**Doctoral Dissertation**

# Studies on Cross-Oligomerization Reactions via Oxidative Cyclization of Tetrafluoroethylene and Ethylene with Nickel

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# Preface and Acknowledgement

The study in this thesis has been carried out under the direction of Professor Dr. Sensuke Ogoshi at the Department of Applied Chemistry, Faculty of Engineering, Osaka University from April 2013 to March 2019. The thesis described cross-oligomerization reactions via oxidative cyclization of tetrafluoroethylene and ethylene with nickel.

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# Contents

## Abbreviations

The following abbreviations are used in the thesis.

| | |
|---|---|
| *α* | alpha |
| Å | angstrom |
| anal. | elemental analysis |
| Ar | aryl |
| atm | atmospheric pressure |
| *β* | beta |
| br | broad |
| Bu | butyl |
| calcd | calculated |
| cat. | Catalyst |
| cf. | confer |
| CI | chemical ionization |
| cod | 1,5-cyclooctadiene |
| Cy | cyclohexyl |
| °C | degrees Celsius |
| d | doublet |
| *d* | deuterated |
| δ | chemical shift of NMR signal in ppm |
| *η* | eta |
| e.g. | for example |
| eq, equiv | equivalent |
| EI | electron ionization |
| Et | ethyl |
| GC | gas chromatography |
| h | hour(s) |
| HFP | hexafluoropropyrene |
| HPLC | high performance liquid chromatography |
| HRMS | high-resolution mass spectrometry |
| Hz | hertz |
| *i* | iso |

| | |
|---|---|
| i.e. | that is |
| IPr | 1,3-bis(2,6-diisopropylphenyl)imidazol-2-ylidene |
| *J* | coupling constant in NMR |
| L | ligand |
| LLDPE | linear low-density polyethylene |
| m | multiplet |
| *m* | meta |
| MAO | methylaluminoxane |
| min | minute(s) |
| mL | milliliter |
| M | metal |
| Me | methyl |
| μL | microliter |
| MS | mass spectrometry |
| *n* | normal |
| NHC | *N*-heterocyclic carbene |
| Ni | nickel |
| NMR | nuclear magnetic resonance |
| *o* | ortho |
| ORTEP | Oak Ridge thermal ellipsoid plot |
| *p* | para |
| $\pi$ | pi |
| Ph | phenyl |
| pin | pinacolato |
| Pr | propyl |
| $PR_3$ | trialkyl- or triaryl-phosphine |
| PS | polystyrene |
| q | quartet |
| quant | quantitative |
| rt | room temperature |
| s | singlet |
| t | triplet |
| *t, tert* | tertiary |

| | |
|---|---|
| temp | temperature |
| TFE | tetrafluoroethylene |
| THF | tetrahydrofuran |
| TMS | trimethylsilyl |
| tol | tolyl |
| TON | turnover number |

# Chapter 1

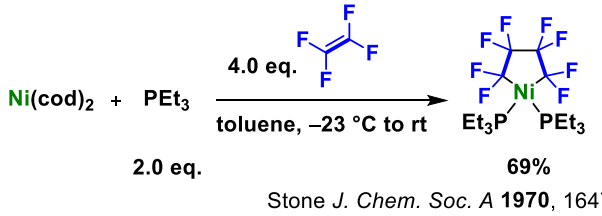
# General Introduction

Organofluorine compounds have attracted much attention due to their remarkable applications in pharmaceutical and materials science.[1] Thus, a great deal of efforts have been directed toward the development of synthetic methods for the organofluorine compounds. One of the fundamental methods in the synthesis of organofluorine compounds is a fluorination that enables the introduction of one fluorine atom into organic compounds, and a variety of efficient and selective fluorination reactions have been achieved with fluorination reagents.[2] In addition to fluorination, a number of methods for the introduction of a $CF_3$ group, so-called trifluoromethylation, have been developed.[3] On the other hand, in the case of the synthesis for multi-fluorinated compounds, the use of an excess amount of costly fluorination reagents is highly undesirable. Thus, the development of straightforward and efficient synthetic methods for them have been highly demanded.

Tetrafluoroethylene (TFE) is an industrially economical feedstock in organofluorine chemistry and is used in the production of poly(tetrafluoroethylene) and co-polymers with other alkenes.[4] It is also an environmentally-benign feedstock with zero ozone depletion potential and near-zero global warming potential. For these reasons, although TFE is an ideal starting material for the production of multi-fluorinated compounds, the synthetic method for transforming TFE into organofluorine compounds remain largely unexplored.

On the other hand, the oxidative cyclization with low-valent transition metals has received considerable attention because the reaction enables the construction of a C–C bond between a variety of unsaturated compounds, and the resulting five-membered metallacycles are assumed to be key reaction intermediates in transition-metal-catalyzed cycloaddition as well as multicomponent coupling reactions.[5] Among transition-metal candidates, nickel has shown great promise as a catalyst, because a number of oxidative cyclization reactions have yielded nickelacycles when using two unsaturated compounds with Ni(0).[6] Because of strong coordination of electron poor TFE to Ni(0), a five-membered nickelacycle generated by the oxidative cyclization of two molecules of TFE

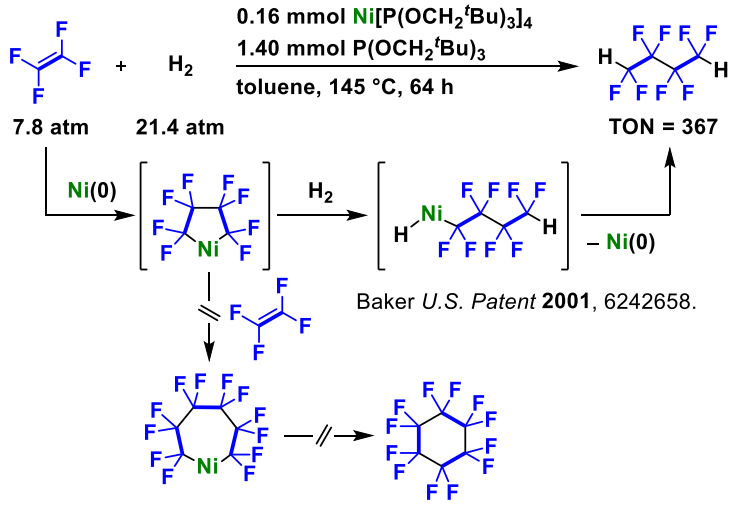
has also been known (Scheme 1.1).[7]




Stone *J. Chem. Soc. A* **1970**, 1647.

**Scheme 1.1.** Oxidative Cyclization of Two-Molecules of TFE with Ni(0).

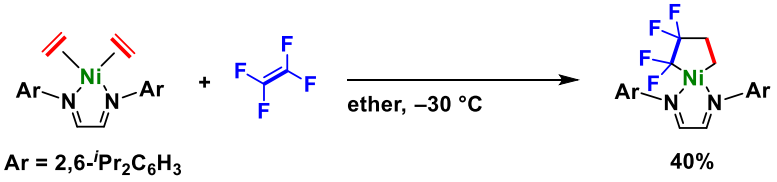
The first catalytic reaction of TFE via a nickelacycle was reported by Baker. In the presence of Ni(0) catalyst and phosphine ligand, the reaction of TFE with $H_2$ produces 1,1,2,2,3,3,4,4-octafluorobutane with a turnover number of 367 (Scheme 1.2).[8] This catalytic reaction might proceed via an octafluoronickelacyclopentane and a Ni–H species generated via hydrogenolysis. However, due to the unique inertness of the bonds between transition-metals and perfluoroalkyl ligands,[9] insertion of unsaturated compounds like TFE to the Ni–$CF_2$ bond, which leads to ring-expansion, is exceptionally difficult. In addition, reductive elimination from Ni–$CF_2$ that forms new C–C bonds is also difficult. On the other hand, reductive elimination from H–M–R (M: transition-metal, R: alkyl group) rather than R–M–R, in general, occurs much more easily. In fact, in the Baker's report, reductive elimination forming the C–H bond have been achieved. Therefore, transformation of TFE via the oxidative cyclization of two molecules of TFE with Ni(0) was limited to the reaction with $H_2$.




Baker *U.S. Patent* **2001**, 6242658.

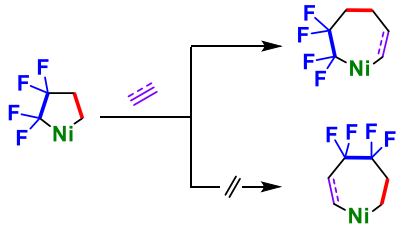
**Scheme 1.2.** First Catalytic Reaction of TFE via a Nickelcycle.

An unsymmetrical five-membered nickelacycle generated by the oxidative cyclization of TFE and ethylene has also been reported (Scheme 1.3).[10,11] However, the reactivity of this nickelacycle has not been studied at all. When regioselective insertion of unsaturated compounds to the Ni–$CH_2$ bond rather than the Ni–$CF_2$ bond might occur, the generated seven-membered nickelacycle enables further transformation of TFE (Scheme 1.4). Moreover, in general, oxidative cyclization between an electron-rich and -deficient substrate using Ni(0) is kinetically much more favorable than those occurring between other substrate combinations.[12] Based on this concept, ethylene should be a good substrate for the oxidative cyclization of TFE with Ni(0) due to its rich electron density and less steric hindrance.



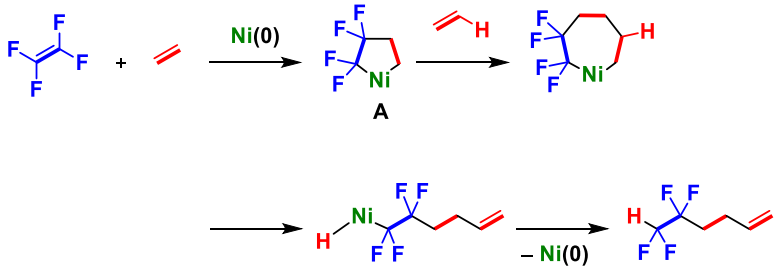

Pörschke *J. Organomet. Chem.* **1991**, 408, C25.

**Scheme 1.3.** Oxidative Cyclization of TFE and Ethylene with Ni(0).



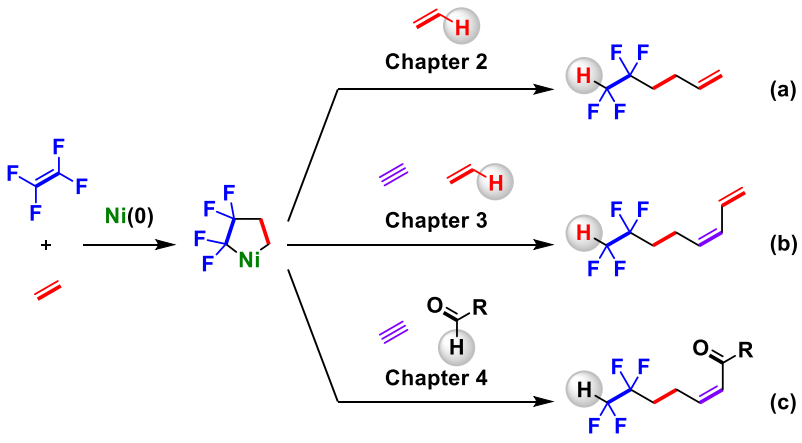

**Scheme 1.4.** Selective Insertion of Unsaturated Compounds to a Nickelacycle Generated by the Oxidative Cyclization of TFE and Ethylene.

On the basis of aforementioned background, we envisioned that the development of a catalytic reaction of TFE with ethylene (Scheme 1.5). First, the oxidative cyclization of TFE and ethylene with Ni(0) yields a kinetically-favored five-membered nickelacycle (**A**). Then, due to the exclusive coordination of the relatively electron-rich ethylene rather than TFE to the Ni(II) center in **A**, the migratory insertion of another ethylene to the Ni−$CH_2$ bond takes place to give a seven-membered nickelacycle intermediate. $\beta$-Hydride elimination followed by reductive elimination affords a co-trimer and regenerates a Ni(0) species.




**Scheme 1.5.** Working Hypothesis for transformation of TFE via a Nickelacycle.

In this thesis, the purpose of this study is the development of cross-oligomerization reactions via the oxidative cyclization of TFE and ethylene with Ni(0). This thesis consists of the general introduction and the following three chapters (Scheme 1.6). In chapter 2, the isolation of a five-membered nickelacycle generated by the oxidative cyclization of TFE and ethylene is described (Scheme 1.6 (a)). A Ni(0)-catalyzed co-trimerization reaction of TFE and ethylene is also described in this chapter. Chapter 3 deals with a Ni(0)-catalyzed cross-tetramerization reaction of TFE, ethylene, and alkyne (Scheme 1.6 (b)). In chapter 4, the development of a Ni(0)-catalyzed cross-tetramerization reaction of TFE, ethylene, alkyne, and aldehyde is discussed (Scheme 1.6 (c)). Finally, this thesis is summarized in conclusion.




**Scheme 1.6.** This thesis: a) Ni(0)-catalyzed co-trimerization reaction of TFE and ethylene. b) Ni(0)-catalyzed cross-tetramerization reaction of TFE, ethylene, and alkyne. c) Ni(0)-catalyzed cross-tetramerization reaction of TFE, ethylene, alkyne, and aldehyde.

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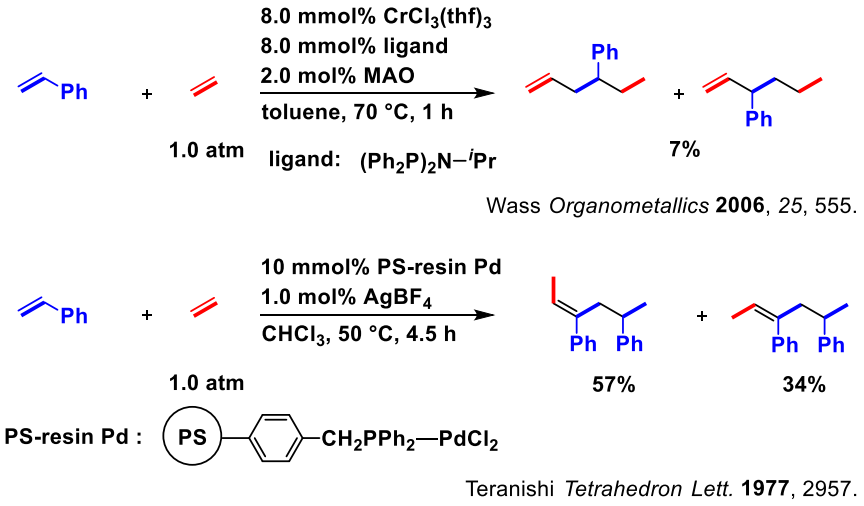
# Chapter 2

# Ni(0)-Catalyzed Co-Trimerization Reaction of TFE and Ethylene

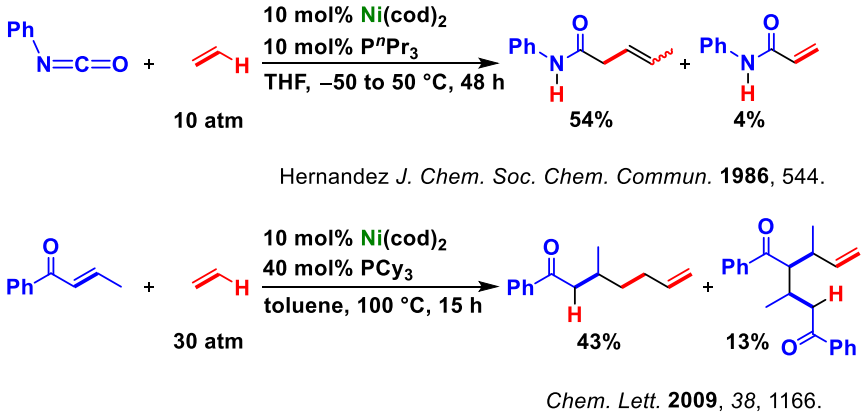
## 2.1 Introduction

Oxidative cyclization with low-valent transition-metal species has received increasing attention as a straightforward and environmentally benign route to the construction of a C−C bond between varieties of two unsaturated compounds. The generated five-membered metallacycles are assumed to be key reaction intermediates in multicomponent coupling reactions as well as in cycloaddition reactions.[1,2] The transition-metal-catalyzed trimerization reaction of ethylene to 1-hexene, which is used as a co-monomer with ethylene to produce linear low-density polyethylene (LLDPE), has been proposed to proceed via oxidative cyclization of two ethylenes.[3,4] Since $\alpha$-olefins can be co-polymerized with ethylene to afford polymers with improved properties, it is worthwhile to develop such an oligomerization leading to $\alpha$-olefins with a terminal functional group.[5] Nevertheless, selective co-trimerization reactions between ethylene and other alkenes have rarely been investigated. Limited reactions between ethylene and styrene are known to be catalyzed by chromium and palladium species (Scheme 2.1).[6,7]




**Scheme 2.1.** Transition-Metal-Catalyzed Co-Trimerizations of Ethylene and Styrene.

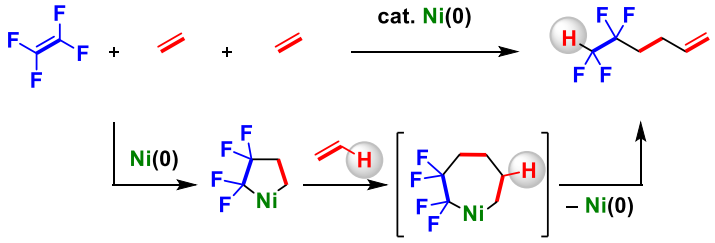
The Ni-catalyzed co-trimerization reactions with ethylene were also demonstrated (Scheme 2.2).[8,9]




**Scheme 2.2.** Ni(0)-Catalyzed Co-Trimerizations with Ethylene.

On the basis of the aforementioned early study employing ethylene and styrene with chromium,[7] it is possible that the five-membered nickelacycle generated via the oxidative cyclization of TFE and ethylene with Ni(0) may serve as an intermediate for a co-trimerization of TFE and ethylene.

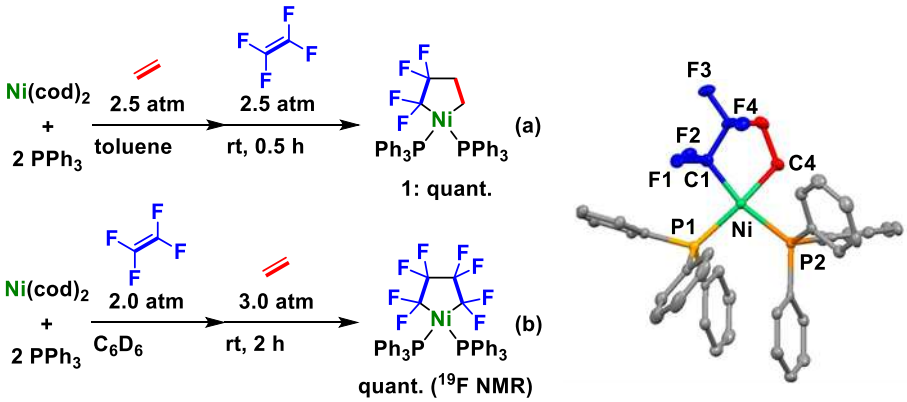
Described in this chapter is a Ni(0)-catalyzed co-trimerization reaction of TFE and ethylene (Scheme 2.3). In the presence of $PPh_3$, oxidative cyclization of TFE and ethylene with Ni(0) took place to give a five-membered nickelacycle, which was found to further react with ethylene to afford a co-trimer. A novel Ni(0)-catalyzed co-trimerization reaction of TFE and ethylene was also established.




**Scheme 2.3.** Ni(0)-Catalyzed Co-Trimerization Reaction of TFE and Ethylene.

## 2.2 Oxidative Cyclization of TFE and Ethylene with Ni(0)

Successive treatment of a mixture of $Ni(cod)_2$ and $PPh_3$ with ethylene followed by TFE in toluene for 0.5 h led to quantitative formation of a five-membered nickelacycle, $(CF_2CF_2CH_2CH_2)Ni(PPh_3)_2$ (**1**) (Scheme 2.4 (a)). In contrast, before the ethylene treatment, the prior exposure of TFE to the Ni(0)/$PPh_3$ mixture gave the known $(CF_2CF_2CF_2CF_2)Ni(PPh_3)_2$ (Scheme 2.4 (b)).[10] The X-ray diffraction study of **1** clearly demonstrated that the nickelacyclopentane framework was derived from one TFE and one ethylene unit. One of the structural features is a distorted square planar geometry of nickel, as indicated by the sum of the angles around the nickel (363.5°) as well as the difference in bond distances between Ni−C1 and Ni−C4 (1.922(4) and 1.993(4) Å, respectively). Conversely, the Ni−P1 bond length of 2.2182(12) Å was slightly shorter than the Ni−P2 bond (2.2589(12) Å), which reflected the difference in the trans influence between the $CH_2$ and the $CF_2$ groups.

