
	292.5	64.4	292.5	+4.34	294sh	96.7	292sh	+5.54
	285sh	48.4	285sh	+2.82				
			278.5sh	+1.82				
			231.5	0.0			243.5	,0.0
	215sh	1100	216.5sh	-2.21			214	-5.62
			211.5	-3.98				
			205	0.0	200*	4570	204	0.0
	196.5	4750	193.5	+18.0			195*	+14.1
			185*	+11.6				
(+) – <u>4</u>	323sh	25.8	323.5	+0.385	320sh	25.8	320sh	+0.301
	314	58.9	312.0	+1.09	310sh	60.0	308sh	+1.01
	394.0	76.5	301.5	+1.29	298sh	86.1	298.5	+1.45
	294	72.0	292.5	+1.23	294	87.9	291.5	+1.47
	287sh	56.9	284.5	+0.925	285	76.9	285	+1.24
	277	40.8	277sh	+0.596				
			269.5sh	+0.355				
х. — — — — — — — — — — — — — — — — — — —			242.5	0.0			249.5	0.0
			222.5	-0.915			223.5	-0.747
			214.5	0.0			216	0.0
	206	3280	200sh	+3.19				
	191.5	2340	193	+3.98	198.5	5020	197.0	+4.22

Table 18. U.v. and c.d. spectra of (1R,5R)-(+)-bicyclo[3.3.0]oct-7-en-2-one (3) and (1S,5R)-(+)-cis-8-methylenebicyclo[3.3.0]octan-2-one (4).

* Shortest wavelength reached.

region is opposite to those of 3 and the saturated ketone 11 with respect to the same configuration of bicyclo[3.3.0]octan-2-one skeleton. Since the conformation of the skeleton would not be so much defferent between three ketones 3, 4 and 11, the contribution from the cyclopentane ring (or more precisely, from the bicyclo[3.3.0]octanone structure) to the Cotton effect is assumed to be almost the same for the three ketones. According to Kirk's method of generalization,²⁾ the magnitude of contribution is well estimated by the c.d. of saturated ketone 11, that is, $\Delta \varepsilon =$ -1.52 (in isooctane) for (1R, 5R)-bicyclo[3.3.2]octan-2-one skeleton. Hence it is clear that the positive c.d. sign of 4 is opposite to the expectation from the contribution of bicyclo[3.3.0]octanone skeleton, and this behavior is easily attributed to the introduction of exocyclic C=C



Figure 34. U.v. and c.d. spectra of (1S,5R)-(+)cis-8-methylenebicyclo[3.3.0]octan-2-one (<u>4</u>) in isooctane (-----) and methanol (----).

double bond in β -position. The c.d. sign is, however, opposite to the prediction from the generalized octant rule even if the slight flexibility of bicyclo[3.3.0]octane skeleton is taken into account (C=C double bond always lies in the lower left or upper tight rear octant). Thus, it is now evident that the c.d. sign in the n $\rightarrow \pi^*$ region is dependent on the direction of the double bond as well as its position in the carbonyl octant.





In addition, the fact that the hydrogenation product (<u>60</u>) shows negative c.d. in the $n \rightarrow \pi^*$ region obviously indicates that the olefinic double bond functions as a particular chromophore whose geometric desposition in a particular octant is sufficient for the determination of the sign of the $n \rightarrow \pi^*$ Cotton effect, as stated by Moscowitz in the original generalized octant rule. The contribution of double bond in <u>4</u> to the c.d. in $n \rightarrow \pi^*$ region is roughly estimated as 2.8 (1.47 + 1.29), which is comparable to the $\Delta \varepsilon_{max}$ of <u>2</u>(-3.14). In fact, the relative array of C=C double bond and carbonyl group in 4 somewhat resembles to that in <u>2</u>, though not exactly the same. The ketone <u>4</u> will surely propose another type of the arrangement of a carbonyl group and a ethylenic linkage, making the applicability of the octant rule to β,γ -unsaturated ketones more difinite.

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VI. Theoretical calculation of circular dichroism - I

Each compound studied has two chromophores (C=C and/or C=O) at the so-called homoconjugated position. Optical rotatory power of this type of compounds can be considered to result from the interaction between two chromophores in the molecule. Various treatments have been proposed for the calculation of optical rotatory power caused by the interaction of the chromophores. Of these, Bosnich's formalism¹ here adopted is relatively simple but proved effective, and, moreover, the result of this method facilitates the understanding of the contributions of individual chromophores. Since Bosnich's method deals only with the interaction of electrically allowed transition, some modification was made for the application of this method to the present system.

1. General procedure

a. Electronic states

Suppose that the molecule under consideration has two chromophores A and B (which may or may not be the same type) with ground state functions specified by ϕ_0^A and ϕ_0^B , respectively, and that there is no interaction between two chromophores at the ground state. The total ground state function Ψ_0 is given by

$$\Psi_0 = \phi_0^{\mathbf{A}} \phi_0^{\mathbf{B}}$$

Consider p and q kinds of excitations for the chromophore A and B, respectively, and i-th excited state of each chromophore given by ϕ_i^A (i = i~p) and ϕ_i^B (i = i~q). Then the j-th local excited state functions, \bar{x}_j (j = $1 \sim p+q$), of the whole system are represented by

$$\overline{\Phi}_{j} = \phi_{j}^{A} \phi_{0}^{B} (j = 1 \sim p)$$

$$\overline{\Phi}_{j} = \phi_{0}^{A} \phi_{j-p}^{B} (j = p+1 \sim p+q)$$

The total wave function, Ψ_i , corresponding to the i-th excited state of the molecule, is expressed as a linear combination of the unperturbed singly

excited state functions, Φ_j , with the mixing coefficients C_{ij} associated with the j-th function of the i-th level

$$\Psi_{i} = \sum_{j=1}^{n} C_{ij} \Phi_{j} \qquad (n = p+q)$$

where $j = 1, 2, \dots, n$. The application of the variation theorem leads to the set of n simultaneous equations.

$$\sum_{i=1}^{n} (H_{ij} - S_{ij}E)C_{ij} = 0 \quad (j = 1 \sim n)$$

$$H_{ij} = \langle \Phi_i | H | \Phi_j \rangle$$

$$S_{ij} = \langle \Phi_i | \Phi_j \rangle$$

H is the Hamiltonian of the system, and E is the appropriate energy. In order to obtain nontrivial solutions, the secular determinant is set to zero and the allowed energies are found by solving for E

$$|H_{ij} - S_{ij}E| = 0$$

If normalized bases functions are used, S_{ij} is given as follows

$$i = j$$
 $S_{ij} = 1$
 $i \neq j$ $S_{ij} = 0$

The second equation needs some comment. If each local transition is set orthogonal to each other in a chromophore, S_{ij} (i \neq j) in a chromophore is natural to be zero. In case of S_{ij} between two chromophres, however, it is necessary for $S_{ij} = 0$ to assume that there is no overlap integral between two chromophores. In this paper this supposition was used because of the simplification of the calculation. Moreover, it is consistent with the previous assumption that there is no interaction between chromophores at the ground state.

Provided that the system is weakly coupled through electrostatic forces, the total Hamiltonian, H, of the system can be split up

$$H = \sum_{i=1}^{n} H_{i} + \sum_{i < j}^{n} V_{ij}$$

where H_i is the Hamiltonian of the i-th state, and v_{ij} is an electrostatic multipole interaction operator between the i-th and j-th states. These two terms are calculated as follows.

i)
$$W_{ij} = \langle \overline{\Phi}_i | \sum_{i=1}^n H_i | \overline{\Phi}_j \rangle$$

 $W_{ij} = 0 \quad \text{for } i \neq j$
 $W_{ij} = E_i \quad \text{for } i = j$

where E_i is the local transition energy of the i-th transition.

ii)
$$v_{ij} = \langle \Phi_i | \sum_{i < j}^n v_{ij} | \Phi_j \rangle$$

In a chromophre $V_{ij} = 0$, because each transition is orthogonal to each other in A and B chromophores, respectively. The interactions between two transitions which belong to the different chromophores are evaluated in the following way.

The interaction between electrically allowed transitions as well as between magnetically allowed transitions are estimated by the point-dipole approximation. The dipole-dipole interaction is given as below.

$$\mathbf{v}_{ij} = \frac{1}{\underset{\mathbf{R}_{ij}^{3}}{\overset{\rightarrow}{\mathbf{H}_{i}, \mu_{j}}}} + \frac{3(\underset{\mathbf{\mu}_{i} \cdot \mathbf{R}_{ij})}{\overset{\rightarrow}{\mathbf{H}_{ij}, \mu_{j}}} + \frac{3(\underset{\mathbf{\mu}_{i} \cdot \mathbf{R}_{ij})}{\overset{\rightarrow}{\mathbf{R}_{ij}, \mu_{j}}} + \frac{3(\underset{\mathbf{\mu}_{i} \cdot \mathbf{R}_{ij}, \mu_{j}})}{\overset{\rightarrow}{\mathbf{R}_{ij}, \mu_{j}}$$

where R_{ij} is the vector distance between the centers of the transition moments (the positions of point-dipoles) of the i-th and j-th transitions (from i to j). $\vec{\mu}_i$ and $\vec{\mu}_j$ are the i-th and j-th transition moments defined by

$$\vec{\mu}_{i} = \langle \underline{\sigma}_{0} | \vec{M} | \underline{\sigma}_{i} \rangle$$
$$\vec{\mu}_{j} = \langle \underline{\sigma}_{0} | \vec{M} | \underline{\sigma}_{j} \rangle$$

where M is the electric or magnetic dipole operator.

On the contrary, there is no interaction between the magnetic and electric dipole moments. In other words, magnetic dipoles do not couple directly with electric dipoles. However, all magnetic transitions which are associated with the orbital motions of electrons must produce electric moments as well. If the chromophore has a center or a plane of symmetry, the electric moments can be dipole moments perpendicular to the magnetic moments, quadrupole moments, etc. In particular, if the transition is of the $n \rightarrow \pi *$ type involving a p-p quantum jump in the atomic orbitals, the magnetic transition invariably is associated with a large quadrupole moment. This quadrupole moment can interact with the electric dipole moment. When i-th transition is magnetically allowed and j-th transition is electrically allowed, the dipole-quadrupole interaction can be evaluated as follows.²⁾

$$V_{ij} = \frac{\vec{R}_{ij} \cdot Q_i \cdot \vec{\mu}_{ij}}{R_{ij}^5} - \frac{5}{2} \frac{\vec{R}_{ij} \cdot Q_i \cdot \vec{R}_{ij} \cdot \vec{R}_{ij} \cdot \vec{R}_{ij} \cdot \vec{\mu}_{ij}}{R_{ij}^7}$$

 Q_i is the quadrupole tensor of the i-th transition and is most easily represented by the matrix shown in the next equation.

$$Q = \begin{pmatrix} 2Q_{XX} - Q_{YY} - Q_{ZZ} & 3Q_{XY} & 3Q_{XZ} \\ 3Q_{XY} & 2Q_{YY} - Q_{XX} - Q_{ZZ} & 3Q_{YZ} \\ 3Q_{XZ} & 3Q_{YZ} & 2Q_{ZZ} - Q_{XX} - Q_{YY} \end{pmatrix}$$

The components of quadrupole moment are calculated by means of

$$Q_{\alpha\beta}^{i} = e \int \Phi_{i\alpha\beta}\Psi_{0} d\tau \quad (\alpha,\beta = X,Y,Z)$$

where e is the electronic charge.

b) Calculation of transition moment and quadrupole tensor of local transition by molecular orbital treatment

In the quantum mechanical system,³⁾ the electric and magnetic transition moments, $\vec{\mu}_k^e$ and $\vec{\mu}_k^m$, respectively, from the ground state Ψ_0 to the k-th local excited state Φ_k are defined as

$$\vec{\mu}_{k}^{e} = \langle \Psi_{0} | M_{e} | \Phi_{k} \rangle$$

$$\vec{\mu}_{k}^{m} = \langle \Psi_{0} | M_{m} | \Phi_{k} \rangle$$

The electric and magnetic moment operator are given by

$$M_{e} = e\vec{r}$$

$$M_{m} = \frac{e}{2mc} \vec{r} \times \vec{p} = \frac{eh}{4\pi imc} \vec{r} \times \vec{\nabla}$$

where e is electronic charge and m is mass of electron, c is the velocity of light. \vec{r} is the position vector with respect to the center of the transition.

Suppose k is not more than p, that is, local transition in chromophore A, next equation is available.

$$\begin{aligned} \overrightarrow{\mu}_{k}^{e} &= \langle \phi_{0}^{A} \phi_{0}^{B} | M_{e} | \phi_{k}^{A} \phi_{0}^{B} \rangle \\ &= \langle \phi_{0}^{A} | M_{e} | \phi_{k}^{A} \rangle \langle \phi_{0}^{B} | \phi_{0}^{B} \rangle \\ &= \langle \phi_{0}^{A} | M_{e} | \phi_{k}^{A} \rangle \end{aligned}$$

Similarly, in the case of magnetic moment;

$$\dot{\mu}_{k}^{m} = \langle \phi_{0}^{A} | \mathbf{M}_{m} | \phi_{k}^{A} \rangle$$

In the molecular orbital approximation, the wave functions ϕ_0^A and ϕ_k^A are constructed by the products of one electron functions ψ_i , which, after multiplication by appropriate spin functions, can be antisymmetrized. This ASMO — though it is important for energy calculations — does not need to concern us for the calculation of transition moments since the same results are obtained even from the following simple treatment.⁴⁾

Suppose 2r electrons are related to p kinds of transitions on chromophore A. Write the ground state as

 $\phi_0^{A} = (\psi_1)^2 (\psi_2)^2 \cdots \psi_r (j) \psi_r (k)$

and an excited singlet state as

$$\phi_{k}^{A} = (\psi_{1})^{2} (\psi_{2})^{2} \cdots (\psi_{r-1})^{2} \{\psi_{r}(j)\psi_{r+1}(k) + \psi_{r+1}(j)\psi_{r}(k)\} \frac{1}{\sqrt{2}}$$

It is obvious that the orthogonality of the molecular orbitals ψ leads to

$$\vec{\mu}_{k}^{e} = \langle \phi_{0}^{A} | M_{e} | \phi_{k}^{A} \rangle$$

$$= \frac{1}{\sqrt{2}} \{ \langle \psi_{r}(j) | M_{e} | \psi_{r+1}(j) \rangle + \langle \psi_{r}(k) | M_{e} | \psi_{r+1}(k) \rangle \}$$

$$= \sqrt{2} \langle \psi_{r} | M_{e} | \psi_{r+1} \rangle$$

The same transformation can be applied to the magnetic moment so that, aside from the factor $\sqrt{2}$, only one electric transition moment needs to be considered

$$\dot{\mu}_{\mathbf{k}}^{\mathbf{m}} = \sqrt{2} \langle \psi_{\mathbf{r}} | \mathbf{M}_{\mathbf{m}} | \psi_{\mathbf{r+1}} \rangle$$

In the current definitions of electric and magnetic moments, these quantities are not formulated on an equal footing. This may be set right by the equivalent formulation³⁾

$$\langle \psi_{k} | M_{e} | \psi_{1} \rangle = - \frac{eh}{4\pi^{2}mv_{k1}} \langle \psi_{k} | \psi_{1} \rangle = - \frac{ie}{2\pi mv_{k1}} \langle \psi_{k} | \psi_{1} \rangle$$

where $hv_{kl} = E_k - E_l$. This equality holds if ψ_k and ψ_l are exact eigenfunctions of a Hamiltonian with eigen values E_k and E_l . Molecular orbitals, however, are usually approximations to exact solutions of a Schrödinger equation. Hence the above expressions are not rigorously equivalent, but one of great practical value.

Next, quadrupole tensor is treated in an analogous way. Let us suppose i-th local transition to be magnetically allowed and to correspond to transition from k-th molecular orbital ψ_k to 1-th molecular orbital ψ_1 . The components of quadrupole moment are easily derived as follows.

$$Q_{\alpha\beta}^{i} = e < \Phi_{i} |\alpha\beta| \Psi_{0} > = \sqrt{2} e < \psi_{k} |\alpha\beta| \psi_{1} > (\alpha, \beta = x, y, z)$$

where the next relationship was used since quadrupole tensor operator is a Hermitian.

$$\langle \Phi_{i} | \alpha \beta | \Psi_{0} \rangle = \langle \Psi_{0} | \alpha \beta | \Phi_{i} \rangle$$

c) Rotational strengthe

Rotational strength R of the transition from Ψ_0 to Ψ_ex state is given as follows from Rosenfeld's equation⁵⁾

$$\mathbf{R}_{ex} = \mathbf{Im} < \Psi_{0} | \mathbf{M}_{e} | \Psi_{ex} > \cdot < \Psi_{ex} | \mathbf{M}_{m} | \Psi_{0} >$$

Thus the calculation of R_{ex} requires that the electric and magnetic transition moments are on an equal footing.

i) Electric transition moment

The electric transition moment E_i from the ground state to the i-th electronic state can be written as follows.⁶⁾

$$\stackrel{\star}{\mathbf{E}_{i}} = \langle \Psi_{0} | \mathbf{M}_{e} | \Psi_{i} \rangle$$

$$= - \frac{eh}{4\pi^{2}m\nu_{0i}} \langle \Psi_{0} | \vec{\nabla} | \Psi_{i} \rangle$$

$$= - \frac{ie}{2\pi m\nu_{0i}} \langle \Psi_{0} | \vec{p} | \Psi_{i} \rangle \quad (\text{since } \vec{p} = \frac{h}{2\pi i} \vec{\nabla})$$

As the result from the solution of Secular determinant, $\frac{\Psi}{i}$ is expressed as the linear combination of local transitions

$$\Psi_{i} = \sum_{j=1}^{n} C_{ij} \Phi_{j}$$

Then the electric moment \mathbf{E}_{i} is given by

$$\vec{E}_{i} = - \frac{ie}{2\pi m v_{0i}} < \Psi_{0} |\vec{p}| \Psi_{i} >$$

$$= - \frac{ie}{2\pi m v_{0i}} < \Psi_{0} |\vec{p}| \sum_{j} C_{ij} \Phi_{j} >$$

$$= - \frac{ie}{2\pi m v_{0i}} \sum_{j} C_{ij} < \Psi_{0} |\vec{p}| \Phi_{j} >$$

When P, is defined as follows,

$$\dot{\vec{P}}_{j} = \langle \Psi_{0} | \dot{\vec{p}} | \Phi_{j} \rangle$$

P. represents one electron transition moment of j-th local transition irresj pective of its transitional energy. Then

$$\dot{\vec{E}}_{i} = - \frac{ie}{2\pi\pi\nu_{0i}} \overset{n}{\underset{j}{\sum}} C_{ij} P_{j}$$

The electric moments thus obtained by nabla method are independent on the choice of the origin.

ii) Magnetic transition moment

The magnetic transition moment M_i can be rewitten as given below.

$$\begin{aligned} \vec{A}_{i} &= \langle \Psi_{0} | \vec{M}_{m} | \Psi_{i} \rangle \\ &= \frac{e}{2mc} \langle \Psi_{0} | \vec{r} \times \vec{p} | \Psi_{i} \rangle \\ &= \frac{e}{2mc} \langle \Psi_{0} | \vec{r} \times \vec{p} | \sum_{j=1}^{n} C_{ij} \Phi_{j} \rangle \\ &= \frac{e}{2mc} \sum_{j=1}^{n} C_{ij} \langle \Psi_{0} | \vec{r} \times \vec{p} | \Phi_{j} \rangle \end{aligned}$$

Here \vec{r} is the position vector with respect to the origin arbitrarily chosen. The magnetic moment, therefore, does depend on the choice of origin. This point requires some explanation.

If R_j indicates the position of the center of the j-th local transition $\Psi_0 \rightarrow \Phi_j$, and \vec{r}_j^0 locates at an arbitrary point with respect to this point, next equations hold.

$$\vec{r}_{j} = \vec{R}_{j} + \vec{r}_{j}^{0}$$

$$\frac{e}{2mc} < \Psi_{0} | \vec{r} \times \vec{p} | \Psi_{j} > = \frac{e}{2mc} < \Psi_{0} | (\vec{R}_{j} + \vec{r}_{j}^{0}) \times \vec{p} | \Psi_{j} >$$

$$= \frac{e}{2mc} \{ < \Psi_{0} | \vec{R}_{j} \times \vec{p} | \Psi_{j} > + < \Psi_{0} | \vec{r}_{j}^{0} \times \vec{p} | \Psi_{j} >$$

$$= \frac{e}{2mc} \stackrel{\rightarrow}{R_{j}} \times \stackrel{\rightarrow}{P_{j}} + \stackrel{\rightarrow}{\mu_{j}}^{m}$$

$$\stackrel{\rightarrow}{M_{i}} = \frac{e}{2mc} \stackrel{n}{\sum} \stackrel{\rightarrow}{C_{ij}R_{j}} \times \stackrel{\rightarrow}{P_{j}} + \stackrel{n}{\sum} \stackrel{C_{ij}\stackrel{\rightarrow}{\mu_{j}}^{m}}{\sum}$$

The last formula clearly shows two types of magnetic transition moments. One is attributed to the "intrinsic" or "group" magnetic moment that the local transition possisses if any (the second term of the last equation). The other comes from the coupling of the electric transition dipole moments (the first term of the last equation). Though the latter type of magnetic moment is origin dependent, the resultant rotational strength is given as origin independent (See Appendix). 2. Application to the spirosystems

a. Molecular conformation

Condidering from Dreiding models, the molecular conformations of spiro-compounds are postulated as follows:

- i) The conformations of the spiro-compounds are made up of two puckered cyclopentane derivatives, that is, cyclopentanone, methylenecyclopentane and cyclopentene. In these spiro[4.4]nonane derivatives, the approximation is allowed that the plane (σ_1) made by the carbons 1, 4 and 5 of spiro[4.4]nonane is perpendicular to that (σ_2) made by the carbons 5, 6 and 9, and that a common line exists which bisects both the angles 4154 and 4659, irrespective of the conformations of the five-membered rings.
- ii) Bond lengths and bond angles of three planar cyclopentane derivatives are approximated to those given in Table 19.
- iii) In a puckered form, the carbons 2 and 3 come above or below the plane σ_1 , that is, the direction of the displacements of C2 and C3 from the plane σ_1 are opposite to each other in half-chair forms and

Table 19. Bond lengths and bond angles of five membered rings.

	Bond length (Å)	Bond angle (°)
0 ⁶	1 - 5 1.52	41-5-4 10F
2 5	1 - 6 1.20	∠5 -1-6 122
3-4		25-1-2 116
⁶ CH ₂	1 - 5 1.52	L1-5-4 106
2 5	1 - 6 1.34	45-1-6 122
3_4		∠5-1 - 2 116
3	1 - 5, 1.52	L1-5-4 106
4-5	1 - 2 1.34	5-1-2 110

the same in envelope forms. If the changes in bond length and bond angle caused by the conformational change from the planer form to the puckered one are uniformly scattered on the whole system, the bond lengths and bond angles given in Table 19 would little deviate from the true values. Then, for the first approximation, the position and direction of the chromophore in a puckered form are obtained by twisting the chromophore around 1-5 bond (resulting in a departure of the chromophore from the plane σ_1) with bond length and bond angles of the same size as those in Table 19.