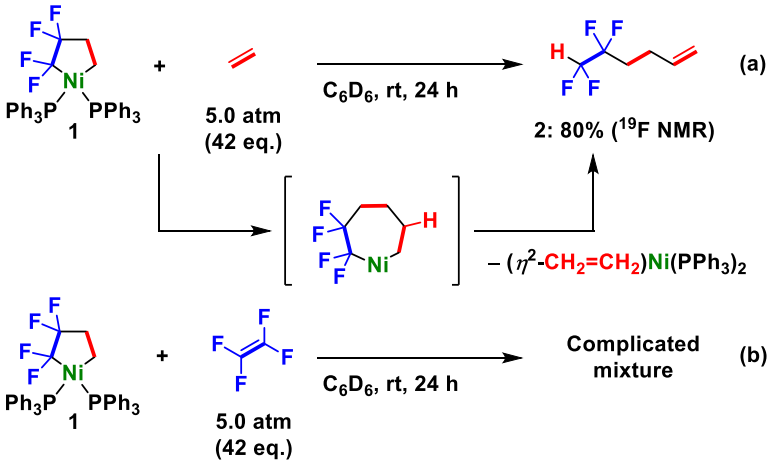



**Scheme 2.4.** Oxidative Cyclization of TFE and Ethylene with Ni(0).

## 2.3 Reactivities of 1

When complex **1** was treated with ethylene in $C_6D_6$ at room temperature for 24 h, generation of 5,5,6,6-tetrafluoro-1-hexene (**2**) was detected in 80% yield (estimated by $^{19}F$ NMR analysis; Scheme 2.5 (a)). In the $^{31}P$ NMR spectrum of the crude reaction mixture, concomitant formation of $(\eta^2\text{-}CH_2{=}CH_2)Ni(PPh_3)_2$ was observed. The co-trimer **2** was obtained as the sole product, and neither 3,3,4,4-tetrafluoro-1-hexene nor any $C_8$ or higher products were detected in the crude product. This clearly indicated the following: (a) migratory insertion of ethylene to the Ni−$CH_2$ bond rather than to the Ni−$CF_2$ bond in **1** occurred selectively to give a seven-membered nickelacycle

intermediate, although spectroscopic evidence could not be obtained, and (b) *β*-hydride elimination from a seven-membered nickelacycle would be substantially faster than further ethylene insertion into the Ni−$CH_2$ bond in a seven-membered nickelacycle (or larger-membered nickelacycles). On the other hand, the reaction of **1** with TFE gave a complicated mixture, albeit with complete consumption of starting complex **1** (Scheme 2.5 (b)).

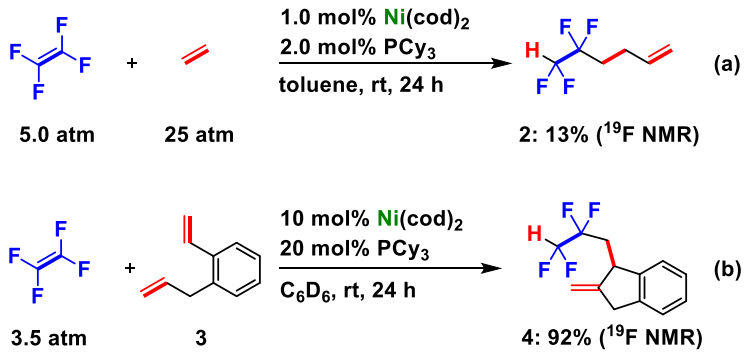



**Scheme 2.5.** Reactivities of **1**.

### 2.4 Ni(0)-Catalyzed Co-Trimerization Reactions with TFE

The selective co-trimerization reaction of TFE and ethylene, leading to **2**, proceeded catalytically, as anticipated from the regeneration of the Ni(0) complex (Scheme 2.5 (a)). Thus, optimization of the reaction conditions revealed that exposing TFE (5 atm) followed by ethylene (25 atm) to a toluene solution of $Ni(cod)_2$/$PCy_3$ catalyst gave the best results, **2** was obtained as a sole product albeit in low yield (Scheme 2.6 (a)). On the other hand, the co-trimerization hardly proceeded in the presence of a catalytic amount of $Ni(cod)_2$ and $PPh_3$, which was probably due to the oxidative cyclization of two-molecules of TFE with Ni(0). In addition, employing 2-allylstyrene (**3**) as a substrate resulted in smooth progress for the catalytic reaction with TFE, yielding a 2-methylene-2,3-dihydroindene derivative (**4**). An elaborate investigation of the reaction conditions concluded that TFE reacted with **3** in the presence $Ni(cod)_2$ and $PCy_3$ (10 and 20 mol%, respectively) to afford **4** in 92% yield (Scheme 2.6 (b)). The oxidative addition of a C−F bond of TFE to Ni(0) gradually occurred to yield *trans*-$(PCy_3)_2Ni(F)(CF{=}CF_2)$ at 40 ℃, leading to a deactivation of the

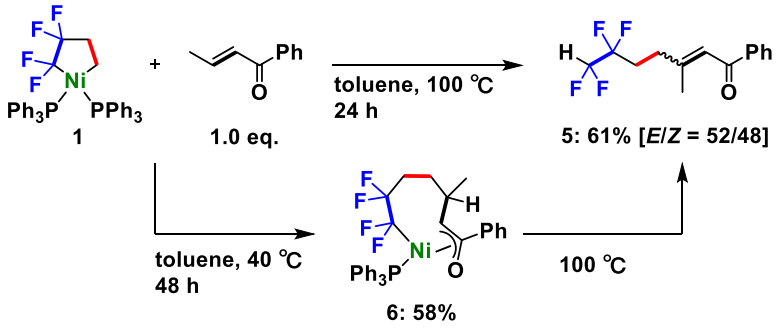
catalyst.[10]




**Scheme 2.6.** Ni(0)-Catalyzed Co-Trimerization Reactions with TFE.

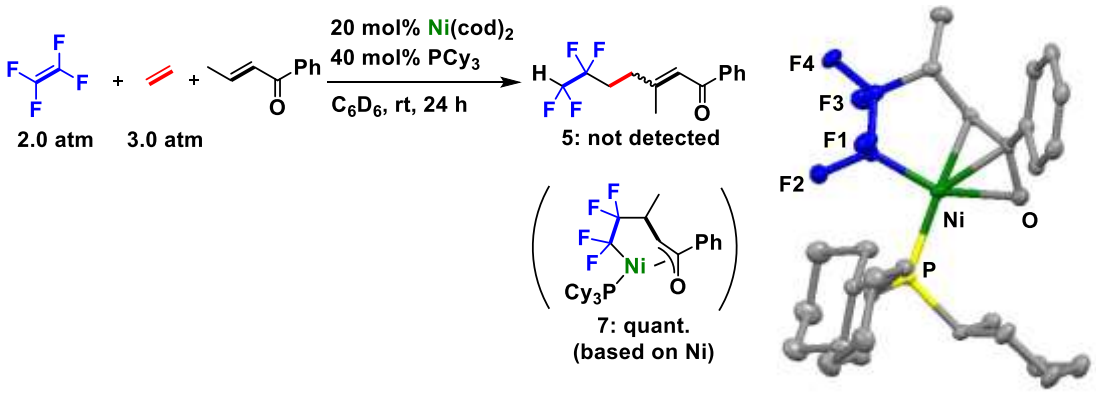
## 2.5 Michael Addition of 1 toward *α,β*-Unsaturated Carbonyl Compound

Nickelacycle **1** was found to be very useful for the stoichiometric preparation of cross-trimerization product of TFE, ethylene, and *α,β*-unsaturated carbonyl compound. The reaction with phenyl 1-propenyl ketone led to the formation of an *E*/*Z* mixture of 6,6,7,7-tetrafluoro-3-methyl-1-phenyl-2-hepten-1-one (**5**) in 61% yield (Scheme 2.7). When the reaction was carried out with phenyl 1-propenyl ketone at 40 °C for 24 h, a seven-membered nickelacycle (**6**) was generated via the insertion of the enone into the Ni−$CH_2$ bond in **1**. Thermolysis of **6** in $C_6D_6$ at 100 °C yielded **5**.



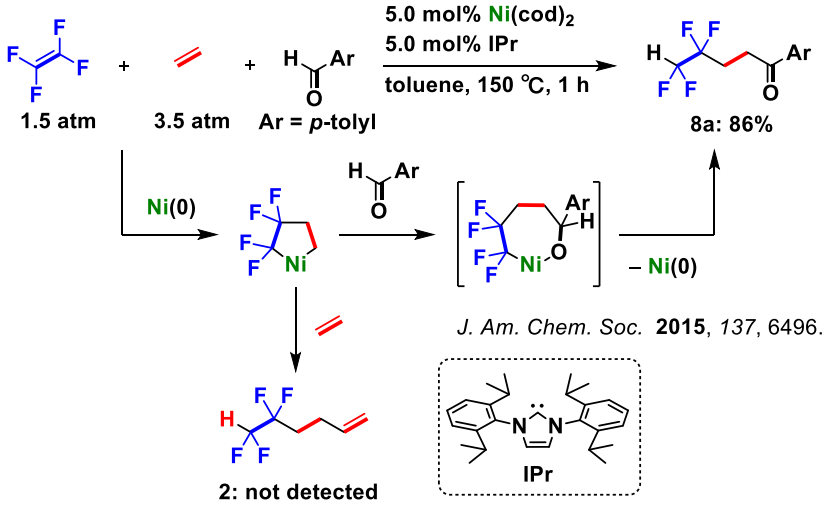

**Scheme 2.7.** Michael Addition of **1** toward *α,β*-Unsaturated Carbonyl Compound.

An attempt to apply this stoichiometric reaction to the catalytic formation of **5** failed. One of the reasons for this failure was formation of the oxidative cyclization product derived from TFE and phenyl 1-propenyl ketone. The corresponding oxidative cyclization product [($\eta^1$:$\eta^3$-$CF_2CF_2C$(H)MeCHC(O)Ph)Ni($PCy_3$)] (**7**), generated in the reaction mixture, did not react with ethylene or enone, presumably due to its stable $\eta^3$-oxallyl structure (Scheme 2.8).




**Scheme 2.8.** Attempt to Catalytic Reaction.

Moreover, in anticipation of the occurrence of a nucleophilic addition of the resultant five-membered nickelacycle to aldehyde, we found a Ni(0)-catalyzed cross-trimerization reaction of TFE, ethylene, and aldehyde, giving fluorine-containing ketone derivative (**8a**; Scheme 2.9).[11]




**Scheme 2.9.** Ni(0)-Catalyzed Cross-Trimerization of TFE, Ethylene, and Aldehyde.

## 2.6 Conclusion

In chapter 2, the Ni(0)-catalyzed co-trimerization of TFE and ethylene is described. Oxidative cyclization of TFE and ethylene with Ni(0) resulted in the formation of a five-membered nickelacycle and the structure was determined by X-ray analysis. This nickelacycle was found not only to react stoichiometrically with enone to give a cross-trimer but also to be a key reaction intermediate in the Ni(0)-catalyzed co-trimerization reaction of TFE and ethylene, leading to 5,5,6,6-tetrafluoro-1-hexene.

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### 2.8 Experimental Section

**General remarks compatible to all the experimental part in this thesis**

All manipulations were conducted under a nitrogen atmosphere using standard Schlenk or dry box techniques. $^{1}H$, $^{13}C$, $^{19}F$, and $^{31}P$ nuclear magnetic resonance (NMR) spectra were recorded on Bruker Avance III 400 spectrometer. The chemical shifts in $^{1}H$ and $^{13}C$ NMR spectra were recorded relative to residual protonated solvent $CDCl_3$ ($\delta$ 7.26 ppm for $^{1}H$ NMR and $\delta$ 77.16 ppm for $^{13}C$ NMR) and $C_6D_6$ ($\delta$ 7.16 ppm for $^{1}H$ NMR and $\delta$ 128.06 ppm for $^{13}C$ NMR). The chemical shifts in $^{19}F$ NMR spectra were recorded relative to $\alpha,\alpha,\alpha$-trifluorotoluene ($\delta$ –65.4 ppm) as an internal standard. The chemical shifts in $^{31}P$ NMR spectra were recorded using 85% $H_3PO_4$ as external standard. Mass spectra were obtained using a Shimadzu GCMS-QP 2010 instrument with an ionization voltage of 70 eV. Analytical gas chromatography was carried out on a Shimadzu GC-2014 gas chromatograph, equipped with a flame ionization detector. High resolution mass spectrometry (HRMS) was performed at Instrumental Analysis Center, Faculty of Engineering, Osaka University.

**Material for all the experimental part in this thesis**

All commercially available reagents were used as received unless otherwise noted. $C_6D_6$ and toluene were distilled from sodium benzophenone ketyl. Fluoroalkenes were kindly supplied by Daikin Industries, Ltd.

**Caution**: TFE is suspected to be carcinogens. The reaction mixture must be handled in a well-ventilated fume hood.

**Isolation of 1 (Scheme 2.4 (a))**

$Ni(cod)_2$ (275 mg, 1.00 mmol) and $PPh_3$ (525 mg, 2.00 mmol) were dissolved into 15 mL of toluene. The toluene solution was transferred into an autoclave reactor. Ethylene (2.5 atm) and TFE (2.5 atm) was charged into the reactor, and the reaction mixture was stirred at room temperature for 30 min. Gradual formation of yellow precipitate was observed. All volatiles were removed under reduced pressure, and then yellow residue was washed with hexane, affording 711 mg of **1** (1.00 mmol, 100%) as yellow solid. Single crystals for X-ray diffraction analysis were prepared by recrystallization from acetone/pentane at room temperature.

$^1$H NMR (400 MHz, $C_6D_6$, rt, δ/ppm): 1.41 (m, 2H), 2.07 (m, 2H), 6.75–6.99 (m, 18H), 7.31–7.52 (m, 6H), 7.52–7.68 (m, 6H). $^{13}C\{^1H\}$NMR (100 MHz, $C_6D_6$, rt, δ/ppm): 22.2 (m), 33.1 (t, $J_{CP}$ = 21.3 Hz), 129.5, 129.7, 133.7 (d, $J_{CP}$ = 36.0 Hz), 134.4 (d, $J_{CP}$ = 10.8 Hz), 134.7 (d, $J_{CP}$ = 11.9 Hz). Resonances attributable to the $CF_2CF_2$ moiety could not be detected due to multiple $^{13}C$–$^{19}F$ couplings, and those attributable to the *m*-$C_6H_5$ were obscured by $C_6D_6$. $^{31}P\{^1H\}$ NMR (162 MHz, $C_6D_6$, rt, δ/ppm): 30.1 (tm, $J_{PF}$ = 22.0 Hz, 1P), 35.0 (tm, $J_{PF}$ = 27.2 Hz, 1P). $^{19}$F NMR (376 MHz, $C_6D_6$, rt, δ/ppm): –121.0 (m, 2F), –101.4 (ddm, $J_{FP}$ = 27.2, 22.0 Hz, 2F). Anal. Calcd for $C_{40}H_{34}F_4P_2Ni$: C, 67.54; H, 4.82. Found: C, 66.93; H, 5.00.

**Formation of $(CF_2CF_2CF_2CF_2)Ni(PPh_3)_2$ (Scheme 2.4 (b))**

A $C_6D_6$ solution of $Ni(cod)_2$ (8.3 mg, 0.03 mmol), $PPh_3$ (15.7 mg, 0.06 mmol), and $\alpha,\alpha,\alpha$-trifluorotoluene (5.0 μL, as an internal standard) was transferred into a pressure-tight NMR tube. TFE (2.0 atm) and ethylene (3.0 atm) was charged in this

order into the reactor. The reaction was monitored at room temperature by $^{19}F$ NMR spectroscopy. After 2 h, the quantitative formation of the title compound was detected. $^{31}P\{^{1}H\}$ NMR (162 MHz, $C_6D_6$, rt, δ/ppm): 25.8 (quin, $J_{PF}$ = 24.2 Hz, 2P). $^{19}F$ NMR (376 MHz, $C_6D_6$, rt, δ/ppm): –139.0 (s, 4F), –101.0 (t, $J_{FP}$ = 24.2 Hz, 4F). Spectral data was identical to the previously-reported data.[S1]

**Stoichiometric reaction of 1 with ethylene (Scheme 2.5 (a))**

To a $C_6D_6$ solution (0.5 mL) of **1** (7.1 mg, 0.01 mmol) was added $\alpha,\alpha,\alpha$-trifluorotoluene (5.0 μL, as an internal standard). The solution was transferred into a pressure-tight NMR tube and ethylene (5.0 atm) was charged into the reactor. The reaction was monitored at room temperature by $^{19}F$ NMR spectroscopy. After 24 h, the formation of 5,5,6,6-tetrafluoro-1-hexene (**2**) was obtained in 80% yield.
$^{19}F$ NMR (376 MHz, $C_6D_6$, rt, δ/ppm): –138.7 (d, $J_{FH}$ = 54.6 Hz, 2F), –119.7 (t, $J_{FH}$ = 17.4 Hz, 2F). Spectral data of **2** was identical to the previously-reported data.[S2]

**Stoichiometric reaction of 1 with TFE (Scheme 2.5 (b))**

To a $C_6D_6$ solution (0.5 mL) of **1** (7.1 mg, 0.01 mmol) was added $\alpha,\alpha,\alpha$-trifluorotoluene (5.0 μL, as an internal standard). The solution was transferred into a pressure-tight NMR tube and TFE (5.0 atm) was charged into the reactor. The reaction was monitored at room temperature by $^{19}F$ NMR spectroscopy. After 24 h, complex **1** was completely consumed to give a complicated mixture.

**Ni(0)-catalyzed co-trimerization reaction of TFE with ethylene (Scheme 2.6 (a))**

A toluene solution (10.0 mL) of $Ni(cod)_2$ (275 mg, 1.0 mmol) and $PCy_3$ (560 mg, 2.0 mmol) was transferred into an autoclave reactor. TFE (5.0 atm) and ethylene (25.0 atm) was charged in this order into the reactor. The reaction mixture was stirred at 40 °C for 24 h. The yield of **2**, determined by $^{19}F$ NMR (using $\alpha,\alpha,\alpha$-trifluorotoluene as an internal standard) was estimated to 13% yield. An attempt to isolate the title compound **2** failed due to its higher volatility.

**Ni(0)-catalyzed co-trimerization reaction of TFE and 3 (Scheme 2.6 (b))**

To a $C_6D_6$ solution (0.5 mL) of $Ni(cod)_2$ (8.3 mg, 0.03 mmol) and $PCy_3$ (16.8 mg, 0.06 mmol) were added **3** (45.9 μL, 0.30 mmol) and $\alpha,\alpha,\alpha$-trifluorotoluene (5.0 μL, an internal standard). The solution was transferred into a pressure-tight NMR tube and TFE (3.5 atm) was charged into the reactor. The reaction tube was thermostated at room temperature and was monitored by $^{19}F$ NMR spectroscopy.

$^1H$ NMR (400 MHz, $CDCl_3$, rt, δ/ppm): 2.31–2.55 (m, 2H), 3.62–3.84 (AB quartet, $J_{HH}$ = 20.2 Hz, 2H), 4.15 (br, 1H), 5.24 (br, 2H), 5.77 (tt, $J_{HF}$ = 54.2, 2.9 Hz, 1H), 7.19–7.28 (m, 4H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$, rt, δ/ppm): 36.9 (t, $J_{CF}$ = 21.1 Hz), 38.6, 42.2, 109.4, 110.5 (tt, $J_{CF}$ = 249.5, 41.2 Hz), 118.0 (tt, $J_{CF}$ = 247.5, 29.2 Hz), 124.6, 124.7 (br), 127.1, 127.4, 141.5, 144.9, 152.4. $^{19}F$ NMR (376 MHz, $CDCl_3$, rt, δ/ppm): –139.3 ~ –137.4 (doublet of AB quartet, $J_{FH}$ = 54.2, $J_{FF}$ = 301.0 Hz, 2F), –117.3 ~ –115.5 (multiplet of AB quartet, $J_{FF}$ = 270.4 Hz, 2F). HRMS Calcd for $C_{13}H_{12}F_4$ 244.0875, Found m/z 244.0876.

**Stoichiometric reaction of 1 with phenyl 1-propenylketone (Scheme 2.7)**

To the toluene solution (30 mL) of **1** (427 mg, 0.60 mmol) was added phenyl-1-propenyl ketone (86.4 μL, 0.60 mmol). The resulting solution was transferred into a sealed tube reactor, and the reaction mixture was thermostated at 100℃ for 24 h. Purification by silica gel column chromatography gave **5** as a yellow liquid (100 mg, 61%).

**(*E*)-5**: $^1H$ NMR (400 MHz, $CDCl_3$, rt, δ/ppm): 2.21 (s, 3H), 2.25 (m, 2H), 2.53 (m, 2H), 5.77 (tt, $J_{HF}$ = 54.1, 2.5 Hz, 1H), 6.84 (s, 1H), 7.40–8.05 (m, 5H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$, rt, δ/ppm): 19.5, 28.0 (t, $J_{CF}$ = 22.2 Hz), 31.9 (t, $J_{CF}$ = 3.8 Hz), 122.5, 127.8–139.2 (m), 157.2, 190.8. $^{19}F$ NMR (376 MHz, $CDCl_3$, rt, δ/ppm): –138.2 (d, $J_{FH}$ = 53.4 Hz, 2F), –119.3 (t, $J_{FH}$ = 17.8 Hz, 2F).

**(*Z*)-5**: $^1H$ NMR (400 MHz, $CDCl_3$, rt, δ/ppm): 2.05 (s, 3H), 2.25 (m, 2H), 2.84 (m, 2H), 5.80 (tt, $J_{HF}$ = 53.8, 3.2 Hz, 1H), 6.77 (s, 1H), 7.40–8.05 (m, 5H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$, rt, δ/ppm): 25.6 (t, $J_{CF}$ = 4.5 Hz), 25.7, 28.5 (t, $J_{CF}$ = 22.6 Hz), 121.7, 127.8–139.2 (m), 156.0, 191.6. $^{19}F$ NMR (376 MHz, $CDCl_3$, rt, δ/ppm): –138.7 (d, $J_{FH}$ = 52.9 Hz, 2F), –119.9 (t, $J_{FH}$ = 17.6 Hz, 2F). HRMS Calcd for $C_{14}H_{14}F_4O$ 274.0981,

Found m/z 274.0980 (as an *E*/*Z* mixture).