Based on these approximations, the calculation of the rotational strength was made for five conformations in which the dihedral angles between the plane σ_1 and the plane defined by C5 and the double bond (chromophore) are +20°, +10°, 0°, -10° and -20°, respectively. In the spirosystem, therefore, twenty-five kinds of conformations are considered. But when the molecule has C₂ symmetry, as in the compounds <u>5</u>, <u>8</u> and <u>9</u>, only five conformers were considered. Plus-signed directions of torsion angles are shown in Figure 36.

b. Local excited states and their energies

The kinds of transitions of the component chromophores considered for the calculation of the transition energies of the spiro-system are shown in Table 20. These energy values except for the $\pi + \pi^*$ transition

Chromophore	Transition	Energy eV (nm)	Transition Moment $\mu^{e} \qquad \mu^{m} \qquad Q(xy)$ $(\bar{x}10^{-17}) (x10^{-20}) (x10^{-26})$
C=0	n → π* n → σ* π → π*	4.132 (300) 6.000 (207) 7.500 (165)	0.0 0.9694 0.42 0.1390 0.1840 — 0.3099 0.0 0.0
C=C	π → π *	6.500 (191)	0.3363 0.0 0.0

Table 20. Transitions of the component chromophores considered for the calculation and their transition energies.

of carbonyl group are decided by taking into account the observed data, though they are not necessarily the exact values for the cyclopentane derivatives (monomeric chromophores). The energy of $\pi \star \pi^*$ transition of the carbonyl that could not be reached in the observed u.v. spectra was taken from the data in the literature.⁷⁾ These energy values are used as the diagonal elements of the secular determinant. As can easily be conceived, there would arise little differences in the results of calculation even if slightly different values were used for these energies. Therefore little attention was given to the refinement of these energy values.



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Figure 36. Torsion angles around the C_1-C_5 and C_5-C_6 bonds.

c. Centers of transitions

The centers of the transitions must be determined for the calculation of magnetic transition moments and of off-diagonal elements of secular determinants. The decision of the transition center is sometimes a serious problem. When the chromophore is benzene or such aromatic ring, there is a considerable arbitrariness in deciding the position of the center, and this may give rise to the marked change in the result of calculation. In the present case, however, it seems reasonable to consider that the center of the transition moment lies between the two atoms of the chromophore. Hence the center of the transition was assumed to be located at the midpoint of the double bond. The trivial displacement of the transition center along the double bond would be attended by little change in the calculated rotational strength.*

* Schellman proposed a definition of the position of the local origin (center of transition) as follows:⁸⁾ the position of the local origin, $\vec{R_i}$, is chosen so as to minimize the matrix element of $\vec{m_i}$ for a given transition. Any arbitrariness which remains after the minimization of the matrix element can be removed by minimizing the magnitudes of the quadrupole or higher multipole components. This treatment, though seems appropriate at a glance, soon proved ineffective as shown below.

The magnetic and quadrupole moments of $n \rightarrow \pi^*$ transition of carbonyl are origin independent and the local origin could not be determined.

The magnetic and quadrupole moments of $n+\sigma^*$ transition of carbonyl are origin dependent because $n+\sigma^*$ transition is both magnetically and electrically allowed. When the magnetic moment is set zero, the quadrupole moment remains, and vise versa. This causes the non-zero interaction between electric moment and zero-magnetic moment, or no interaction between electric and magnetic moments. It is also difficult to determine unequivocally the position of the origin for a transition with magnetic and quadrupole moments both of which have non-zero and significant values, since there exists infinite number of such points. d. LCAO-MO of C=C and C=O double bonds.

Molecular orbitals are written as linear combinations of atomic orbitals, for which Slater functions are chosen (See Apendix 4 and 5).

For carbon-carbon double bond, let the coordinates of two carbon atoms Cl and C2 be located as in Figure 37. One electron molecular orbitals ψ_{π} and ψ_{π}^{*} are given by

$$\begin{split} \psi_{\pi} &= \frac{1}{\sqrt{2}} (\chi_{2\text{px}}^{\text{Cl}} + \chi_{2\text{px}}^{\text{C2}}) \\ \psi_{\pi}^{*} &= \frac{1}{\sqrt{2}} (\chi_{2\text{px}}^{\text{Cl}} - \chi_{2\text{px}}^{\text{C2}}) \end{split}$$

For the calculation of transition moments of carbonyl the SCF-LCAO-MO of formaldehyde are adopted, whose dimensions are shown in Figure 38. The molecular orbitals are given by

$$\begin{split} \psi_{n} &= -0.3684(\chi_{1s}^{H1} - \chi_{1s}^{H2}) - 0.2704\chi_{2px}^{C} + 0.9054\chi_{2px}^{O} \\ \psi_{\pi} &= 0.655\chi_{2py}^{C} + 0.626\chi_{2py}^{O} \\ \psi_{\pi}^{*} &= 0.788\chi_{2py}^{C} - 0.812\chi_{2py}^{O} \\ \psi_{\sigma}^{*} &= 0.796(\chi_{1s}^{H1} + \chi_{1s}^{H2}) - 0.0142\chi_{1s}^{C} + 0.101\chi_{2s}^{C} \\ &+ 1.298\chi_{2pz}^{C} - 0.0729\chi_{1s}^{O} - 0.746\chi_{2s}^{O} + 0.595\chi_{2pz}^{O} \end{split}$$



Figure 37.

Figure 38.

e. Transition moments

i) C=C double bond

 $\pi \! \! \to \! \! \pi^*$ transition of C=C double bond is only electrically allowed and its electric moment is given by

$$\vec{\mu}_{\pi\pi^*}^{\mathbf{e}} = -\frac{\mathrm{i}e\sqrt{2}}{2\pi\mathrm{m}v_{\pi\pi^*}} \langle \psi_{\pi} | \vec{p} | \psi_{\pi^*} \rangle = -\frac{\mathrm{eh}}{4\pi^2\mathrm{m}v_{\pi\pi^*}} \sqrt{2} \langle \psi_{\pi} | \vec{\nabla} | \psi_{\pi^*} \rangle$$

And with LCAO expression, $\langle \psi_{\pi} | \vec{\nabla} | \psi_{\pi \star} \rangle$ is rewritten by

From symmetry consideration (See Appendix 4)

$$\langle \psi_{\pi} | \vec{\nabla} | \psi_{\pi *} \rangle = - \langle \chi_{2px}^{C1} | \vec{\nabla} | \chi_{2px}^{C2} \rangle$$

With numerical calculations (See Appendix 1 and 4)

$$\langle \chi_{2px}^{C1} | \vec{\nabla} | \chi_{2px}^{C2} \rangle = 0.444 \times 10^8$$

Then

 $\dot{\mu}_{\pi\pi^*}^{e} = 0.3368 \times 10^{-17} \text{ e.s.u.}$

ii) C=O double bond

 $n\!\!\rightarrow\!\!\pi^*$ transition of carbonyl double bond is only magnetically allowed. Its magnetic moment is given by

$$\dot{\vec{\mu}}_{n \to \pi^{\star}}^{m} = \frac{e}{2mc} \sqrt{2} < \psi_{n} | \vec{r} \times \vec{p} | \psi_{\pi^{\star}} >$$
$$= \frac{eh}{4\pi i mc} \sqrt{2} < \psi_{n} | \vec{r} \times \vec{\nabla} | \psi_{\pi^{\star}} >$$
and

$$\langle \psi_{n} | \vec{r} \times \vec{\nabla} | \psi_{\pi^{*}} \rangle = -0.2903 \{ \langle \chi_{1s}^{H1} | \vec{r} \times \vec{\nabla} | \chi_{2py}^{C} \rangle - \langle \chi_{1s}^{H2} | \vec{r} \times \vec{\nabla} | \chi_{2py}^{C} \rangle \}$$

- 0.213 $\langle \chi_{2px}^{C} | \vec{r} \times \vec{\nabla} | \chi_{2py}^{C} \rangle + 0.2196 \langle \chi_{2px}^{C} | \vec{r} \times \vec{\nabla} | \chi_{2py}^{O} \rangle$
- 0.713 $\langle \chi_{2px}^{O} | \vec{r} \times \vec{\nabla} | \chi_{2py}^{C} \rangle - 0.735 \langle \chi_{2px}^{O} | \vec{r} \times \vec{\nabla} | \chi_{2py}^{O} \rangle$

where the integrals between the non-neiboring atoms are neglected since they are small. In addition, the integrals concerning the atomic orbitals χ_{1s}^{H1} , χ_{1s}^{H2} and χ_{1s}^{C} are also neglected because their coefficients in formaldehyde cannot be used in ketones. With the following numerical values,

$$<\chi^{C}_{2px}|\vec{r} \times \vec{\nabla}|\chi^{C}_{2py}> = 1.0 \text{ k}$$

$$<\chi^{C}_{2px}|\vec{r} \times \vec{\nabla}|\chi^{O}_{2py}> = 0.2232 \text{ k}$$

$$<\chi^{O}_{2px}|\vec{r} \times \vec{\nabla}|\chi^{C}_{2py}> = 0.2232 \text{ k}$$

$$<\chi^{O}_{2px}|\vec{r} \times \vec{\nabla}|\chi^{O}_{2py}> = 0.2232 \text{ k}$$

we obtain

1

$$\dot{\mu}_{n \to \pi^*}^{m}$$
 = 0.9694 x 10⁻²⁰ k e.s.u.*

For the quadrupole of Figure 38, only one component Q_{xy} takes non-zero value.

$$Q_{xy}^{n \to \pi^*} = \sqrt{2} e < \psi_n |xy| \psi_{\pi^*} >$$

* If χ_{ls}^{H} and etc. were taken into account, the following values were obtained.

$$\dot{\mu}_{n \to \pi^{*}}^{m} = 1.23 \times 10^{-20} \text{ k e.s.u.}$$

 $\rho_{xy}^{n\pi^{*}} = 0.723 \times 10^{-26} \text{ e.s.u.}$

With the following numerical values

$$<\chi^{C}_{2px} |xy| \chi^{C}_{2py} > = 0.159 \times 10^{-16}$$

$$<\chi^{C}_{2px} |xy| \chi^{O}_{2py} > = 0.034 \times 10^{-16}$$

$$<\chi^{O}_{2px} |xy| \chi^{C}_{2py} > = 0.034 \times 10^{-16}$$

$$<\chi^{O}_{2px} |xy| \chi^{O}_{2py} > = 0.081 \times 10^{-16}$$

$$\varphi^{n \to \pi^{*}}_{xy} = 0.423 \times 10^{-26} |k \text{ e.s.u.}$$

we obtain

The $n \rightarrow \sigma^*$ transition is both electrically and magnetically allowed. Its electric moment is given by

$$\dot{\psi}_{n \neq \sigma^{\star}}^{e} = - \frac{eh}{4\pi^{2} m \nu_{n\sigma^{\star}}} \sqrt{2} < \psi_{n} |\vec{\nabla}| \psi_{\sigma^{\star}} >$$

The term $\langle \psi_n | \vec{\nabla} | \psi_{\sigma*} \rangle$ was calculated in the same manner as above to give

$$\dot{\mu}_{n+\sigma^{*}}^{e} = 0.139 \times 10^{-17}$$
 i e.s.u.

The magnetic moment is given by

$$\dot{\mu}_{n \to \sigma^*}^{m} = 0.184 \times 10^{-20}$$
 j e.s.u.

The quadrupole moment was neglected in this case because taking it into consideration makes the calculation very troublesome in spite of its very small contribution to the c.d. in the $n \rightarrow \pi^*$ transition.

The transition moment of the electrically allowed $\pi \rightarrow \pi^*$ transition was calculated in a similar manner as above.

* See note in the preceding page.

$$\vec{\psi}_{\pi\pi*}^{e} = -\frac{eh}{4\pi^{2}m\nu_{\pi\pi*}} \sqrt{2} < \psi_{\pi} |\vec{\nabla}| \psi_{\pi*} >$$
$$= 0.337 \times 10^{-17} k \quad e.s.u.$$

These calculated values of transition moments are listed in Table 20.

f. Results and Discussions

i) β, γ -Unsaturated ketones 1 and 2

The calculated results for <u>1</u> and <u>2</u> are summarized in Table 21 and 22 together with the observed data. In the case of <u>1</u>, almost all conformations considered gave positive c.d. sign in $n \rightarrow \pi^*$ transition.

In the most stable conformation of <u>1</u>, the puckering mode of fivemembered ring is assumed to be similar to that defined for diketone <u>5</u> from X-ray analysis and Valence-Force calculation, that is, the conformer of $(+10^{\circ}, +10^{\circ})$.* This form gave negative sign, whereas the assumed next stable conformation $(-10^{\circ}, -10^{\circ})$ gave relatively large positive sign. Hence a consideration upon the population of conformers can well explain the observed positive sign of c.d. Moreover, based on these two conformers, the reported temperature dependence of the c.d. spectra in which the positive sign decreased at lower temperature⁹ can be explained satisfactorily by the use of these calculated results.

In $n \rightarrow \sigma^*$ transition a good agreement was also seen between the calculated and the observed c.d. signs based on the same consideration of conformation.

In the case of the ketone 2, the observed negative sign in $n + \pi *$ region is well reproduced in almost all conformation, and the large rotational strength of 2 compared to that of 1 is also exhibited in the calculation. The negative sign of $n + \pi *$ transition in the observed c.d. spectra is also in fair agreement with the computed results.

* Plus sign of θ_2 designates such twisting that C=C double bond approaches to and depart from the carbonyl in <u>1</u> and <u>2</u>, respectively (see Figure 36). Table 21. The calculated and observed values for (R)-6-methy-lenespiro[4.4]nonan-l-one (1).

Table 22. The calculated and observed values for (S)-spiro-[4.4]non-6-en-2-one (2).

	the second data and the se			The second s			
		Calcula	ted Results	Calculated Results			
	θl	θ2	Rotational Strength for $n \rightarrow \pi^*$ transition $(x10^{-40})$	θι	θ2	Rotational Strength for $n \rightarrow \pi^*$ transition (x10 ⁻⁴⁰)	
	-20	-20	1.98	-20	+20	-0.056	
	-20	-10	1.63	-20	+10	-0.488	
	-20	0	1.21	-20	0	-0.836	
	-20	10	0.76	-20	-10	-1.041	
	-20	20	0.32	-20	- 20	-1.043	
	-10	-20	1.69	-10	+20`	-0.026	
	-10	-10	1.27	-10	+10	-0.553	
	-10	0	0.82	-10	• 0	-1.023	
	-10	10	0.38	-10	-10	-1.373	
	-10	20	0.01	-10	-20	-1.527	
	0	-20	1.23	0	+20	0.066	
	0	-10	0.81	0	+10	-0.522	
	0	0	0.39	0	0	-1.095	
	0	10	0.04	0	-10	-1.592	
	0	20	-0.17	0	-20	-1.935	
	10	-20	0.71	10	+20	0.218	
	10	-10	0.34	10	+10	-0.377	
	10	0	0.03	10	• 0	-1.004	
•	10	10	-0.14	10	-10	-1.617	
	10	20	-0.12	10	-20	-2.144	
	20	-20	0.24	20	+20	0.401	
	20	-10	0.01	20	+10	-0.138	
	20	0	-0.10	20	. 0	-0.748	
	20	10	-0.03	20	-10	-1.406	
	20	20	0.26	20	-20	-2.061	
		·····	·				
		Observ	ved Data		Obse	rved Data	
	u.v	7.	c.d.		u.v.	c.d.	
	λ	D	λ R	λ	D	λ R	
	302 8.	$.9 \times 10^{-3}$	38 305 +4.5 x 10 ⁻⁴⁰	306	1.2 x 10	-37 310 -9.9×10^{-40}	
	204 6.	8×10^{-3}	36 207 +2.6 x 10 ⁻³⁹	197	6.8 x 10	-36 205 -3.3×10^{-39}	
	183 1.	.3 x 10 ⁻³	35				
-				L			

One general trend in the calculated results is that the sign of c.d. in $n+\pi^*$ region is always dominated by the mixing of $\pi+\pi^*$ transition of C=C double bond and that it is independent on the mixing of $n+\sigma^*$ and $\pi+\pi^*$ transitions of carbonyl which can mix with $n+\pi^*$ transition indirectly only through the interaction with $\pi+\pi^*$ of C=C bond.* This was also confirmed by the calculation in which $n+\sigma^*$ transition was not taken into account. Thus the same sign was calculated for $n+\pi^*$ transition with or without consideration of $n+\sigma^*$ transition.

The other trend which is more important is that the sign of mixing coefficient of $\pi \rightarrow \pi^*$ of C=C with $n \rightarrow \pi^*$ transition is invariable for a given absolute configuration, that is, positive both for <u>1</u> and <u>2</u>, irrespective of their conformations in the feasible extent of puckering. Therefore, the sign of c.d. is entirely dependent upon the mutual orientation of the C=C double bond and carbonyl group, namely, the intersecting angle between the electric and magnetic moments.

ii) diketone 5

The results are shown in Table 23. The calculation always shows two Cotton effects of opposite sign in the $n \rightarrow \pi^*$ region. The relative magnitude of rotational strength for two transitions varies depending upon the conformations. In (+10°, +10°) conformer, which is similar to that determined by X-ray analysis¹⁰⁾, the Cotton effect at the shorter wavelength side was calculated to be larger than that at the longer one. On the contrary, a larger value was given at the longer wavelength side for $(-10^{\circ}, -10^{\circ})$ conformer. This result is well in accord with the observed temperature dependence of the c.d. spectra, though the calculation by Lightner gave another explanation.¹¹⁾ In any event, the relative magnitude of the two transitions is very sensitive to the method of calculation apart from the sensitivity to the conformation, and, at present, a quantitative conclusion cannot be drawn based on these rough approximations.

* The $n \rightarrow \sigma^*$ and $\pi \rightarrow \pi^*$ transitions of carbonyl cannot mix with $n \rightarrow \pi^*$ in the first- order treatment of perturbation theory.

With regard to the splitting of two $n \rightarrow \pi^*$ transitions, very small value was given because of the negligibly small order of interaction between magnetic moments inputted to the calculation. When the point monopole method* was adopted for the calculation of interaction between $n \! \rightarrow \! \pi^*$ transitions as an alternative, a larger value was obtained (0.0637 ev) though the computation was very troublesome.

	Calculated Results							
	θι	^θ 2	eV	R x10 ⁻³⁹	eV	R x10 ⁻³⁹		
I	-20	-20	4.131876	-0.0693	4.131865	+0.3078		
	-10	-10	4.131881	-0.1107	4.131869	+0.2475		
	0	0	4.131906	-0.1243	4.131892	+0.1427		
	+10	+10	4.131893	-0.0653	4.131883	+0.0211		
	+20	+20	4.131759	+0.0883	4.131752	-0.0699		
II	-20	-20	4.131876	-0.0682	4.131867	+0.3100		
	-10	-10	4.131887	-0.1051	4.131879	+0.2534		
	0	0	4.131937	-0.1130	4.131931	+0.1543		
	+10	+10	4.131994	-0.0496	4.131991	+0.0392		
	+20	+20	4.131980	+0.1049	4.131975	-0.0470		
	.		Obs	served Data				
			u.v.		c.d.			
			λ D	λ	R			
			301 1.7 x 1	10 ⁻³⁷ 317	-4.6×10^{-40}			
			217 1.1 x 1	288 10 ⁻³⁶ 222	$+6.7 \times 10^{-40}$			
			202 2.1 x 1	10-36	-9×10^{-40}			

Table 23. The calculated and observed values for (R)-spiro[4.4]nonan-1,6-dione (5).

I: $n \rightarrow \sigma^*$ transitions are considered. II: $n \rightarrow \sigma^*$ transitions are not considered.

* See Chapter VIII-2.

iii) Dienes

The results of calculation for dienes $\underline{8}$, $\underline{9}$ and $\underline{10}$ are shown in Table 24, 25 and 26, respectively, together with the observed data. These results are entirely the same as the qualitative examination by exciton model as expected, except for the magnitude. Every conformer gave a satisfactory sign for diene $\underline{9}$ and $\underline{10}$ but not for $\underline{8}$, as already expected by exciton model. A noticeable point for $\underline{8}$ is that only the most unstable conformation can give the c.d. sign consistent with the observed one, but that the magnitude is very small compared to those of other conformers. This disagreement of the exciton theory with the observation for $\underline{8}$ may be partly attributed to the homoconjugation of double bonds which is more effective in $\underline{8}$ than in $\underline{9}$ and $\underline{10}$ because of the relatively parallel arrangement of double bonds in $\underline{8}$. Accordingly further calculation was carried out for $\underline{8}$ by use of the method of composite molecule (See the following chapter).

Table 24. The calculated and observed values for (R)-spiro-[4.4]nona-1,6-diene (8). Table 25. The calculated and observed values for (R)-1,6- dimethylenespiro[4.4]nonane (9).

			Contraction of the local division of the loc			
	Calcu	ilated Results		Calcu	lated Results	5
θι	θ2	Rotational Strength for longer wavelength (xl0 ⁻³⁸)	θι	- θ ₂	Rotational for longer (x10	Strength wavelength ⁻³⁷)
- 20	-20	-0.19	-20	-20	+0.	.17
-10	-10	+0.34	-10	-10	+0.	.20
0	0	+0.76	0	0.	+0.	22
+10	+10	+1.02	+10	+10	+0.	22
+20	+20	+1.10	+20	+20	+0.	20
					· · · · · · · · · · · · · · · · · · ·	
-	Ovse	rved Data		Obser	ved Data	
u	.v.	c.d.	υ	1.V.	c.d	•
λ	D	λ R	λ	D	λ	R
198	1.6 x 1	0^{-35} 198 -3.7 x 10^{-39}	187	2.9 x 10	35 211 +8	$.0 \times 10^{-39}$

Table 26. The calculated and observed values for (S)-6-methylenespiro[4.4]non-l-ene (10).

	Calculated Results.				
θι	θ2	Rotational Strength for longer wavelength (x10 ⁻³⁷)			
+20	+20	-0.16			
+10	+10	-0.17			
0	0	-0.15			
-10	10	-0.12			
-20	-20	-0.08			
	Observed Data				
u.v.		c.d.			
λ	D	λ R			
186	2.6 x	10^{-35} 200 -5.0 x 10^{-39}			

3. Application to the β,γ - unsaturated bicyclooctanone <u>3</u> and <u>4</u>.

The calculation was made for only one conformer of each ketone, in which the five-membered rings were assumed to be planar and the dihedral angle between two rings was set at 120°. Bond lengths and bond angles adopted here are shown in Figure 39.





Only two transitions $(n \neq \pi^* \text{ of carbonyl and } \pi \neq \pi^* \text{ of } C=C$ double bond) were taken into account for this calculation because other transitions have already proved to have little effect on the c.d. of $n \neq \pi^*$ transition.

The results of calculation based on the disposition shown in Figure 40 are given in Table 27, which predicts relatively large positive and



- 110

small negative Cotton effects for (1R,5R)-3 and (1R,5S)-4, respectively. The predicted consignate behavior of 3 and dissignate behavior of 4 agree well with the observed c.d. spectra for these ketones (Figure 33, 34; Table 19), showing again the usefulness of the μ -m coupling theory for β,γ -unsaturated ketones.

One remarkable feature in the calculated results is that the interaction between two transition has the same sign of mixing coefficient in 3 and 4, and that the sign of Cotton effect is only dependent upon the mutual orientation of the double bond and carbonyl group, as was already shown in the case of spiro system.

Comj	pound	(1R,ŠR)- <u>3</u>	(1R,5S)- <u>4</u>		
Magnetic	Position	(0.00, 0.00, 0.00)	(0.00, 0.00, 0.00)		
Moment	Direction	C ₂ → O (0.00, 0.00, 1.00)	C ₂ + O (0.00, 0.00, 1.00)		
Electric	Position	(+2.08, -1.59, -1.84) (+2.36, -1.43,			
Moment	Direction	$C_8 \rightarrow C_7$ (+0.03, -0.61, -0.85)	C ₈ → C ₉ (+0.44, -0.27, +0.86)		
R		3.2 Å	2.8 Å		
	v	0.0223 eV	0.0022 eV		
Rotationa	l Strength*	$+0.799 \times 10^{-39}$	-0.078×10^{-39}		

Table 27. The calculated results for (1R,5R)-bicyclo[3.3.0]oct-7-en-2-one (3) and (1R,5S)-8-methylenebicyclo[3.3.0]octan-2-one (4).

* Mixing coefficients obtained by perturbation theory were used.

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VII. Theoretical calculation II. Composite molecule method for endoendo diene $\underline{8}$

Electronic states of $\underline{8}$ was calculated based on the composite molecule method^{1,2)} in order to estimate the effect of charge transfer transitions.

The method of calculation is almost the same as that in the preceding chapter except that the charge transfer transitions were considered. Spiro[4.4]nona-1,6-diene ($\underline{8}$) is regarded to be composed of two ethylene chromophores. The assumptions regarding the molecular geometry of $\underline{8}$ are as follows. The two five-membered rings are planar and set perpendicular to each other. The planes, ClC5C4 and C6C5C9, bisect the angles, \angle C6C5C9 and \angle ClC5C4, respectively. The bond lengths and bond angles adopted are the same as those in the preceding chapter.

In this calculation, the π - electron approximation and zero-differential overlap approximation were adopted, and the β -value of ethylene was tentatively assigned as -2.37 eV so that the calculated transition energy of ethylene coinsides with the observed one (λ_{max} , 187 nm). Electron repulsion integrals can be obtained by Pariser-Parr method³⁾ when $2p\pi$ orbitals are parallel to each other. In case of the integral between C_{2p}^1 and C_{2p}^6 which are not parallel to each other, the integral is divided into σ and π components, which are determined from the table of ab initio two center repulsion integrals by Roothaan.⁴⁾ These values in table are, however, sometimes far apart from the observed ones.⁵⁾ Hence the modified values from the following equation are employed,

 $(ii/jj) = (ii/jj) \frac{P - (ii/jj)_{\tau}^{R}}{(ii/jj)_{\pi}^{R}}$

where $(ii/jj)^P$ is the value from Parriser-Parr approximation, and $(ii/jj)^R_{\tau}$ or $(ii/jj)^R_{\pi}$ are the values obtained from Roothaan's table in which both the π and σ components, or only the π components are considered, respectively. This modification did not result in any large differences in the electronic states of spirodiene. One center electron repulsion integral was assumed to be 10.84 eV based on the data of Pritchard and Skinner.⁶ Resonance integrals β_{ij} (for example, between C_1 and C_6) are calculated by the following equation,

$$\beta_{ij} = \frac{s_{ij}}{s_{12}} \beta_{12}$$

where S_{ij} is the overlap integrals between C_i and C_j . All orbitals are assumed to be of Slater type, and the charge transfer energy are estimated by Murrell's method.⁷⁾ The numerical values used in this calculation are listed in Table 14.

Table 14

 $\beta_{12} = -2.37 \text{ eV}$ $S_{12} = 0.277 \qquad S_{16} = 0.0356 \qquad S_{17} = S_{26} = 0.000236$ $S_{27} = 0.000088$ <11|11> = 10.84 eV <11|22> = 7.06 eV <11|66> = -5.20 eV <11|77> = <22|66> = 3.97 eV <22|77> = 3.05 eV

From these data the secular determinant was solved to give the results shown in Table 15.

Tab	le	15
Tan	TC	

Transition energy (eV)	Wave functions*
8.0115 7.9694 6.9311 6.2700	$\Psi_{5} = -0.1783 \ \Psi_{L}^{A} + 0.9840 \ \Psi_{CT}^{A}$ $\Psi_{4} = -0.0380 \ \Psi_{G} + 0.0389 \ \Psi_{L}^{S} + 0.9985 \ \Psi_{CT}^{S}$ $\Psi_{3} = -0.0017 \ \Psi_{G} - 0.9993 \ \Psi_{L}^{S} + 0.0386 \ \Psi_{CT}^{S}$ $\Psi_{2} = 0.9840 \ \Psi_{L}^{A} + 0.1781 \ \Psi_{CT}^{A}$ $\Psi_{2} = 0.9840 \ \Psi_{L}^{A} + 0.0002 \ \Psi_{CT}^{S} + 0.0381 \ \Psi_{CT}^{S}$
$\begin{array}{c} \Psi_{1} \rightarrow \Psi_{2} \\ \Psi_{1} \rightarrow \Psi_{3} \end{array}$	197.3 nm (Rotational strength) ₁₊₂ -8.48 X 10^{-39} e.s.u. 178.5 nm (Rotational strength) ₁₊₃ +7.89 X 10^{-39} e.s.u.

* On the notation one is referred to the literature below: S. Nagakura, "Yuki Denshi Riron", p.132 (1966), Baifukan.

The rotational strength of the lowest two transitions are strengthened

compared to that obtained by exciton theory $(R = 7.1 \times 10^{-39})$, but the sign is still opposite to the observed one. The relatively large rotational strength of the lowest energy transiton compared to that of the second transition is contrary to the prediction from CNDO calculation by Wagnière⁸ who regarded the c.d. of (S)-(+)-8 as the overlapping of a large positive c.d. in the shorter wavelength on a weak negative one in the longer wavelength.

In contrast, Wynberg⁹⁾ calculated on the basis of CNDO method to give the same result as the exciton theory and described that only the unstable conformation could give the sign compatible with the experiment. This result agrees essentially with the present calculation. Inapplicability of the composite molecule method as well as of exciton theory to the diene 8 clearly shows that the effect of σ - bond is dominantly large for this system and the failure of CNDO method seems to exhibit the imperfect nature of its approximation for the calculation of transition states. References

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VIII. General discussions

1. Historical consideration of theoretical treatment of β , γ -unsaturated ketones.

Optical properties of dissymmetric β,γ -unsaturated ketones have received much experimental and theoretical attention in many laboratories.^{1 \circ 7)} The dissymmetric β,γ -unsaturated ketones are peculiar among ketones in which their lowest $n \rightarrow \pi^*$ singlets, which lie in the vicinity of 300 nm, exhibit enhanced absorption and optical activity.

As early as 1950, Alpen, Kumler, and Strait,⁸⁾ in order to account for the exaltation of the 295 nm band in substituted phenylacetones, suggested that "interaction between carbonyl and phenyl groups takes place directly through space". This interpretation is now known to be essentially correct. Further, in 1950, Woodward and Kovach¹⁾ remarked that "the high rotation and the abnormally high carbonyl absorption intensity (of parasantonide at 300 nm) have a common basis", that is, spectroscopic interactions between a carbonyl group and a β,γ -double bond are accompanied by high optical activity. This observation was continually reported by some groups.^{2v7}

The earliest meaningful mechanism for the enhanced intensity of β , γ unsaturated ketone was advanced by Labhart and Wagnière³⁾ who called attention to the overlap of the nonbonding orbital in the carbonyl group with the π -system of the neighboring ethylenic moiety. They adopted an orbital viewpoint, and showed that because of the non-orthogonality, the non-bonding orbital was better represented as $(n + \lambda \pi')$, where λ is a small mixing parameter determined by perturbation theory, and π' is the highest bonding π -orbital of the whole π -system. The lowest singlet transition is therefore better described as $(n + \lambda \pi') + \pi^*$, so that the transition is partially $\pi + \pi^*$ in character (roughly parallels to the extent λ) and hence weakly allowed. Labhart and Wagnière used a Hückel-type approach to show that their mechanism led to a reasonable order of magnitude for the absorption enhancement observed.

In the initial work on the optical activity⁵⁾ which presented the generalized octant rule for the first time, Moscowitz followed the lead

of Labhart and Wagnière and adopted their model and simple orbital formalism. He also pointed out that as far as the correlation of the sign of the 300 nm Cotton effect with absolute configuration was concerned, this would be determined by the sign of the overlap of an idealized non-bonding orbital, situated solely on the oxygen atom, with the highest bonding π -orbital. In this simple orbital picture, the sign of the overlap was sufficient to fix the relative phases of the orbitals involved in the transition, and hence the sign of λ . Labhart and Wabnière themselves were not concerned with the sign of λ since the enhancement of absorption intensity depends only on the absolute magnitude of this quantity. Moscowitz gave the correct sign of λ and assigned the correct absolute configurations (and even estimated the order of magnitude in some cases) based on this simple Hückel approach.

On the contrary, S. F. Mason⁴⁾ erroneously criticised Moscowitz' extension and use of the Hückel-formulated model of Labhart and Wagnière. The most serious criticism offered was, though without foundation, that Moscowitz' model predicts different wavelengths for corresponding electronic transitions in enantiomeric β,γ -unsaturated ketones. Still based on Labhart and Wagnière formalism, Mason claimed that the intensity enhancement and optical activity of the 300 nm carbonyl absorption is attributed to the direct overlap of the carbonyl lone-pair and the olefin π -orbital, which appears as the mixing of the electric dipole forbidden $n + \pi^*$ transition of the carbonyl group with an allowed charge-transfer transition of a π -electron from the carbon-carbon double bond to the antibonding π^* -orbital of the carbonyl group. Based on Mason's formalism, the absoption at 300 nm of asymmetric ketones is due to the transition of an electron to the carbonyl antibonding π^* -orbital from a mixed orbital, ψ . It can be written,

$\psi = a 2 p_y(0) + b \phi,$

where $2p_y(0)$ and ϕ refer, respectively, to the oxygen lone-pair orbital and the donor orbital from which the charge-transfer originates, and a and bare such coefficients that a >> b and $(a^2 + b^2) = 1$. The value of a is always near to unity in the series considered. The rotational strength, R, of the transition is given by the scalar product of the magnetic and

the electric dipole transition moments. The $n \rightarrow \pi^*$ component of the mixed transition has a magnetic dipole transition moment, μ , directed along the carbonyl axis, and the charge-transfer component has an electric dipole transition moment, ρ , directed at an angle θ to the carbonyl bond axis, giving

$\mathbf{R} = ab\mu\rho cos\theta$

The intensity enhancement of the ketone absoption at 300 nm depends upon the dipole strength, D, of the charge-transfer component of the mixed transition, where

$$D = (b\rho)^2$$

so that

$$\mathbf{R} = a\mu cos\theta \sqrt{\mathbf{D}}$$

That is,

$$R = \frac{1}{2}logD + log(a\mu cos\theta)$$

Thus the rotatory power of asymmetric ketones should be proportional to the square root of the intensity enhancement of the absorption at 300 nm if θ does not vary greatly from compound to compound, because α and μ are almost unity and constant.

Mason's formalism was supported by Cookson,²⁾ who provided straight relationship by plotting *loge* against *logAe* for the long wavelength band of bicyclo[2.2.2]octenone, bicyclo[2.2.1]heptenone and the bornenone derivarives, approximating R by Ae and D by e, though the gradient was about 0.3 rather than 0.5 as expected.

Although this method of plotting was preferentially used by some authors^{9,10)} for the theoretical basis of optical activity of β , γ -unsaturated ketones, the success of this treatment does not give any proof for the validity of Mason's and Cookson's formalism, because the same relationship comes even from Moscowitz' formalism.

However, these treatments of homoconjugation and mixing of charge transfer are, both based on Labhart and Wagnière formalism, unsuccesful for the clear-cut elucidation of enhanced absorptions of different intensity in various β,γ -unsaturated ketones. According to the quantum mechanical treatment and perturbation theory, coefficients λ and b, respectively, by Moscowitz and Mason, are both proportional to the resonance integral β' (which correlates to overlap integral S) between carbonyl carbon and β -carbon. In β,γ -unsaturated ketones studied at that time, β' is almost invariable irrespective of the mutual disposition of carbonyl and olefinic double bonds, since the relative position and direction of orbitals of carbonyl carbon and β -carbon is not so much altered and, moreover, the overlap integral S is relatively insensitive to the slight conformational changes.

In Moscowitz' formalism, the enhanced dipole strength is just proportional to λ^2 and the rotational strength to λ because the transition moment is essentially that derived from the $\pi \star \pi \star$ transition of the carbonyl, which directs along the bond axis of carbonyl. Therefore, the D and R must be almost constant in any cases, when the mutual arrangement of C=O and C=C is not so much altered.

In Mason's formalism, the direction of charge transfer transition is from the β -carbon to carbonyl carbon, since other transitions, e.g., that from olefinic carbon to carbonyl oxygen, are negligibly small because of very small overlap integrals. The intensity of charge transfer transition is almost proportional to the resonance integral β ', and therefore almost constant. Hence the rotational strength calculated by Mason has no variables and should be constant.

On the contrary, the observed ϵ and $\Delta \epsilon$ is very diverse even in the structurally related compounds.

The most important shortcoming of their formalism is that they are based on the Hückel method which makes no inquiry into the nature and origin of the coupling between chromophores nor, in its simplest form, takes account of configuration interaction effects.

Moscowitz himself, recognizing this shortcoming, re-investigated⁶) the optical activity of β , γ -ketone (bicyclo[2.2.2]oct-5-en-2-one) on the basis of Longuet-Higgins-Murrell formalism¹¹) which is particularly suitable for the consideration of mixing of charge transfer as well as the configuration interaction between local transitions. Moreover, this formalism allows for maximum utilization of empirical absorption data.

Table	28
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				S	CF coeffic	ients	• ·	· · ·
5	Symbol	Description	×ı	×2	x ₃	X4	X ₃	×4
	θ.	C=C bonding T	$1/\sqrt{2}$	$1/\sqrt{2}$	0	0	0	0
	θο	C=C antibonding π	$1/\sqrt{2}$	$-1/\sqrt{2}$	0	0	0	0
	(i) -	C=O bonding T	0.	0	0.62789	0.77830	0	0
	ωc 1	C=0 nonbonding n	0	0	0	0	-0.55024	0.83501
	ω_2	C=O antibonding π	0	0	-0.77830	0.62789	0	0
		Excited States						
	θ , $\overline{\theta}$	Locally excited C=	C π→π*					
	$\omega_1^{\perp} = 1 \omega_2^{\perp}$	Locally excited C=	O π→π *					
	$\omega_2^{\perp-1}\omega_3^{\prime}$	Locally excited C=	0 n→π*					
	$\theta_1^{2-1}\omega_3$	Charge transfer		•				
	$\omega_1^{-1}\theta_2$	Charge transfer					· ·	
	$\omega_2^{\perp-1}\theta_2$	Charge transfer						

Table 29

Transition		Mixing coefficient
ethylenic $\pi \rightarrow \pi$	$\theta_1^{-1}\theta_2$	+0.072
charge transfer	$\omega_2^{-1}\theta_2$	-0.017
carbonyl $\pi \rightarrow \pi$	ω ⁻¹ ω ₃	+0.0036



Figure 41

All transitions he considered are shown in Table 28. The results are given in Table 29, which clearly shows that the mixing of $\pi \to \pi^\star$ transition of ethylene $(\theta_2^{-1}\theta_2)$ is the more dominant factor for the enhancement of absorption than that of the charge transfer state $\omega_2^{-1}\theta_2$ or the locally excited carbonyl $\omega_1^{-1}\omega_3$ state. This is very remarkable, compared to the previous approach based on the Hückel model. In addition, the rotational strength is also dependent upon the sign of mixing coefficient of the locally excited ethylenic $\theta_1^{-1}\theta_2$ state, and the absolute configuration of bicyclooctenone was correctly assigned based on this sign. Moreover, the important interaction potential giving rise to the mixing is not the conjugative effect associated with the interchromophoric β 's but the electrostatic effect associated with the repulsion integrals. This was clearly shown by setting the interchromophoric β 's equal to zero which changed by less than 0.1 % the coefficient of mixing of the locally excited ethylenic state $\theta_1^{-1}\theta_2$ with the $n \to \pi^*$ state $\omega_2^{-1}\omega_3$. In general, it was the dissymmetric repulsion integrals involving atomic orbitals such as are depicted in Figure 41 that make the most significant contributions to the interaction potential. This point is very important for further theoretical treatment in the following section.

It is surprising that the simple Huckel-type MO model extended by Moscowitz⁵⁾ could lead to successful assignments of absolute configuration. Moscowitz provided some insight into the reasons for this, based on his configuration interaction treatment.⁶⁾

Certainly the main reason for the success of the model, also including Mason's formalism, lies in its essentially correct estimation of the basic symmetry of the situation, i.e., the situation posed by the intrinsic geometries of nearby C=O and unsaturated groups, and their associated electronic structures. For example, consider the overlap of the ideally localized nonbonding carbonyl orbital with the neighboring π -system. This overlap presents the same variation in sign with changes in the mutual disposition of the molecular fragments as do the important electrostatic interaction integrals. According to the more informative configuration interaction treatment cited above, it is these electrostatic terms that are primarily responsible for the coupling between fragments and the concomitant mixing of states that leads to the enhanced intensity of ab-

sorption and Cotton effect for the 300 nm transition. Moreover, the magnitudes of both the overlap and the electrostatic terms will increase or decrease as the distance between atomic centers decreases or increases. Hence the $n - \pi'$ overlap in the simple MO picture will correlate with just those terms of the configuration interaction treatment which mix, say, the locally excited ethylenic state with the $n + \pi^*$ state of the carbonyl group in bicyclooctenone. In this connection, it is interesting to note that the simple MO model also attributes the enhanced absorption and optical activity to a $n + \pi^*$ transition that overwhelmingly has the character of the same local ethylenic excitation. In summary, enough of the important symmetry and orbital characteristics that govern the lowest optical transitions of β , γ -unsaturated ketones are contained in the simple Labhart and Wagnière model and its extension as to make it extremely successful for correlating molecular structure with optical activity measurements.

Although Moscowitz justified his treatment of Hückel model as described above, the most important difference between the results from extended Labhart and Wagnière model by Moscowitz and Mason and those from electrostatic coupling model is that the former gives the octant nature of activity of $n \rightarrow \pi^*$ transition, whilst the latter gives the octant nature of coupling mode. This concept is more clearly expressed as follows; the former predicts that the sign of c.d. of $n + \pi^*$ of β, γ -unsaturated ketones is solely dependent upon the octant position of double bond regardless of its direction, and the latter exhibits the dependence of optical activity on the direction as well as the position of double bond.

This significant difference should have been noticed at the time of 1964, but Moscowitz exploited his meaningful results only for the justification of his simple Hückel treatment presented before.

2. Inspection of μ -m coupling method.

From the results of Moscowitz,⁶ it was shown that what governs the sign of Cotton effect of $n \rightarrow \pi^*$ of carbonyl is, not the mixing of the charge transter transition with $n \rightarrow \pi^*$ of carbonyl, but the coupling of $n \rightarrow \pi^*$ (of carbonyl) and $\pi \rightarrow \pi^*$ (of C=C). This type of coupling , sometimes called μ - m coupling (μ and m mean electric and magnetic transition moments, respectively), has now become the important factor for the c.d. of carbonyl.

There have been reported some methods of calculation for $\mu - m$ coupling. One is the molecular orbital method in which the transitions are splitted into atomic orbitals and the interaction energy can be obtained as the sum of electron repulsion integrals. This method, adopted by Moscowitz, is, though seems most appropriate, requires very troublesome calculation, including the integrals of the type $\langle pq | rr \rangle (\langle \chi_3 \chi'_3 | \chi_2 \chi_2 \rangle$ in Figure 41), although Moscowitz did not show the precise equation of integrals.

In the other mothod, magnetic moment, which is essentially the rotation of electron, can be expanded into multipole form, that is, "quadrupole". This electric dipole-quadrupole interaction, adopted in the present paper, was first introduced into the calculation of optical activity by Schellman¹²⁾ and Weigang,¹³⁾ independently.* This method has been proved very useful for the calculation of c.d. of benzobicyclo[2.2.2]octan-2-one derivatives.¹⁶⁾

* Shellman¹⁴⁾ and Woody¹⁵⁾ also proposed the monopole approximation method in which $n \rightarrow \pi^*$ and $\pi \rightarrow \pi^*$ transitions are expressed by charged sphere as shown in Figure.



This method, though its calculation is troublesome, can give more appropriate interaction energy than point-dipole - point-quadrupole approximation. 3. Proposal of a symmetry rule for β, γ -unsaturated ketones.

The most characteristic feature of the calculated results in this paper is, as stated before, that the coupling mode for the magnetic moment of carbonyl $n + \pi^*$ and the electric moment of C=C $\pi + \pi^*$ is always the same in any conformation considered. In other words, the coupling mode for four β,γ -unsaturated ketone $1 \sim 4$ is such that the magnetic moment with $C \neq 0$ direction always couples with the electric moment with $C_{\beta} + C_{\gamma}$ direction in cases that the C=C is placed at the upper right or lower left ' carbonyl octant.

 μ - m interaction V is reformulated as follows,¹²⁾

$$v = \frac{3Q_{xy}}{R^7} \left[\left(R^2 - 5x^2 \right) Y \mu_{2x} + \left(R^2 - 5Y^2 \right) X \mu_{2y} - 5 \left(XYZ \right) \mu_{2z} \right]$$
(1)

Equation (1) present the symmetry character of V, since V changes its sign when the double bond is reflected by σ - plane of carbonyl (for example; $\mu_{2x} \rightarrow -\mu_{2x}$, $X \rightarrow -X$). Hence the sign of Cotton effect by μ - m coupling is expressed as follows,

$$(sign) = -XYZ \cos \theta$$
 (2)

where X, Y, Z are the position of C=C in carbonyl octant and θ is the angle between C+O and $C_{\beta} + C_{\gamma}$ vectors. The equation (2) constitutes the <u>generalized</u> octant rule for β,γ -unsaturated ketones in the true meaning. This equation clealy shows that what is important for the sign of c.d. is, not the array of two chromophores (cisoid or transoid as was pointed out by Lightner¹⁷⁾ and showed in Figure 42, but the angle between two chromophores.



Figure 42

This new symmetry rule can clearly explain the sign of c.d. of β , γ unsatureated ketones of transoid type, as well as those of cisoid type hitherto investigated (See Figure 43).



* Angle between two chromophores is larger than 90° at planar conformation. For detail discussion, see Capter IV.



Figure 43.

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IX. Experimental section

1. General procedure

Melting and boiling points are uncorrected. Melting points were determined on a Mettler EP2 apparatus. IR spectra were measured on a Hitach EPI-G3 grating infrared spectrophotometer, a Hitach EPI-S infrared spectrophotometer, or a Jasco DS-402G in frared spectrophotometer by KBrdisk method unless otherwise stated. ¹H NMR spectra were recorded on a Varian XL-100, a Varian T-60, a Varian A-60, or a Hitach R-24 (60 MHz) spectrometer and are reported in δ from tetramethylsilane as an internal standard. Unless otherwise stated CDCl₃ was used as solvent. Optical rotations were obtained with a Perkin-Elmer 141 polarimeter or a Union PM-71 polarimeter. UV spectra were recorded on a Hitach EPS-3T spectrometer. CD spectra were recorded on a Jasco ORD/UV-5 spectropolarimeter equipped with a CD attachment or a Jasco J-20 spectropolarimeter. Silica gel for column chromatography refers to Merck Kiesel gel 60 (70-23- mesh ASTM). Alumina refers to Merck Aluminumoxid 90, II-III (70-230 mesh ASTM). TLC was carried out on plates prepared with Merck Kiesel gel GF254 containing CaSO, and fluorescent indicator.

2. Spiro[4.4] nonane derivatives.

Ethyl 4-Bromobutyrate (15).

A solution of Υ -butyrolactone (200 g, 2.33 mol) in absolute ethanol (300 mL) was cooled in an ice bath while a stream of dry hydrogen bromide (generated by bromine with tetralin) was introduced. The passage of gas was continued over 6 h, the alcoholic solution of the product was kept for 24 h at 0 °C and then poured onto ice-cold water (1 L). The oily layer was separated, and the aqueous layer was extracted with ether (2 x 100 mL). The combined oil and extracts was washed with ice-cold 2% potassium hydroxide solution then with very dilute hydrochloric acid, and finally with water. The organic layer was dried over sodium sulfate, the solvent was removed under reduced pressure and the residual crude ester was distilled to give a colorless oil (380 g, 84 % yield).

15: bp 69 - 70.5 °C at 6.5 mmHg

Triethyl 1,1,4-Butanetricarboxylate (16).

Some pieces of sodium (11.73 g, 0.51 mol) was added to anhydrous ethanol (500 mL) at 0 °C under nitrogen atmosphere. After the evolution of hydrogen ceased, diethyl malonate (84.57 g, 0.628 mol) was added over a period of 15 min at 0 °C and then ethyl 4-bromobutyrate (<u>15</u>) (100 g, 0.51 mol) added over 15 min at room temperature. After refluxing for 1.5 h, 400 mL of ethanol was distilled off and cold water (400 mL) added. The yellow oily layer was separated and the aqueous layer extracted with ether. The combined organic layer was washed with saturated brine (3 x 70 mL) and dried over sodium sulfate. Solvent removal gave the mixture of triester <u>16</u> and tetraester <u>17</u>, which was separated by high vacuum distillation to give 16 (94.8 g, 67.8 %) and 17 (13.6 g, 13.7 %).