**Isolation of 6 (Scheme 2.7)**

To a toluene suspension (2.5 mL) of **1** (71 mg, 0.10 mmol) was added phenyl-1-propenyl ketone (14.4 $\mu$L, 0.10 mmol). The resulting solution was transferred into a sealed tube reactor, and the reaction mixture was thermostated at 40℃ for 48 h. All volatiles were removed under reduced pressure, and the residue was purified by recrystallization from toluene/hexane at –30 °C, giving the title compound **6** (34 mg, 0.058 mmol, 58%) as yellow solid.

$^{1}$H NMR (400 MHz, $C_6D_6$, rt, δ/ppm): 0.88 (d, $J_{HH}$ = 6.3 Hz, 3H), 1.60–1.75 (m, 1H), 2.01–2.31 (br m, 2H), 2.80 (br, 1H), 3.11 (br, 1H), 4.93 (br, 1H), 6.87–7.09 (m, 11H), 7.12–7.19 (obscured by $C_6D_5H$, 1H), 7.53–7.65 (br, 2H), 7.70–7.89 (m, 6H). $^{13}$C{$^{1}$H}NMR (100 MHz, $C_6D_6$, rt, δ/ppm): 23.3, 30.7 (br), 33.3, 79.9 (m), 127.7, 128.7 (d, $J_{CP}$ = 9.7 Hz), 128.8, 130.5, 131.3 (br s), 132.1 (d, $J_{CP}$ = 42.4 Hz), 134.7 (d, $J_{CP}$ = 12.3 Hz), 157.6 (m). Resonances attributable to the $CF_2CF_2$ moiety could not be detected due to multiple $^{13}$C–$^{19}$F couplings. $^{31}$P{$^{1}$H} NMR (162 MHz, $C_6D_6$, rt, δ/ppm): 26.3 (d, $J_{PF}$ = 61.9 Hz, 1P). $^{19}$F NMR (376 MHz, $C_6D_6$, rt, δ/ppm): –113.5 (d, $J_{FF}$ = 247.5 Hz, 1F), –110.3 (d, $J_{FF}$ = 247.5 Hz, 1F), –93.1 (dd, $J_{FF}$ = 246.1, $J_{FP}$ = 61.9 Hz, 1F), –87.8 (d, $J_{FF}$ = 246.1 Hz, 1F). Anal. Calcd for $C_{32}H_{29}F_4NiOP$: C, 64.57; H, 4.91. Found: C, 65.04; H, 4.98.

**An attempt to the Ni(0)-catalyzed cross-trimerization reaction of TFE, ethylene and phenyl 1-propenyl ketone (Scheme 2.8)**

A $C_6D_6$ solution of $Ni(cod)_2$ (8.3 mg, 0.03 mmol), $PCy_3$ (16.8 mg, 0.06 mmol), phenyl-1-propenyl ketone (24.4 μL, 0.17 mmol), and $\alpha,\alpha,\alpha$-trifluorotoluene (5.0 μL, as an internal standard) was transferred into a pressure-tight NMR tube. TFE (2.0 atm) and ethylene (3.0 atm) was charged in this order into the reactor. The reaction tube was monitored at room temperature by $^{19}$F NMR spectroscopy. After 24 h, $^{19}$F NMR analysis indicated the occurrence of the undesired oxidative cyclization of TFE and phenyl-1-propenyl ketone, giving an $\eta^3$-oxallyl nickelacycle (**7**).

Spectral data for **7**: $^{1}$H NMR (600 MHz, $C_6D_6$, rt, δ/ppm): 1.14–1.30 (m, 6H), 1.31 (d,

$J_{HH}$ = 6.8 Hz, 3H), 1.60–1.84 (m, 18H), 1.88–2.08 (m, 6H), 2.18–2.25 (m, 3H), 2.77 (qddd, $J_{HC}$ = 6.8, 11.6, $J_{HF}$ = 4.1, 23.7 Hz, 1H), 4.38 (ddm, $J_{HC}$ = 11.6, $J_{HP}$ = 2.0 Hz, 1H), 7.10–7.20 (m, 3H), 7.83 (d, $J_{HH}$ = 7.8 Hz, 2H). $^{13}C\{^{1}H\}$NMR (150 MHz, $C_6D_6$, rt, δ/ppm): 11.3 (q, $J_{CH}$ = 129.0 Hz), 26.5 (t, $J_{CH}$ = 129.0 Hz), 27.8 (td, $J_{CH}$ = 127.2, $J_{PC}$ = 10.0 Hz), 28.0 (td, $J_{CH}$ = 125.2, $J_{CP}$ = 11.6 Hz), 29.7 (t, $J_{CH}$ = 128.5 Hz), 30.8 (td, $J_{CH}$ = 129.0, $J_{CP}$ = 1.2 Hz), 34.0 (dd, $J_{CH}$ = 128.8, $J_{CP}$ = 19.9 Hz), 37.4 (ddd, $J_{CH}$ = 127.2, $J_{CF}$ = 23.2, 23.7 Hz), 74.8 (ddd, $J_{CH}$ = 154.8, $J_{CP}$ = 7.4, $J_{CF}$ = 11.6 Hz), 128.8 (dd, $J_{CH}$ = 160.2, 5.6 Hz), 129.0 (ddd, $J_{CH}$ = 159.1, 6.3, 6.3 Hz), 130.1 (m), 131.7 (dt, $J_{CH}$ = 161.1, 7.4 Hz), 136.1 (m), 136.3, 159.1. $^{31}P\{^{1}H\}$ NMR (162 MHz, $C_6D_6$, rt, δ/ppm): 37.1 (d, $J_{PF}$ = 15.6 Hz, 1P). $^{19}F$ NMR (564 MHz, $C_6D_6$, rt, δ/ppm): –91.6 (dd, $J_{FF}$ = 8.3, 241.6 Hz, 1F), –104.4 (dddd, $J_{FF}$ = 3.0, 18.6, 241.6, $J_{FP}$ = 15.6 Hz, 1F), –106.1 (dddd, $J_{FF}$ = 3.0, 8.3, 222.5, $J_{FH}$ = 4.1 Hz, 1F), –132.2 (ddd, $J_{FF}$ = 18.6, 222.5, $J_{FH}$ = 23.7 Hz, 1F).

**References for Experimental Section**


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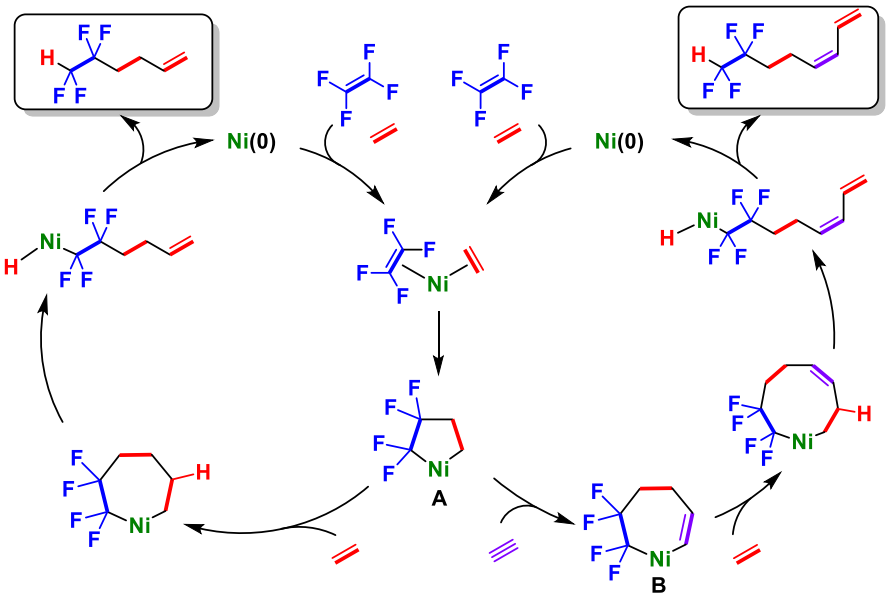
S2 W. R. Dolbier Jr., X. X. Rong, M. D. Bartberger, H. Koroniak, B. E. Smart, Z.-Y. J. Yang, *Chem. Soc., Perkin Trans. 2* **1998**, 219.

# Chapter 3

# Ni(0)-Catalyzed Cross-Tetramerization Reaction of TFE, Ethylene, and Alkyne

## 3.1 Introduction

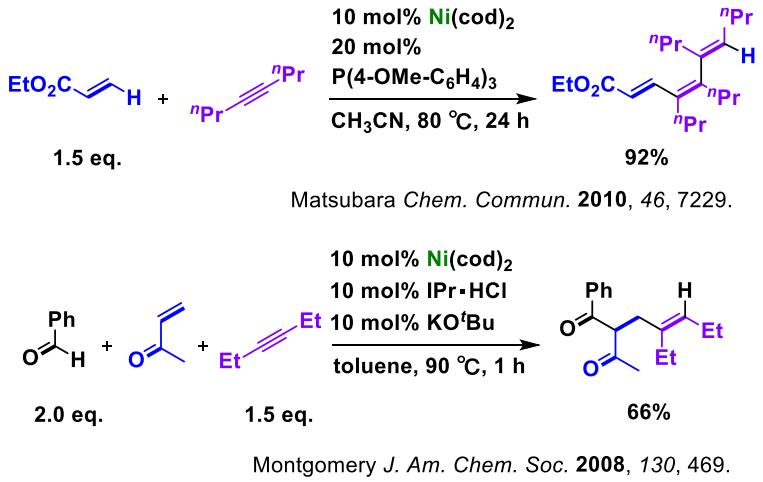
As organofluorine compounds are important components for a variety of commercial products, such as agrochemicals, drugs, and advanced materials,[1] economical organofluorine feedstocks are needed in bulk as starting materials for their syntheses. In this context, we are interested in broadening the scope of TFE as a synthetic reagent. Previously, we have reported the coupling of TFE with various organometallic reagents to yield (*α*,*β*,*β*-trifluoro)styrene derivatives.[2] Recently, we became interested in the incorporation of TFE into organic frameworks as tetrafluoroethylene bridges (−$CF_2CF_2$−).[3]




**Scheme 3.1.** Working Hypothesis.

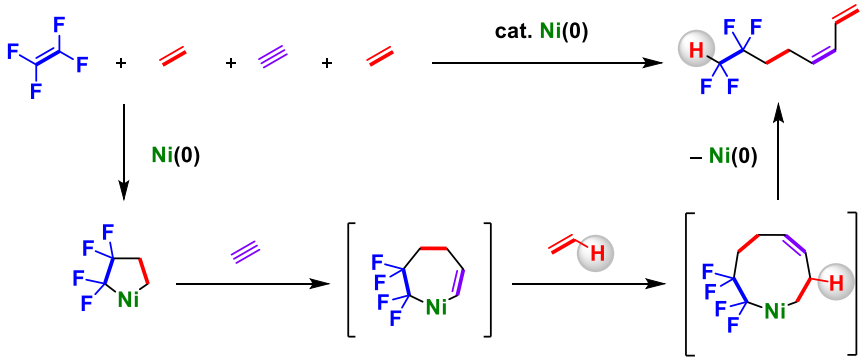
As described in Chapter 2, we discovered that **A**, generated by the oxidative cyclization of TFE and ethylene with Ni(0), is a key reaction intermediate in the Ni(0)-catalyzed co-trimerization of TFE and ethylene (Scheme 3.1, left). We envisioned that the migratory insertion of an alkyne rather than ethylene into the Ni−$CH_2$ bond in **A**,

even in the presence of an excess amount of TFE and ethylene, should provide a synthetic route to a cross-tetramer that consists of TFE, two molecules of ethylene, and an alkyne (Scheme 3.1, right). This cross-tetramer should be formed due to the inability of the seven-membered nickelacycle (**B**) to undergo *β*-hydride elimination. Although a few transition-metal-catalyzed co- or cross-trimerizations of unsaturated compounds have been reported,[4] a cross-tetramerization has not yet been reported (Scheme 3.2).




**Scheme 3.2.** Ni(0)-Catalyzed Co- or Cross-Trimerization Reactions.

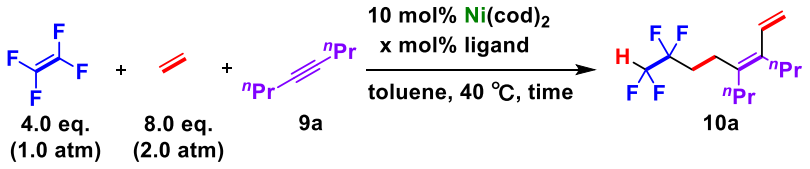
Described in this chapter is a Ni(0)-catalyzed cross-tetramerization reaction of TFE, ethylene, and alkyne (Scheme 3.3). In addition, a Ni(0)-catalyzed cross-tetramerization of TFE, styrene, alkyne, and ethylene was developed. These catalytic reactions might proceed via partially fluorinated five- and seven-membered nickelacycle key intermediates.



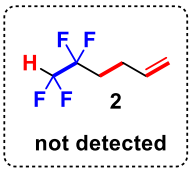

**Scheme 3.3.** Ni(0)-Catalyzed Cross-Tetramerization of TFE, Ethylene, and Alkyne.

### 3.2 Optimization of Reaction Conditions

Based on the optimum reaction conditions in the co-trimerization of TFE and ethylene, the toluene solution of 4-octyne (**9a**) at 40 °C was exposed for 24 h to a gas mixture containing TFE (partial pressure = 1.0 atm) and ethylene (partial pressure = 2.0 atm) in the presence of $Ni(cod)_2$ and $PCy_3$ (10 and 20 mol %, respectively). As a result, a desired cross-tetramer (**10a**), a 1,3-diene derivative with a 3,3,4,4-tetrafluorobutyl chain, was formed in quantitative yield (Table 3.1). Encouraged by this result, optimization of the reaction conditions by varying the ligands was conducted (runs 1−3). However, all attempts confirmed that $PCy_3$ is indeed the optimal ligand in this cross-tetramerization, similar to the co-trimerization of TFE and ethylene. Subsequently, the effect of the $PCy_3$/Ni(0) ratio on the catalytic performance was examined. The use of 4 equiv of $PCy_3$ relative to $Ni(cod)_2$ accelerated the catalytic reaction, while using 1 equiv of $PCy_3$ led to notable retardations (runs 4−6). Thus, the optimal reaction conditions were determined as 10 mol % $Ni(cod)_2$ and 40 mol % $PCy_3$ in toluene at 40 °C. It should be emphasized that the potential side-reaction products, i.e., the co-trimer **2** consists of TFE and two molecules of ethylene, the cyclic trimer of **9a** were not generated under the optimal reaction conditions.




| run | ligand (x mol%) | time (h) | $^{19}$F NMR yield (%) |
|---|---|---|---|
| 1 | $PCy_3$ (20) | 24.0 | > 99 |
| 2 | $PPh_3$ (20) | 24.0 | 32 |
| 3[a] | IPr (10) | 24.0 | 0 |
| 4 | $PCy_3$ (10) | 24.0 | 6 |
| 5 | $PCy_3$ (20) | 0.5 | 7 |
| 6 | $PCy_3$ (40) | 0.5 | > 99 |



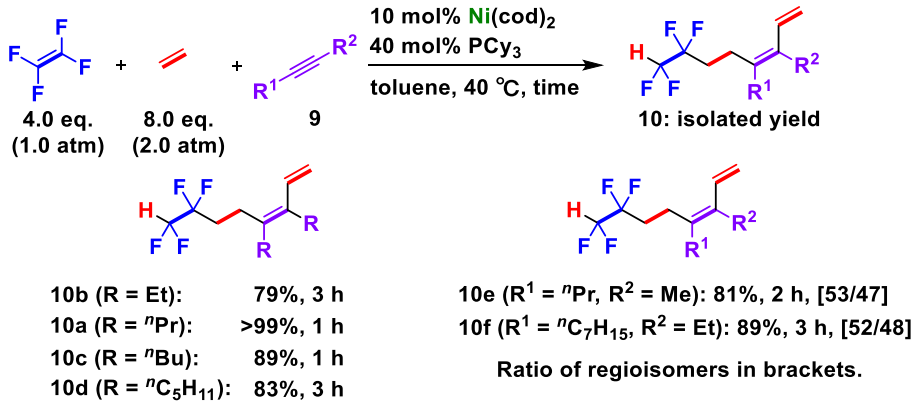

[a]The cyclic trimer of 9a was formed in 100% yield.

**Table 3.1.** Optimization of Reaction Conditions.

### 3.3 Substrate Scope

With the optimal reaction conditions in hand, the scope and limitations of this Ni(0)/$PCy_3$-catalyzed cross-tetramerization with respect to various alkynes was

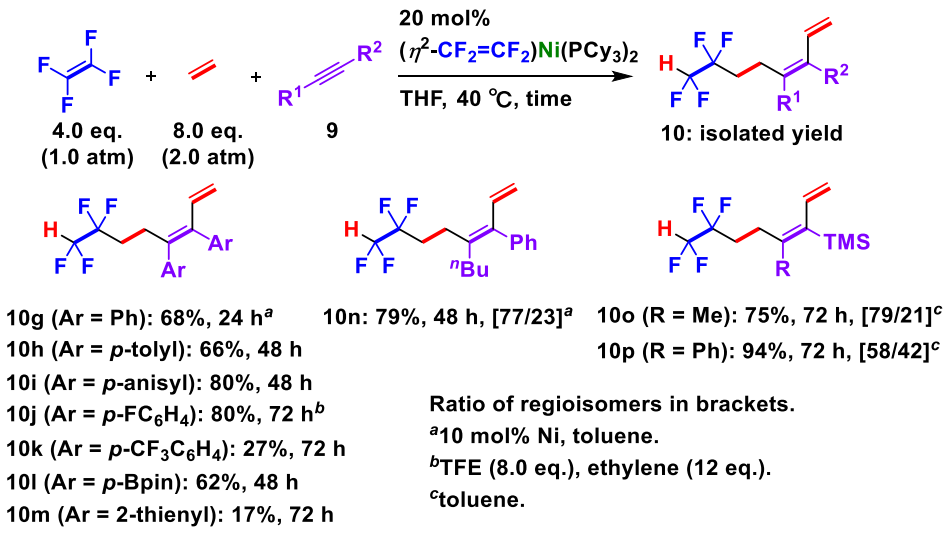
examined (Scheme 3.4). Compound **10a** could be successfully isolated in quantitative yield from the reaction of **9a** with a gas mixture containing TFE and ethylene. The use of symmetrical aliphatic alkynes, such as 3-hexyne (**9b**), 5-decyne (**9c**), and 6-undecyne (**9d**), afforded the corresponding products (**10b**, **10c**, and **10d**) in good to excellent yields, whereas the unsymmetrical aliphatic alkynes (**9e** and **9f**) yielded a mixture of regioisomers (**10e** and **10f**) in poor selectivity.




**Scheme 3.4.** Substrate Scope (Alkyne 1).

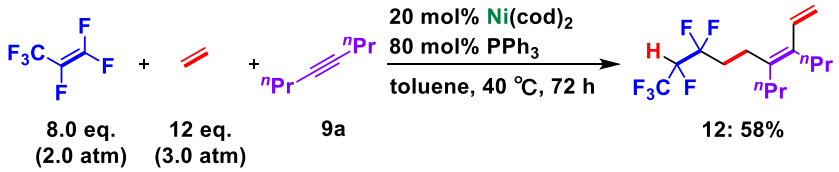
When diphenylacetylene (**9g**) was used, the corresponding cross-tetramer (**10g**) was obtained in 9% yield (estimated by $^{19}$F NMR spectroscopy) due to the rapid trimerization of **9g** prior to pressurization with TFE and ethylene. To inhibit this undesirable trimerization of **9g**, ($\eta^2$-$CF_2$=$CF_2$)Ni($PCy_3$)$_2$ (**11**) was used as a catalyst precursor instead of Ni(cod)$_2$/$PCy_3$.[5] As a result, **9g** was transformed into **10g** in 68% yield (Scheme 3.5).

Under these reaction conditions, a variety of diarylacetylenes were able to participate in this cross-tetramerization (**10g**–**10m**). The use of unsymmetrical alkyne (**9n**) gave the corresponding product (**10n**) with moderate regioselectivity. Moreover, the reactions with 1-methyl-2-(trimethylsilyl)acetylene (**9o**) and 1-phenyl-2-(trimethylsilyl)acetylene (**9p**) furnished the corresponding 1,3-diene derivatives (**10o** and **10p**) in excellent yield. In the case of a terminal alkyne such as 1-octyne, a desired product was not obtained at all due to the rapid trimerization of the alkyne.