16: bp 120 °C at 0.035 mmHg

NMR 1.10 and 1.22 (9H, t each, methyls), 1.76 (4H, m, methylenes), 2.31 (2H, t, CH₂-CO), 3.35 (1H, t, methine), 4.10 and 4.18 (6H, q each, O-CH₂-).

17: bp 150-155 °C at 0.035 mmHg
NMR 1.06 (12H, t, methyls), 1.62 (8H, b m, methylenes),
2.15 (4H, m, -CH₂CO-), 3.98 (8H, q, -OCH₂-).

Tetraethyl 1,1,4,7-Heptanetetracarboxylate (17).

Under nitrogen atmosphere, sodium (24.4 g, 1.06 mol) was added to absolute ethanol (600 mL) at 0 °C, and the triester <u>16</u> (290.8 g, 1.06 mol) was added over a period of 10 min and then the ester <u>15</u> (207.7 g, 1.06 mol) at room temperature over 10 min. The mixture was allowed to stir at room temperature and heated at the time when sodium bromide began to precipitate. After 2.5h of reflux, 400 mL of ethanol was distilled off, and water (200 mL) and ether (200 mL) were added. The organic layer was separated , washed with water, dried over sodium sulfate and distilled to give the recovered <u>16</u> (103.2 g) and <u>17</u> (216.1 g, 52.5 %).

17: mp 28 °C

Anal. Calcd for C₁₉H₃₂O₈: C; 58.74, H; 8.26 Found: C; 58.74, H; 8.30

1,1,4,7-Heptanetetracarboxylic Acid (18).

A mixture of <u>17</u> (23.1 g, 0.0615 mol), potassium hydroxide (18.16 g, 0.312 mol) and water (96 mL) was refluxed for 12 h to give a homogeneous solution. Concentrated hydrochloric acid (27.8 mL, 0.344 mol) was added and the mixture was concentrated to dryness under reduced pressure below 40 °C. The redidual solid was pulverized and washed with anhydrous ether to remove hydrochloric acid. The colorless solid was extracted continuously with acetone and the extracts were concentrated to afford the colorless solid of 18 (14.85 g, 97.8 %).

<u>18</u>: mp 162.8-172.7 °C (dec. with evolution of a gas) For further reaction a mixture of <u>18</u> and potassium chloride was used without any separation.

(\pm) -Spiro[4.4]nonane-1,6-dione (5).

A mixture of <u>18</u> (14.85 g, 0.0538 mol) and acetic anhydride (97 mL) was allowed to stier at 60 °C for 24 h and concentrated at 80 °C under reduced pressure to give the brown viscous oil, which was pyrolyzed at 250 °C under 28 mmHg to give a brown solid in a dry ice bath. The crude product was distilled under vacuum to yield 3.8 g of <u>5</u> (0.025 mol, 46.5 %), which was recrystallized from methanol and purified by sublimation.

(±) -5: bp 126 5 °C at 22.5 mmHg mp 38.0-38.5 °C IR (KBr) 1743, 1716 cm⁻¹

> Anal. Calcd for C₉H₁₂O₂: C; 71.02, H; 7.95 Found: C; 70.97, H; 7.89

(±)-trans, trans-Spiro[4.4] nonane-1, 6-diol (19).

A solution of 5 (6.0 g, 0.0395 mol) in anhydrous ether (150 mL) was added over a period of 50 min to a solution of lithium aluminum hydride (6.0 g, 0.158 mol) in ether (150 mL). The mixture was refluxed for 3 h, and heated for 1h after dropping ethyl acetate (30 mL) at 0°C. Water (20 mL) was then added at 0 °C over 0.5 h and the mixture was stirred for 6 h at room temperature. The white precipitate; were filtered and washed with ethyl acetate. The combined filtrate and the washing were concentrated under vacuum to give a mixture of three diols (6.15 g, 99.7 %), which was dissolved in ethyl acetate-benzene (2:1, 80 mL) and chromatographed on silica gel (1 kg) eluting with ethyl acetate-benzene (2:1, 200 mL-fractions). Fraction 11-18 gave a colorless oil (4.85 g), and fraction 19 and 20 yielded a colorless viscous oil (0.67 g). Fraction 21-26 afforded colorless crystals (0.41 g, mp 113-121 °C) which was recrystallized from benzene to give colorless prisms of <u>19</u>.

(±)-19: mp 124.2-125.0 °C

IR (KBr) 3280 cm^{-1}

Anal. Calcd for C₉H₁₆O₂: C; 69.19, H; 10.32 Found: C; 69.44, H; 10.33

Fractions 19 and 20 were rechromatographed for separation and fractions 11-18 were oxidized with Jones' reagent to give 5.

3-Bromo-d-camphoric Anhydride.

A mixture of d-camphoric acid (150 g, 0.75 mol) and phosphorous pentachloride (315 g, 1.5 mol) was stirred slowly to give a homogenous solution which was allowed to stir overnight, and bromine (43.5 mL, 0.74 mol) was added dropwise over 5 h at 90 °C. The mixture was poured onto cold water (500 mL, exothermic!!) to give white solid and yellow solution. The aqueous solution was decanted off and the residue was stirred with acetic acid (240 mL) and water (60 mL) at 70 °C for 1 h. Water (600 mL) was added, and the mixture was stirred for 0.5 h and filtered. The light yellow needles were washed three times with ethanol and dried to give 132 g of anhydride (mp 215.4-217.2 °C, sublimable).

d-Camphanic Acid.

A solution of 3-bromo-d-camphoric anhydride (160 g, 0.61 mol) and potassium acetate (110 g) in acetic acid (600 mL) and acetic anhydride (6 mL) was refluxed for 4 days and concentrated at 90 °C under reduced pressure. The residue was dissolved in hot water (300 mL) and decolorized by activated charcoal powder (3 g). The solution was acidified with concentrated hydrochloric acid (200 mL), and the resultant precipitate WAS filtered to give 95.7 g of acid. The filtrated aqueous solution was extracted with ether (2 x 300 mL) and the ether layer dried over magnesium sulfate. Solvent removal gave 22.2 g of acid. The combined products

were recrystallized from benzene-ethyl acetate (60:1) to give colorless crystals (95 g, 85 %).

mp 204.3-206.3 °C IR (KBr) 2972, 1756 cm⁻¹ Anal. Calcd for $C_{10}H_{14}O_4$: C; 60.59, H; 7.12 C; 60.63, H; 7.25

(-)-d-Camphanyl Chloride.

A solution of d-camphanic acid (9.1 g, 0.046 mol) in thionyl chloride (52.5 g) was heated at reflux for 2.5 h and the thionyl chloride was evaporated under reduced pressure at room temperature to give colorless solid (9.53 g, 96 %) which was sublimed at 70 °C for purification.

mp 68.9-70.1 °C

Anal. Calcd for C₁₀H₁₃O₃Cl: C; 55.43, H; 6.04, Cl; 16.36 Found: C; 55.56, H; 6.02, Cl; 16.33

(1R,5S,6R)-(-)- and (1S,5R,6S)-(+)-trans,trans-1,6-Dicamphanyloxyspiro-[4.4]nonane (19'a and 19'b). Optical Resolution of 19.

To a solution of $(\pm)-\underline{19}$ (0.85 g, 5.52 mmol) in dry pyridine (15 mL) was added (-)-camphanyl chloride (3.58 g, 16.6 mmol) and the solution was allowed to stir for 16 h at room temperature. Water (200 mL) was added, and the reaction mixture was extracted with benzene, and washed successively with hydrochloric acid, 5 % sodium bicarbonate and saturated brine. After drying over sodium sulfate solvent removal gave colorless solid (2.77 g, 97.1 %, mp 160.9-200 °C), which was dessolved in methylene chloride (30 mL) and chromatographed on silica gel (1 kg) eluting with cyclohexane-ethyl acetate (2:1, 200 mL-fraction). Fraction 18-20 gave 0.86 g of <u>19'b</u> which was recrystallized four times from cyclohexane-ethyl acetate (1:1) to give diastereomerically pure crystals.

(+)-19'b: mp 173.6-174.8 °C

[\(\alpha\)]_{589} +51.3° (c 1.0, methylene chloride) IR (KBr) 1792, 1738 cm⁻¹ NMR 0.978, 1.07, 1.12 (3H each, s each, methyls), 1.4-2.7 20H, m, methylenes), 5.04 (1H, bm, -0-CH-). Anal. Calcd for C₂₉H₄₀O₈: C; 67.42, H; 7.80 Found: C; 67.77, H; 7.80 Fraction 22-25 gave 2.82 g of crystals which was recrystallized from the same solvent and again recrystallized four times together with the crystals from fraction 26-28 (0.58 g) to give diastereomerically pure (-)-19'a.

(-)-<u>19'a</u>: mp 220.2-220.4 °C

Anal. Calcd for C₂₉H₄₀O₈: C; 67.42, H; 8.70 Found: C; 67.78, H; 7.81

Fraction 21 and all mother liquours were combined and rechromatographed for further separation.

(1R,5S,6R)-(-)-trans,trans-Spiro[4.4]nonane-1,6-diol (19).

A solution of $(-)-\underline{19'a}$ (0.50 g, 0.969 mmol) in ethanol (30 mL) and 2N potassium hydroxide (10 mL) was refluxed for 14 h, concentrated to 7 mL, and extracted with ethyl acetate to give 152.03 mg of crude <u>19</u>, which was recrystallized from benzene to give colorless rods.

(-)-<u>19</u>: mp 132.5-132.7 °C
[d]₅₈₉ -58.8° (c 1.0, ethanol)
IR (KBr) 3240 cm⁻¹
Anal. Calcd for C₉H₁₆O₂: C; 69.19, H; 10.32
Found: C; 69.57, H; 10.25

(R) - (+) - and (S) - (-) - Spiro[4.4]nonane-1, 6-dione (5).

To a solution of $(-)-\underline{19}$ (121.68 mg, 0.779 mmol) in acetone (15 mL) was rapidly added Jones' reagent (0.45 mL) at -10 °C. After stirring for 5 min benzene was added (150 mL), and the mixture was passed through **a** celite column. Solvent removal under reduced pressure gave 108.14 mg (91.2 %) of crude 5 which was sublimed for purification to afford colorless rods of 5.

> (-)-<u>5</u>: mp 63.5-65.2 °C [&]₅₈₉ -129.8° (c 0.5, cyclohexane)

UV and CD Figure 11, 12 and 18, and Table 7, 8 and 10. Anal. Calcd for C₉H₁₂O₂: C; 71.02, H; 7.95 Found: C; 70.79, H; 7.95

(±)-cis- and trans-6-Hydroxyspiro[4.4]nonan-1-one (20 and 21).

After prereducing of Adamas catalyst (0.5 g) in 99% ethanol (20 mL) with hydrogen at atmospheric pressure, dione 5 (4.9 g, 32.2 mmol) in ethanol (80 mL) was added and the reduction allowed to proceed until equimolar hydrogen was taken up (ca. 800 mL at 25 °C). Filtration and solvent removal yielded a colorless oil (4.83 g). Column chromatography on silica gel (150 g) with benzene - ethyl acetate (3:1) eluted cis-ketol 20 (2.55 g) as a colorless oil.

(±)-20: bp 110-111 °C at 12 mmHg.

IR (CCl₄, 0.1 M) 3500, 1727 cm^{-1} .

NMR (CCl₄) 1.2-2.7 (12H, m, cyclic methylenes), 3.50 (1H, s, OH), 3.90 (1H, m, -CH-OH).

Anal. Calcd for C₉H₁₄O₂: C; 70.10, H; 9.15 Found: C; 69.99, H, 9.21

Further elution gave a colorless oil of trans-ketol 21 (0.10 g).
(±)-21: IR (CCl₄, 0.1 M) 3680, 3450, 1736 cm⁻¹
NMR (CCl₄) 1.0-2.7 (12H, m, cyclic methylenes), 3.45 (1H, s,

OH), 4.02 (1H, br t, -CH-OH).

Further elution with benzene-ethyl acetate (1:1) gave fully hydrogenated product, spiro[4.4]nonane-1,6-diol (1.30 g).

(5R, 6R)-(-)- and (5S, 6S)-(+)-cis-6-(Camphanyloxy)spiro[4.4]nonan-1one (20, a and 20, b). Optical resolution of 20.

A solution of cis-ketol 20 (0.38 g, 2.46 mmol) and (-)- camphanyl chloride (0.73 g, 3.23 mmol) in anhydrous pyridine (10 mL) was allowed to stand for 2 days at room temperature. The mixture was diluted with water (100 mL) and extracted with benzene (2 x 100 mL). The extract was washed with 10% hydrochloric acid, 5% aqueous sodium bicarbonate and water, and dried over sodium sulfate. After removal of solvent the residual colorless

solid (0.67 g) was chromatographed on silica gel (80 g) with benzeneethyl acetate (10:1, 100 mL-fractions). Fraction 7 (colorless crystals, 90 mg) was five times recrystallized from cyclohexane to give colorless plates of 20'b.

(+)-<u>20'b</u>: mp 110.5-111.3 °C [a]²⁰ +40.2° (c 0.116, ethanol)

IR 1793, 1736 cm^{-1}

NMR 0.95, 1.04, 1.07 (3H each, s each, methyls), 1.2-2.5 (16H, m, cyclic methylenes), 5.05 (1H, m, -CH-O).
Anal. Calcd for C₁₉H₂₆O₅: C; 68.24, H; 7.84.
Found: C, 68.28, H; 7.88.

Fraction 10-14 gave colorless crystals (240 mg) which were purified in the same manner to yield colorless plates of 20'a.

(-)-<u>20'</u>a: mp 115.2-115.5 °C

[x]²⁰₅₈₉ -68.8° (c 0.583, ethanol)
IR 1784, 1747 cm⁻¹
NMR 0.96, 1.02, 1.07 (3H each, s each, methyls), 1.2-2.5
 (16H, m, cyclic methylenes), 5.1 (1H, m, CH-O).
Anal. Calcd for C₁₉H₂₆O₅: C; 68.24, H; 7.84
 Found: C; 68.51, H; 7.78

Fraction 8 and 9 gave a mixture of <u>20'a</u> and <u>20'b</u> (280 mg) which was combined with the mother liquors of the recrystallizations and submitted to further chromatography.

(5S,6R)-(-)-trans-6-(Camphanyloxy)spiro[4.4]nonan-1-one (21'a). Optical resolution of 21.

trans-Ketol <u>21</u> (0.25 g, 1.62 mmol) in pyridine (10 mL) was treated with (-)-camphanyl chloride (0.50 g, 2.31 mmol) and worked up in the same manner as cis-ketol <u>20</u>. The resulting oil (0.53 g) was crystallized and recrystallized (three times) from hexane to give the ester <u>21'a</u> (180 mg) as fine needles.

NMR 0.90, 1.02, 1.07 (3H each, s each, methyls), 1.2-2.5
 (16H, m, cyclic methylenes), 5.2 (1H, m, CH-O).
Anal. Calcd for C₁₉H₂₆O₅: C; 68.24, H; 7.84
 Found: C; 67.98, H; 7.79

(R)-(+)- and (S)-(-)-Spiro[4.4]nonane-1,6-dione (5). Determination of absolute configuration of 20'a and 21'a.

<u>A. From (-)-20'a.</u> Lithium aluminum hydride (0.50 g) in anhydrous ether (30 mL) was refluxed for 1 h and cooled. (-)-cis-Camphanate 20'a(0.50 g, 14.9 mmol) in ether (35 mL) was added dropwise over 0.5 h. The mixture was refluxed for 1 h, cooled, and the excess lithium aluminum hydride was decomposed by adding ethyl acetate-ether (1:1, 10 mL) under stirring. Water (2 mL) was then added carefully and the solution was stirred for 3 h until the color of the precipitate changed from gray to white. The slurry reaction mixture was filtered and the solid washed with ethyl acetate. The solvent was removed and the residue chromatographed on silica gel. Elution with benzene-ethyl acetate (2:3) gave diol 27 as a colorless oil (0.24 g, quantitative yield).

 $(-)-\frac{27}{589}$: $[\alpha]_{589}^{20}$ -80.5° (c 1.2, ethyl acetate).

This diol was oxidized with rapid addition of Jones' reagent. Workingup of the reaction mixture according to Gerlach's procedure gave a crude solid of (+)-dione 5 (0.21 g, 93% yield from 20'a).

 $(+) - 5: [\alpha]_{589}^{20} + 135^{\circ} (c \ 0.457, cyclohexane)$

Recrystallization from methanol gave analytically pure sample of 5.

5: mp 64.3-65.1 °C IR 1743, 1715 cm⁻¹ NMR (CCl₄) 1.4-2.6 (12H, m, methylenes) Anal. Calcd for C₉H₁₂O: C; 71.02, H; 7.95 Found: C; 70.98, H; 7.96

<u>B. From 21'a.</u> (-)-trans-Camphanate <u>21'a</u> (75 mg, 0.23 mmol) was converted in the same manner to (-) dione <u>5</u> (30.5 mg, 84% yield from <u>21'a</u>). (-)-5: $[\alpha]_{589}^{20}$ -130° (c 0.312, cyclohexane).
(±)-cis-6-Methylenespiro[4.4]nonan-1-ol (22).

Under a nitrogen atmosphere potassium t-butoxide (6.7 mmol) in tbutyl alcohol (6.3 mL) was added to a stirred suspension of triphenylmethyl phosphonium bromide (2.5 g, 7.0 mmol) in anhydrous benzene (25 mL), and the resulting orange-yellow solution was stirred for 0.5 h. cis-Ketol 20 (0.50 g, 3.24 mmol) in benzene (20 mL) was dropped in 1 h and the mixture was stirred until the starting material was not detected by TLC examination (1 h). Water (100 mL) and benzene (100 mL) were added and the separated organic layer was washed with water (100 mL) and filtered through silica gel column. After evaporation of solvent the crude material was chromatographed on silica gel (80 g). Benzene fraction gave an unidentified hydrocarbon (77.7 mg) and benzene-ether (15:1) fraction yielded a colorless oil (89 mg, 18%) of unsaturated alcohol 22, which was micro-distilled to afford a pure sample.

(±)-22: bp 90°C (bath temperature) at 20 mmHg
IR (neat) 3430, 3050, 1650, 885 cm⁻¹
NMR (CCl₄) 1.2-2.2 (loH, m, cyclic methylenes), 1.55 (lH, s,
OH), 2.37 (2H, m, allylic), 3.43 (lH, m, CH-O),
4.86 (lH, m, olefinic), 5.05 (lH, m, olefinec).
Anal. Cacld for C₁₀H₁₆O: C; 79.05, H; 10.61
Found: C; 78.89 H; 10.59

(1R,5R)-(-)- and (1S,5S)-(+)-cis-l-(Camphanyloxy)-6-methylenespiro-[4.4]nonane (22'a and 22'b).

<u>A. Optical resolution of 22.</u> A mixture of (\pm) -alcohol <u>22</u> (222 mg, 1.45 mmol), (-)-camphanyl chloride (493 mg, 2.28 mmol), and pyridine (10 mL) was left to stand for 4 days and worked up in the usual way to give crude material (489 mg), which was chromatographed on silica gel (140 g) with benzene-ether (40:1, 80 mL-fractions). Fraction 5-7 gave crude crystals of <u>22'b</u> (200 mg) which was twice recrystallized from pentane to yield colorless crystals (94.5 mg).

22'b: mp 91.0-91.6 °C [\$\alpha]_{589}^{20} 0.0^{\circ}, [\$\alpha]_{350}^{20} -25.7^{\circ} (c 2.91, ethanol) IR 3070, 1788, 1716, 1647 cm⁻¹ NMR 0.93, 1.01, 1.08 (3H each, s each, methyls), 1.2-2.6 (16H, m, cyclic methylenes), 4.92 (3H, m, olefinic and -CH-O).

Anal. Calcd for C₂₀H₂₈O₄: C; 72.26, H; 8.49 Found: C; 72.52, H; 8.52

Further elution gave several fractions containing mainly <u>22'b</u> (total 200 mg), which on twice recrystallization from cyclohexane yielded color-less needles (84 mg).

22'b: mp 132.2-132.4 °C
[d]²⁰₅₈₉ -2.8°, [d]²⁰₃₅₀ -8.4° (c 2.14, ethanol)
IR 3070, 1783, 1742, 1648 cm⁻¹
NMR 0.92, 1.04, 1.08 (3H each, s each, methyls), 1.3-2.6
(16H, m, cycloic methylenes), 4.9 (3H, m, olefinic
and CH-O).

Anal. Calcd for C₂₀H₂₈O₄: C; 72.26, H; 8.49 Found: C; 72.57, H; 8.64

<u>B. Wittig reaction of 20'a.</u> A solution of (-)-cis-eater <u>20'a</u> (98 mg, 0.29 mmol) in benzene (10 mL) was added under nitrogen to a solution of triphenylmethylene phosphorane prepared from triphenylmethyl phosphonium bromide (400 mg) in benzene (15 mL) and potassium t-butoxide (0.8 mmol) in t-butyl alcohol (0.6 mL). After 1.5 h stirring, the mixture was treated with water, and dried over sodium sulfate. Removal of solvent followed by column chromatography on silica gel (15 g) with benzene-ether (20:1) gave colorless crystals of 22'a (17.3 mg, 18%).

22'a: mp 128-131 °C

Other spectral data were identical with those of 22'a in A.

(1R,5R)-(-)-cis-6-Methylenespiro[4.4]nonan-1-ol (22).

A solution of (-)-cis-ester 22'a (117 mg, 3.5 mg) in methanol (8 mL) and 1N potassium hydroxide (1.5 mL) was refluxed for 4 h. The reaction mixture was worked up with pentane-water, washed with saturated brine, and dried over sodium sulfate. Removal of solvent and column chromatography on silica gel (15 g) with pentane-ether (15:1) gave (-)-22 as a colorless oil (39.8 mg, 73%). 22: [d]²⁰₅₈₉ -51.8° (c 0.80, methylene chloride)

NMR and IR spectra were identical with those of the racemate.

(R)-(+)-6-Methylenespiro[4.4]nonan-l-one (1).

A. Wittig reaction of (R)-(+)-dione 5. A solution of triphenylmethylene phosphorane, prepared from triphenylmethyl phosphonium bromide (6.0 g, 16.8 mmol), potassium t-butoxide (15.8 mmol) in t-butanol (16 mL) and anhydrous benzene (50 mL), was added during 1 h to a solution of (R)-(+)-dione 5 (620 mg, 4.07 mmol) in benzene (30 mL) under nitrogen atmosphere. Water was then added to decompose the excess phosphorane, and the mixture was worked up in the usual way. The crude material was chromatographed twice on silica gel and the pentane-ether (20:1) eluate was distilled in vacuo. Further chromatography followed by distillation gave (+)-unsaturated ketone <u>1</u> (106 mg, 17%) as a colorless oil.

(+)-1: bp 71-75 °C (bath temperature) at 35 mmHg
[a]²⁰₅₈₉ +134.5° (c 0.525, methanol)
IR (neat) 3080, 1738, 1650 cm⁻¹
NMR 1.80 (8H, m, cyclic methylenes), 2.35 (4H, m, allylic
and -CH₂-CO), 4.72 (1H, t, J = 2.3Hz, olefinic), 4.98
(1H, t, J = 2.1 Hz, olefinic).
UV and CD Figure 4 and Table 5.
Anal. Calcd for C₁₀H₁₄O: C; 79.95, H; 9.39
Found: C; 79.67, H; 9.41

<u>B.</u> Oxidation of (1R,5R)-(-)-alcohol 22. To a solution of chromium trioxide (149.7 mg) in anhydrous pyridine (2 mL) and methylene chloride (2 mL) was added a solution of (-)-alcohol <u>22</u> (39.8 mg, 0.26 mmol) in methylene chloride (3 mL) and stirred for 5 h at room temperature. The reaction mixture was taken up in pentane and worked up in the usual way. The curde material (25.5 mg) was purified by repeated chromatography as in A, giving (+)-ketone 1 (6.22 mg, 16%) as a colorless oil.