**Scheme 3.5.** Substrate Scope (Alkyne 2).

When the scope and limitations with respect to the perfluoroalkene component was examined, hexafluoropropylene (HFP) could participate in this cross-tetramerization by employing a $Ni(cod)_2/PPh_3$ catalyst to afford desired cross-tetramer (**12**) in 58% yield as a single regioisomer (Scheme 3.6). $PPh_3$ was used as a ligand due to the occurrence of an undesired reaction between HFP and $PCy_3$.[6]

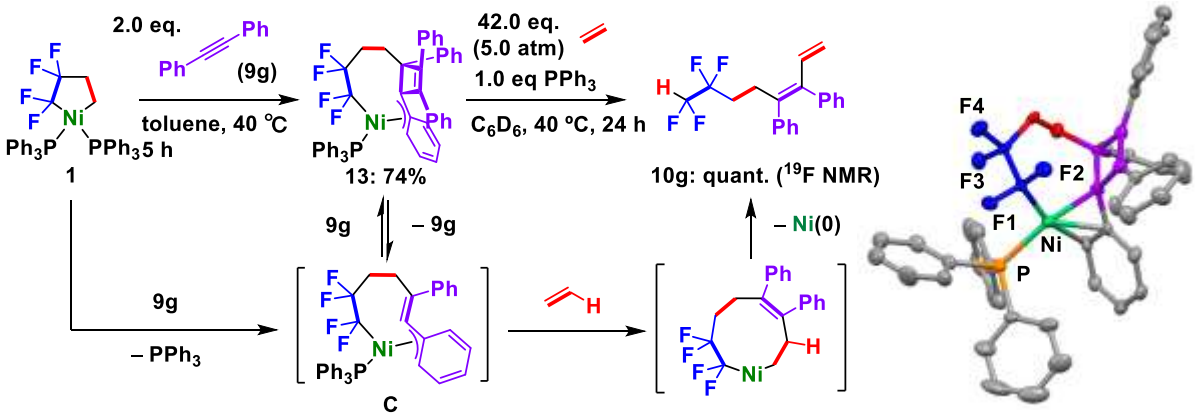



**Scheme 3.6.** Substrate Scope (Perfluoroalkene).

### 3.4 Stoichiometric Reactions

To explore the reaction mechanism, stoichiometric reaction between **1** and 2 equiv of **9g** in toluene at 40 °C for 5 h to furnish nickelacycle **13** in 74% isolated yield (Scheme 3.7).[7] The X-ray diffraction study of **13** clearly demonstrated that the phenyl ring in **13** coordinated to nickel to possess an $\eta^3$-$\pi$-benzyl structure and that a cyclobutene ring should be formed via a [2+2] cycloaddition of **9g** and a C=C bond in a tentative seven-membered nickelacycle (**C**), generated by an insertion of another molecule of **9g** into a Ni−$CH_2$ bond in **1**.

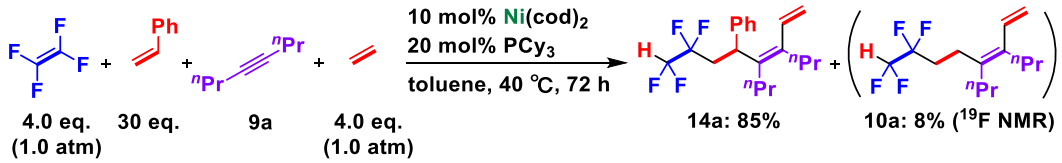
When **13** in $C_6D_6$ was treated in the presence of an equimolar amount of $PPh_3$ with ethylene (5.0 atm) at 40 °C for 24 h, cross-tetramer **10g** was obtained in quantitative yield (Scheme 3.7). This result clearly indicates that an equilibrium between **13** and **C** exists, and that a gradual insertion of ethylene to **C** should occur to yield **10g**. In other words, **13** would be located outside the catalytic cycle and exist as a resting state. In the $^{31}P$ NMR spectrum of the crude reaction mixture, the concomitant formation of $(\eta^2\text{-}CH_2{=}CH_2)Ni(PPh_3)_2$ was observed.[8]




**Scheme 3.7.** Formation and Reactivity of Nickelacycle **13**.

### 3.5 Ni(0)-Catalyzed Cross-Tetramerization Reaction with Styrene

Previously, our group reported the oxidative cyclization of TFE and styrene with Ni(0), together with the reactivity of the generated five-membered nickelacycle.[9] Based on this report, styrene was employed as a fourth component, which resulted in smooth progress of the catalytic reaction with TFE, **9a**, and ethylene, yielding 7,7,8,8-tetrafluoro-5-phenyl-3,4-dipropyl-1,3-octadiene (**14a**) in 85% yield (Scheme 3.8). In this case, **10a** (8%) was also observed as a minor product. In the catalytic reaction with styrene, the formation of a kinetically less favored five-membered nickelacycle generated by the oxidative cyclization of TFE and styrene with Ni(0) requires the use of an excess of styrene.




**Scheme 3.8.** Ni(0)-Catalyzed Cross-Tetramerization Reaction with Styrene.

## 3.6 Conclusion

In chapter 3, the Ni(0)-catalyzed cross-tetramerization reaction of TFE, ethylene, and alkyne is described. This is an unprecedented example of a highly selective transition-metal-catalyzed cross-tetramerization. This reaction allows the effective use of TFE as a starting material for the preparation of organofluorine compounds via the oxidative cyclization of TFE and unsaturated compounds with Ni(0).

## 3.7 References and Notes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[2] a) M. Ohashi, T. Kambara, T. Hatanaka, H. Saijo, R. Doi, S. Ogoshi, *J. Am. Chem. Soc.* **2011**, *133*, 3256; b) M. Ohashi, H. Saijo, M. Shibata, S. Ogoshi, *Eur. J. Org. Chem.* **2013**, *2013*, 443; c) H. Saijo, H. Sakaguchi, M. Ohashi, S. Ogoshi, *Organometallics* **2014**, *33*, 3669; d) K. Kikushima, H. Sakaguchi, H. Saijo, M. Ohashi, S. Ogoshi, *Chem. Lett.* **2015**, *44*, 1019.

[3] a) H. Saijo, M. Ohashi, S. Ogoshi, *J. Am. Chem. Soc.* **2014**, *136*, 15158; b) M. Ohashi, T. Adachi, N. Ishida, K. Kikushima, S. Ogoshi, *Angew. Chem. Int. Ed.* **2017**, *56*, 11911.

[4] a) T. Sambaiah, L.-P. Li, D.-J. Huang, C.-H. Lin, D. K. Rayabarapu, C.-H. Cheng, *J. Org. Chem.* **1999**, *64*, 3663; b) A. Herath, W. Li, J. Montgomery, *J. Am. Chem. Soc.* **2008**, *130*, 469; c) Y. Nakao, H. Idei, K. S. Kanyiva, T. Hiyama, *J. Am. Chem. Soc.* **2009**, *131*, 15996; d) H. Horie, T. Kurahashi, S. Matsubara, *Chem. Commun.* **2010**, *46*, 7229; e) S. Ogoshi, A. Nishimura, M. Ohashi, *Org. Lett.* **2010**, *12*, 3450; f) M. Kobayashi, K. Tanaka, *Chem. Eur. J.* **2012**, *18*, 9225.

[5] M. Ohashi, M. Shibata, H. Saijo, T. Kambara, S. Ogoshi, *Organometallics* **2013**, *32*, 3631.

[6] D. J. Burton, S. Shinya, R. D. Howells, *J. Am. Chem. Soc.* **1979**, *101*, 3689.

[7] When the reaction of **1** was conducted with an equimolar amount of **9g**, 50% of **1** was converted into **13** while the rest remained unchanged.

[8] K. R. Pörschke, Y. H. Tsay, C. Krüger, *Angew. Chem.* **1985**, *97*, 334.

[9] M. Ohashi, Y. Ueda, S. Ogoshi, *Angew. Chem. Int. Ed.* **2017**, *56*, 2435.

## 3.8 Experimental Section

**Optimization of reaction conditions for Ni(0)-catalyzed cross-tetramerization reaction of TFE, ethylene, and 4-octyne (9a) (Table 3.1)**

All catalytic reactions were conducted by using an autoclave reactor (BüchiGlasuster, tinyclave steel: volume: 50.0 mL). The yield of **10a** was determined by $^{19}$F NMR analysis using *α*,*α*,*α*-trifluorotoluene as an internal standard.

**The evaluation of ligands (Table 3.1; runs 1–3)**

A toluene (1.5 mL) solution of $Ni(cod)_2$ (13.7 mg, 0.05 mmol), a given ligand (0.05 or 0.10 mmol), and **9a** (0.50 mmol) was transferred into the autoclave reactor. Then, TFE (1.0 atm, c.a. 2.0 mmol) and ethylene (2.0 atm, c.a. 4.0 mmol) was charged in this order into the reactor. The reactor was thermostated at 40 °C for 24 h.

**The evaluation of the amount of the ligand (Table 3.1; runs 4–6)**

A toluene (1.5 mL) solution of $Ni(cod)_2$ (13.7 mg, 0.05 mmol), $PCy_3$ (0.05, 0.10 or 0.20 mmol), and **9a** (0.50 mmol) was transferred into the autoclave reactor. Then, TFE (1.0 atm, c.a. 2.0 mmol) and ethylene (2.0 atm, c.a. 4.0 mmol) was charged in this order into the reactor. The reactor was thermostated at 40 °C for a given time.

**Scope of substrate with respect to alkynes in the Ni(0)-catalyzed cross-tetramerization reaction (Schemes 3.4 and 3.5)**

**General procedure *A* for isolation of the product**

A toluene solution (1.5 mL) of $Ni(cod)_2$ (13.7 mg, 0.05 mmol), $PCy_3$ (56.0 mg, 0.20 mmol), and alkyne (**9**: 0.50 mmol) was transferred into an autoclave reactor (volume: 50.0 mL). Then, TFE (1.0 atm, c.a. 2.0 mmol) and ethylene (2.0 atm, c.a. 4.0 mmol) was charged in this order into the reactor. The reaction mixture was stirred at 40 °C for a given time. After redundant TFE and ethylene were purged from the reactor (*caution*: The reaction mixture must be handled in well ventilated fume hood!!), the reaction mixture was exposed to air to quench the catalyst. Insoluble was removed by filtration, and all volatiles were then removed under reduced pressure. The crude product was purified by silica gel column chromatography, giving the title compound **10**.

**General procedure *B* for isolation of the product**

A toluene solution (1.5 mL) of ($\eta^2$-$CF_2$=$CF_2$)$Ni(PCy_3)_2$ (**11**: 35.9 mg, 0.05 mmol) and alkyne (**9**: 0.50 mmol) was transferred into an autoclave reactor (volume: 50.0 mL). Then, TFE (1.0 atm, c.a. 2.0 mmol) and ethylene (2.0 atm, c.a. 4.0 mmol) was charged in this order into the reactor. The reaction mixture was stirred at 40 °C for a given time. After redundant TFE and ethylene were purged from the reactor (*caution*: The reaction mixture must be handled in well ventilated fume hood!!), the reaction mixture was exposed to air to quench the catalyst. Insoluble was removed by filtration, and all volatiles were then removed under reduced pressure. The crude product was purified by silica gel column chromatography, giving the title compound **10**.

**General procedure *C* for isolation of the product**

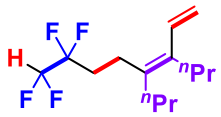
A THF solution (6.0 mL) of **11** (71.8 mg, 0.10 mmol) and alkyne (**9**: 0.50 mmol) was transferred into an autoclave reactor (volume: 50.0 mL). Then, TFE (1.0 atm, c.a. 2.0 mmol) and ethylene (2.0 atm, c.a. 4.0 mmol) was charged in this order into the reactor. The reaction mixture was stirred at 40 °C for a given time. After redundant TFE and ethylene were purged from the reactor (*caution*: The reaction mixture must be handled in well ventilated fume hood!!), the reaction mixture was exposed to air to quench the

catalyst. Insoluble was removed by filtration, and all volatiles were then removed under reduced pressure. The crude product was purified by silica gel column chromatography, giving the title compound **10**.

**General procedure *D* for isolation of the product**

A toluene solution (3.0 mL) of **11** (71.8 mg, 0.10 mmol) and alkyne (**9**: 0.50 mmol) was transferred into an autoclave reactor (volume: 50.0 mL). Then, TFE (1.0 atm, c.a. 2.0 mmol) and ethylene (2.0 atm, c.a. 4.0 mmol) was charged in this order into the reactor. The reaction mixture was stirred at 40 °C for a given time. After redundant TFE and ethylene were purged from the reactor (*caution*: The reaction mixture must be handled in well ventilated fume hood!!), the reaction mixture was exposed to air to quench the catalyst. Insoluble was removed by filtration, and all volatiles were then removed under reduced pressure. The crude product was purified by silica gel column chromatography, giving the title compound **10**.

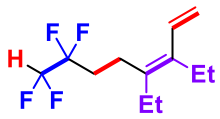
**(*Z*)-7,7,8,8-tetrafluoro-3,4-dipropyl-1,3-octadiene (10a)**




By following the general procedure ***A***, the reaction with 4-octyne (**9a**: 73.2 μL, 0.50 mmol) was conducted for 1 h to give **10a** (135.2 mg, >99%) as colorless oil.

$^{1}$H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): 0.85 (t, $J_{HH}$ = 7.6 Hz, 3H), 0.86 (t, $J_{HH}$ = 7.6 Hz, 3H), 1.22–1.38 (m, 4H), 1.85–1.99 (m, 2H), 2.00 (t, $J_{HH}$ = 8.0 Hz, 2H), 2.12 (t, $J_{HH}$ = 8.0 Hz, 2H), 2.31–2.35 (m, 2H), 4.98 (d, $J_{HH}$ = 10.8 Hz, 1H), 5.11 (d, $J_{HH}$ = 17.2 Hz, 1H), 5.63 (t, $J_{HF}$ = 54.0 Hz, 1H), 6.53 (dd, $J_{HH}$ = 10.8, 17.2 Hz, 1H). $^{13}$C{$^{1}$H} NMR (100 MHz, $CDCl_3$, rt, δ/ppm): 14.3, 14.3, 22.0, 22.3 (t, $J_{CF}$ = 4.0 Hz), 22.6, 29.6 (t, $J_{CF}$ = 24.0 Hz), 29.8, 35.3, 110.3 (tt, $J_{CF}$ = 248.0, 42.0 Hz), 112.9, 117.7 (tt, $J_{CF}$ = 246.0, 29.0 Hz), 133.7, 136.7, 136.7. $^{19}$F NMR (376 MHz, $CDCl_3$, rt, δ/ppm): –119.9 (t, $J_{FH}$ = 18.8 Hz, 2F), –138.5 (d, $J_{FH}$ = 52.6 Hz, 2F). HRMS Calcd for $C_{14}H_{22}F_4$ 266.1658, Found *m*/*z* 266.1654.

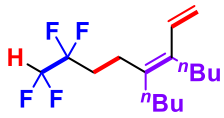
**(*Z*)-3,4-diethyl-7,7,8,8-tetrafluoro-1,3-octadiene (10b)**




By following the general procedure ***A***, the reaction with 3-hexyne (**9b**: 56.8 μL, 0.50 mmol) was conducted for 3 h to give **10b** (95.2 mg, 79%) as colorless oil.

$^{1}$H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): 0.92 (t, $J_{HH}$ = 7.6 Hz, 3H), 0.95 (t, $J_{HH}$ = 7.6 Hz, 3H), 1.85–1.99 (m, 2H), 2.05 (q, $J_{HH}$ = 7.6 Hz, 2H), 2.18 (q, $J_{HH}$ = 7.6 Hz, 2H), 2.31–2.36 (m, 2H), 5.00 (d, $J_{HH}$ = 11.2 Hz, 1H), 5.14 (d, $J_{HH}$ = 17.6 Hz, 1H), 5.64 (tt, $J_{HF}$ = 54.4, 2.4 Hz, 1H), 6.52 (dd, $J_{HH}$ = 11.2, 17.6 Hz, 1H). $^{13}$C{$^{1}$H} NMR (100 MHz, $CDCl_3$, rt, δ/ppm): 13.2, 14.0, 20.4, 21.9 (t, $J_{CF}$ = 4.0 Hz), 25.8, 29.5 (t, $J_{CF}$ = 22.0 Hz), 110.3 (tt, $J_{CF}$ = 248.0, 43.0 Hz), 112.8, 117.7 (tt, $J_{CF}$ = 245.0, 30.0 Hz), 133.2, 134.7, 137.7. $^{19}$F NMR (376 MHz, $CDCl_3$, rt, δ/ppm): –119.9 (t, $J_{FH}$ = 18.8 Hz, 2F), –138.5 (d, $J_{FH}$ = 56.4 Hz, 2F). HRMS Calcd for $C_{12}H_{18}F_4$ 238.1345, Found *m/z* 238.1347.

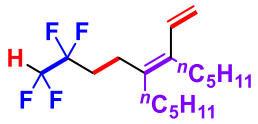
**(*Z*)-3,4-dibutyl-7,7,8,8-tetrafluoro-1,3-octadiene (10c)**




By following the general procedure ***A***, the reaction with 5-decyne (**9c**: 89.7 μL, 0.50 mmol) was conducted for 1 h to give **10c** (131.6 mg, 89%) as colorless oil.

$^{1}$H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): 0.75 (t, 3H, $J_{HH}$ = 7.6 Hz), 0.85 (t, 3H, $J_{HH}$ = 7.6 Hz), 1.34–1.53 (m, 8H), 1.98–2.10 (m, 2H), 2.15 (t, $J_{HH}$ = 8.0 Hz, 2H), 2.27 (t, $J_{HH}$ = 8.8 Hz, 2H), 2.44–2.48 (m, 2H), 5.11 (d, $J_{HH}$ = 10.8 Hz, 1H), 5.25 (d, $J_{HH}$ = 17.6 Hz, 1H), 5.76 (tt, $J_{HF}$ = 54.0, 2.8 Hz, 1H), 6.66 (dd, $J_{HH}$ = 10.8, 17.6 Hz, 1H). $^{13}$C{$^{1}$H} NMR (100 MHz, $CDCl_3$, rt, δ/ppm): 13.9, 14.0, 22.4 (t, $J_{CF}$ = 4.0 Hz), 23.0, 23.1, 27.4, 29.6 (t, $J_{HH}$ = 22.0 Hz), 31.0, 31.7, 32.8, 110.3 (tt, $J_{CF}$ = 248.0, 41.0 Hz), 112.7, 117.7 (tt, $J_{CF}$ = 245.0, 29.0 Hz), 133.7, 136.8, 136.8. $^{19}$F NMR (376 MHz, $CDCl_3$, rt, δ/ppm): –119.9 (t, $J_{FH}$ = 18.8 Hz, 2F), –138.5 (d, $J_{FH}$ = 52.6 Hz, 2F). HRMS Calcd for $C_{16}H_{26}F_4$ 294.1971, Found *m/z* 294.1965.

**(*Z*)-7,7,8,8-tetrafluoro-3,4-dipentyl-1,3-octadiene (10d)**

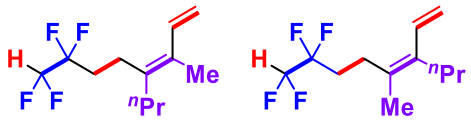



By following the general procedure ***A***, the reaction with 6-dodecyne (**9d**: 106.3 μL, 0.50 mmol) was conducted for 3 h to give **10d** (136.1 mg, 83%) as colorless oil.

$^1$H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): 0.92 (t, 3H, $J_{HH}$ = 7.7 Hz), 1.04 (t, 3H, $J_{HH}$ = 7.7 Hz), 1.29–1.54 (m, 12H), 2.11–2.12 (m, 2H), 2.16 (t, $J_{HH}$ = 8.0 Hz, 2H), 2.29 (t, $J_{HH}$ = 8.8 Hz, 2H), 2.44–2.50 (m, 2H), 5.13 (d, $J_{HH}$ = 10.8 Hz, 1H), 5.26 (d, $J_{HH}$ = 17.2 Hz, 1H), 5.77 (tt, $J_{HF}$ = 54.0, 2.8 Hz, 1H), 6.68 (dd, $J_{HH}$ = 10.8, 17.2 Hz, 1H). $^{13}$C{$^1$H} NMR (100 MHz, $CDCl_3$, rt, δ/ppm): 13.9, 14.0, 22.4 (t, $J_{CF}$ = 4.0 Hz), 22.5, 27.7, 28.5, 29.2, 29.6 (t, $J_{CF}$ = 24.0 Hz), 32.1, 32.3, 33.1, 33.1, 110.3 (tt, $J_{CF}$ = 248.0, 41.0 Hz), 112.7, 117.7 (tt, $J_{CF}$ = 245.0, 29.0 Hz), 133.7, 133.7, 136.7. $^{19}$F NMR (376 MHz, $CDCl_3$, rt, δ/ppm): –119.9 (t, $J_{FH}$ = 18.8 Hz, 2F), –138.5 (d, $J_{FH}$ = 52.6 Hz, 2F). HRMS Calcd for $C_{18}H_{30}F_4$ 322.2284, Found *m/z* 322.2281.

**(*Z*)-7,7,8,8-tetrafluoro-3-methyl-4-propyl-1,3-octadiene (10e)**

**(*Z*)-7,7,8,8-tetrafluoro-4-methyl-3-propyl-1,3-octadiene (10e')**



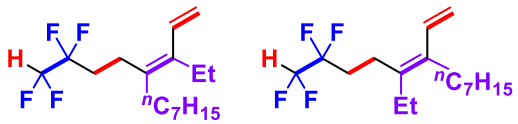

By following the general procedure ***A***, the reaction with 2-hexyne (**9e**: 56.1 μL, 0.50 mmol) was conducted for 2 h to give a mixture of **10e** and **10e'** (97.0 mg, 81%, **10e**/**10e'** = 53/47) as colorless oil.

Spectrum data for **10e**: $^1$H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): 1.00 (t, $J_{HH}$ = 6.0 Hz, 3H), 1.41–1.58 (m, 2H), 1.84 (s, 3H), 2.01–2.12 (m, 2H), 2.18 (t, $J_{HH}$ = 8.0 Hz, 2H), 2.48–2.52 (m, 2H), 5.12 (d, $J_{HH}$ = 10.4 Hz, 1H), 5.25 (d, $^3J_{HH}$ = 18.4 Hz, 1H), 5.77 (tt, $J_{HF}$ = 54.0, 2.8 Hz, 1H), 6.81 (dd, $J_{HH}$ = 10.4, 18.4 Hz, 1H). $^{13}$C{$^1$H} NMR (100 MHz, $CDCl_3$, rt, δ/ppm): 13.4, 14.1, 21.8, 22.8 (t, $J_{CF}$ = 4.0 Hz), 29.5 (t, $J_{CF}$ = 22.0 Hz), 35.6, 110.3 (tt, $J_{CF}$ = 247.0, 41.0 Hz), 112.8, 117.7 (tt, $J_{CF}$ = 245.0, 29.0 Hz), 128.8, 133.5, 134.8. $^{19}$F NMR (376 MHz, $CDCl_3$, rt, δ/ppm): –120.0 (t, $J_{FH}$ = 15.0 Hz, 2F), –138.5 (d, $J_{FH}$ = 52.6 Hz, 2F).

Spectrum data for **10e'**: $^{1}$H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): 0.99 (t, $J_{HH}$ = 6.0 Hz, 3H), 1.41–1.58 (m, 2H), 1.86 (s, 3H), 2.01–2.12 (m, 2H), 2.28 (t, $J_{HH}$ = 8.0 Hz, 2H), 2.48–2.52 (m, 2H), 5.10 (d, $J_{HH}$ = 10.8 Hz, 1H), 5.25 (d, $^{3}J_{HH}$ = 18.4 Hz, 1H), 5.77 (tt, $J_{HF}$ = 54.0, 2.8 Hz, 1H), 6.72 (dd, $^{3}J_{HH}$ = 10.8, 18.4 Hz, 1H). $^{13}$C{$^{1}$H} NMR (100 MHz, $CDCl_3$, rt, δ/ppm): 14.2, 19.1, 21.9, 24.7 (t, $J_{CF}$ = 4.0 Hz), 28.9 (t, $J_{CF}$ = 23.0 Hz), 30.0, 110.3 (tt, $J_{CF}$ = 247.0, 41.0 Hz), 112.4, 117.8 (tt, $J_{CF}$ = 245.0, 29.0 Hz), 132.1, 133.6, 136.8. $^{19}$F NMR (376 MHz, $CDCl_3$, rt, δ/ppm): –119.8 (t, $J_{FH}$ = 18.8 Hz, 2F), –138.5 (d, $J_{FH}$ = 56.4 Hz, 2F). HRMS Calcd for $C_{12}H_{18}F_4$ 238.1345, Found *m/z* 238.1347 (as a mixture of **10e** and **10e'**).

**(*Z*)-3-ethyl-7,7,8,8-tetrafluoro-4-heptyl-1,3-octadiene (10f)**

**(*Z*)-4-ethyl-7,7,8,8-tetrafluoro-3-heptyl-1,3-octadiene (10f')**



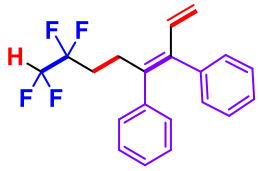

By following the general procedure ***A***, the reaction with 3-undecyne (**9f**: 97.4 μL, 0.50 mmol) was conducted for 3 h to give a mixture of **10f** and **10f'** (137.2 mg, 89%, **10f**/**10f'** = 52/48) as colorless oil.

Spectrum data for **10f**: $^{1}$H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): 0.85–1.05 (br, 3H), 1.09 (t, $J_{HH}$ = 7.2 Hz, 3H), 1.26–1.54 (br, 10H), 2.02–2.14 (m, 2H), 2.14–2.24 (m, 2H), 2.24–2.39 (m, 2H), 2.39–2.56 (m, 2H), 5.12 (d, $J_{HH}$ = 10.8 Hz, 1H), 5.29 (d, $J_{HH}$ = 17.2 Hz, 1H), 5.76 (tt, $J_{HF}$ = 54.0, 2.4 Hz, 1H), 6.66 (dd, $J_{HH}$ = 10.8, 17.2 Hz, 1H). $^{13}$C{$^{1}$H} NMR (100 MHz, $CDCl_3$, rt, δ/ppm): 13.9, 14.0, 22.4 (t, $J_{CF}$ = 3.0 Hz), 22.6, 25.9, 27.6, 29.2, 29.6 (t, $J_{CF}$ = 23.0 Hz), 29.9, 31.8, 33.0, 110.3 (tt, $J_{CF}$ = 247.0, 42.0 Hz), 112.7, 117.7 (tt, $J_{CF}$ = 245.0, 29.0 Hz), 133.2, 133.7, 136.4. $^{19}$F NMR (376 MHz, $CDCl_3$, rt, δ/ppm): –119.9 (t, $J_{FH}$ = 18.8 Hz, 2F), –138.5 (d, $J_{FH}$ = 52.6 Hz, 2F).

Spectrum data for **10f'**: $^{1}$H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): 0.85–1.05 (br, 3H), 1.05 (t, $J_{HH}$ = 7.2 Hz, 3H), 1.26–1.54 (br, 10H), 2.02–2.14 (m, 2H), 2.14–2.24 (m, 2H), 2.24–2.39 (m, 2H), 2.39–2.56 (m, 2H), 5.12 (d, $J_{HH}$ = 10.8 Hz, 1H), 5.28 (d, $J_{HH}$ = 17.2 Hz, 1H), 5.76 (tt, $J_{HF}$ = 54.0, 2.4 Hz, 1H), 6.67 (dd, $J_{HH}$ = 10.8, 17.2 Hz, 1H). $^{13}$C{$^{1}$H} NMR (100 MHz, $CDCl_3$, rt, δ/ppm): 13.1, 14.0, 20.6, 21.9 (t, $J_{CF}$ = 6.0 Hz), 25.9, 27.6, 28.9, 29.6 (t, $J_{CF}$ = 21.0 Hz), 30.0, 31.9, 33.0, 110.3 (tt, $J_{CF}$ = 247.0, 42.0 Hz), 112.8,

117.7 (tt, $J_{CF}$ = 245.0, 29.0 Hz), 133.4, 135.0, 137.9. $^{19}$F NMR (376 MHz, $CDCl_3$, rt, δ/ppm): –119.9 (t, $J_{FH}$ = 18.8 Hz, 2F), –138.5 (d, $J_{FH}$ = 52.6 Hz, 2F). HRMS Calcd for $C_{17}H_{28}F_4$ 308.2127, Found *m/z* 308.2126 (as a mixture of **10f** and **10f'**).

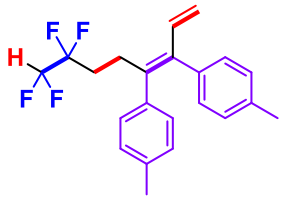
**(*Z*)-7,7,8,8-tetrafluoro-3,4-diphenyl-1,3-octadiene (10g)**



By following the general procedure ***B***, the reaction with diphenylacetylene (**9g**: 89.0 mg, 0.50 mmol) was conducted for 24 h to give **10g** (114.1 mg, 68%) as colorless oil.

$^1$H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): 1.90–2.03 (m, 2H), 2.87–2.92 (m, 2H), 4.83 (d, $J_{HH}$ = 16.8 Hz, 1H), 5.21 (d, $J_{HH}$ = 10.8 Hz, 1H), 5.58 (t, $J_{HH}$ = 54.0 Hz, 1H), 6.70–6.89 (m, 4H), 6.89–7.06 (m, 7H). $^{13}$C{$^1$H} NMR (100 MHz, $CDCl_3$, rt, δ/ppm): 24.9 (t, $J_{CF}$ = 4.0 Hz), 28.8 (t, $J_{CF}$ = 22.0 Hz), 110.3 (tt, $J_{CF}$ = 248.0, 41.0 Hz), 117.8 (tt, $J_{CF}$ = 246.0, 30.0 Hz), 119.3, 126.3, 126.4, 127.5, 127.8, 129.3, 131.0, 134.9, 138.5, 138.8, 139.4, 141.6. $^{19}$F NMR (376 MHz, $CDCl_3$, rt, δ/ppm): –119.6 (t, $J_{FH}$ = 18.8 Hz, 2F), –138.2 (d, $J_{FH}$ = 52.6 Hz, 2F). HRMS Calcd for $C_{20}H_{18}F_4$ 334.3576, Found *m/z* 334.1340.

**(*Z*)-7,7,8,8-tetrafluoro-3,4-bis(*p*-tolyl)-1,3-octadiene (10h)**

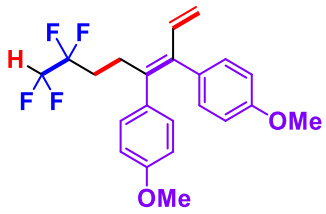


By following the general procedure ***C***, the reaction with 1,2-bis(*p*-tolyl)acetylene (**9h**: 103.0 mg, 0.50 mmol) was conducted for 48 h to give **10h** (119.7 mg, 66%) as colorless oil.

$^1$H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): 1.88–2.01 (m, 2H), 2.00 (s, 3H), 2.01 (s, 3H), 2.84–2.88 (m, 2H), 4.81 (dd, $J_{HH}$ = 1.4, 17.2 Hz, 1H), 5.16 (dd, $J_{HH}$ = 1.4, 10.8 Hz, 1H), 5.56 (tt, $J_{HF}$ = 54.0, 2.4 Hz, 1H), 6.71–6.85 (m, 4H), 6.90–6.97 (m, 4H), 6.94 (dd, $J_{HH}$ = 10.8, 17.2 Hz, 1H). $^{13}$C{$^1$H} NMR (100 MHz, $CDCl_3$, rt, δ/ppm): 19.9, 20.0, 23.9 (t, $J_{CF}$ = 4.0 Hz), 27.8 (t, $J_{CF}$ = 22.0 Hz), 109.2 (tt, $J_{CF}$ = 247.8, 40.9 Hz), 116.7 (tt, $J_{CF}$ = 244.9,

29.1 Hz), 117.7, 127.2, 127.4, 128.1, 129.8, 134.2, 134.5, 134.7, 135.4, 137.1, 137.2, 137.6. $^{19}$F NMR (376 MHz, $CDCl_3$, rt, δ/ppm): –119.7 (t, $J_{FH}$ = 18.8 Hz, 2F), –138.3 (d, $J_{FH}$ = 52.6 Hz, 2F). HRMS Calcd for $C_{22}H_{22}F_4$ 362.1658, Found *m/z* 362.1658.

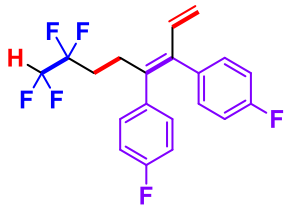
**(*Z*)-7,7,8,8-tetrafluoro-3,4-bis(*p*-anisyl)-1,3-octadiene (10i)**




By following the general procedure ***C***, the reaction with 1,2-bis(*p*-anisyl)acetylene (**9i**: 119.0 mg, 0.50 mmol) was conducted for 48 h. Further purification was carried out by using a recycle HPLC, affording **10i** (159.2 mg, 80%) as colorless oil.

$^1$H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): 1.88–2.05 (m, 2H), 2.83–2.91 (m, 2H), 3.58 (s, 3H), 3.60 (s, 3H), 4.84 (dd, $J_{HH}$ = 1.6, 16.9 Hz, 1H), 5.16 (dd, $J_{HH}$ = 1.6, 10.6 Hz, 1H), 5.59 (tt, $J_{HF}$ = 53.9, 2.7 Hz, 1H), 6.52 (d, $J_{HH}$ = 8.7 Hz, 2H), 6.57 (d, $J_{HH}$ = 8.6 Hz, 2H), 6.76 (d, $J_{HH}$ = 8.6 Hz, 2H), 6.78 (d, $J_{HH}$ = 8.7 Hz, 2H), 6.93 (dd, $J_{HH}$ = 10.6, 16.9 Hz, 1H). $^{13}$C{$^1$H} NMR (100 MHz, $CDCl_3$, rt, δ/ppm): 22.7 (t, $J_{CF}$ = 4.0 Hz), 26.6 (t, $J_{CF}$ = 22.0 Hz), 52.7, 108.0 (tt, $J_{CF}$ = 247.8, 40.9 Hz), 110.8, 110.9, 115.5 (tt, $J_{CF}$ = 244.9, 29.0 Hz), 116.4, 128.2, 129.6, 129.8, 131.7, 133.1, 135.5, 135.5, 155.6, 155.6. $^{19}$F NMR (376 MHz, $CDCl_3$, rt, δ/ppm): –119.7 (t, $J_{FH}$ = 18.8 Hz, 2F), –138.4 (d, $J_{FH}$ = 52.6 Hz, 2F). HRMS Calcd for $C_{22}H_{22}F_4O_2$ 394.1556, Found *m/z* 394.1553.

**(*Z*)-7,7,8,8-tetrafluoro-3,4-bis(*p*-fluorophenyl)-1,3-octadiene (10j)**

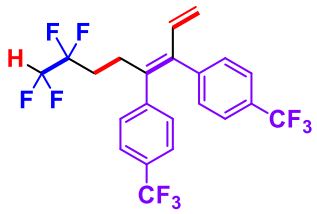



A THF solution (6.0 mL) of **11** (71.8 mg, 0.10 mmol) and 1,2-bis(*p*-fluorophenyl)acetylene (**9j**: 107.0 mg, 0.50 mmol) was transferred into an autoclave reactor (volume: 50.0 mL). Then, TFE (2.0 atm, c.a. 4.0 mmol) and ethylene (3.0 atm, c.a. 6.0 mmol) was charged in this order into the reactor. The reaction mixture

was stirred at 40 °C for 72 h. After redundant TFE and ethylene were purged from the reactor (*caution*: The reaction mixture must be handled in well ventilated fume hood!!), the reaction mixture was exposed to air to quench the catalyst. Insoluble was removed by filtration, and all volatiles were then removed under reduced pressure. The crude product was purified by silica gel column chromatography, giving the title compound **10j** (149.4 mg, 80%) as colorless oil.

$^{1}$H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): 1.84–2.03 (m, 2H), 2.80–2.91 (m, 2H), 4.79 (dd, $J_{HH}$ = 1.4, 17.0 Hz, 1H), 5.20 (dd, $J_{HH}$ = 1.4, 10.7 Hz, 1H), 5.58 (tt, $J_{HF}$ = 53.9, 2.6 Hz, 1H), 6.63–6.74 (m, 4H), 6.74–6.85 (m, 4H), 6.93 (dd, $J_{HH}$ = 10.7, 17.0 Hz, 1H). $^{13}$C{$^{1}$H} NMR (100 MHz, $CDCl_3$, rt, δ/ppm): 25.0 (t, $J_{CF}$ = 4.0 Hz), 28.5 (t, $J_{CF}$ = 22.0 Hz), 110.2 (tt, $J_{CF}$ = 247.8, 41.0 Hz), 114.6 (d, $J_{CF}$ = 21.3 Hz), 114.9 (d, $J_{CF}$ = 21.1 Hz), 117.7 (tt, $J_{CF}$ = 245.0, 29.2 Hz), 119.5, 130.9 (d, $J_{CF}$ = 7.9 Hz), 132.5 (d, $J_{CF}$ = 7.8 Hz), 134.7, 135.1 (d, $J_{CF}$ = 3.3 Hz), 137.3 (d, $J_{CF}$ = 3.5 Hz), 137.9, 138.1, 160.1 (d, $J_{CF}$ = 247.3 Hz), 162.6 (d, $J_{CF}$ = 246.3 Hz). $^{19}$F NMR (376 MHz, $CDCl_3$, rt, δ/ppm): –118.4 (m, 1F), –118.9 (m, 1F), –119.6 (t, $J_{FH}$ = 18.8 Hz, 2F), –138.3 (d, $J_{FH}$ = 52.6 Hz, 2F). HRMS Calcd for $C_{20}H_{16}F_6$ 370.1156, Found *m/z* 370.1152.

**(*Z*)-7,7,8,8-tetrafluoro-3,4-bis(*p*-trifluoromethylphenyl)-1,3-octadiene (10k)**

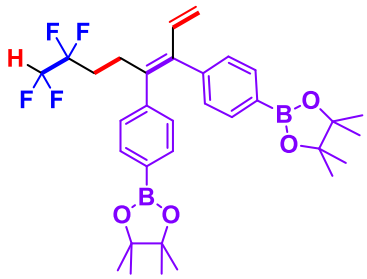



By following the general procedure ***C***, the reaction with 1,2-bis(*p*-trifluoromethylphenyl)acetylene (**9k**: 157.1 mg, 0.50 mmol) was conducted for 72 h to give **10k** (64.4 mg, 27%) as colorless oil.

$^{1}$H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): 1.84–2.04 (m, 2H), 2.87–2.96 (m, 2H), 4.77 (d, $J_{HH}$ = 17.0 Hz, 1H), 5.28 (d, $J_{HH}$ = 10.7 Hz, 1H), 5.61 (t, $J_{HF}$ = 53.8 Hz, 1H), 6.92–7.02 (m, 5H), 7.26–7.31 (m, 4H). $^{13}$C{$^{1}$H} NMR (100 MHz, $CDCl_3$, rt, δ/ppm): 23.9 (t, $J_{CF}$ = 3.3 Hz), 27.4 (t, $J_{CF}$ = 22.3 Hz), 109.2 (tt, $J_{CF}$ = 250.4, 41.3 Hz), 116.5 (tt, $J_{CF}$ = 246.7, 30.4 Hz), 119.6, 123.7 (q, $J_{CF}$ = 3.9 Hz), 124.0 (q, $J_{CF}$ = 3.8 Hz), 127.8 (q, $J_{CF}$ = 32.4 Hz), 128.5, 130.1, 133.0, 137.0, 137.7, 141.7, 143.8. Resonance attributable to an

aromatic carbon was obscured by an overlapping with others, and resonance assignable to the *C*$F_3$ carbon could not be detected due to multiple $^{13}C$–$^{19}F$ couplings. $^{19}F$ NMR (376 MHz, $CDCl_3$, rt, δ/ppm): –65.8 (s, 3F), –65.9 (s, 3F), –119.6 (t, $J_{FH}$ = 18.0 Hz, 2F), –138.3 (d, $J_{FH}$ = 53.8 Hz, 2F). HRMS Calcd for $C_{22}H_{16}F_{10}$ 470.1092, Found *m/z* 470.1093.

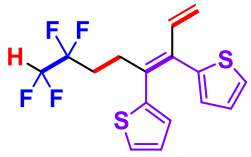
**(*Z*)-7,7,8,8-tetrafluoro-3,4-bis(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)-1,3-octadiene (10l)**




By following the general procedure ***C***, the reaction with 1,2-bis(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)acetylene (**9l**: 215.1 mg, 0.50 mmol) was conducted for 48 h to give **10l** (185.3 mg, 62%) as white solid.

$^1H$ NMR (400 MHz, $CDCl_3$, rt, δ/ppm): 1.22 (s, 12H), 1.24 (s, 12H), 1.85–2.05 (m, 2H), 2.82–2.94 (m, 2H), 4.78 (d, $J_{HH}$ = 16.8 Hz, 1H), 5.21 (d, $J_{HH}$ = 10.8 Hz, 1H), 5.59 (t, $J_{HF}$ = 54.0 Hz, 1H), 6.88 (d, $J_{HH}$ = 6.8 Hz, 4H), 6.94 (dd, $J_{HH}$ = 10.8, 16.8 Hz, 1H), 7.43 (d, $J_{HH}$ = 7.9 Hz, 2H), 7.46 (d, $J_{HH}$ = 7.8 Hz, 2H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$, rt, δ/ppm): 24.9, 24.9, 28.7 (t, $J_{CF}$ = 22.0 Hz), 83.7, 83.7, 110.2 (tt, $J_{CF}$ = 248.0, 41.0 Hz), 117.7 (tt, $J_{CF}$ = 245.0, 29.0 Hz), 119.6, 128.6, 130.3, 134.0, 134.3, 134.7, 134.7, 138.4, 138.7, 142.3, 144.4, 144.4. Resonance attributable to the -*C*$H_2$$CH_2$$CF_2$- was obscured by that of the *C*$H_3$ group of Bpin. $^{19}F$ NMR (376 MHz, $CDCl_3$, rt, δ/ppm): –119.7 (t, $J_{FH}$ = 18.8 Hz, 2F), –138.3 (d, $J_{FH}$ = 52.6 Hz, 2F). HRMS Calcd for $C_{32}H_{40}F_4O_4B_2$ 586.3049, Found *m/z* 586.3051.

**(*Z*)-7,7,8,8-tetrafluoro-3,4-bis(2-thienyl)-1,3-octadiene (10m)**

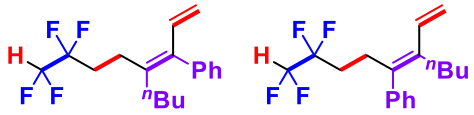


By following the general procedure ***C***, the reaction with 1,2-bis(2-thienyl)acetylene (**9m**: 95.1 mg, 0.50 mmol) was conducted for 72 h. Further purification was carried out by using a recycle HPLC, affording **10m** (30.9 mg, 17%) as colorless oil.