 $(+)-\underline{1}: [\alpha]_{589}^{20} +139.8^{\circ} (c \ 0.124, \text{ methanol})$

Other spectral data were identical with those of $\underline{1}$ in A.

(R) - (+) - 1, 6-Dimethylenespiro [4.4] nonane (9).

To a solution of triphenylmethylenephosphorane prepared from triphenylmethylphosphonium bromide (400 mg, 11.2 mmol) and 1.11 N potassium t-butoxide (0.65 mL of t-butyl alcohol solution) in spectroscopically pure n-pentane (15 mL) was added under nitrogen atmosphere a solution of (+)-1(55.8 mg, 0.372 mmol) in n-pentane (10 mL) in 20 min. The solution was allowed to stir for 2.5 h at room temperature and the excess phosphorane was decomposed with water. After usual workup, the reaction mixture was chromatographed on silica gel (5 g) with pentane, and the pentane was distilled off. Benzene formed from phosphorane was evaporated under reduced pressure at room temperature and the residue was distilled to give a colorless oil of 9 (9.7 mg, 17.6%).

(+)-9: [d]₅₈₉ +190° (c 0.0432, isooctane)

IR (neat) 3080, 1665 cm^{-1}

NMR (CDCl₂) 1.3-1.9 (8H, m, methylenes), 2.45 (4H, m, allylic methylenes), 4.71 and 4.88 (2H each, m each, J = 1.08 Hz, olefinic). UV and CD Figure 23 and Table 13. Anal. Calcd for C11H16: C; 89.12, H; 10.88 Found:

C; 88.53, H; 11.07

(1R,5R,6R)-cis,cis-(-)- and (1S,5R,6R)-trans,cis-(-)-6-(Camphanyloxy)spiro[4.4]nonan-1-ol (28 and 29).

(-)-cis-Ester 20'a (6.0 g, 17.9 mmol) was hydrogenated in ethanol (100 mL) over Adams catalyst (470 mg). Filtration followed by evaporation of solvent gave a mixture of alcohols 28 and 29 whose ratio was ca. 4:1 by ¹H-NMR examination. Five times recrystallization from benzene-cyclohexane (3:4) gave $(-)-\underline{29}$ (1.0 g) as feebly hygroscopic colorless fine needles.

> (-)-29: mp 185.7-186.1 °C [\$\mathcal{\mathcal{A}}]_{589}^{20} -139.9° (c 1.07, ethanol) IR 3500, 1777, 1742 cm⁻¹ IR $(CCl_{A}, 10^{-2} \text{ M})$ 3500, 1801, 1738 cm⁻¹ NMR 1.00, 1.07, 1.10 (3H each, s each, methyls), 1.2

2.6 (16H, m, cyclic methylenes), 2.21 (1H, s, OH), 3.95 (1H, br s, -CH-OH), 5.23 (1H, br s, -CH-OCO). Anal. Calcd for C₁₉H₂₈O₅: C; 67.83, H; 8.39 Found: C; 67.45, H; 8.33

Combined crops from the mother liquors were treated with cyclohexane to remove sparingly soluble 29. Repeated recrystallization from benzene-cyclohexane (1:2) gave (-)-28 (2.30 g) as colorless rods.

(±)-cis-6-(Tetrahydropyranyloxy)spiro[4.4]nonan-l-one (24).

To an ice-cooled mixture of (\pm) -cis-ketol <u>20</u> (3.59 g, 23.3 mmol) and dihydropyrane (2.20 g, 26.2 mmol) was added a small piece of toluenesulfonic acid. The solution was stirred for 1 h, **and** potassium carbonate (2 g) was added. The mixture was left to stir for 1 additional hour, filtered and washed with benzene. The combined organic phase was distilled to give a colorless liquid of <u>24</u> (3.92 g). The residue was chromatographed and distilled to give additional 0.63 g of <u>24</u> (total yield 82%).

(±)-24: bp 148-149 °C at 10 mmHg

IR (neat) 1734, 1038, 1023 cm⁻¹ Anal. Calcd for C₁₄H₂₂O₃: C; 70.55, H; 9.31 Found: C; 70.41, H; 9.33

(5R,6R)-cis-6-(Tetrahydropyranyloxy)spiro[4.4]nonan-1-one (24).

To a solution of (-)-alcohol <u>28</u> (4.26 g, 12.7 mmol) in chloroform (80 mL) were added dihydropyrane (2.0 g, 23.8 mmol) and toluenesulfonic acid (1 small piece) and stirred for 2.7 h under cooling on an ice bath.

The mixture was directly chromatographed on silica gel with benzene-ethyl acetate (10:1) and the volatiles were removed in vacuo (room temperature, 20 mmHg). The residual oil was taken up in anhydrous ether and added dropwise to a solution of lithium alminum hydride (5.0 g, 130 mmol) in ether (200 mL). The reaction mixture was refluxed for 1 h and worked up in the usual way. The product (5.0 g) was chromatographed on silica gel (Wakogel 140 g) with benzene-ethyl acetate (7:1) to give the hydroxy-ether as a colorless oil (3.0 g, 98% yield from 28). Oxidation with a solution of chromium trioxide (8 g), pyridine (150 mL) and methylene chloride (250 mL) gave, after usual work up and distillation, a colorless oil of 24 (0.76 g, 25% yield from 28).

24: bp 150 °C (bath temperature) at 10 mmHg

NMR (CCl₄) 1.0-2.8 (18H, m, cyclic methylenes), 3.2-4.3 (3H, m, $-CH_2-O$, -CH-OTHP), 4.5 (1H, m, O-CH-O). IR spectrum was identical with that of the racemate. Anal. Calcd for $C_{14}H_{22}O_3$: C; 70.55, H; 9.31 Found: C; 70.39, H; 9.33

(±)-cis-6-(Tetrahydropyranyloxy)hydrazone (25).

A solution of (\pm) -cis-ketol <u>24</u> (0.30 g, 12.6 mmol), toluenesulfonyl hydrazide (0.23 g, 12.6 mmol) and pyridine (1 drop) in anhydrous ethanol (5 mL) was refluxed for 2.5 h. The volatiles were removed in vacuo and the residue chromatographed on silica gel (20 g). Eluting with benzene gave the recovered ketone (0.16 g). Benzene-ether (20:1) eluate gave the hydrazone <u>25</u> (0.20 g, 39%) as colorless crystals which were recrystallized from methanol-pyridine (75:1) to give colorless prisms.

25: mp 126.4-134.2 °C

IR (nujol) 3175, 1608 cm⁻¹

NMR 1.0-2.5 (21H, m, NH and cyclic methylenes), 2.40 (3H, s, methyl), 3.2-4.2 (3H, br m, -CH₂O- and -CH-OTHP), 4.3-5.05 (1H, m, O-CH-O), 7.3, 7.9 (4H, A₂B₂ pattern, aromatic).

Anal. Calcd for C₂₁H₃₀O₄S: C; 62.04, H; 7.44, N; 6.89, S; 7.89 Found: C; 61.92, H; 7.47, N; 6.88, S; 7.85

(±)-cis-l-(Tetrahydropyranyloxy)spiro[4.4]non-6-ene (26).

To a stirred suspension of finely pulverized (\pm) -hydrazone 25 (3.10 g, 7.63 mmol) in dry ether (100 mL) was added under nitrogen n-butyllithium (25.4 mmol) in ether (28 ml). After disappearance of white powder of 25, the resulting yellow solution was stirred for 2.5 h. Aqueous workup, drying over sodium sulfate, removal of solvent, and chromatography (silica gel, pentane-ether 20:1) gave a colorless oil of (\pm) -ether <u>26</u> (1.20 g, 71%), which was microdistilled for further purification.

 $(\pm)-\underline{26}$: bp 130 °C (bath temperature) at 33 mmHg IR (neat) 1605 cm⁻¹

> NMR 1.0-2.0 (14H, m, cyclic methylenes), 2.37 (2H, br t, allylic), 3.2-4.0 (3H, m, -OCH₂ and CH-OTHP), 4.6 (1H, m, -OCH-O), 5.5-5.9 (2H, m, olefinic). Anal. Calcd for C₁₄H₂₂O₂: C; 75.63, H; 9.77 Found: C, 75.68, H; 9.95

(\pm) -cis-Spiro[4.4]non-6-en-1-ol (23).

A solution of (\pm) -ether <u>26</u> (1.20 g, 5.4 mmol) in methanol (10 mL) was mixed with hydrochloric acid (2 drops) and allowed to Stand for 1 day at room temperature. The mixture was taken up in pentane (40 mL), washed successively with aqueous sodium bicarbonate and water, and dried over sodium sulfate. Chromatography on silica gel (40 g) with pentane-ether (10:1)followed by distillation gave a colorless oil of (\pm) -<u>23</u> (0.51 g). A small sample was chromatographed and distilled again for analysis.

 $(\pm)-23$: bp 100 °C (bath temperature) at 27 mmHg

IR (neat) 3380, 3050, 1612 cm⁻¹

NMR (CCl₄) 1.2-2.2 (8H, m, cyclic methylenes), 2.2-2.6 (2H, m, allylic), 3.73 (1H, br t, CH-O), 5.72 (2H, m, olefinic).

Anal. Calcd for C₉H₁₄O: C; 78.21, H; 10.21 Found: C; 78.13, H; 10.29

(<u>1R,5S</u>)-(-)- and (<u>1S,5R</u>)-(+)-cis-(Camphanyloxy)spiro[4.4]non-6-ene (<u>23'a and 23'b</u>).

A. Optical resolution of 23. (±)-Alcohol 23 (0.90 g, 6.73 mmol)

and (-)-camphanyl chloride (2.0 g, 9.23 mmol) in pyridine were treated in the usual way to give a mixture of esters (crystals, 1.97 g). Six times recrystallization from hexane gave 23'a (528 mg) as colorless rods with a constant specific rotation.

(-)-23'a: mp 130-131.3 °C

 $[\alpha]_{589}^{20}$ -131.7° (c 0.50, methanol) IR 3050, 1787, 1741 cm⁻¹

NMR 0.95, 1.05, 1.10 (3H each, s each, methyls), 1.5-2.7 (14H, m, cyclic methylenes), 5.0 (1H, br d, CH-O), 5.60 (1H, td, J = 1.80, 5.8 Hz, olefinic), 5.77 (1H, td, J=2.05, 5.8 Hz, olefinic).

Anal. Calcd for $C_{19}H_{26}O_4$: C; 71.67, H; 6.23 Found: C; 71.73, H; 8.24

The mother liquor of the first recrystallization yielded colorless crystals (580 mg) which were recrystallized twice from hexane, then from methanol, giving 23'b as colorless prisms (282 mg).

(+)-23'b: mp 83.8-85.2 °C $[\alpha]_{589}^{20}$ +125.0° (c 0.32, ethanol) IR; 3045, 1790, 1734 cm⁻¹ NMR; 0.97, 1.06, 1.11 (3H each, s each, methyls), 1.5-2.6 (14H, cyclic methylenes), 5.05 (1H, br d, CH-O), 5.70 (1H, td, J=1.63, 5.70 Hz, olefinic), 5.80 (1H, td, J=1.80, 5.70 Hz, olefinic). Anal. Calcd for C₁₉H₂₆O₄: C; 71.67, H; 8.23 Found: C; 71.48, H; 8.16

<u>B. 23'a from (5R,6R)-ketoether 24.</u> (5R,6R)-cis-Ketoether <u>24</u> (0.64 g, 2.7 mmol) was converted to (-)-alcohol <u>23</u> (72 mg, 19%) in the same manner as the racemic series. This (-)-alcohol was treated with (-)-camphanyl chloride in pyridine and worked up in the usual way. The resulting product (85.76 mg) was dissolved in benzene-ethyl acetate (15:1) and passed through silica gel column (10 g) to give colorless crystals of <u>23'a</u>.

(-)-23'a: mp 127-129 °C

 $[\alpha]_{589}^{20}$ -122° (c 0.50, methanol) NMR spectrum was identical with that of 23'a obtained in A.

(1R,5S)-(-)-cis-Spiro[4.4]non-6-en-1-ol (23).

A solution of (-)-cis-ester 23'a (500 mg, 1.57 mmol) in methanol (20 mL) and 1 N potassium hydroxide (5 mL) was allowed to stand for 7 days at room temperature and worked up in the usual way. Column chromatography on silica gel (30 g) with pentane-ether (6:1) gave a colorless oil of (-)-23 (215 mg, quantitative) containing no impurities by TLC examination.

(-)-23: $[\alpha]_{589}^{20}$ -86.9° (c 0.3392, pentane) IR (neat) 3350, 3050, 1612 cm⁻¹

(±)-Spiro[4.4]non-6-en-1-one (2).

A solution of (\pm) -alcohol 23 (240 mg, 1.74 mmol) in methylene chloride was added to a solution of chromium trioxide (1.04 g) and pyridine (20 mL) in methylene chloride (30 mL) at 0 °C. Stirring was continued for 2 h, after usual workup, the crude material was chromatographed (silica gel 40 g, pentane-ether 30:1) and distilled to give a colorless oil of (\pm) ketone 2 (108 mg, 50%).

 $(\pm)-2$: bp 100 °C (bath temperature) at 31 mmHg

NMR 1.5-2.7 (10H, m, cyclic methylenes), 5.49 (1H, td, J = 2.0, 5.4 Hz, olefinic), 5.98 (1H, td, J = 2.2, 5.4 Hz, olefinic).

Anal: Calcd for C₉H₁₂O: C; 79.37, H; 8.88 Found: C; 79.07, H; 8.84

(S) - (-) - Spiro[4.4] non-6-en-1-one (2).

(1R,5S)-(-)-Alcohol 23 (200 mg, 1.45 mmol) was allowed to react with chromium trioxide (900 mg) in pyridine and methylene chloride for 5 h. Three times chromatography gave 47 mg (24%) of (-)-2.

(-)-<u>2</u>: [\propto]²⁰₅₈₉ -317° (c 0.125, iso-octane) IR (neat) 3048, 1738, 1612 cm⁻¹ UV and CD Figure 5 and Table 5

(S)-(+)-6-Methylenespiro[4.4]non-1-ene (10).

To a solution of triphenylmethlenephosphorane prepared from triphenylmethyl phosphonium bromide (1.0 g, 2.8 mmol) and 0.834 N potassium t-butoxide solution in t-butyl alcohol (2.5 mL) in spectroscopically pure n-pentane (25 mL) under nitrogen atmosphere was added a solution of (+)-2 (158 mg) in n-pentane (15 mL) over a period of 30 min and the mixture was stirred for 1.5 h at room temperature. The solution was washed with water (three times) and stored overnight in a refrigerator for triphenylphosphine oxide to precipitate. The filtered solution was passed through silica gel column, the pentane distilled, and the vacuum distillation gave $(+)-\underline{10}$ (68 mg, 44 % yield).

(+)-10: bp 70 °C (bath temperature at 100 mmHg

[α]₅₈₉ +109° (c 0.0367, isooctane) NMR (CDCl₃) 1.5-2.05 (6H, m, methylenes), 2.2-2.7 (4H, m, allylic methylenes), 4.78 (2H, m, J=1.2 Hz, exo-olefinic), 5.49 (1H, dt, J=5.6 and 1.9 Hz, endo-oldfinic), 5.78 (1H, dt, J= 5.6 and 2.2 Hz, endo-olefinic).

UV and CD Figure 24 and Table 13.

Anal. Calcd for C₁₀H₁₄: C; 89.41, H; 10.51 C; 89.54, H; 10.50

(±)-1,6-Di(hydroxyimindspiro[4.4]nonane (30).

A mixture of $(\pm)-5$ (5.0 g, 32.9 mmol), hydroxylamine hydrochloride (5.0 g, 32.9 mmol), anhydrous pyridine (25 mL) and absolute ethanol (25 mL) was heated at reflux for 2 h and the solvents were removed under reduced pressure at 50 °C leaving a colorless oil which crystallized when cooled. The solid was triturated with water, filtered and dried to give white granules of <u>30</u> (5.70 g, 95.2 %) which were recrystallized from methanol to give colorless prisms.

(±)-<u>30</u>: mp 243.5-244.1 °C

IR (KBr) 3280, 1668 cm⁻¹

UV $\lambda_{max}(\epsilon)$ 200.0sh (10,000), 197.5 (10,800) Anal. Calcd for $C_{9}H_{14}O_{2}N_{2}$: C; 59.32, H; 15.37, N; 7.74 C; 59.25, H; 15.22, N; 7.75

(±)-1,6-Diaminospiro[4.4]nonane (31).

A suspension of dioxime 30 (4.0 g, 22.0mmol) and platinum oxide catalyst

(0.5 g) in glacial acetic acid (50 mL) was shaken under hydrogen atmosphere for 2 days. The solution was filtered, the solvent removed under reduced pressure, and the residue was made alkaline with 15 % sodium hydroxide solution. After filtration, the aqueous alkaline solution was extracted with ether (three times) and dried over anhydrous potassium carbonate. Filtration of the mixture and removal of the solvent from the filtrate gave the amine which was distilled in vacuo to yield an oil (1.4 g, 41 %).

(±)-31: bp 110-113 °C at 10.5 mmHg

(±)-1,6-Bis(dimethylamino)spiro[4.4]nonane(32).

90 % formic acid (4.27 g, 93 mmol) was cooled to 0 °C and the diamine 31 (1.0 g, 6.49 mmol) was added gradually. To this solution was added 35 % aqueous formaldehyde (3.25 g, 38 mmol), and the mixture was heated to 100 °C im 0.5 h and kept at 100 °C for 4 h beyond the period during which gas bubbles were evolved. The solution was allowed to cool to room temperature, 15 % hydrochloric acid (2.5 mL) was added, the the mixture was evaporated under reduced pressure. The residue was made alkaline with 25 % sodium hydroxide (6 mL), the solution was saturated with potassium carbonate and extracted with ether. The ether extract was dried, the solvent evaporated and the amine 32 was distilled under reduced pressure to give cololess oil of 32 (0.69 g, 50.6 %).

(±)-32: bp 110 °C at 5 mmHg

(±)-1,6-Bis(dimethylamino)spiro[4.4]nonane Dimethiodide (33).

A mixture of <u>33</u> (2.02 g, 9.26 mmol) and methyl iodide (9.38 g) was kept in a refrigerator under nitrogen atmosphere. The resulting yellow solid was filtered and recrystallized from methanol to give very hygroscopic powder of <u>33</u> (2.0 g, 42.1 %).

(±)-<u>33</u>: mp 211.6-211.8 °C

IR (KBr) 3480, 1480 cm⁻¹

Anal. Calcd for C₁₅H₃₂N₂I₂: C; 36.42, H; 6.47, N; 5.66,

I; 51.36

Found:

C; 36.47, H; 6.70, N; 5.55, I; 51.20 (5S)-(+)-1,6-Bis(dimethylamino)spiro[4.4]nonane Dimethiodide (33).

(5S)-(+)-33 was prepared from (S)-(-)-dione 5 in the same manner as racemate.

(+)-<u>33</u>: mp 222.7-223.0 °C

[α]₅₈₉ +2.8°, [α]₃₆₅ +12.3° (c 0.1, methanol) Anal. Calcd for C₁₅H₃₂N₂I₂: C; 36.42, H; 6.47, N; 5.67, I; 51.36 Found: C; 36.31, H; 6.52, N; 5.69, I; 51.11

(±)-Spiro[4.4]nona-1,6-diene (8).

To a solution of methiodide $\underline{33}$ (2.0 g) in water (10 mL) was added freshly prepared (alkali-free) silver oxide (prepared from 1.41 g of silver nitrate and 0.44 g of sodium hydroxide). The mixture was stirred, first at room temperature for 1 h and then at 50 °C for 1 h. The silver iodide was collected and washed with water. The combined filtrate and washings were evaporated to dryness at 40 °C (20 mmHg), and the residue was pyrolyzed at 100 °C (20 mmHg), the distillate being collected in a dry ice-ethanol trap. The distillate was then acidified with cold 15 % sulfuric acid (30 mL), and the olefin was extracted with pentane (3 x 30 mL). The pentane extract was washed with sodium bicarbonate solution (10 mL), with water (10 mL) and dried over sodium sulfate. After passing through 20 alumina column (12 g), the solvent was evaporated through a Vigreux column, and the residue was distiiled at atmospheric pressure to give a colorless oil (116 mg).

(±)-8: NMR (CCl₄) 1.85 (4H, m, methylenes), 2.3 (4H, allylic methylenes), 5.55 (4H, m, olefinic).

(S)-(+)-Spiro[4.4]nona-1,6-diene (8).

(+)-8 was prepared from (+)-dimethiodide 33 (0.4 g) in the same manner as racemate to give a colorless oil (309.5 mg) as a mixture with n-pentane.

(+)-<u>8</u>: [a]₅₈₉ +119.3° (c 0.07, n-pentane)

UV and CD Figure 22 and Table 13.

(S)-Spiro[4.4]nonane Disemicarbazone (6).

A mixture of (-)-5 (100.17 mg, 0.659 mmol) and semicarbazide reagent

(2.8 ml, prepared from 0.5 g of semicarbazide hydrochloride and 0.8 g of sodium acetate with 9 mL of methanol by filtration) was allowed to stir overnight and concentrated. The residue was washed successively with 5 % sodium bicarbonate (2 x 2 mL) and water to give 177.9 mg of $\underline{6}$, which was recrystallized from water and then methanol to give colorless crystals.

(-)-<u>6</u>: mp >270 °C

[α]₅₈₉ -134.6° (c 0.005, methanol)
 IR (KBr) 3484, 1688, 1574 cm⁻¹
 UV and CD Figure 20 and Table 11
 Anal. Calcd for C₁₁H₁₈O₂N₆: C; 49.61, H; 6.81, N; 31.56
 Found: C; 49.82, H; 7.06, N; 30.33

(S)-(-)-Spiro[4.4]nonane Bis(2,4-dinitrophenyl)hydrazone (7).

A solution of (-)-5 (79.21 mg), 2,4-dinitrophenylhydrazide (199.96 mg) in ethanol (50 mL) and acetic acid (1 drop) was heated at reflux for 2 days and concentrated to 20 mL to give yellow crystals when cooled. The filtration and recrystallization from ethyl acetate gave 49.17 mg of <u>7</u>.

(-)-7: mp 185.2-187.3°C

[α]₅₈₉ -231.8° (c 0.01, methanol)

IR 1620, 1590 cm^{-1}

UV and CD Figure 21 and Table 12

Anal. Calcd for C₂₁H₂₀O₈N₈: C; 49.22, H; 3.93, N; 21.87 Found: C; 49.36, H; 4.19, N; 21.88

(1S,5R,6S)-(+)-trans,trans-1,6-Dibenzoyloxyspiro[4.4]nonane (34).

To a solution of (+)-diol <u>34</u> (39.37 mg) in anhydrous pyridine (2 mL) was added benzoyl chloride (81.78 mg), and the solution was heated at 100 °C for 40 min and cooled. Benzene (10 mL) and methylene chloride (20 mL) were added to the reaction mixture and the solution was washed successively with 3 N hydrochloric accid (2 x 15 mL), saturated brine, 5% sodium bicarbonate solution and again saturated brine. The organic layer was dried over sodium sulfate and the solvent removal gave a colorless oil (79.68 mg), which was crystallized from methanol to yield colorless crystals (31.15 mg).

(+)-<u>34</u>: mp 59.1-62.3 °C

[α]₅₈₉ +129.2° (c 0.13, methanol)

IR 1724 cm^{-1}

UV and CD Figure 26 and Table 14 Anal. Calcd for C₂₃H₂₄O₄: C; 75.80, H; 6.64 Found: C; 75.29, H; 6.59 2. Bicyclo[3.3.0]octane derivatives.

Peroxybenzoic acid.