$^{1}$H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): 2.04–2.24 (m, 2H), 2.93–3.05 (m, 2H), 5.03 (dd, $J_{HH}$ = 1.2, 16.7 Hz, 1H), 5.30 (dd, $J_{HH}$ = 1.2, 10.6 Hz, 1H), 5.68 (tt, $J_{HF}$ = 54.1, 2.7 Hz, 1H), 6.49–7.43 (m, 7H). $^{13}$C{$^{1}$H} NMR (100 MHz, $CDCl_3$, rt, δ/ppm): 25.0 (t, $J_{CF}$ = 4.6 Hz), 29.3 (t, $J_{CF}$ = 22.5 Hz), 110.3 (tt, $J_{CF}$ = 248.9, 40.5 Hz), 117.7 (tt, $J_{CF}$ = 247.1, 29.9 Hz), 120.1, 138.6, 139.6, 143.0. Resonances attributable to the 2-thienyl group could not identified due to low S/N ratio. $^{19}$F NMR (376 MHz, $CDCl_3$, rt, δ/ppm): –119.6 (t, $J_{FH}$ = 17.7 Hz, 2F), –138.1 (d, $J_{FH}$ = 54.5 Hz, 2F). HRMS Calcd for $C_{16}H_{14}F_4S_2$ 346.0473, Found *m/z* 346.0471.

**(*E*)-4-butyl-7,7,8,8-tetrafluoro-3-phenyl-1,3-octadiene (10n)**

**(*E*)-3-butyl-7,7,8,8-tetrafluoro-4-phenyl-1,3-octadiene (10n')**

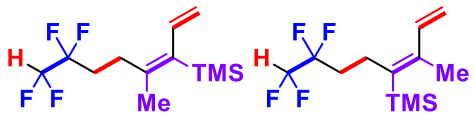



By following the general procedure ***B***, the reaction with 1-phenyl-1-hexyne (**9n**: 87.6 μL, 0.50 mmol) was conducted for 48 h to give a mixture of **10n** and **10n'** (125.4 mg, 79%, **10n**/**10n'** = 77/23) as colorless oil.

Spectrum data for **10n**: $^{1}$H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): 0.64 (t, $J_{HH}$ = 7.3 Hz, 3H), 0.98–1.07 (m, 2H), 1.16–1.26 (m, 2H), 1.77 (t, $J_{HH}$ = 8.5 Hz, 2H), 1.95–2.13 (m, 2H), 2.47–2.52 (m, 2H), 4.46 (d, $J_{HH}$ = 16.4 Hz, 1H), 5.00 (d, $J_{HH}$ = 11.6 Hz, 1H), 5.65 (tt, $J_{HF}$ = 54.0, 2.5 Hz, 1H), 6.77 (dd, $J_{HH}$ = 11.6, 16.4 Hz, 1H), 6.94 (m, 1H), 7.00 (m, 1H), 7.13–7.20 (m, 1H), 7.20–7.28 (m, 2H). $^{13}$C{$^{1}$H} NMR (100 MHz, $CDCl_3$, rt, δ/ppm): 13.7, 21.6 (t, $J_{CF}$ = 3.7 Hz), 22.6, 29.4 (t, $J_{CF}$ = 22.2 Hz), 30.3, 33.6, 110.4 (tt, $J_{CF}$ = 249.0, 43.0 Hz), 117.2, 117.8 (tt, $J_{CF}$ = 245, 30.0 Hz), 126.5, 128.0, 129.8, 134.7, 137.5, 138.3, 139.6. $^{19}$F NMR (376 MHz, $CDCl_3$, rt, δ/ppm): –119.7 (t, $J_{FH}$ = 18.8 Hz, 2F), –138.3 (d, $J_{FH}$ = 52.6 Hz, 2F). HRMS Calcd for $C_{18}H_{22}F_4$ 314.1658, Found *m/z* 314.1660 (as a mixture of **10n** and **10n'**).

**(*E*)-7,7,8,8-tetrafluoro-4-methyl-3-(trimethylsilyl)-1,3-octadiene (10o)**

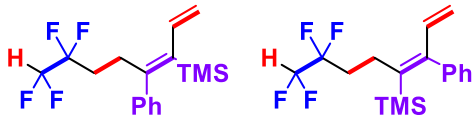
**(*E*)-7,7,8,8-tetrafluoro-3-methyl-4-(trimethylsilyl)-1,3-octadiene (10o')**




By following the general procedure ***D***, the reaction with 1-methyl-2-(trimethylsilyl)acetylene (**9o**: 74.5 μL, 0.50 mmol) was conducted for 72 h to give a mixture of **10o** and **10o'** (101.7 mg, 75%, **10o**/**10o'** = 79/21) as colorless oil. Spectrum data for **10o**: $^{1}$H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): 0.00 (s, 9H), 1.70 (s, 3H), 1.80–1.93 (m, 2H), 2.19–2.28 (m, 2H), 4.61 (d, $J_{HH}$ = 18.4 Hz, 1H), 4.92 (d, $J_{HH}$ = 12.8 Hz, 1H), 5.54 (t, $J_{HF}$ = 56.4 Hz, 1H), 6.14 (dd, $J_{HH}$ = 12.8, 18.4 Hz, 1H). $^{13}$C{$^{1}$H} NMR (100 MHz, $CDCl_3$, rt, δ/ppm): 0.0, 21.3, 26.3 (t, $J_{CF}$ = 4.0 Hz), 28.1 (t, $J_{CF}$ = 23.0 Hz), 109.7 (tt, $J_{CF}$ = 248.0, 41.0 Hz), 114.3, 117.3 (tt, $J_{CF}$ = 245.0, 29.0 Hz), 136.8, 138.6, 144.1. $^{19}$F NMR (376 MHz, $CDCl_3$, rt, δ/ppm): –119.9 (t, $J_{FH}$ = 18.8 Hz, 2F), –138.7 (d, $J_{FH}$ = 52.6 Hz, 2F). HRMS Calcd for $C_{12}H_{20}F_4Si$ 268.1270, Found *m/z* 268.1267 (as a mixture of **10o** and **10o'**).

**(*Z*)-7,7,8,8-tetrafluoro-4-phenyl-3-(trimethylsilyl)-1,3-octadiene (10p)**

**(*Z*)-7,7,8,8-tetrafluoro-3-phenyl-4-(trimethylsilyl)-1,3-octadiene (10p')**




By following the general procedure ***D***, the reaction with 1-phenyl-2-(trimethylsilyl)acetylene (**9p**: 97.0 μL, 0.50 mmol) was conducted for 72 h to give a mixture of **10p** and **10p'** (156.4 mg, 94%, **10p**/**10p'** = 58/42) as colorless oil. Spectrum data for **10p**: $^{1}$H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): 0.00 (s, 9H), 2.22–2.36 (m, 2H), 2.82–2.98 (m, 2H), 4.89 (d, $J_{HH}$ = 16.8 Hz, 1H), 5.44 (d, $J_{HH}$ = 11.6 Hz, 1H), 5.95 (t, $J_{HF}$ = 54.0 Hz, 1H), 7.21 (dd, $J_{HH}$ = 11.6, 16.8 Hz, 1H), 7.28 (d, $J_{HH}$ = 6.6 Hz, 1H), 7.33 (d, $J_{HH}$ = 7.5 Hz, 1H), 7.42–7.58 (m, 3H). $^{13}$C{$^{1}$H} NMR (100 MHz, $CDCl_3$, rt, δ/ppm): 0.0, 21.6 (t, $J_{CF}$ = 3.0 Hz), 30.7 (t, $J_{CF}$ = 22.0 Hz), 110.4 (tt, $J_{CF}$ = 248.0, 42.0 Hz), 117.7 (tt, $J_{CF}$ = 244.0, 30.0 Hz), 119.7, 127.1, 120.7, 130.4, 134.5, 138.9, 141.1, 151.0. $^{19}$F NMR (376 MHz, $CDCl_3$, rt, δ/ppm): –119.5 (t, $J_{FH}$ = 18.8 Hz, 2F),

–138.3 (d, $J_{FH}$ = 56.4 Hz, 2F).

Spectrum data for **10p'**: $^{1}$H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): 0.00 (s, 9H), 2.01–2.20 (m, 2H), 2.82–2.98 (m, 2H), 5.19 (d, $J_{HH}$ = 16.4 Hz, 1H), 5.40 (d, $J_{HH}$ = 11.6 Hz, 1H), 5.81 (tt, $J_{HF}$ = 56.4, 2.4 Hz, 1H), 6.69 (dd, $J_{HH}$ = 11.6, 16.4 Hz, 1H), 7.28 (d, $J_{HH}$ = 6.6 Hz, 1H), 7.33 (d, $J_{HH}$ = 7.5 Hz, 1H), 7.42–7.58 (m, 3H). $^{13}$C{$^{1}$H} NMR (100 MHz, $CDCl_3$, rt, δ/ppm): 0.1, 27.6 (t, $J_{CF}$ = 2.0 Hz), 28.7 (t, $J_{CF}$ = 22.0 Hz), 110.2 (tt, $J_{CF}$ = 240.0, 41.0 Hz), 115.5, 117.7 (tt, $J_{CF}$ = 240.0, 29.0 Hz), 127.3, 128.1, 128.8, 138.8, 140.9, 143.3, 150.0. $^{19}$F NMR (376 MHz, $CDCl_3$, rt, δ/ppm): –119.8 (t, $J_{FH}$ = 18.8 Hz, 2F), –138.6 (d, $J_{FH}$ = 52.6 Hz, 2F). HRMS Calcd for $C_{17}H_{22}F_4Si$ 330.1427, Found *m/z* 330.1425 (as a mixture of **10p** and **10p'**).

**Ni(0)-catalyzed cross-tetramerization of HFP, ethylene, and 9a (Scheme 3.6)**

A toluene solution (1.5 mL) of $Ni(cod)_2$ (27.5 mg, 0.10 mmol), $PPh_3$ (104.9 mg, 0.40 mmol), and **9a** (73.2 μL, 0.50 mmol) was transferred into an autoclave reactor (volume: 50.0 mL). Then, HFP (2.0 atm, c.a. 4.0 mmol) and ethylene (3.0 atm, c.a. 6.0 mmol) was charged in this order into the reactor. The reaction mixture was stirred at 40 °C for 72 h. After redundant HFP and ethylene were purged from the reactor, the reaction mixture was exposed to air to quench the catalyst. Insoluble was removed by filtration, and all volatiles were then removed under reduced pressure. The crude product was purified by Kugelrohr distillation, giving **12** (92.3 mg, 58%) as colorless oil.

$^{1}$H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): 0.85 (t, $J_{HH}$ = 7.5 Hz, 3H), 0.87 (t, $J_{HH}$ = 7.5 Hz, 3H), 1.20–1.54 (m, 4H), 1.91–2.06 (m, 2H), 2.00 (t, $J_{HH}$ = 8.8 Hz, 2H), 2.13 (t, $J_{HH}$ = 7.8 Hz, 2H), 2.32–2.35 (m, 2H), 4.67 (dm, $J_{FH}$ = 44.2 Hz, 1H), 4.99 (d, $J_{HH}$ = 11.1 Hz, 1H), 5.12 (d, $J_{HH}$ = 17.2 Hz, 1H), 6.51 (dd, $J_{HH}$ = 11.1, 17.2 Hz, 1H). $^{13}$C{$^{1}$H} NMR (100 MHz, $CDCl_3$, rt, δ/ppm): 13.3, 13.3, 20.9, 21.5, 21.7 (t, $J_{CF}$ = 5.0 Hz), 28.8, 31.4 (t, $J_{CF}$ = 23.0 Hz), 34.2, 85.1 (dm, $J_{CF}$ = 228.5 Hz), 112.0, 117.8 (td, $J_{CF}$ = 247.8, 22.3 Hz), 132.6, 132.9, 135.3. Resonance attributable to the *C*$F_3$ could not be detected due to multiple $^{13}$C–$^{19}$F couplings. $^{19}$F NMR (376 MHz, $CDCl_3$, rt, δ/ppm): –77.5 (m, 3F), –108.7~ –115.8 (mutiplet of AB quartet, $J_{FF}$ = 270.7 Hz, 2F), –213.3 (dm, $J_{FH}$ = 45.1 Hz, 1F). HRMS Calcd for $C_{15}H_{22}F_6$ 316.1626, Found *m/z* 316.1628.

**Isolation of 13 (Scheme 3.7)**

A toluene solution (5.0 mL) of **1** (71.1 mg, 0.10 mmol) and **9g** (35.6 mg. 0.20 mmol) was transferred into a sealed tube, and the reaction mixture was thermostated at 40 ℃ for 5 h. All volatiles were removed under reduced pressure, and then brown residue was washed with hexane, affording **13** (59.6 mg, 74%) as brown solid.

$^{1}$H NMR (400 MHz, $C_6D_6$, rt, δ/ppm): 1.91–2.12 (m, 1H), 2.41–2.49 (m, 1H), 2.65–2.86 (m, 1H), 3.35–3.48 (m, 1H), 5.82–5.91 (m, 2H), 5.91–6.00 (m, 1H), 6.25–6.32 (m, 1H), 6.77–6.89 (m, 3H), 6.89–7.05 (m, 11H), 7.05–7.08 (m, 2H), 7.20–7.27 (m, 2H), 7.34–7.42 (m, 4H), 7.42–7.52 (m, 7H), 8.62 (d, $J_{HH}$ = 7.4 Hz, 2H). $^{13}$C{$^{1}$H} NMR (100 MHz, $C_6D_6$, rt, δ/ppm): 26.7 (br), 29.1 (br), 59.5 (d, $J_{CP}$ = 3.4 Hz), 73.4 (br), 100.1 (br), 110.4, 110.5, 126.1, 126.5 (d, $J_{CP}$ = 17.0 Hz), 128.6, 128.6, 128.9, 129.5, 129.5 (d, $J_{CP}$ = 2.0 Hz), 131.3, 132.6, 132.6, 133.0, 134.3 (d, $J_{CP}$ = 13.0 Hz), 135.4, 141.6, 141.7, 145.0, 150.8 (d, $J_{CP}$ = 2.0 Hz). Resonances attributable to the $CF_2CF_2$ and some aromatic carbons could not be detected due to multiple $^{13}$C–$^{19}$F couplings and overlapping with other aromatic resonances. $^{31}$P{$^{1}$H} NMR (162 MHz, $C_6D_6$, rt, δ/ppm): 31.2 (dd, $J_{PF}$ = 5.6, 78.4 Hz, 1P). $^{19}$F NMR (376 MHz, $C_6D_6$, rt, δ/ppm): –86.4 (dm, $J_{FF}$ = 244.4 Hz, 1F), –88.6 (dd, $J_{FF}$ = 244.4, $J_{PF}$ = 78.4 Hz, 1F), –106.7 (dm, $J_{FF}$ = 249.3 Hz, 1F), –110.0 (br d, $J_{FF}$ = 249.3 Hz, 1F). Anal. Calcd for $C_{50}H_{39}F_4NiP$: C, 74.55; H, 4.88. Found: C, 74.40; H, 5.26.

**Stoichiometric reaction of 13 with ethylene (Scheme 3.7)**

To a $C_6D_6$ solution (0.5 mL) of **13** (8.1 mg, 0.01 mmol) and $PPh_3$ (2.6 mg, 0.01 mmol) was added *α,α,α*-trifluorotoluene (5.0 μL, as an internal standard). The solution was transferred into a pressure-tight NMR tube and ethylene (5.0 atm) was charged into the reactor. The reaction was monitored at 40 °C by means of $^{19}$F NMR spectroscopy. After 24 h, quantitative formation of **10g** was confirmed and ($\eta^2$-$CH_2$=$CH_2$)Ni($PPh_3$)$_2$[S1] was generated concomitantly.

**Ni(0)-catalyzed cross-tetramerization reaction with styrene (Scheme 3.8)**

A toluene solution (0.75 mL) of Ni(cod)$_2$ (13.7 mg, 0.05 mmol), $PCy_3$ (28.0 mg, 0.10 mmol), styrene (0.75 mL, 15.0 mmol), and **9a** (73.2 μL, 0.50 mmol) was transferred

into an autoclave reactor (volume: 50.0 mL). TFE (1.0 atm, c.a. 2.0 mmol) and ethylene (1.0 atm, c.a. 2.0 mmol) were then charged in this order into the reactor. The reaction mixture was stirred at 40 °C for 72 h. After redundant TFE and ethylene were purged from the reactor (*caution*: The reaction mixture must be handled in well ventilated fume hood!!), the reaction mixture was exposed to air to quench the catalyst. Insoluble was removed by filtration, and all volatiles were then removed under reduced pressure. The crude product was purified by silica gel column chromatography, isolating the cross-tetramerization product **14a** (145.4 mg, 85%) as colorless oil. NMR analysis of the crude product revealed that a small amount of **10a** (8%, estimated by $^{19}$F NMR) was also contained as a minor product.

$^{1}$H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): 0.42–0.55 (m, 1H), 0.50–0.72 (m, 3H), 0.72–1.00 (m, 3H), 1.00–1.14 (m, 1H), 1.29–1.41 (m, 2H), 1.70–1.82 (m, 1H), 1.82–1.98 (m, 1H), 2.03–2.21 (m, 2H), 2.33–2.65 (m, 2H), 4.56–4.71 (m, 1H), 5.11 (dd, $J_{HH}$ = 4.6, 11.0 Hz, 1H), 5.22 (d, $J_{HH}$ = 4.6, 17.2 Hz, 1H), 5.59 (tt, $J_{HF}$ = 54.1, 2.8 Hz, 1H), 6.90 (dd, $J_{HH}$ = 11.0, 17.2 Hz, 1H), 7.08–7.22 (m, 3H), 7.22–7.38 (m, 2H). $^{13}$C{$^{1}$H} NMR (100 MHz, $CDCl_3$, rt, δ/ppm): 14.4, 14.8, 22.1, 23.5, 31.0, 31.5 (t, $J_{CF}$ = 21.1 Hz), 31.9, 38.1, 110.1 (tt, $J_{CF}$ = 247.3, 42.2 Hz), 114.1, 117.9 (tt, $J_{CF}$ = 247.7, 28.5 Hz), 126.4, 127.5, 128.2, 134.1, 134.2, 139.6, 141.9. $^{19}$F NMR (376 MHz, $CDCl_3$, rt, δ/ppm): –116.9 ~ –118.5 (multiplet of AB quartet, $J_{FF}$ = 272.0 Hz, 2F), –137.9 ~ –139.7 (doublet of AB quartet, $J_{FH}$ = 54.1, $J_{FF}$ = 299.8 Hz, 2F). HRMS Calcd for $C_{20}H_{26}F_4$ 342.1971, Found *m/z* 342.1441.

**References for Experimental Section**

S1 K. R. Pörschke, Y. H. Tsay, C. Krüger, *Angew. Chem.* **1985**, *97*, 334.

# Chapter 4

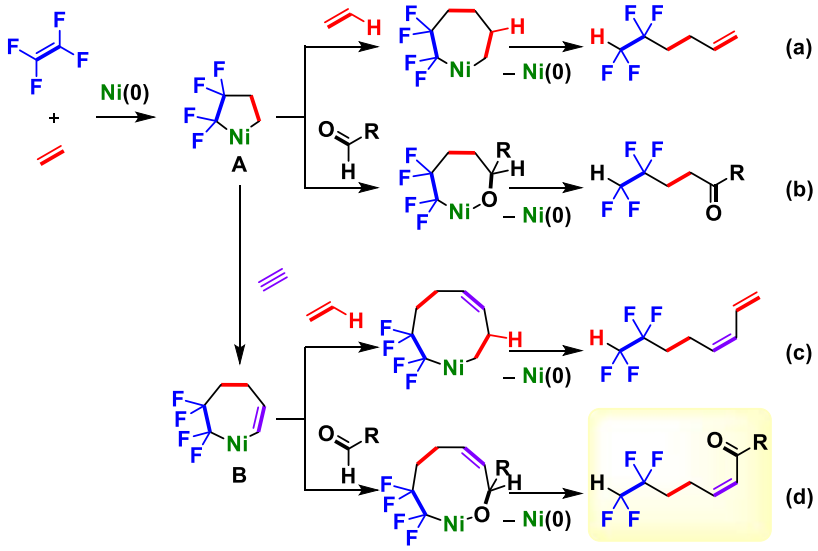
# Ni(0)-Catalyzed Cross-Tetramerization Reaction of TFE, Ethylene, Alkyne, and Aldehyde

## 4.1 Introduction

Oxidative cyclizations with low-valent transition-metal complexes have received increasing attention as a straightforward and environmentally benign route to the construction of C−C bonds between two unsaturated compounds.[1,2] Representative examples are the transition-metal-catalyzed linear trimerization or tetramerization of ethylene to 1-hexene or 1-octene, respectively, via a five-membered metallacycle generated by the oxidative cyclization of two molecules of ethylene.[3] The development of such oligomerizations represents an attractive research target given that $\alpha$-olefins can be co-polymerized with ethylene to afford polymers with improved properties.[4] On the other hand, transition-metal-catalyzed cross-trimerizations or -tetramerizations of unsaturated compounds allow generating complicated molecular structures in a highly atom-economical manner and a single step. However, the number of hitherto developed cross-trimerizations of unsaturated compounds remains low, most likely due to potential side reactions that generate e.g. homo-coupling products.[5] Cross-tetramerizations, especially those using four different unsaturated compounds, have not yet been reported.

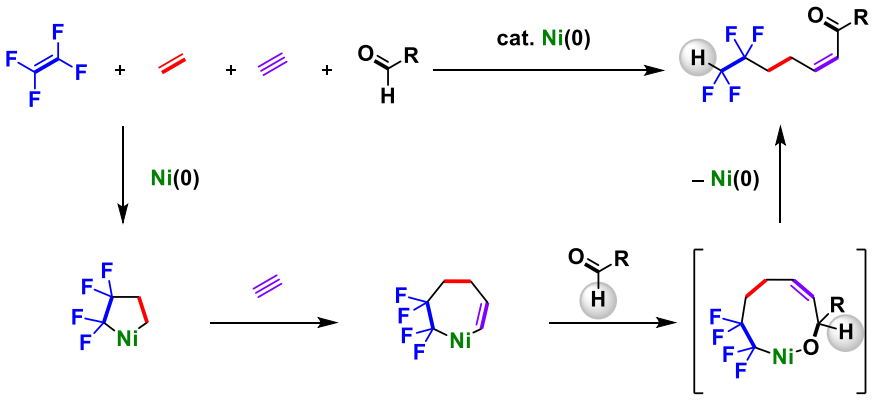
We have been focusing on the usage of TFE as an ideal C2 building block for the introduction of fluorinated functionalized groups.[6] As described in chapter 2, we have developed chemo- and regio-selective co- or cross-trimerizations of TFE with unsaturated compounds in the presence of a Ni(0) catalyst (Scheme 4.1 (a) and (b)).[7] In addition, as described in chapter 3, we have discovered the Ni(0)-catalyzed cross-tetramerization of TFE, alkyne, and two molecules of ethylene that affords 7,7,8,8-tetrafluoro-1,3-octadiene derivatives (Scheme 4.1 (c)). We envisioned a further expansion of this three-component cross-tetramerization into a chemo-selective cross-tetramerization of four different unsaturated compounds. As aldehyde exhibits a

reactivity toward the five-membered nickelacycle **A** that is higher than that of ethylene (Scheme 4.1 (b)), a nucleophilic addition of **B** to an aldehyde rather than to ethylene should provide the targeted cross-tetramer (Scheme 4.1 (d)).




**Scheme 4.1.** Working Hypothesis.

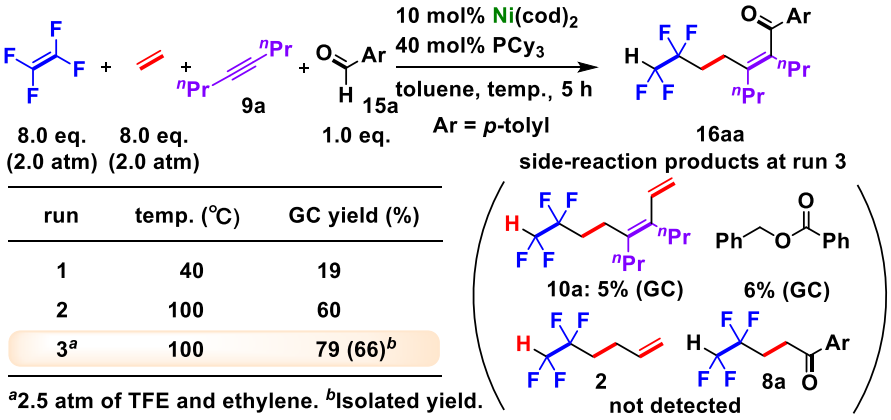
Described in this chapter is a Ni(0)-catalyzed cross-tetramerization reaction of TFE, ethylene, alkyne, and aldehyde (Scheme 4.2). This reaction is the first example of a highly selective cross-tetramerization between four different unsaturated compounds. Stoichiometric reactions revealed that the present reaction involves partially fluorinated five- and seven-membered nickelacycles as key reaction intermediates.




**Scheme 4.2.** Ni(0)-Catalyzed Cross-Tetramerization Reaction with Aldehyde.

### 4.2 Optimization of Reaction Conditions

Based on the optimal ligand and ligand/Ni(0) ratio in the cross-tetramerization that leads to the tetrafluoro-1,3-diene derivatives **10**, a toluene solution of **9a** and *p*-tolaldehyde (**15a**) was exposed for 5 h at 40 °C to a gas mixture containing TFE (2.0 atm) and ethylene (2.0 atm) in the presence of $Ni(cod)_2$ and $PCy_3$ (10 and 40 mol%, respectively). Under these conditions, cross-tetramer (**16aa**), a fluorine-containing enone derivative, was formed in 19% yield (Scheme 4.3; run 1). Encouraged by this result, we attempted to optimize the ligands and the ligand/Ni(0) ratio; however, all our attempts confirmed that $PCy_3$ is indeed the optimal ligand and that the use of 4 equiv of $PCy_3$ relative to $Ni(cod)_2$ accelerates the catalytic reaction.




| run | temp. (℃) | GC yield (%) |
|---|---|---|
| 1 | 40 | 19 |
| 2 | 100 | 60 |
| 3[a] | 100 | 79 (66)[b] |

[a]2.5 atm of TFE and ethylene. [b]Isolated yield.

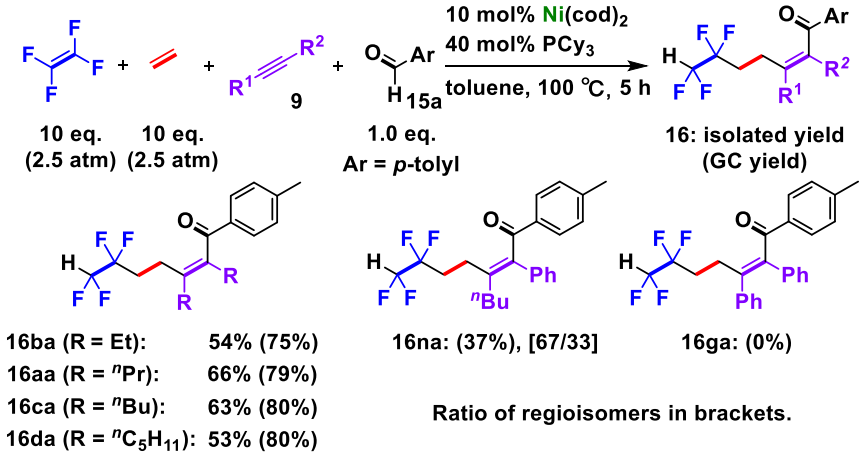
**Scheme 4.3.** Optimization of Reaction Conditions.

However, we discovered that the reaction temperature is of paramount importance to this reaction, i.e., increasing the temperature to 100 °C improved the yield of **16aa** to 60% (run 2). Moreover, increasing the gas pressure (2.5 atm each) allowed isolating **16aa** in 66% yield (79% GC yield; run 3). The crude reaction mixture also contains the three-component cross-tetramer **10a** (5%) consisting of TFE, **9a**, and two molecules of ethylene, the Tishchenko reaction product (6%).[8] However, co-trimer **2** or cross-trimer **8a** were not generated at all. The required purification procedure, which includes column chromatography on silica gel followed by recycling HPLC, is responsible for the relatively low isolated yield of **16aa**. Consequently, the optimal reaction conditions were determined as: 10 mol% $Ni(cod)_2$ and 40 mol% $PCy_3$ in toluene at 100 °C under an atmosphere of a gas mixture of TFE and ethylene (2.5 atm each). It should be emphasized that an equimolar mixture of the alkyne and aldehyde is sufficient to

facilitate the desired cross-tetramerization, which stands in stark contrast to another type of four-component cross-tetramerization with TFE, styrene, alkyne, and ethylene (Scheme 3.8).[9]

### 4.3 Substrate Scope

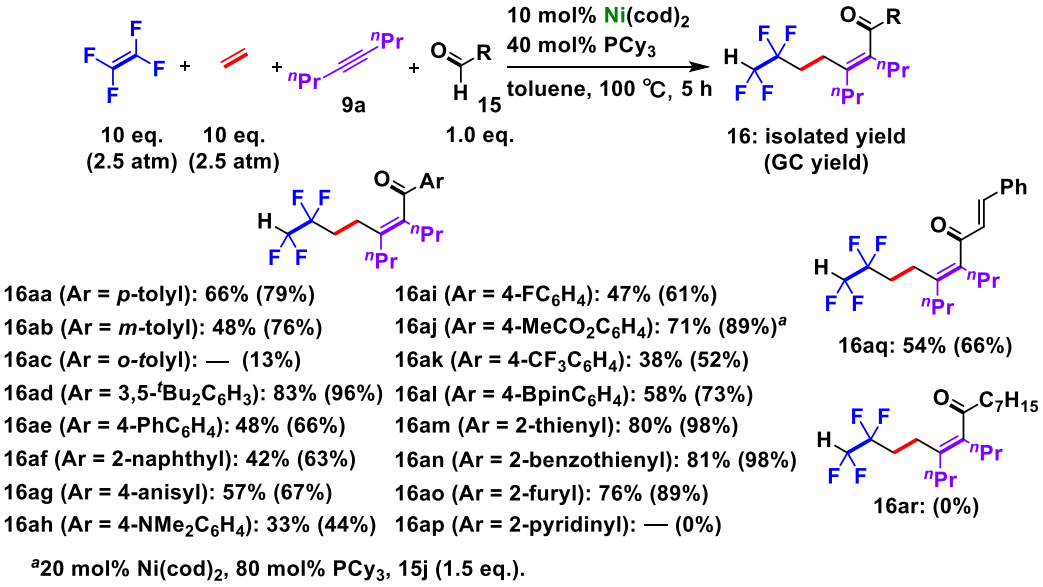
With the optimal reaction conditions in hand, the scope and the limitations of this Ni(0)-catalyzed cross-tetramerization with respect to the alkyne substrates was investigated (Scheme 4.4). The use of symmetrical aliphatic alkynes, such as **9a**, **9b**, **9c**, and **9d**, furnished the desired cross-tetramers (**16aa**–**16da**). The use of **9n** afforded the desired product (**16na**) with moderate regioselectivity, albeit the yield was low. When **9g** was used, the desired cross-tetramer (**16ga**) was not obtained due to the trimerization of **9g** and the Tishchenko reaction of **15a**.




**Scheme 4.4.** Substrate Scope (Alkyne).

Subsequently, the substrate scope with respect to various aldehydes was explored (Scheme 4.5). *m*-Tolualdehyde (**15b**) furnished the corresponding cross-tetramer (**16ab**) in 48% yield while *o*-tolualdehyde (**15c**) afforded a diminished yield, which is probably due to its increased steric demand. The reaction with 3,5-di-*tert*-butylbenzaldehyde (**15d**) yielded the corresponding cross-tetramer (**16ad**) in 83% yield. The reaction using 4-phenyl benzaldehyde (**15e**) and 2-naphthaldehyde (**15f**) afforded the corresponding cross-tetramers (**16ae** and **16af**) in moderate yield. 4-Anisaldehyde (**15g**), 4-dimethylaminobenzaldehyde (**15h**), 4-fluorobenzaldehyde (**15i**), and methyl 4-formylbenzoate (**15j**) afforded the corresponding cross-tetramers (**16ag**-**16aj**) in 57%,

33%, 47%, and 71% yield, respectively. However, using 4-trifluoromethylbenzaldehyde (**15k**) yielded the desired cross-tetramerization product (**16ak**) in 38% yield together with a considerable amount of **10a** (55% GC yield in the crude mixture). Using *p*-boronate-substituted benzaldehyde (**15l**) furnished the corresponding cross-tetramer (**16al**) in 58% yield, and the boronate moiety could be used in subsequent cross-coupling reactions to synthesize highly functionalized derivatives. In this catalytic system, thienyl aldehydes (**15m** and **15n**) and furyl aldehyde (**15o**) are also applicable. Among these, **15m** and **15n** yielded the cross-tetramers (**16am** and **16an**) in excellent yield (**16am**: 80% isolated and 98% GC yield; **16an**: 81% isolated and 98% GC yield). On the other hand, the use of 2-pyridinecarboxaldehyde (**15p**) did not yield the desired cross-tetramer (**16ap**). *Trans*-cinnamaldehyde (**15q**) engages in the reaction, leading to the desired cross-tetramer (**16aq**) in 54% yield. Conversely, aliphatic aldehyde, such as octanal (**15r**), cannot be used in this catalytic reaction due to the formation of **10a**.

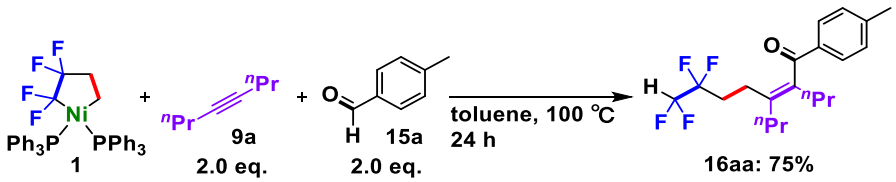



**Scheme 4.5.** Substrate Scope (Aldehyde).

### 4.4 Stoichiometric Reaction

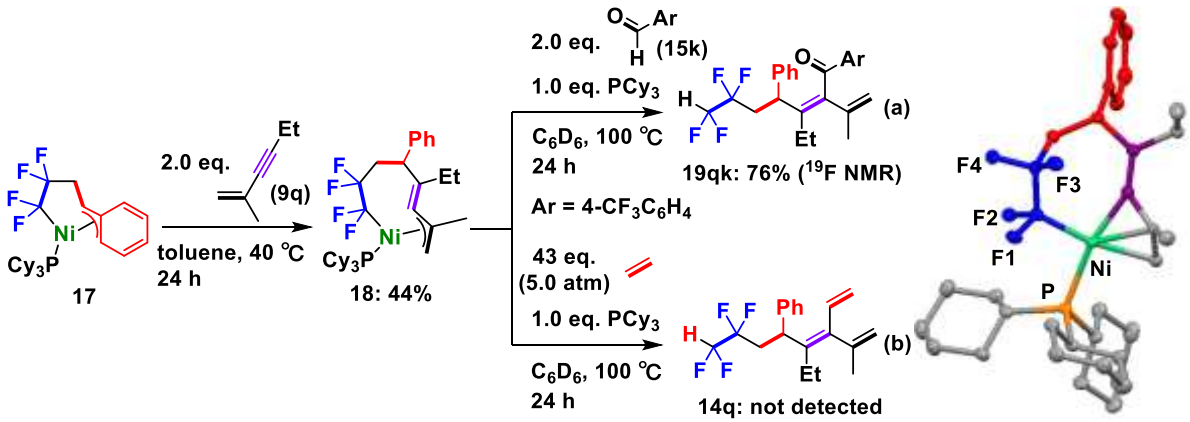
To gain deeper insight into the reaction mechanism as well as the origin of the unique chemoselectivity in this cross-tetramerization, several stoichiometric reactions were carried out. The treatment of **1** with 2 equiv of **9a** and **15a** in toluene at 100 °C for 24 h led to the formation of the corresponding cross-tetramer **16aa** in 75% yield

(Scheme 4.6). It should be emphasized that an expected cross-trimer **8a** that consists of TFE, ethylene, and **15a** was not generated, which stands in contrast to our previous observation that the corresponding cross-trimer was obtained from the reaction of **1** with benzaldehyde.[7] This result clearly supports the notion that the insertion of the alkyne into the Ni–$CH_2$ bond in the five-membered nickelacycle is much faster than that of the aldehyde.




**Scheme 4.6.** Stoichiometric Reaction of **1** with a mixture of **9a** and **15a**.

Next, a stoichiometric reaction of ($\eta^1$:$\eta^3$-$CF_2CF_2CH_2CHPh$)Ni($PCy_3$)[9] (**17**) with 2 equiv of 2-methyl-1-hexen-3-yne (**9q**) was conducted in order to trap a potential seven-membered nickelacycle intermediate (Scheme 4.7). Indeed, we managed to isolate the corresponding seven-membered nickelacycle (**18**) in 44% yield, and its molecular structure was unambiguously determined by X-ray diffraction analysis. Further treatment of **18** with 2 equiv of **15k** in the presence of an equimolar amount of $PCy_3$ in $C_6D_6$ at 100 °C for 24 h afforded the corresponding four-component cross-tetramer (**19qk**) in 76% yield (Scheme 4.7 (a)). In contrast, complex **18** exhibited lower reactivity toward ethylene, i.e., the reaction of **18** with ethylene (5 atm) did not furnish the corresponding cross-tetramer (**14q**; Scheme 4.7 (b)). These results are consistent with our working hypothesis (Scheme 4.1).[10]




**Scheme 4.7.** Synthesis and Reactivities of Seven-Membered Nickelacycle **18**.

## 4.5 Conclusion

In chapter 4, the Ni(0)-catalyzed cross-tetramerization reaction of TFE, ethylene, alkyne, and aldehyde is described. This is the first example of a highly selective cross-tetramerization using four different unsaturated compounds. The key reaction intermediates are the partially fluorinated five- and seven-membered nickelacycles.

## 4.6 References and Notes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[9] M. Ohashi, Y. Ueda, S. Ogoshi, *Angew. Chem. Int. Ed.* **2017**, *56*, 2435.

[10] The cross-tetramerization of TFE, ethylene, **9q**, and **15a** gave a desired cross-tetramer in <1 % yield.

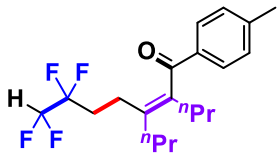
## 4.7 Experimental Section

**Scope of substrate with respect to alkynes in the Ni(0)-catalyzed cross-tetramerization reaction (Scheme 4.4)**

**General procedure *A* for isolation of the product**

A toluene solution (1.5 mL) of $Ni(cod)_2$ (13.7 mg, 0.05 mmol), $PCy_3$ (56.0 mg, 0.20 mmol), alkyne (**9**: 0.50 mmol), and *p*-tolualdehyde (**15a**: 58.8 μL, 0.50 mmol) was transferred into an autoclave reactor (BüchiGlasuster, tinyclave steel: volume: 50.0 mL). Then, TFE (2.5 atm, c.a. 5.0 mmol) and ethylene (2.5 atm, c.a. 5.0 mmol) was charged in this order into the reactor. The reaction mixture was stirred at 100 °C for 5 h. After redundant TFE and ethylene were purged from the reactor (*caution*: The reaction mixture must be handled in well ventilated fume hood!!), the reaction mixture was exposed to air to quench the catalyst. Insoluble was removed by filtration, and all volatiles were then removed under reduced pressure. The crude product was purified by silica gel column chromatography. Further purification was conducted by recycle HPLC, giving the title compound **16**.

**(*Z*)-6,6,7,7-tetrafluoro-2,3-dipropyl-1-(*p*-tolyl)hept-2-en-1-one (16aa)**

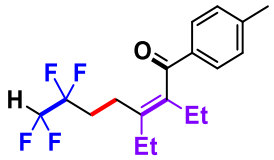



By following the general procedure ***A***, the reaction with 4-octyne (**9a**: 73.2 μL, 0.50 mmol) was conducted to give **16aa** (118.1 mg, 66%) as colorless oil.

$^1$H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): 0.79 (t, $J_{HH}$ = 7.3 Hz, 3H), 0.94 (t, $J_{HH}$ = 7.7 Hz, 3H), 1.22–1.32 (m, 2H), 1.43–1.52 (m, 2H), 1.86–2.05 (m, 4H), 2.08 (t, $J_{HH}$ = 7.4 Hz, 2H), 2.20 (t, $J_{HH}$ = 8.1 Hz, 2H), 2.32 (s, 3H), 5.52 (tt, $J_{HF}$ = 53.8, 2.6 Hz, 1H), 7.17 (d, $J_{HH}$ = 7.9 Hz, 2H), 7.69 (d, $J_{HH}$ = 7.9 Hz, 2H). $^{13}$C{$^1$H} NMR (100 MHz, $CDCl_3$, rt, δ/ppm): 13.9, 14.3, 21.6, 21.7, 21.9, 24.2 (t, $J_{CF}$ = 4.4 Hz), 29.3 (t, $J_{CF}$ = 22.3 Hz), 32.4, 32.6, 110.1 (tt, $J_{CF}$ = 244.3, 37.9 Hz), 117.4 (tt, $J_{CF}$ = 242.2, 27.9 Hz), 129.3, 129.3, 134.3, 136.6, 138.1, 144.1, 200.5. $^{19}$F NMR (376 MHz, $CDCl_3$, rt, δ/ppm): –120.2 (t, $J_{FH}$ = 17.9 Hz, 2F), –138.8 (d, $J_{FH}$ = 53.8 Hz, 2F). HRMS Calcd for $C_{20}H_{26}F_4O$

358.1920, Found *m/z* 358.1917.

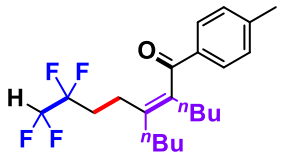
**(*Z*)-6,6,7,7-tetrafluoro-2,3-diethyl-1-(*p*-tolyl)hept-2-en-1-one (16ba)**




By following the general procedure ***A***, the reaction with 3-hexyne (**9b**: 56.8 μL, 0.50 mmol) was conducted to give **16ba** (89.7 mg, 54%) as colorless oil.