90% Hydrogen peroxide (13.4 mL, 0.45 mol) was added dropwise with efficient agitation to a partial solution of benzoic acid (36.6 g, 0.30 mol) in methanesulfonic acid (86.5 g, 0.90 mol) in a 500-mL tall-form The reaction temperature is maintained at 25-30° by means of an beaker. The reaction was exothermic during the hydrogen peroxide ice-water bath. addition, which required approximately 30 minutes. During this period the benzoic acid completely dissolved. The solution is stirred for an additional 2 hours and was then cooled to 15°. Fifty grams of chopped ice and 75 ml. of ice-cold saturated ammonium sulfate solution were cautiously added in sequence while the temperature is maintained below The contents of the beaker were transferred to 25° during the dilution. a separatory funnel, and the peroxybenzoic acid solution was extracted with three 50-ml. portions of benzene at room temperature. The aqueous layer was discarded, and the combined benzene extracts were washed twice with cold saturated ammonium sulfate solution (15 mL) to ensure complete removal of methanesulfonic acid and hydrogen peroxide, dried over anhydrous sodium sulfate, and filtered. A 1-mL aliquot of the benzene solution of peroxybenzoic acid was pipetted into an iodine flask, the walls of the flask were rinsed with a small quantity of chloroform, and 15 ml. of acetic acid was added. Two milliliters of a saturated aqueous solution of analytical reagent grade sodium iodide was added. After a reaction period of about 5 minutes, 75 mL of water was added, and the liberated iodine was titrated with 0.1N sodium thiosulfate solution The yield was 81% . This solution was used directly (starch indicator). for epoxidation without further treatment.

3,4-Epoxycyclooctene (36).

To an ice-cold, mechanically stirred solution of 1,3-cyclooctadiene (35) (80 g, 0.740 mol) in benzene (200 ml) was added dropwise a solution of peroxybenzoic acid (0.63 mol) in benzene over 1 h. The mixture was allowed to stand overnight at room temperature washed successively with

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10% sodium hydroxide (200 mL x 3) and water. Drying over magnesium sulfate, solvent removal and vacuum distillation gave the epoxide 36 (76 g, 97%).

36: bp 75 °C at 20 mm Hg

(±)-endo-cis-Bicyclo[3.3.0]oct-7-en-2-ol (37).

To an ice-cold solution of diethylamine (32 g, 0.438 mol) in anhydrous ether (500 mL) was added commercial 15% butyllithium in hexane (270 mL) under a nitrogen atmosphere. A solution of epoxide <u>36</u> (21.8 g, 0.175 mol) in anhydrous ether (400 mL) was added and the mixture was heated to reflux for 2 days. The reaction mixture was cooled and poured onto water, and the organic layer separated. The aqueous layer was extracted with ether and the combined organic layers were washed with 1N hydrochloric acid, saturated sodium bicarbonate solution, and water.

Drying over magnesium sulfate, solvent removal and vacuum distillation gave the alcohol 37 (16.1 g, 74% yield).

(±)-<u>37</u>: bp 42-50 °C at 6 mmHg

IR(neat) 3300, 3000 cm⁻¹ (CCl₄ 0.15 M) 3635, 3605, 3595, 3500 cm⁻¹ (CCl₄ 0.015 M) 3635, 3605, 3595 cm⁻¹ NMR 0.8-2.0 (4H, m, cyclic methylenes), 2.2 (1H, m, bridgehead), 2.43 (1H, s, OH), 2.6 (2H, m, allylic methylene), 3.2 (1H, m, allylic methine), 4.1 (1H, q, -CH-O), 5.7 (2H, t, olefinic).

(1R, 2R, 5R) - (+) - and (1S, 2S, 5S) - (-) - endo-cis-2-Camphanyloxybicyclo-[3.3.0]oct-7-en (37'a and 37'b). Optical resolution of <u>37</u>. A solutionof (±)-alcohol <u>37</u> (6.18 g, 49.8 mmol) in dry pyridine (75 ml) was droppedinto an ice-cold, stirred solution of (-)-camphanyl chloride (15.0 g, 69.2mmol) in dry pyridine (75 ml). The mixture was allowed to stand overnight,poured onto water (1 L), and extracted with benzene (3 x 150 ml). Theorganic layer was washed with 2N hydrochloric acid (9 x 100 ml), 5% aquous sodium bicarbonate, and saturated brine. After drying over sodium sulfate evaporation of solvent gave a colorless solid (14.36 g, 94.8%). Recrystallization from haxane (3 times) and methanol (twice) gave 3.44 g of <u>37'a</u>.

(+)-<u>37'a</u>: mp 111.4-111.8 °C

 $[\alpha]_{589}^{18} +129.0^{\circ} (c \ 0.592, \ \text{ethanol})$ IR (KBr disk) 3050, 1785, 1738 cm⁻¹ NMR 0.96, 1.04, 1.10 (each 3H, each s, methyls), 1.20-2.90 (12H, m), 5.30 (1H, q J=6 Hz, -CH-OCO), 5.44 (1H, m, olefinic), 5.75 (1H, m, olefinic). Anal. Calcd for $C_{18}H_{24}O_4$: C; 71.02, H; 7.95 Cound: C; 70.78, H; 8.02

Crystals from the mother liquor of the first recrystallization was

recrystallized from methanol (twice) to give 0.88 g of 37'b

(-)-<u>37'b</u>: mp 78.8-80.6 °C

[α]²⁰₅₈₉ -139.8° (c 0.661, ethanol) IR (KBr disk) 3060, 1780, 1740 cm⁻¹ NMR 0.97, 1.04, 1.10 (each 3H, each s, methyls), 1.30-2.90 (12H, m), 5.25 (1H, q J=6 Hz, -CH-OCO), 5.46 (1H, m, olefinic), 5.76 (1H, m, olefinic). Anal. Calcd for C₁₈H₂₄O₄: C; 71.02, H; 7.95 Found: C; 71.10, H; 8.01.

All mother liquors were combined and concentrated to give a crude diastereomeric mixture which was chromatographed on silica gel (200 g) with benzene-ethyl acetate (100:1, 200 ml-fraction). The ratio of 37'a and 37'b in each fraction was checked by HPLC (Merk SI-100, 8 x 500 nm, solvent; n-hexane-ether 10:3. Retention time: <u>37'a</u>, 19 min; <u>37'b</u>, 17 min.) and the crystals from each fraction were again fractionally recrystallized to give <u>37'a</u> or <u>37'b</u>, according to its diastereomeric content.

(+)-3-Camphanyloxy-2-oxycarbonylcyclopentaneacetic Acid (38).

(+)-37'a (3.0 g, 9.86 mmol) was treated with sodium metaperiodate (11.4 g) and ruthenium dioxide (0.15 g) by the procedure reported elswhere. The crude product was passed through a silica gel column (20 g) with ether to give 3.42 g (94.2%) of a colorless solid, which was recrystallized from ethyl acetate-benzene (3:8) to yield colorless prisms of 38 (2.50 g).

(+)-<u>38</u>: mp 157.0-157.4 °C

[α]¹⁵₅₈₉ +3.16°, [α]¹⁵₄₀₅ +7.77° (c 1.65, ethanol) IR (KBr disk) 1780, 1742, 1710 cm⁻¹ NMR 0.95, 1.06, 1.11 (3H each, s each, methyls), 1.50-2.50 (4H, m), 2.53 (3H, br s, methine and -CH₂CO), 3.33 (1H, m, -CH-CO), 5.58 (1H, q J=5.5 Hz, -CH-OCO), 11.56 (2H, s, COOH). Anal. Calcd for C₁₈H₂₄O₈: C; 58.69, H; 6.57

Found: C; 58.84, H; 6.59.

(-)-Methyl 3-Hydroxy-2-methoxycarbonylcyclopentaneacetate (39).

A solution of (+)-38 (2.35 g, 6.38 mmol) in absolute methanol (150 mL) and conc. sulfuric acid (1 mL) was refluxed for 20 hr. Sodium bicarbonate (5.5 g) was added and, after stirring, the solid was filtered The filtrate was concentrated under reduced presure, diluted with off. saturated aquous sodium chloride (50 mL) and extracted with ether (3 x 50 ml). The ether layer was washed with saturated ageuous sodium bicarbonate and saturated brine and dried over sodium sulfate. Solvent removal left an oil (2.62 g) which was chromatographed on silica gel (90 g). Elution with benzene (100 ml-fractrion) gave, successively, the olefin 41 (34 mg), methyl camphanate 42 (516 mg), triester 40 (2.1 g), and the alcohol 39 (439 mg colorless oil). (-)-40 (1.7 g) was refluxed for 7 days with anhydrous methanol (200 ml) saturated with hydrogen chloride. After evaporation of solvent, the reaction mixture was treated in the usual manner to give 1.6 g of an oil, which was chromatographed (silica gel, 80 g) to yield 597 mg of 42 and 626 mg of 39. Recrystallization of 42 from benzene-n-hexane (1:5) afforded colorless rods.

(-)-39: bp 120 °C (bath temperature) at 3 mmHg

 $\left[\alpha\right]_{589}^{15}$ -11.8° (c 2.09, ethanol) IR (neat) 3500, 1735 cm⁻¹

NMR 1.70-3.10 (8H, m), 3.70, 3.75 (each 3H, wach s, OCH₃), 3.58 (1H, br s, OH), 4.45 (1H, m, -CH-O) Anal. Calcd for $C_{10}H_{16}O_5$: C; 55.54, H; 7.46 Found: C; 55.51, H; 7.50.

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(-)-40:	$[\alpha]_{589}^{15}$ -4.87° (c 1.85, ethanol).								
	IR (neat) 1780, 1730 cm^{-1}								
	NMR 0.96, 1.06, 1.12 (each 3H, each s, methyls),								
	1.60-2.50 (4H, m, -CH ₂ -), 2.58 (3H, m, -CH- and								
	-CH ₂ CO-), 3.30 (1H, t J=6.5 Hz, -CH-CO), 3.71								
	(6H, s, OCH ₃), 5.53 (1H, q J=6.5 Hz, -CH-OCO)								
(+)- <u>41</u> :	$[\alpha]_{589}^{24}$ +54.1° (c 0.821, carbon tetrachloride)								
	IR 3070, 1743, 1726, 1630 cm^{-1}								
	NMR 1.50-3.70 (7H, m), 3.73, 3.80 (each 3H, each s,								
	OCH_3), 6.90 (1H, m, olefinic).								
(-)-42:	mp 108.4-108.5 °C.								
	[d] 15 -12.4 ° (c 2.17, ethanol)								
	IR (KBr disk) 1783, 1730 cm ⁻¹								
e .	NMR 0.98, 1.08, 1.13 (each 3H, each s, methyls),								
	1.60-2.80 (4H, m, -CH ₂ -), 3.88 (3H, s, OCH ₃).								
	Anal. Calcd for $C_{11}H_{16}O_4$: C; 62.25, H; 7.60								
	Found: C; 62.22, H; 7.57								

(-)-Methyl 2-Methoxycarbonyl-3-oxocyclopentaneacetate (43).

1.1 ml of Jones' reagent $(CrO_3 \ 10 \ g, \ H_2SO_4 \ 10 \ ml, \ H_2O \ 25 \ ml)$ was added dropwise to an ice-cold solution of $(-)-\underline{39}$ (810 mg, 3.75 mmol) in acetone (30 ml). After stirring for three minutes, the reaction mixture was diluted with benzene (300 ml) and passed through a celite column and concentrated. The product was chromatographed on silica gel (30 g) eluting with benzene-ether (15:1) to yield colorless oil of <u>43</u> (628 mg, 78%) and recovered <u>39</u> (147 mg, 18% recovery).

(-)- <u>43</u> :	bp 130 °C (bath	a temperature) at 4 mmHg
	[x] ¹⁸ -66.8° (c	: 1.42, methanol)
	IR (neat) 1730	$0-1770 \text{ cm}^{-1}$
	NMR 1.10-3.40	(4H, m), 3.72, 3.80 (each 3H, each s,
	осн ₃)	
	UV (methanol)	λ_{max} nm 290 sh (ϵ 54.5), 252 (490), 237
		sn (398)
	CD (methanol)	△£ (nm) -1.65 (295), +0.028 (237).
	Anal. Calcd for	r С ₁₀ H ₁₄ O ₅ : С; 56.07, Н; 6.59
	Found.	C: 56.13. H; 6.70.

(-)-3-Oxocyclopentaneacetic Acid (44) via (-)-Methyl 3-Oxocyclopentaneacetate (45).

The ester <u>43</u> (579 mg, 2.7 mmol) was mixed with conc. hydrochloric acid (130 mL) and refluxed for 5 hr. Removal of hydrochloric acid by repeated azeotropic distillation with benzene under reduced pressure gave a brown oil of <u>44</u> (400 mg); $[\alpha]_{589}^{20}$ -116.5° (c 6.99, chloroform). Crude acid <u>44</u> was mixed with methanol (50 ml) containing 1 mL of conc. hydrochloric acid and refluxed overnight. The reaction mixture was worked up in the usual way to give 333 mg of a colorless oil, which was chromatographed on silica gel (30 g) with benzene-ether (10:1, 30 mL-fraction). Fraction 6-10 gave 304 mg of <u>45</u> in 72% yield from the ketone <u>43</u>. Vacuum distillation afforded 268 mg of a colorless oil.

> (-) $-\underline{45}$: $[\alpha]_{589}^{18}$ -115.4° (c 1.13, methanol) $[\alpha]_{589}^{18}$ -121.0° (c 1.47, chloroform) IR (neat) 1740 cm⁻¹ NMR 1.40-2.80 (9H, m), 3.73 (3H, s, OCH₃) UV (methanol) λ_{max} nm 286.5 (ε 23.0), 205 sh (99.2) CD (methanol) $\Delta \varepsilon$ (nm) -1.82 (291), -0.022 (207.5). Anal. Calcd for $C_{8}H_{12}O_{3}$: C; 61.59, H; 7.75 Found: C; 61.80, H; 7.84.

A solution of (-)-45 (122 mg, 0.783 mmol) in methanol (5 mL) and water (1 mL) with potassium hydroxide (100 mg) was allowed to stand for 3 hr and diluted with water (20 mL). After washing with ether, aquous layer was acidified with conc. hydrochloric acid (5 mL) and extracted five times with ether. After usual workup, solvent removal gave 72 mg of the acid <u>44</u>.

> (-)-<u>44</u>: [α]²³₅₈₉ -111.5° (c 1.42, chloroform) IR (neat) 3400-2400, 1740 cm⁻¹ NMR 1.00-3.00 (9H, m), 10.96 (1H, s, COOH).

(1R, 2R, 5R)-(+)-Bicyclo[3.3.0]oct-7-en-2-ol (37).

A solution of (+)-37'a (3.0 g, 9.86 mmol) in ethanol (150 mL) was mixed with a solution of potassium hydroxide (1.5 g) in water (20 mL) and refluxed for 1.5 hr. After usual workup, the reaction product was chromatographed on silica gel (10 g) with benzene-ether (2:1) to give a

colorless oil of <u>37</u> (1.14 g, 92.7%).

(+) - <u>37</u> :	bp 50 °C at 3 mmHg
	[α] ²⁰ ₅₈₉ +210.6° (c 0.729, methanol)
	IR (neat) 3350, 3045 cm^{-1}
j.	NMR 1.00-3.50 (9H, m), 4.23 (1H, m, -CH-O), 5.78 (2H,
•	m, olefinic)
	UV (methanol) ε 4300 (197 nm)
	CD (methanol) $\Delta \epsilon$ +11.4 (195 nm)(shortest wave length reached)
	Anal. Calcd for $C_8H_{12}O$: C; 77.37, H; 9.74
	Found: C: 77.00, H: 9.85.

(1R, 5R)-(+)-Bicyclo[3.3.0]oct-7-en-2-one (3).

A solution of (+)-37 (0.3 g, 2.41 mmol) in methylene chloride (10 mL, dried over molecular sieve 5A) was added in one portion to a solution of chromium trioxide (1.45 g, 14.5 mmol) in dry pyridine (2.3 g, 29 mmol) and methylene chloride (40 mL) cooled with an ice-salt bath. The mixture was stirred for 130 min at room temperature and decanted. The residue was washed with ether and the combined organic layer was washed successively with 5% sodium hydroxide, 5% hydrochloric acid, dilute sodium bicarbonate and saturated brine. After drying over sodium sulfate, solvent removal gave colorless oil of <u>3</u> (0.17g, 57.3% yield, TLC pure).

> (+)-3: $[\alpha]_{589}^{20}$ +619° (c 0.67, isooctane) $[\alpha]_{589}^{20}$ +720° (c 0.0461, methanol) bp 100 °C (bath temperature) at 25 mmHg IR (neat) 3086, 1740 cm⁻¹ NMR 1.7-3.5 (8H, m, methylenes and methines), 5.7 (2H, m, olefinic) UV and CD Figure 33 and Table 19 Anal. Calcd for C₈H₁₀O: C; 78.65, H; 8.25 Found: C, 78.50, H; 8.30

(1R, 5R)-(+)-8-Methylenebicyclo[3.3.0]oct-7-ene (14).

A solution of (+)-3 (120 mg, 0.98 mmol) in spectroscopically pure n-pentane (10 mL) was added to a solution of methylenetriphenylphosphorane (prepared from 1.7 g of triphenylmethylphosphonium bromide and 2.5 mL of 15% n-butyllithium in n-pentane 30 mL) at room temperature under nitrogen atomosphere. The mixture was stirred for 3 h at 0 °C, washed with water, and dried over magnesium sulfate. The solution was passed through silica gel (20 mL) and concentrated. Column chromatography over silica gel (10 g) eluting with spectroscopically pure n-pentane (2 mL-fraction) gave the diene <u>14</u> in fraction 4 and 5.

(+)-14: IR (CCl₄ solution); 3050, 1660, 1615

NMR (CCl₄) 1.5-3.0 (7H, m, methylenes and methine), 3.5 (lH, m, allylic methine), 4.75 (2H, m, exo-methylene), 5.48 (2H, s, endo-olefinic). UV and CD Figura 32 and Table 16.

(1R,2R,5R)-(+)-2-Tosyloxybicyclo[3.3.0]oct-7-ene (48).

To a solution of $(+)-\underline{37}$ (387.65 mg, 3.12 mmol) in dry pyridine (3 mL) was added a solution of tosyl chloride (1.0 g, 5.24 mmol) in pyridine (3 mL) at 0 °C. The solution was allowed to stir overnight at room temperature and poured onto ice-water (80 mL). The mixture was extracted with ether (3 x 50 mL), washed successively with 1N hydrochloric acid (2 x 50 mL), sodium bicarbonate solution, and saturated brine. After drying over magnesium sulfate, solvent removal gave a colorless oil which was chromatographed on silica gel (20 g). Elution with n-hexane-benzene (10:1, 400 mL) gave the excess tosyl chloride and benzene-eluate (300 mL) gave a colorless oil of <u>48</u>(822.5 mg, 94.6 %).

(1R,5R)-(+)-Bicyclo[3.3.0]oct-2-ene (13).

A mixture of lithium aluminum hydride (800 mg) and absolute ether was stirred for 1 h at room temperature and a solution of (+)-48 (747 mg, 2.68

mmol) in ether (20 mL) was added dropwise. The mixture was stirred overnight at room temperature and water (4 mL) was added cautiously. The resultant slurry white solution was filtered and the solid washed with ether. The filtrate and washing were combined and the ether was substituted by pentane using Vigreux column. The pentane solution was concentrated to 2 mL and the residue chromatographed on silica gel (5 g). The first eluate (5 mL) was concentrated and chromatographed again. Evaporation of solvent and vacuum distillation gave colorless oil of <u>13</u> (68.65 mg, 23.7 %).

(+)-13: bp 80 °C (bath temperature) at 35 mmHg

 $[\alpha]_{589}^{23}$ +88.0° (c 0.104, isooctane) IR (CCl₄) 3070, 1620 cm⁻¹

NMR (CDCl₃) 1.0-2.3 (7H, m, methine and methylenes), 2.4-3.0 (2H, m, allylic methylene), 3.17 (1H, m,

allylic methine), 5.55 (2H, m, olefinic).

UV and CD Figure 31 and Table 16

Anal. Calcd for C₈H₁₂: C; 88.82, H; 11.18 Found: C; 88.85, H; 11.49

(1R, 2S, 5R) - (-) - 2 - Camphanyloxybicyclo[3.3.0]octane (49).

A mixture of (-)-37'b (3.9 g, 12.6 mmol) and platinum dioxide (100 mg)in methanol (150 mL) was vigorously stirred under hydrogen atmosphere for 1.5 h. Filtration and evaporation of solvent gave a colorless oil (4.07 g), which was chromatographed on silica gel (40 g) eluting with benzene-ethyl acetate (20:1, 200 mL) and crystallized from methanol to give colorless crystals (3.03 g, 85.5 %).

(lR,2S,5R)-(-)-Bicyclo[3.3.0]octan-2-ol (50).

A mixture of $(-)-\underline{49}$ (3.0 g, 9.79 mmol) in ethanol (40 mL) and potassium hydroxide (1.7 g, 30 mmol) in water (10 mL) was heated at reflux for 1 h and allowed to stand overnight at room temperature. The solution was concentrated to 30 mL, poured onto ice-water (80 mL) and extracted with ether (3 x 50 mL). The ether extracts were washed with saturated brine (50 mL), dried over magnesium sulfate and filtered. Evaporation of solvent and vacuum distillation gave 943.4 mg of <u>50</u> (76.4 %).

(1R,5R)-(-)-Bicyclo[3.3.0]octan-2-one (11):

Jones' reagent (2.06 mL) was added rapidly to a solution of $(-)-\underline{50}$ (900 mg, 7.13 mmol) in acetone (15 mL) cooled with an ice-salt bath and the mixture was stirred for 5 min at -10 °C. Pentane (100 mL) was added, and the reaction mixture was passed through celite column (Wako 545, 10 g). Solvent removal and vacuum distillation gave a colorless oil of <u>11</u> (689.9 mg, 5.556 mmol).

> (-)-<u>11</u>: bp 103 °C at 43 mmHg $[\alpha]_{589}^{24}$ -176° (c 3.29, isooctane) IR (neat) 1742 cm⁻¹ NMR (CDCl₃) 1.0-3.2 (m) UV and CD Figure 29 and Table 15 Anal. Calcd for C₈H₁₂O: C; 77.37, H; 9.74 Found: C; 77.56, H; 9.89

(±)-endo-cis-2-(Tetrahydropyranyloxy)bicyclo[3.3.0]oct-2-ene (51).

To a mixture of $(\pm)-37$ (40.0 g, 0.322 mol) and dihydropyrane (33 g, 0.392 mol) cooled with an ice-bath was added a catalytic amount of phospho-

rousoxychloride (1.0 g) and the solution was stirred for 2 h at room temperature. The YCaction mixture was then cooled with an ice bath and 5 % aqueous potassium hydroxide solution (100 mL) added. The mixture was extracted three times with ether (500 mL), washed with saturated brine and dried over magnesium sulfate. Evaporation of solvent gave 70.8 g of reddish brown oil, which was chromatographed over alumina (600 g) with n-hexane to give 62.6 g of 51 (93.3 %). Analytical sample was further purified by column chromatography over silica gel with n-hexane-ether (20: 1) and vacuum distilled to yield pure 51.

(±)-<u>51</u>: bp 89.0-89.5 °C

IR (neat) 3050

(±)-Epoxide of endo-cis-2-(Tetrahydropyranyloxy)bicyclo[3.3.0]oct-2-ene (52).

To a mixture of $(\pm)-\underline{51}$ (55.0 g, 0.264 mol) in methylene chloride (3 L) and 0.5 M aqueous sodium bicarbonate solution (1.2 L) was added m-chloroperbenzoic acid (65.0 g, 0.264 mol as 70 % content) and the mixture was allowed to stir for 26 h. The organic layer was separated, washed with 1N sodium hydroxide and water successively, and dried over magnesium sulfate. Filtration and solvent removal gave 64.9 g of crude product, which was chromatographed over alumina (600 g) with benzene to yield 53.0 g of $\underline{52}$ (89.6 %).

(±)-<u>52</u>: bp 137-138 °C at 5 mmHg
IR (neat) 3025 cm⁻¹
Anal. Calcd for C₁₃H₂₀O₃: C; 69.61, H; 8.99
Found: C; 69.43, H; 9.08

(±)-endo-cis-8-(Tetrahydropyranyloxy)bicyclo[3.3.0]octan-2- and 3-ol (53).

To a solution of lithium aluminum hydride (35 g, 0.922 mol) in dry ether (1.7 L) was added dropwise a solution of $(\pm)-52$ (49 g, 0.218 mol)

in ether (300 mL). The mixture was refluxed for 28 h and cooled with an ice-bath. A solution of ethyl acetate (100 mL) in ether (200 mL) was added and then water (160 mL) added cautiously. After stirring overight, the white precipitates formed were filtered off. The filtrate and the ether washing were combined and dried over sodium sulfate. Evaporation of solvent gave $(\pm)-53$ (49.8 g, quantitative yield), which showed four spots on silica gel TLC with benzene-ethyl acetate (10:1). This mixture was further oxidized without anyl separation and purification.

 $(\pm) - 53$: IR (neat) 3410 cm⁻¹

(±)-endo-cis-8-(Tetrahydropyranyloxy)bicyclo[3.3.0]octan-2- and 3-one (54).

To a mixture of dry pyridine (20 mL) and dry methylene chloride (300 mL) cooled with an ice-salt bath was added chromium trioxide (14 g, 0.14 mol) and the mixture was stirred for 3 h at room temperature. A solution of (\pm) -<u>53</u> (3.4 g, 15 mmol) in methylene chloride (50 mL) was added at o °C and allowed to stir for 1 h at o °C. The dark brown organic layer was decanted and the residual black harz washed with ether (300 mL). The combined organic layer was washed with water (200 mL), 5 % sodium hydroxide solution (3 x 200 mL) and saturated brine successively, and dried over magnesium sulfate. After removal of solvent, the crude product was chromatographed over alumina (100 g) eluting with hexane (300 mL), benzene (500 mL) and benzene-ether (50:1, 500 mL), successively. Benzene and benzene-ether eluate gave 3.3 g of <u>54</u> in quantitative yield.

 $(\pm) - 54$: bp 129-132 °C at 3 mmHg IR (neat) 1740 cm⁻¹

> Anal. Calcd for C₁₃H₂₀O₃: C; 69.61, H; 8.99 Found: C; 69.87, H; 9.16

(±)-endo-cis-7- and 8-Methylene-2-(tetrahydropyranyloxy)bicyclo[3.3. 0]octane (55).

Commercially available n-butyllithium in hexane (6.3 mL, 10.08 mmol) was added to a mixture of triphenylmethylphosphonium bromide (4.0 g, 11.16 mmol) in dry benzene (100 mL) under nitrogen atmosphere. After 2 h-stirring, a solution of $(\pm)-54(1.0 \text{ g}, 4.5 \text{ mmol})$ in dry benzene (20 mL) was

added dropwise at 10 °C and allowed to stir for 21 h at room temperature. Water (0.5 mL) and pentane (50 mL) was added, and the filtered organic layer was washed with water (50 mL), dried over magnesium sulfate and concentrated. The residual oil (1.3 g) was triturated with n-hexane to filter off triphenylphosphin oxide. Yellow oil thus obtained (1.0 g) was chromatographed over alumina (20 g). n-Hexane eluted the reaction products and benzene **c**luted the recovered ketone (305 mg). n-Hexane eluate was chromatographed again on silica gel (10 g) eluting with benzene to give 55 (310 mg, 52 % yield by considering the recovery).

(±)-55: bp 100 °C (bath temperature) at 3 mmHg

IR (neat) 3070, 1652 cm^{-1}

NMR (CDCl₃) 1.1-2.05 (16H, m, cyclic methylenes), 2.05-3.1 (4H, m, allylic methylene and bridgehead), 3.2-4.0 (2H, m, O-CH₂), 4.2 (1H, m, THP-O-CH-), 4.77 (2H, m, olefinic and O-CH-O), 4.96 (1H, m, olefinec).

HPLC (Merck SI-100, 8 \emptyset x 500 mm, n-hexane-ethyl acetate 50:1) 2 peaks (intensity ratio 7.2) Anal. Calcd for $C_{14}H_{22}O_2$: C; 75.63, H; 9.97

Found: C; 75.96, H; 10.14

(±)-endo-cis-7- and 8-Methylenebicyclo[3.3.0]octan-2-ol (57 and 56).

To a mixture of $(\pm)-\underline{55}$ (2.65 g, 11.9 mmol), methanol (25 mL) and water (1 mL) was added concentrated hydrochloric acid (0.2 mL) at 0 °C and the mixture was allowed to stir overnight at room temperature under argon atmosphere. Ether (50 mL), water (50 mL) and potassium carbonate (4 g) were added and the reaction mixture was stirred for 0.5 h. The organic layer was separated and the aqueous layer extracted twice with ether (50 mL x 2). The combined organic layer was washed with saturated brine and dried over magnesium sulfate. Filtration, evaporation of solvent and column chromatography on silica gel (40 g) eluting with pentane-ether (10:1) gave <u>56</u> (1.0 g, 7.6 mmol) and <u>57</u> (270 mg, 2.0 mmol), successively. Analytical samples were vacuum distilled for purification.

> $(\pm)-\underline{56}$: bp 90 °C (bath temperature) at 35 mmHg IR (CCl₄ 0.2 M) 3571, 3068, 1647 cm⁻¹ (CCl₄ 0.02 M) 3571, 3068 cm⁻¹

> > 164

NMR (CDCl₃) 1.3-2.1 (6H, m, cyclic methylenes), 1.92 (1H, s, OH), 2.34 (2H, m, allylic methylene), 2.65 (1H, m, bridgehead), 2.98 (1H, br t, J = 8.0 Hz, allylic bridgehead), 4.18 (1H, m, CH-O), 4.86, 5.14 (1H each, m each, olefinic).

Anal. Calcd for C₉H₁₄O: C; 78.21, H; 10.21

Found: C; 77.83, H; 10.32

(±)-57: bp 125 °C (bath temperature) at 35 mmHg

IR (CCl₄ 0.2 M) 3630, 3600sh, 3480, 3070, 1660 cm⁻¹ (CCl₄ 0.02 M) 3630, 3600sh cm⁻¹

NMR (CDCl₃) 1.2-2.8 (10H, m, cyclic methylenes, bridgehead and allylic methylene), 1.42 (1H, s, OH), 4.22 (1H, m, CH-O), 4.79 (2H, m, olefinic).

(1R,2R,5S)-(-)- and (1S,2S,5R)-(+)-2-Camphnyloxy-8-methylenebicyclo-[3.3.0]octane (56'a and 56'b). Optical Resolution of 56.

A mixture of (\pm) -56 (350 mg, 2.53 mmol), (-)-camphanyl chloride (2.0 g, 9.23 mmol) and dry pyridine (10 mL) was allowed to stir overnight at room temperature. Crashed ice (100 g) was added, and the mixture was extracted with ether (80 mL x 2), washed with 1 N hydrochloric acid (2 x 100 mL) and saturated brine. Drying over magnesium sulfate and evaporation of solvent gave the diastereomeric mixture of camphanates (0.9 g).

1.0 g of the mixture was chromatographed on silica gel (30 g) eluting with benzene-ethyl acetate (200:1) to give the less polar part (540 mg) and the more polar part (380 mg). HPLC (Merck SI-100, 8 \emptyset x 500 mm, n-hexane-ethyl acetate 10:1) of the less polar part showed two peaks in the ratio 3:1. Recrystallization twice from methanol gave diastereomerically pure (+)-56'b (275 mg).

4.93 (lH each, m each, olefinic), 5.5 (lH,

С; 71.62, Н; 8.29

m, -CH-O).

Anal. Calcd for C₁₉H₂₆O₄: C; 71.67, H; 8.23

Found:

HPLC of the more polar part showed two peaks in the ratio of 1:5. Recrystallization twice from methanol gave the pure (-)-56'a.

Anal. Calcd for $C_{19}H_{26}O_4$: C; 71.67, H; 8.23 Found: C; 71.40, H; 8.31

(1S,2S,5R)-(+)-8-Methylenebicyclo[3.3.0]octan-2-o1 (56).

A mixture of $(+)-\underline{56'b}$ (265 mg, 0.83 mmol) in ethanol (10 mL) and 1N potassium hydroxide solution (3 mL) was heated at reflux for 3 h and poured onto ice-water (30 mL). The mixture was extracted with ether (3 x 15 mL), washed with saturated brine, and dried over sodium sulfate. Solvent removal and column chromatography on silica gel eluting with pentane-ether (3:1) gave a colorless oil of <u>56</u> (101.5 mg, 88 %).

(+) -56: IR and NMR were identical with those of racemate. $[\alpha]_{589}^{22}$ +103.9° (c 1.015, pentane)

(1S,2S,5R)-(+)-8-Methylene-2-tosyloxybicyclo[3.3.0]octane (58).

To a solution of $(+)-\underline{56}$ (14.2 mg, 0.103 mmol) in dry pyridine (1 mL) was added tosyl chloride (24.42 mg) at 0 °C and the mixture was stirred for 3 days at room temperature. Ether (20 mL) was added and the mixture washed successively with water (2 x 5 mL), 1N hydrochloric acid (10 mL), saturated sodium bicarbonate solution (5 mL) and water (5 mL). After drying over sodium sulfate and solvent removal, the residual oil (mixture

of <u>58</u> and the recovered <u>56</u>) was chromatographed on silica gel eluting with benzene gave a colorless oil of <u>58</u> (14.86 mg).

(+) -58: [\$\alpha]_{589}^{23} +97.6° (c 1.486, carbon tetrachloride)
NMR (CDCl₃) 1.2-2.8 (9H, m, methine and methylene), 2.44
(3H, s, methyl), 2.97 (1H, bt, allylic methine),
4.65 (1H, bs, -CH-O), 4.9 (2H, m, olefinic),
7.30, 7.77 (2H each, AA'BB' pattern, aromatic).

(1R,5R)-(-)-2-Methylenebicyclo[3.3.0]octane (12).

<u>A. From (-)-11.</u> To a phosphorane solution (prepared from 2.7 g of triphenylmethylphosphonium bromide and 4.4 mL of 15 % n-butyllithium in 30 mL of spectroscopically pure pentane) was added a solution of $(-)-\underline{11}$ (360 mg, 2.9 mmol) in pentane (10 mL) at 5 °C under nitrogen atmosphere. The mixture was stirred overnight, washed with water (2 x 10 mL) and passed through alumina column (12 g). The eluate was concentrated with Vigreux column to 3 mL and the residue chromatographed on silica gel (10 g). Solvent removal gave 40 mg of $\underline{12}$ which contained some n-pentane by NMR examination (ca. 0.3 mole fraction).

 $(-)-\underline{12}$: IR (CCl₄) 3070, 1658 cm⁻¹

NMR (CDCl₃) 1.0-3.0 (12H, m, methine and methylenes), 4.75 (2H, m, olefinic).

UV and CD Figure 30 and Table 16

<u>B. From (+)-58.</u> To a mixture of lithium aluminum hydride (30 mg) in anhydrous ether (5 mL) was added a solution of (+)-58 (14 mg) in ether (2 mL) and the mixture was allowed to stir overnight at room temperature. Water (0.3 mL) was added and the mixture was stirred until the grayish solution became white. Pentane (10 mL) was added and the filtered solution was passed through the column of sodium sulfate (5 g) and silica gel (1 g) to give the solution with dextro rotation, which was concentrated under reduced pressure (50 mmHg) and chromatographed on silica gel (1 g) eluting with pentane (3 mL fraction). Fraction 1 was TLC pure and UV and CD were measured without isolation.

(+)-12: UV identical pattern with that of 12 in A CD antipodal to that of 12 in A

(1S, 5R) - (+) - 8-Methylenebicyclo[3.3.0]octan-2-one (4).

To a mixture of pyridinium chlorochromate (200 mg) and sodium acetate (80 mg) in dry methylene chloride (1.5 mL) was added a solution of (+)-<u>56</u> (77.2 mg, 0.56mmol) in methylene chloride (2 mL) and the mixture was stirred for 3.5 h at room temperature (29 °C). Ether (10 mL) was added and decanted. The residue was washed with ether (2 x 20 mL). The combined brown ether layer was passed through the column of silica gel (1 g) and sodium sulfate (3 g) to give a light yellow solution, which was washed successively with 1 % sodium bicarbonate solution (2 x 5 mL) and saturated brine (3 x 5 mL) and dried over sodium sulfate. Filtration and solvent removal gave a light yellow oil, which was passed through silica gel column (2 g) eluting with benzene (20 mL), and distilled to afford a colorless oil of 4 (20.3 mg, 27 %).

(+)-4: bp 90 °C (bath temperature) at 35 mmHg $[\alpha]_{589}^{23}$ +80.3° (c 0.685, isooctane) IR (CCl₄) 3080, 1750, 1652 cm⁻¹ NMR (CCl₄) 1.2-2.5 (8H, m, methylenes), 2.98 (2H, m, methine), 4.94, 5.10 (2H each, m each, olefinic). UV and CD Figure 34 and Table 18 Anal. Calcd for C₉H₁₂O: C; 79.37, H; 8.88 Found: C; 79.26, H; 9.03

(1S,5R)-8-Methylbicyclo[3.3.0]octan-2-one (60).

A methanolic solution of (+)-4 (2 mL, 0.50 x 10^{-2} mol/1) with palladium-charcoal (10 mg) was stirred overnight at hydrogen atmosphere. The solution was filtered and the catalyst was washed with methanol (2 x 1 mL). The filtrate and the washings Were combined and diluted with methanol to 5 mL, and the solution was directly subjected to CD measurement.

(-)-60: CD Figure 35

(±)-8-Methyl-cis-bicyclo[3.3.0]oct-7-en-2-one (59).

A solution of $(\pm)-4$ (66 mg) in pentane was adsorbed on alumina (20 g) and, after 1 h, was eluted with ether to give a colorless oil (55 mg) of <u>59</u>. $(\pm)-59$: IR (neat) 1710, 1660 cm⁻¹

> UV (n-hexane) λ_{max} (ϵ) 366(20), 350(27), 335(31), 322(30), 248(5400).

General Procedure for Kinetic Resolution.

To a stirred solution of optically active alcohol (ca. 30 mg, x mmol) was added (±)-anhydride (about double the molar quantity, y mmol) and the mixture was stirred for several hours. Water (lmL) was added and the solution was stirred for 1 h to decompose the unreacted anhydride, and benzene (10 mL) and water (10 mL) were added. After stirring for several times, the produced acid was determined by titration with 1/10 N sodium hydroxide solution by phenolphthalein as an indicator (titration volume; z mL). The esterification yield (Y %) is given

$$Y = \frac{2y - z}{m} \times 100$$
 (%)

This equation can be used only for the case that the hydrolysis of unreacted anhydride was complete and that the anhydride used for the reaction was pure and not contaminated by free acid.

0.5 mL of 1/10 N sodium hydroxide was added and the organic layer separated. The aqueous layer was extracted with benzene (2 x 10 mL) and the combined organic layer washed with water (3 x 10 mL). The washings (30 mL) were extracted with benzene (10 mL) and benzene layeres were combined and dried over sodium sulfate. Column chromatography of this solution gave the recovered alcohol from which the esterification yield was easily calculated in cases when the yield was not given by titration method.

The combined aqueous layer (40 mL) was acidified with 1 N hydrochloric acid (pH < 1.0) and extracted with benzene (3 x 15 mL). The benzene layer was washed with water (10 mL) and dried over sodium sulfate. Filtration and solvent removal gave the acid which was dissolved in benzene (10 mL). The optical rotation was measured in 10 cm-cell.

The weight of the acid produced by the reaction (G g), the concentration of the benzene solution (C g/100 mL), and the optical yield of the reaction (e.e.) are given

$$G = \frac{Y}{100} \cdot \frac{xM}{1000} = \frac{YxM}{100000} (g) \qquad C = \frac{100}{10} \cdot G = \frac{YxM}{1000} (g/100 \text{ mL})$$

e.e. = { (100 \cdot \frac{\alpha}{C}) / [\alpha] } \cdot 100 = \frac{10000000\alpha}{YxM[\alpha]} (\%)

where M is the molecular weight of the acid, α is the observed rotation, and $[\alpha]$ is the absolute rotation of the acid. Appendix

1. Physical constants

The values of important physical constants used in the calculations are taken from the tabulation of R. Birge, Rev. Modern Phys., 13, 233 (1941).

Velocity of light Charge of electron Plank's constant Mass of electron Avogadro's number Bohr radius $(h^2/4\pi^2 me^2)$ $c = 2.9976 \times 10^{10} cm \cdot sec^{-1}$ $e = 4.8025 \times 10^{-10}$ abs. e.s.u. $h = 6.6242 \times 10^{-27}$ erg.sec. $m = 9.107 \times 10^{-28} gm$. $N = 6.0228 \times 10^{23} \text{ mol}^{-1}$ $a_0 = 0.5292 \times 10^{-8} \text{ cm}$

2. Coordinates systems

a. Polar coordinates

 $x = rsin\theta cos\psi$ $y = rsin\theta sin\psi$ $z = rcos\theta$ $d\tau = r^2 sin\theta dr d\theta d\psi$ $0 \leq r < \infty$ $0 \leq \theta \leq \pi$ $0 \leq \psi \leq 2\pi$

b. Elliptical coordinates (Figure 1)



(ψ measured from xz plane) $x = dv (\mu^2 - 1) (1 - v^2) \cos \psi$ $y = d\sqrt{(\mu^2 - 1)(1 - \nu^2)}sin\psi$ z = duv $\mu = \frac{1}{2d} (r_a + r_b)$ $v = \frac{1}{2d} (r_a - r_b)$ $\mathbf{r}_{a} = (\mu + \nu)\mathbf{d}$ $r_{\rm b} = (\mu - \nu)d$ $d\tau = d^3(u^2 - v^2) du dv d\psi$ $1 \leq u < \infty$ $-1 \leq v \leq 1$ $0 \leq \psi \leq 2\pi$ 3. Some special integrals

$$\int_{0}^{2\pi} \sin^{2}x dx = \int_{0}^{2\pi} \cos^{2}x dx = \pi$$

$$\int_{0}^{\pi} \sin^{m}x dx = 2\int_{0}^{\pi/2} \sin^{m}x dx$$

$$\int_{0}^{\pi/2} \sin^{m}x dx = \frac{1 \cdot 3 \cdot 5 \cdot (m-1)}{2 \cdot 4 \cdot 6 \cdot m} \cdot \frac{\pi}{2} \quad (m : even)$$

$$= \frac{2 \cdot 4 \cdot 6 \cdot (m-1)}{1 \cdot 3 \cdot 5 \cdot m} \quad (m : odd)$$

$$\int_{0}^{\infty} x^{n} e^{-ax} dx = \frac{n!}{a^{n+1}} \quad n > -1, \quad a > 0$$

$$\int_{1}^{\infty} x^{n} e^{-ax} dx = \frac{n! e^{-a}}{a^{n+1}} \quad \sum_{k=0}^{n} \frac{a^{k}}{k!} \equiv A_{n}(a)$$

$$\int_{-1}^{1} x^{n} e^{-ax} dx = (-1)^{n+1} A_{n}(-a) - A_{n}(a) \equiv B_{n}(a)$$
when a is zero,
$$\int_{-1}^{1} x^{n} dx = \frac{2}{n+1} \quad (n : even)$$

$$= 0 \quad (n : odd)$$

$$\int_{0}^{2} \sin^{2}\psi \cos^{2}\psi d\psi = \frac{1}{4}\pi$$

4. Integrals between two atomic orbitals

Five types of atomic orbitals χ_t^a (t = 1s, 2s, $2p_x$, $2p_y$, and $2p_z$), considered in this paper, are chosen as Slater functions which, in the local coordinate system with its origin at atomic nucleus A, are represented by

$$\chi_{1s}^{a} = \frac{1}{\sqrt{\pi}} (q_{1}^{a})^{3/2} \exp(-q_{1}^{a}r_{a})$$

$$\chi_{2s}^{a} = \frac{1}{\sqrt{3\pi}} (q_{2}^{a})^{5/2}r_{a}\exp(-q_{2}^{a}r_{a})$$

$$\chi_{2px}^{a} = \frac{1}{\sqrt{\pi}} (q_{2}^{a})^{5/2}x_{a}\exp(-q_{2}^{a}r_{a})$$

$$\chi_{2py}^{a} = \frac{1}{\sqrt{\pi}} (q_{2}^{a})^{5/2}y_{a}\exp(-q_{2}^{a}r_{a})$$

$$\chi_{2pz}^{a} = \frac{1}{\sqrt{\pi}} (q_{2}^{a})^{5/2}y_{a}\exp(-q_{2}^{a}r_{a})$$

$$\chi_{2pz}^{a} = \frac{1}{\sqrt{\pi}} (q_{2}^{a})^{5/2}z_{a}\exp(-q_{2}^{a}r_{a})$$

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with $q_{n_t}^a = \frac{z_{n_t}^a}{n_t a_0}$, where n_t are effective principal quantum numbers of t orbitals, a_0 is Bohr radius, and $z_{n_t}^a$ are effective nuclear charges in atom A in case of the effective principal quantum number n_t .

Here we will consistently use right handed cartesian coordinate systems. For the integrals between two atomic orbitals χ_t^a and χ_u^b with the operator \vec{r} and $\vec{r}x\nabla$, the following relationships are available,

$$\langle \chi_{t}^{a} | m | \chi_{u}^{b} \rangle = \pm \langle \chi_{u}^{b} | m | \chi_{t}^{a} \rangle$$
 (1)

where m are components of operator $\vec{\nabla}$, $\vec{r} x \vec{\nabla}$ and $\alpha \beta$, and signs are minus for $\vec{\nabla}$ and $\vec{r} x \vec{\nabla}$, and plus for $\alpha \beta$. Equation (1) can be proved mathematically as follows.

For the operator $\frac{\partial}{\partial x}$, we find

$$\iiint_{-\infty}^{\infty}\chi_{t}^{a}(\frac{\partial}{\partial x}\chi_{u}^{b})dxdydz = \iint_{-\infty}^{\infty}[\chi_{t}^{a}\chi_{u}^{b}]_{x=-\infty}^{x=+\infty}dydz - \iiint_{-\infty}^{\infty}\chi_{u}^{b}(\frac{\partial}{\partial x}\chi_{t}^{a})dxdydz$$

Since $\chi^a\chi^b$ vanishes at infinity, the first integral on the right is zero, hence,

$$\langle \chi_{t}^{a} | \frac{\partial}{\partial x} | \chi_{u}^{b} \rangle = - \langle \chi_{u}^{b} | \frac{\partial}{\partial x} | \chi_{t}^{a} \rangle$$

The same proof holds for every component of $\vec{\nabla}$ and $\vec{r} \times \vec{\nabla}$. From the character of operator $\alpha\beta$, equation (1) for $\alpha\beta$ is apparently confirmed without further demonstration.

a. Integrals between the atomic orbitals χ^a_t and χ^b_u on one nucleus A.

In the present case, χ^a and χ^b belong to the same atom A. Therefore, both local co-cordinate systems coincide with each other, such as

$$r_{a} = r_{b} = r$$

$$x_{a} = x_{b} = x$$

$$y_{a} = y_{b} = y$$

$$z_{a} = z_{b} = z$$

$$q_{t}^{a} = q_{t}^{b}$$

$$\chi_{t}^{a} = \chi_{t}^{b}$$

In Table 1 are shown all possible combinations of two atomic orbitals and components which give non-zero integrals from the symmetry.

	χ^{a}_{1s}	X ^a 2s	X ^a _{2px}	χ^{a}_{2py}	X ^a 2pz	
χ_{1c}^{a}			e _x , -	e _y , -	e _z , -	
χ^{a}_{2s}	_		e _x , -	e _y , -	e _z , -	
χ^{a}_{2px}	e _x , -	e _x , -		- , m _z	- , ^m y	
χ^{a}_{2py}	e _y , -	e _y , -	-, m _z		-, m _x	
χ^{a}_{2pz}	e _z , -	e _z , -	- , m _y	-, m _x		

Table 1. Non-zero components in integrals $\langle \chi_t | \mathbf{m} | \chi_u \rangle$ $(\mathbf{m} = \vec{\nabla}, \vec{r} \times \vec{\nabla}, \alpha \beta)$. e_{α} and \mathbf{m}_{α} show that α -component of integrals $\langle \chi_t | \vec{\nabla} | \chi_u \rangle$ and $\langle \chi_t | \vec{r} \times \vec{\nabla} | \chi_u \rangle$, respectively, differs from zero. Non-zero integrals of the components of Q are omitted since $\mathbf{m}_{\mathbf{x}}$, $\mathbf{m}_{\mathbf{y}}$, and $\mathbf{m}_{\mathbf{z}}$ are inevitably accompanied by $Q_{\mathbf{yz}}$, $Q_{\mathbf{zx}}$, and $Q_{\mathbf{xy}}$, respectively.

In addition to the relationship (1), next equality holds from symmetry.

Hence only four types of integrals $\langle \chi_{2px}^{a} | \vec{\nabla} | \chi_{1s}^{a} \rangle$, $\langle \chi_{2px}^{a} | \vec{\nabla} | \chi_{2s}^{a} \rangle$, $\langle \chi_{2px}^{a} | \vec{r} \times \vec{\nabla} | \chi_{2py}^{a} \rangle$ and $\langle \chi_{2px}^{a} | xy | \chi_{2py}^{a} \rangle$ are worth calculation. The results of calculation are as follows.

$$\begin{aligned} &\langle \chi_{2px}^{a} | \vec{\nabla} | \chi_{1s}^{a} \rangle = -\langle \chi_{1s}^{a} | \vec{\nabla} | \chi_{2px}^{a} \rangle = \langle \chi_{2px}^{a} | \frac{\partial}{\partial x} | \chi_{1s}^{a} \rangle \mathbf{i} \\ &\langle \chi_{2py}^{a} | \vec{\nabla} | \chi_{1s}^{a} \rangle = -\langle \chi_{1s}^{a} | \vec{\nabla} | \chi_{2py}^{a} \rangle = \langle \chi_{2px}^{a} | \frac{\partial}{\partial x} | \chi_{1s}^{a} \rangle \mathbf{j} \\ &\langle \chi_{2pz}^{a} | \vec{\nabla} | \chi_{1s}^{a} \rangle = -\langle \chi_{1s}^{a} | \vec{\nabla} | \chi_{2pz}^{a} \rangle = \langle \chi_{2pz}^{a} | \frac{\partial}{\partial x} | \chi_{1s}^{a} \rangle \mathbf{k} \\ &\langle \chi_{2pz}^{a} | \vec{\nabla} | \chi_{2s}^{a} \rangle = -\langle \chi_{2s}^{a} | \vec{\nabla} | \chi_{2pz}^{a} \rangle = \langle \chi_{2pz}^{a} | \frac{\partial}{\partial x} | \chi_{1s}^{a} \rangle \mathbf{k} \\ &\langle \chi_{2py}^{a} | \vec{\nabla} | \chi_{2s}^{a} \rangle = -\langle \chi_{2s}^{a} | \vec{\nabla} | \chi_{2px}^{a} \rangle = \langle \chi_{2px}^{a} | \frac{\partial}{\partial x} | \chi_{2s}^{a} \rangle \mathbf{i} \\ &\langle \chi_{2py}^{a} | \vec{\nabla} | \chi_{2s}^{a} \rangle = -\langle \chi_{2s}^{a} | \vec{\nabla} | \chi_{2py}^{a} \rangle = \langle \chi_{2py}^{a} | \frac{\partial}{\partial x} | \chi_{2s}^{a} \rangle \mathbf{j} \\ &\langle \chi_{2pz}^{a} | \vec{\nabla} | \chi_{2s}^{a} \rangle = -\langle \chi_{2s}^{a} | \vec{\nabla} | \chi_{2pz}^{a} \rangle = \langle \chi_{2py}^{a} | \frac{\partial}{\partial x} | \chi_{2s}^{a} \rangle \mathbf{k} \end{aligned}$$
$$\langle \chi^{\mathbf{a}}_{2px} | \vec{r} \times \vec{\nabla} | \chi^{\mathbf{a}}_{2py} \rangle = -\langle \chi^{\mathbf{a}}_{2py} | \vec{r} \times \vec{\nabla} | \chi^{\mathbf{a}}_{2px} \rangle = \langle \chi^{\mathbf{a}}_{2px} | x \frac{\partial}{\partial y} - y \frac{\partial}{\partial x} | \chi^{\mathbf{a}}_{2py} \rangle | \mathbf{k}$$

$$\langle \chi^{\mathbf{a}}_{2py} | \vec{r} \times \vec{\nabla} | \chi^{\mathbf{a}}_{2pz} \rangle = -\langle \chi^{\mathbf{a}}_{2pz} | \vec{r} \times \vec{\nabla} | \chi^{\mathbf{a}}_{2py} \rangle = \langle \chi^{\mathbf{a}}_{2py} | x \frac{\partial}{\partial y} - y \frac{\partial}{\partial x} | \chi^{\mathbf{a}}_{2pz} \rangle | \mathbf{k}$$

$$\langle \chi^{\mathbf{a}}_{2pz} | \vec{r} \times \vec{\nabla} | \chi^{\mathbf{a}}_{2pz} \rangle = -\langle \chi^{\mathbf{a}}_{2px} | \vec{r} \times \vec{\nabla} | \chi^{\mathbf{a}}_{2pz} \rangle = \langle \chi^{\mathbf{a}}_{2py} | x \frac{\partial}{\partial y} - y \frac{\partial}{\partial x} | \chi^{\mathbf{a}}_{2pz} \rangle | \mathbf{k}$$

where i, j and k are unit vectors of x, y and z directions, respectively, and

$$<\chi_{2px}^{a} \left| \frac{\partial}{\partial x} \right| \chi_{1s}^{a} > = - \frac{8 (q_{1}^{a} q_{2}^{a})^{5/2}}{(q_{1}^{a} + q_{2}^{a})^{4}} <\chi_{2px}^{a} \left| \frac{\partial}{\partial x} \right| \chi_{2s}^{a} > = - \frac{q_{2}^{a}}{2\sqrt{3}} <\chi_{2px}^{a} \left| \frac{x_{2px}}{y} \right| \chi_{2s}^{a} > = - \frac{q_{2}^{a}}{2\sqrt{3}} <\chi_{2px}^{a} \left| \frac{x_{2px}}{y} \right| \chi_{2s}^{a} > = 1 <\chi_{2px}^{a} \left| \frac{x_{2py}}{y} \right| \chi_{2py}^{a} > = <\chi_{2py}^{a} \left| \frac{y_{2}}{y_{2px}} \right| \chi_{2pz}^{a} > = <\chi_{2pz}^{a} \left| \frac{x_{2px}}{y_{2px}} \right| \chi_{2px}^{a} > \\ = <\chi_{2py}^{a} \left| \frac{x_{2px}}{y_{2py}} \right| \chi_{2px}^{a} > = <\chi_{2pz}^{a} \left| \frac{y_{2}}{y_{2py}} \right| \chi_{2py}^{a} > = <\chi_{2px}^{a} \left| \frac{x_{2px}}{y_{2px}} \right| \chi_{2pz}^{a} > \\ = \frac{3}{2} (q_{2}^{a})^{-2}$$

b. Integrals between the atomic orbitals χ^a_t and χ^b_u on two atomic nuclei A and B.

It is convenient for calculation to express the orbitals χ^a and χ^b in one coordinate system with its origin at the midpoint between the nuclei A and B, and with the z-axis pointing from A toward B, parallel to the local axes Z_a and Z_b . x_a and x_b axes are also set parallel to the new x axis. Figure 2 shows this relation by assuming that the distance between A and B is 2d.

The local coordinate systems are transformed into general ones in the following way.

$$x_{a} = x_{b} = x$$

$$y_{a} = y_{b} = y$$

$$z_{a} = z + d$$

$$z_{b} = z - d$$

$$r_{a} = \sqrt{x^{2} + y^{2} + (z + d)^{2}}$$

$$r_{b} = \sqrt{x^{2} + y^{2} + (z - d)^{2}}$$



Figure 2. General and local coordinate systems.

As in the case of section a, non-zero integrals are listed in Table 2.

	X ^b ls	χ ^b 2s	χ^{b}_{2px}	x ^b 2py	χ^{b}_{2pz}
χ^{a}_{ls}	e _z , -	e _z , -	e _x , m _y	e _y , m _x	e _z , -
X ^a 2s	e _z , -	e _z , -	e _x , m _y	e _y , ^m x	e _z , -
χ^{a}_{2px}	e _x , m _y	e _x , m _y	e _z , -	— ; m _z	e _x , m _y
χ^{a}_{2py}	e _y , m _x	e _y , m _x	-, m _z	e _z , -	e _y , m _x
χ^{a}_{2pz}	e _z , -	e _z , -	e _x , m _y	e _y , m _x	e _z , -

Table 2. Non-zero components in integrals $\langle \chi_t^a | m | \chi_u^b \rangle$ $(m = \vec{\nabla}, \vec{r} \times \vec{\nabla}, \alpha\beta)$. Symbols e_{α} and m_{β} are the same as those in Table 1.

Next relations can be utilized in addition to equation (1).

$$\langle \chi_{t}^{a}(q_{n_{t}}^{a}) | m | \chi_{u}^{b}(q_{n_{u}}^{b}) \rangle = \pm \langle \chi_{u}^{a}(q_{n_{u}}^{b}) | m | \chi_{t}^{b}(q_{n_{t}}^{a}) \rangle$$
(2)

$$\langle \chi_{2px}^{a} | \vec{\nabla} | \chi_{w}^{b} \rangle_{y} = \langle \chi_{2py}^{a} | \vec{\nabla} | \chi_{w}^{b} \rangle_{x}$$
(3)

$$\langle \chi^{a}_{2px} | \vec{r} \times \vec{\nabla} | \chi^{b}_{w} \rangle_{y} = -\langle \chi^{a}_{2py} | \vec{r} \times \vec{\nabla} | \chi^{b}_{w} \rangle_{x}$$
(4)

$$\langle \chi_{2px}^{a} | xz | \chi_{w}^{b} \rangle = \langle \chi_{2py}^{a} | yz | \chi_{w}^{b} \rangle$$
(5)

$$<\chi^{a}_{2px}|xz|\chi^{b}_{2pz} = <\chi^{a}_{2py}|yz|\chi^{b}_{2pz}$$
 (6)

where χ^b_w are χ^b_{1s} and χ^b_{2s} orbitals. Equation (2) can be proved as shown below. From equation (1),

$$<\chi_{t}^{a}(q_{n_{t}}^{a})|m|\chi_{u}^{b}(q_{n_{u}}^{b})> = \pm<\chi_{u}^{b}(q_{n_{u}}^{b})|m|\chi_{t}^{a}(q_{n_{t}}^{a})>$$
(7)

With respect to the coordinate transformation from z to -z, we find

$$\begin{split} \chi^{a}_{t}(q^{a}_{n_{t}}) & \rightarrow \pm \chi^{b}_{t}(q^{a}_{n_{t}}) \\ \chi^{b}_{u}(q^{b}_{n_{u}}) & \rightarrow \pm \chi^{a}_{u}(q^{b}_{n_{u}}) \end{split}$$

where plus sign is for t, u = ls, 2s, 2px and 2py, and minus for t, u = 2pz, and we also find,

$$m \rightarrow \pm m$$

where plus for $m = \frac{\partial}{\partial x}$, $\frac{\partial}{\partial y}$, $x\frac{\partial}{\partial y} - y\frac{\partial}{\partial x}$, xy, and minus for $m = \frac{\partial}{\partial z}$, $y\frac{\partial}{\partial z} - z\frac{\partial}{\partial y}$, $z\frac{\partial}{\partial x} - x\frac{\partial}{\partial z}$, xz, yz,

and we find,

$$\int_{-\infty}^{\infty} dz \rightarrow \int_{-\infty}^{\infty} -dz = \int_{-\infty}^{\infty} dz$$

By the use of these transformations, equation (7) becomes

$$\langle \chi_{t}^{a}(q_{n_{t}}^{a}) | m | \chi_{u}^{b}(q_{n_{u}}^{b}) \rangle = \pm \langle \chi_{u}^{a}(q_{n_{u}}^{b}) | m | \chi_{t}^{b}(q_{n_{t}}^{a}) \rangle$$

$$(2)$$

and the signs will be determined individually.

This equation is applied for the calculation of $\langle \chi_t^a(q_{n_t}^a) | m | \chi_u^b(q_{n_t}^b) \rangle$ when $\langle \chi_u^a(q_{n_u}^a) | m | \chi_t^b(q_{n_t}^b) \rangle$ are given as functions of $q_{n_u}^a$ and $q_{n_t}^b$.

Equations (3), (4), (5), and (6) are easily convinced from symmetry considerations.

The results of calculations are shown below with the abbreviation

$$p = d(q^{a} + q^{b})$$

$$t = \frac{q^{a} - q^{b}}{q^{a} + q^{b}}$$

$$A_{n} = A_{n}(p) \equiv \frac{n!e^{-p}}{p^{n+1}} \sum_{k=0}^{n} \frac{p^{k}}{k!}$$

$$B_{n} = B_{n}(pt) \equiv (-1)^{n+1}A_{n}(-pt) - A_{n}(pt) \quad (t \neq 0)$$

$$= 0 \qquad (t = 0, n; odd)$$

$$= \frac{2}{n+1} \qquad (t \neq 0, n; even)$$

$$\begin{aligned} &<\chi_{1s}^{a} |\vec{\nabla}| \chi_{1s}^{b} > = -2d^{3}(q_{1}^{a})^{3/2}(q_{1}^{b})^{5/2} \{ (A_{2}-A_{0})B_{1} + (B_{2}-B_{0})A_{1} \} k \\ &<\chi_{2s}^{a} |\vec{\nabla}| \chi_{1s}^{b} > = -\frac{2}{\sqrt{3}} d^{4}(q_{2}^{a}q_{1}^{b})^{5/2} \{ (B_{2}-B_{0})A_{2} + (B_{3}-B_{1})A_{1} + (A_{2}-A_{0})B_{2} + (A_{3}-A_{1})B_{1} \} k \\ &<\chi_{2px}^{a} |\vec{\nabla}| \chi_{1s}^{b} > = -d^{4}(q_{2}^{a}q_{1}^{b})^{5/2} \{ (A_{3}-A_{1}) (B_{0}-B_{2}) + (A_{2}-A_{0}) (B_{1}-B_{3}) \} i \\ &<\chi_{2py}^{a} |\vec{\nabla}| \chi_{1s}^{b} > = <\chi_{2px}^{a} |\vec{\nabla}| \chi_{1s}^{b} > x j \\ &<\chi_{2pz}^{a} |\vec{\nabla}| \chi_{1s}^{b} > = -2d^{4}(q_{2}^{a}q_{1}^{b})^{5/2} (A_{3}B_{2}+A_{2}B_{3}-A_{1}B_{0}-A_{0}B_{1}) k \\ &<\chi_{2s}^{a} |\vec{\nabla}| \chi_{2s}^{b} > = \frac{2}{3}d^{4}(q_{2}^{a}q_{2}^{b})^{5/2} [\{ (B_{2}-B_{0})A_{2} + (B_{3}-B_{1})A_{1} + (A_{2}-A_{0})B_{2} + (A_{3}-A_{1})B_{1} \} \\ &-dq_{2}^{b} [(B_{2}-B_{0})A_{3} + (B_{2}-B_{4})A_{1} - (A_{2}-A_{0})B_{3} - (A_{2}-A_{4})B_{1} \}] k \end{aligned}$$

$$<\chi_{2px}^{a} |\vec{\nabla}| \chi_{2s}^{b} > = \frac{1}{\sqrt{3}} d^{4} (q_{2}^{a} q_{2}^{b})^{5/2} [\{ (A_{3} - A_{1}) (B_{0} - B_{2}) + (A_{2} - A_{0}) (B_{1} - B_{3}) \} \\ - dq_{2}^{b} [(A_{4} - A_{2}) (B_{0} - B_{2}) - (A_{2} - A_{0}) (B_{2} - B_{4})]] i$$

$$\begin{aligned} & \langle \chi_{2py}^{a} | \vec{\nabla} | \chi_{2s}^{b} \rangle = \langle \chi_{2px}^{a} | \vec{\nabla} | \chi_{2s}^{b} \rangle_{x} \quad \mathbf{j} \\ & \langle \chi_{2pz}^{a} | \vec{\nabla} | \chi_{2s}^{b} \rangle = \frac{2}{\sqrt{3}} d^{4} (\underline{q}_{2}^{a} \underline{q}_{2}^{b})^{5/2} [(A_{3}^{B} \underline{q} + A_{2}^{B} \underline{q} - A_{1}^{B} \underline{0} - A_{0}^{B} \underline{1}) - d\underline{q}_{2}^{b} (A_{4} + A_{0}^{b} \underline{B}_{2}^{b} - (B_{4} + B_{0}^{b} A_{1}^{b})] \\ & \langle \chi_{2px}^{a} | \vec{\nabla} | \chi_{2px}^{b} \rangle = -d^{5} (\underline{q}_{2}^{a})^{5/2} (\underline{q}_{2}^{b})^{7/2} \{(A_{4} - 2A_{2} + A_{0}^{b}) (B_{1}^{b} - B_{3}^{b}) + (A_{1}^{b} - A_{3}^{b}) (B_{4}^{b} - 2B_{2}^{b} + B_{0}^{b}) \} \\ & \langle \chi_{2py}^{a} | \vec{\nabla} | \chi_{2py}^{b} \rangle = \langle \chi_{2px}^{a} | \vec{\nabla} | \chi_{2px}^{b} \rangle \\ & \langle \chi_{2py}^{a} | \vec{\nabla} | \chi_{2pz}^{b} \rangle = \langle \chi_{2px}^{a} | \vec{\nabla} | \chi_{2px}^{b} \rangle_{z} \quad \mathbf{i} \\ & \langle \chi_{2py}^{a} | \vec{\nabla} | \chi_{2pz}^{b} \rangle = \langle \chi_{2px}^{a} | \vec{\nabla} | \chi_{2px}^{b} \rangle_{z} \quad \mathbf{j} \\ & \langle \chi_{2py}^{a} | \vec{\nabla} | \chi_{2pz}^{b} \rangle = 2d^{4} (\underline{q}_{2}^{a} \underline{q}_{2}^{b})^{5/2} [(A_{3}^{B} \underline{1} - A_{1}^{B} \underline{3} + A_{2}^{B} \underline{0} - A_{0}^{B} \underline{2}) \\ & \quad -d\underline{q}_{2}^{b} [(A_{4}^{-} A_{2}^{b}) \underline{3} + (A_{0}^{-} A_{2}^{b}) \underline{1} + (B_{4}^{-B} \underline{2}) A_{3}^{b} + (B_{0}^{-B} \underline{2}) A_{1}^{b}] \end{bmatrix} \\ \mathbf{k} \end{aligned}$$

$$\begin{aligned} & \langle \chi_{2px}^{a} | \dot{x} \times \ddot{v} | \chi_{1s}^{a} \rangle &= d \langle \chi_{2px}^{a} | \vec{v} | \chi_{1s}^{b} \rangle_{x} \mathbf{I} \\ & \langle \chi_{2px}^{a} | \dot{x} \times \ddot{v} | \chi_{2s}^{b} \rangle &= -d \langle \chi_{2py}^{a} | \vec{v} | \chi_{2s}^{b} \rangle_{x} \mathbf{I} \\ & \langle \chi_{2px}^{a} | \dot{x} \times \ddot{v} | \chi_{2s}^{b} \rangle &= d \langle \chi_{2px}^{a} | \vec{v} | \chi_{2s}^{b} \rangle_{x} \mathbf{I} \\ & \langle \chi_{2py}^{a} | \dot{x} \times \ddot{v} | \chi_{2s}^{b} \rangle &= -d \langle \chi_{2py}^{a} | \vec{v} | \chi_{2ps}^{b} \rangle_{x} \mathbf{I} \\ & \langle \chi_{2py}^{a} | \dot{x} \times \ddot{v} | \chi_{2px}^{b} \rangle &= -d \langle \chi_{2py}^{a} | \chi_{2py}^{b} \rangle \mathbf{K} \\ &= -d \langle q_{2q}^{a} q_{2}^{b} \rangle^{5/2} \{ (\mathbf{A}_{4} - \mathbf{A}_{2}) (\mathbf{B}_{0} - \mathbf{B}_{2}) - (\mathbf{A}_{2} - \mathbf{A}_{0}) (\mathbf{B}_{2} - \mathbf{B}_{4}) \} \mathbf{K} \\ & \langle \chi_{2px}^{a} | \dot{x} \times \ddot{v} | \chi_{2pz}^{b} \rangle &= \{ -\langle \chi_{2py}^{a} | \chi_{2py}^{b} \rangle + d \langle \chi_{2px}^{a} | \vec{v} | \chi_{2px}^{b} \rangle_{z} \} \mathbf{I} \\ & \langle \chi_{2px}^{a} | \dot{x} \times \ddot{v} | \chi_{2pz}^{b} \rangle &= \{ \langle \chi_{2py}^{a} | \chi_{2py}^{b} \rangle - d \langle \chi_{2px}^{a} | \vec{v} | \chi_{2px}^{b} \rangle_{z} \} \mathbf{I} \\ & \langle \chi_{2px}^{a} | \dot{x} x | \chi_{2pz}^{b} \rangle &= \langle \chi_{2py}^{a} | \chi_{2py}^{b} \rangle - d \langle \chi_{2px}^{a} | \vec{v} | \chi_{2px}^{b} \rangle_{z} \} \mathbf{I} \\ & \langle \chi_{2px}^{a} | xz | \chi_{1s}^{b} \rangle &= \langle \chi_{2py}^{a} | yz | \chi_{1s}^{b} \rangle \\ &= d^{6} (q_{2}^{0})^{5/2} (q_{1}^{b})^{3/2} \{ (\mathbf{A}_{5} - \mathbf{A}_{3}) (\mathbf{B}_{1} - \mathbf{B}_{3}) - (\mathbf{A}_{3} - \mathbf{A}_{1}) (\mathbf{B}_{3} - \mathbf{B}_{5}) \} \\ & \langle \chi_{2px}^{a} | xz | \chi_{2s}^{b} \rangle &= \langle \chi_{2py}^{a} | yz | \chi_{2s}^{b} \rangle \\ &= \frac{1}{\sqrt{3}} d^{7} (q_{2}^{a} q_{2}^{b})^{5/2} \{ (\mathbf{A}_{6} - \mathbf{A}_{4}) (\mathbf{B}_{1} - \mathbf{B}_{3}) + (\mathbf{A}_{4} - \mathbf{A}_{2}) (\mathbf{B}_{3} - \mathbf{B}_{5}) \\ & -(\mathbf{A}_{5} - \mathbf{A}_{3}) (\mathbf{B}_{2} - \mathbf{B}_{4}) - (\mathbf{A}_{3} - \mathbf{A}_{1}) (\mathbf{B}_{4} - \mathbf{B}_{6}) \}, \end{aligned}$$

$$<\chi_{2px}^{a} | xy | \chi_{2py}^{b} > = \frac{1}{4} d^{7} (q_{2}^{a}q_{2}^{b})^{5/2} \{ (A_{6}^{-2A_{4}^{}+A_{2}^{}}) (B_{4}^{-2B_{2}^{}+B_{0}^{}}) - (A_{4}^{-2A_{2}^{}+A_{0}^{}}) (B_{6}^{-2B_{4}^{}+B_{2}^{}}) \}$$

$$\langle \chi_{2px}^{a} | xz | \chi_{2pz}^{b} \rangle = \langle \chi_{2py}^{a} | yz | \chi_{2pz}^{b} \rangle$$

$$= d^{7} (q_{2}^{a} q_{2}^{b})^{5/2} \{ (A_{6} - A_{4}) (B_{2} - B_{4}) + (A_{3} - A_{1}) (B_{3} - B_{5})$$

$$- (A_{5} - A_{3}) (B_{1} - B_{3}) - (A_{4} - A_{2}) (B_{4} - B_{6}) \}$$

5. Table of effective nuclear charges in Slater orbitals

	ls	2s,2p	
Н	1.00		
С	5.70	3.25	
0	7.70	4.55	