$^{1}$H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): 1.00 (t, $J_{HH}$ = 7.4 Hz, 3H), 1.17 (t, $J_{HH}$ = 7.7 Hz, 3H), 1.97–2.10 (m, 2H), 2.14–2.18 (m, 2H), 2.24 (q, $J_{HH}$ = 7.4 Hz, 2H), 2.38 (q, $J_{HH}$ = 7.7 Hz, 2H), 2.43 (s, 3H), 5.63 (tt, $J_{HF}$ = 54.1, 2.7 Hz, 1H), 7.28 (d, $J_{HH}$ = 8.1 Hz, 2H), 7.81 (d, $J_{HH}$ = 8.1 Hz, 2H). $^{13}$C{$^{1}$H} NMR (100 MHz, $CDCl_3$, rt, δ/ppm): 13.1, 13.2, 21.5, 23.4, 23.6, 23.9 (t, $J_{CF}$ = 4.6 Hz), 29.1 (t, $J_{CF}$ = 22.1 Hz), 110.1 (tt, $J_{CF}$ = 249.2, 41.2 Hz), 117.4 (tt, $J_{CF}$ = 245.3, 29.5 Hz), 129.3, 129.3, 134.5, 137.5, 138.7, 144.2, 200.4. $^{19}$F NMR (376 MHz, $CDCl_3$, rt, δ/ppm): –120.4 (t, $J_{FH}$ = 18.0 Hz, 2F), –138.9 (d, $J_{FH}$ = 54.1 Hz, 2F). HRMS Calcd for $C_{18}H_{22}F_4O$ 330.1607, Found *m/z* 330.1606.

**(*Z*)-6,6,7,7-tetrafluoro-2,3-dibutyl-1-(*p*-tolyl)hept-2-en-1-one (16ca)**

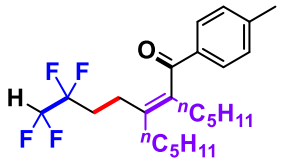



By following the general procedure ***A***, the reaction with 5-decyne (**9c**: 89.7 μL, 0.50 mmol) was conducted to give **16ca** (121.4 mg, 63%) as colorless oil.

$^{1}$H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): 0.74 (t, $J_{HH}$ = 7.1 Hz, 3H), 0.89 (t, $J_{HH}$ = 7.2 Hz, 3H), 1.14–1.27 (m, 4H), 1.30–1.36 (m, 2H), 1.37–1.45 (m, 2H), 1.84–1.95 (m, 2H), 1.98–2.04 (m, 2H), 2.08 (t, $J_{HH}$ = 7.2 Hz, 2H), 2.21 (t, $J_{HH}$ = 7.1 Hz, 2H), 2.30 (s, 3H), 5.51 (tt, $J_{HF}$ = 53.7, 3.0 Hz, 1H), 7.15 (d, $J_{HH}$ = 8.1 Hz, 2H), 7.68 (d, $J_{HH}$ = 8.1 Hz, 2H). $^{13}$C{$^{1}$H} NMR (100 MHz, $CDCl_3$, rt, δ/ppm): 13.7, 13.9, 21.5, 22.6, 22.9, 24.3 (t, $J_{CF}$ = 3.9 Hz), 29.3 (t, $J_{CF}$ = 22.1 Hz), 30.1, 30.3, 30.7, 30.8, 110.1 (tt, $J_{CF}$ = 247.1, 41.0 Hz), 117.4 (tt, $J_{CF}$ = 244.7, 26.7 Hz), 129.3, 129.3, 134.3, 136.7, 138.0, 144.1, 200.4. $^{19}$F

NMR (376 MHz, $CDCl_3$, rt, δ/ppm): –120.3 (t, $J_{FH}$ = 16.9 Hz, 2F), –138.9 (d, $J_{FH}$ = 53.7 Hz, 2F). HRMS Calcd for $C_{22}H_{30}F_4O$ 386.2233, Found *m/z* 386.2237.

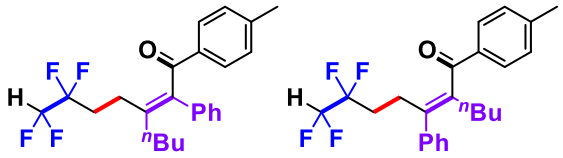
**(*Z*)-2-pentyl-3-(3,3,4,4-tetrafluorobutyl)-1-(*p*-tolyl)oct-2-en-1-one (16da)**



By following the general procedure ***A***, the reaction with 6-dodecyne (**9d**: 106.3 μL, 0.50 mmol) was conducted to give **16da** (107.0 mg, 53%) as colorless oil.

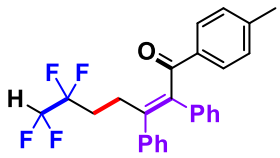
$^1$H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): 0.86 (t, $J_{HH}$ = 6.3 Hz, 3H), 0.97 (t, $J_{HH}$ = 6.3 Hz, 3H), 1.20–1.60 (m, 12H), 1.96–2.06 (m, 2H), 2.10–2.15 (m, 2H), 2.19 (t, $J_{HH}$ = 8.5 Hz, 2H), 2.31 (t, $J_{HH}$ = 8.1 Hz, 2H), 2.43 (s, 3H), 5.63 (t, $J_{HF}$ = 54.0 Hz, 1H), 7.27 (d, $J_{HH}$ = 7.6 Hz, 2H), 7.80 (d, $J_{HH}$ = 7.6 Hz, 2H). $^{13}$C{$^1$H} NMR (100 MHz, $CDCl_3$, rt, δ/ppm): 13.9, 14.0, 21.6, 22.3, 22.5, 24.2 (t, $J_{CF}$ = 3.7 Hz), 28.2, 28.3, 29.2 (t, $J_{CF}$ = 22.2 Hz), 30.4, 30.6, 31.7, 32.0, 110.1 (tt, $J_{CF}$ = 249.0, 39.5 Hz), 117.4 (tt, $J_{CF}$ = 247.3, 29.0 Hz), 129.3, 129.3, 134.3, 136.7, 138.1, 144.1, 200.5. $^{19}$F NMR (376 MHz, $CDCl_3$, rt, δ/ppm): –120.3 (t, $J_{FH}$ = 17.3 Hz, 2F), –138.8 (d, $J_{FH}$ = 54.0 Hz, 2F). HRMS Calcd for $C_{24}H_{34}F_4O$ 414.2546, Found *m/z* 414.2547.

**(*Z*)-3-butyl-6,6,7,7-tetrafluoro-2-phenyl-1-(*p*-tolyl)hept-2-en-1-one (16na)**
**(*E*)-2-butyl-6,6,7,7-tetrafluoro-3-phenyl-1-(*p*-tolyl)hept-2-en-1-one (16n'a)**



By following the general procedure ***A***, the reaction with 1-phenyl-1-hexyne (**9n**: 87.6 μL, 0.50 mmol) was conducted. After redundant TFE and ethylene were purged from the reactor, the reaction mixture was exposed to air to quench the catalyst. Tetradecane (10.0 μL, as an internal standard) was added to the reaction mixture. GC analysis revealed that the yield of a mixture of **16na** and **16n'a** (**16na**/**16n'a** = 67/33) was 37%.

**(*E*)-6,6,7,7-tetrafluoro-2,3-diphenyl-1-(*p*-tolyl)hept-2-en-1-one (16ga)**




By following the general procedure ***A***, the reaction with diphenylacethylene (**9g**: 89.0 mg, 0.50 mmol) was conducted. After redundant TFE and ethylene were purged from the reactor, the reaction mixture was exposed to air to quench the catalyst. Tetradecane (10.0 μL, as an internal standard) was added to the reaction mixture. GC analysis revealed that the target compound **16ga** was not obtained.

**Scope of substrate with respect to aldehydes in the Ni(0)-catalyzed cross-tetramerization reaction (Scheme 4.5)**

**General procedure *B* for isolation of the product**

A toluene solution (1.5 mL) of $Ni(cod)_2$ (13.7 mg, 0.05 mmol), $PCy_3$ (56.0 mg, 0.20 mmol), 4-octyne (**9a**: 73.2 μL, 0.50 mmol), and aldehyde (**15**: 0.50 mmol) was transferred into an autoclave reactor (volume: 50.0 mL). Then, TFE (2.5 atm, c.a. 5.0 mmol) and ethylene (2.5 atm, c.a. 5.0 mmol) was charged in this order into the reactor. The reaction mixture was stirred at 100 °C for 5 h. After redundant TFE and ethylene were purged from the reactor (*caution*: The reaction mixture must be handled in well ventilated fume hood!!), the reaction mixture was exposed to air to quench the catalyst. Insoluble was removed by filtration, and all volatiles were then removed under reduced pressure. The crude product was purified by silica gel column chromatography. Further purification was conducted by recycle HPLC, giving the title compound **16**.

**General procedure *C* for isolation of the product**

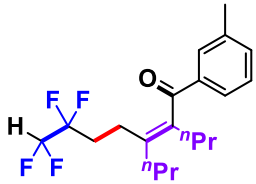
A toluene solution (1.5 mL) of $Ni(cod)_2$ (27.4 mg, 0.10 mmol), $PCy_3$ (112.0 mg, 0.40 mmol), 4-octyne (**9a**: 73.2 μL, 0.50 mmol), and aldehyde (**15**: 0.75 mmol) was transferred into an autoclave reactor (volume: 50.0 mL). Then, TFE (2.5 atm, c.a. 5.0 mmol) and ethylene (2.5 atm, c.a. 5.0 mmol) was charged in this order into the reactor. The reaction mixture was stirred at 100 °C for 5 h. After redundant TFE and ethylene were purged from the reactor (*caution*: The reaction mixture must be handled in well

ventilated fume hood!!), the reaction mixture was exposed to air to quench the catalyst. Insoluble was removed by filtration, and all volatiles were then removed under reduced pressure. The crude product was purified by silica gel column chromatography, giving the title compound **16**.

**General procedure *D* for isolation of the product**

A toluene solution (1.5 mL) of $Ni(cod)_2$ (13.7 mg, 0.05 mmol), $PCy_3$ (56.0 mg, 0.20 mmol), 4-octyne (**9a**: 73.2 μL, 0.50 mmol), and aldehyde (**15**: 0.50 mmol) was transferred into an autoclave reactor (volume: 50.0 mL). Then, TFE (2.5 atm, c.a. 5.0 mmol) and ethylene (2.5 atm, c.a. 5.0 mmol) was charged in this order into the reactor. The reaction mixture was stirred at 100 °C for 5 h. After redundant TFE and ethylene were purged from the reactor (*caution*: The reaction mixture must be handled in well ventilated fume hood!!), the reaction mixture was exposed to air to quench the catalyst. Insoluble was removed by filtration, and all volatiles were then removed under reduced pressure. The crude product was purified by silica gel column chromatography, giving the title compound **16**.

**(*Z*)-6,6,7,7-tetrafluoro-2,3-dipropyl-1-(*m*-tolyl)hept-2-en-1-one (16ab)**

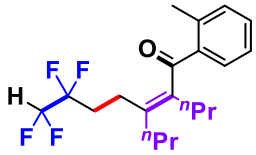



By following the general procedure ***B***, the reaction with *m*-tolualdehyde (**15b**: 58.7 μL, 0.50 mmol) was conducted to give **16ab** (85.4 mg, 48%) as colorless oil.

$^1$H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): 0.91 (t, $J_{HH}$ = 7.2 Hz, 3H), 1.07 (t, $J_{HH}$ = 7.4 Hz, 3H), 1.34–1.44 (m, 2H), 1.55–1.65 (m, 2H), 1.99–2.09 (m, 2H), 2.12–2.17 (m, 2H), 2.21 (t, $J_{HH}$ = 7.9 Hz, 2H), 2.32 (t, $J_{HH}$ = 7.9 Hz, 2H), 2.44 (s, 3H), 5.65 (tt, $J_{HF}$ = 53.6, 2.9 Hz, 1H), 7.37–7.42 (m, 2H), 7.68 (d, $J_{HH}$ = 7.2 Hz, 1H), 7.74 (s, 1H). $^{13}$C{$^1$H} NMR (100 MHz, $CDCl_3$, rt, δ/ppm): 13.9, 14.3, 21.3, 21.7, 21.9, 24.3 (t, $J_{CF}$ = 4.2 Hz), 29.2 (t, $J_{CF}$ = 22.1 Hz), 32.4, 32.6, 110.1 (tt, $J_{CF}$ = 250.3, 40.2 Hz), 117.4 (tt, $J_{CF}$ = 247.0, 25.7 Hz), 126.5, 128.5, 129.4, 134.0, 136.8, 137.0, 138.1, 138.5, 201.0. $^{19}$F NMR (376 MHz, $CDCl_3$, rt, δ/ppm): –120.2 (t, $J_{FH}$ = 17.0 Hz, 2F), –138.8 (d, $J_{FH}$ = 53.6 Hz, 2F). HRMS

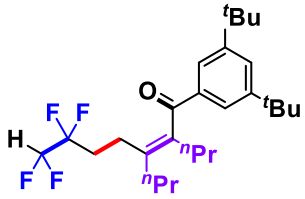
Calcd for $C_{20}H_{26}F_4O$ 358.1920, Found *m/z* 358.1915.

**(*Z*)-6,6,7,7-tetrafluoro-2,3-dipropyl-1-(*o*-tolyl)hept-2-en-1-one (16ac)**



By following the general procedure ***B***, the reaction with *o*-tolualdehyde (**15c**: 58.8 μL, 0.50 mmol) was conducted. After redundant TFE and ethylene were purged from the reactor, the reaction mixture was exposed to air to quench the catalyst. Tetradecane (10.0 μL, as an internal standard) was added to the reaction mixture. GC analysis revealed that the yield of the target compound **16ac** was 13%.

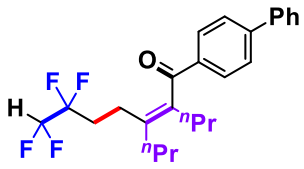
**(*Z*)-1-(3,5-di-*tert*-butylphenyl)-6,6,7,7-tetrafluoro-2,3-dipropylhept-2-en-1-one (16ad)**



By following the general procedure ***B***, the reaction with 3,5-di-*tert*-butylbenzaldehyde (**15d**: 109.0 mg, 0.50 mmol) was conducted to give **16ad** (188.0 mg, 83%) as colorless oil.

$^1$H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): 0.94 (t, $J_{HH}$ = 7.4 Hz, 3H), 1.10 (t, $J_{HH}$ = 7.1 Hz, 3H), 1.39 (s, 18H), 1.40–1.49 (m, 2H), 1.58–1.67 (m, 2H), 1.98–2.18 (m, 4H), 2.24 (t, $J_{HH}$ = 6.8 Hz, 2H), 2.36 (t, $J_{HH}$ = 6.8 Hz, 2H), 5.64 (tt, $J_{HF}$ = 54.0, 2.4 Hz, 1H), 7.69 (s, 2H), 7.80 (s, 1H). $^{13}$C{$^1$H} NMR (100 MHz, $CDCl_3$, rt, δ/ppm): 14.0, 14.2, 21.7, 21.9, 24.2 (t, $J_{CF}$ = 3.9 Hz), 29.1 (t, $J_{CF}$ = 22.4 Hz), 31.3, 32.3, 32.7, 34.9, 110.1 (tt, $J_{CF}$ = 248.6, 39.3 Hz), 117.4 (tt, $J_{CF}$ = 245.8, 26.0 Hz, -$CF_2$-), 123.5, 127.5, 136.4, 136.5, 138.5, 151.2, 201.6. $^{19}$F NMR (376 MHz, $CDCl_3$, rt, δ/ppm): –120.2 (t, $J_{FH}$ = 17.1 Hz, 2F,), –138.7 (d, $J_{FH}$ = 54.0 Hz, 2F). HRMS Calcd for $C_{27}H_{40}F_4O$ 456.3015, Found *m/z* 456.3011.

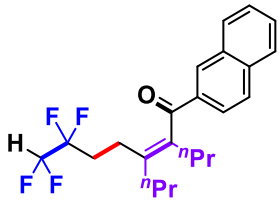
**(*Z*)-1-([1,1'-biphenyl]-4-yl)-6,6,7,7-tetrafluoro-2,3-dipropylhept-2-en-1-one (16ae)**




By following the general procedure ***B***, the reaction with 4-phenylbenzaldehyde (**15e**: 91.1 mg, 0.50 mmol) was conducted to give **16ae** (100.9 mg, 48%) as colorless oil.

$^{1}$H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): 0.96 (t, $J_{HH}$ = 7.2 Hz, 3H), 1.11 (t, $J_{HH}$ = 7.3 Hz, 3H), 1.40–1.50 (m, 2H), 1.60–1.69 (m, 2H), 2.04–2.23 (m, 4H), 2.25 (t, $J_{HH}$ = 7.9 Hz, 2H), 2.39 (t, $J_{HH}$ = 7.4 Hz, 2H), 5.67 (t, $J_{HF}$ = 53.5 Hz, 1H), 7.45 (t, $J_{HH}$ = 7.4 Hz, 1H), 7.52 (dd, $J_{HH}$ = 7.4, 7.4 Hz, 2H), 7.68 (d, $J_{HH}$ = 7.4 Hz, 2H), 7.74 (d, $J_{HH}$ = 7.4 Hz, 2H), 8.01 (d, $J_{HH}$ = 7.4 Hz, 2H). $^{13}$C{$^{1}$H} NMR (100 MHz, $CDCl_3$, rt, δ/ppm): 14.0, 14.3, 21.7, 22.0, 24.3 (t, $J_{CF}$ = 3.9 Hz), 29.3 (t, $J_{CF}$ = 22.0 Hz), 32.5, 32.6, 110.1 (tt, $J_{CF}$ = 250.3, 41.2 Hz), 117.5 (tt, $J_{CF}$ = 246.5, 28.9 Hz), 127.3, 127.4, 128.2, 128.9, 129.8, 135.5, 137.1, 138.1, 139.9, 146.0, 200.4. $^{19}$F NMR (376 MHz, $CDCl_3$, rt, δ/ppm): –120.1 (t, $J_{FH}$ = 17.2 Hz, 2F), –138.7 (d, $J_{FH}$ = 53.5 Hz, 2F). HRMS Calcd for $C_{25}H_{28}F_4O$ 420.2076, Found *m/z* 420.2075.

**(*Z*)-6,6,7,7-tetrafluoro-1-(naphthalen-2-yl)-2,3-dipropylhept-2-en-1-one (16af)**

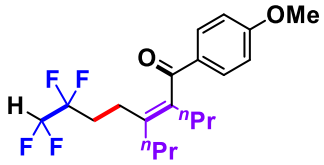



By following the general procedure ***B***, the reaction with 2-naphthaldehyde (**15f**: 78.1 mg, 0.50 mmol) was conducted to give **16af** (84.0 mg, 42%) as colorless oil.

$^{1}$H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): 0.95 (t, $J_{HH}$ = 6.8 Hz, 3H), 1.14 (t, $J_{HH}$ = 7.1 Hz, 3H), 1.42–1.51 (m, 2H), 1.64–1.73 (m, 2H), 2.07–2.26 (m, 4H), 2.29 (t, $J_{HH}$ = 7.1 Hz, 2H), 2.43 (t, $J_{HH}$ = 8.1 Hz, 2H), 5.65 (tt, $J_{HF}$ = 53.9, 2.8 Hz, 1H), 7.57–7.66 (m, 2H), 7.92–8.07 (m, 4H), 8.44 (s, 1H). $^{13}$C{$^{1}$H} NMR (100 MHz, $CDCl_3$, rt, δ/ppm): 14.0, 14.3, 21.7, 22.0, 24.4 (t, $J_{CF}$ = 4.0 Hz), 29.4 (t, $J_{CF}$ = 21.9 Hz), 32.5, 32.8, 110.1 (tt, $J_{CF}$ = 250.4, 38.6 Hz), 117.5 (tt, $J_{CF}$ = 245.4, 28.8 Hz), 124.4, 126.8, 127.8, 128.6, 128.7, 129.6, 131.3, 132.6, 134.1, 135.8, 137.3, 138.1, 200.8. $^{19}$F NMR (376 MHz, $CDCl_3$, rt,

δ/ppm): –120.2 (t, $J_{FH}$ = 18.1 Hz, 2F), –138.7 (d, $J_{FH}$ = 53.9 Hz, 2F). HRMS Calcd for $C_{23}H_{26}F_4O$ 394.1920, Found *m/z* 394.1920.

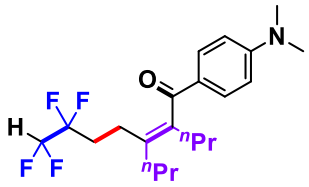
**(*Z*)-6,6,7,7-tetrafluoro-1-(4-anisyl)-2,3-dipropylhept-2-en-1-one (16ag)**




By following the general procedure ***B***, the reaction with 4-anisaldehyde (**15g**: 60.5 μL, 0.50 mmol) was conducted to give **16ag** (107.5 mg, 57%) as colorless oil.

$^1$H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): 0.79 (t, $J_{HH}$ = 7.3 Hz, 3H), 0.94 (t, $J_{HH}$ = 7.5 Hz, 3H), 1.23–1.32 (m, 2H), 1.42–1.51 (m, 2H), 1.86–2.03 (m, 4H), 2.07 (t, $J_{HH}$ = 8.0 Hz, 2H), 2.19 (t, $J_{HH}$ = 8.1 Hz, 2H), 3.78 (s, 3H), 5.53 (tt, $J_{HF}$ = 53.9, 3.0 Hz, 1H), 6.85 (d, $J_{HH}$ = 8.9 Hz, 2H), 7.78 (d, $J_{HH}$ = 8.9 Hz, 2H). $^{13}$C{$^1$H} NMR (100 MHz, $CDCl_3$, rt, δ/ppm): 14.0, 14.3, 21.7, 21.9, 24.2 (t, $J_{CF}$ = 3.9 Hz), 29.2 (t, $J_{CF}$ = 22.0 Hz), 32.4, 32.7, 55.4, 110.1 (tt, $J_{CF}$ = 249.3, 40.3 Hz), 117.5 (tt, $J_{CF}$ = 246.4, 28.8 Hz), 113.8, 129.8, 131.5, 136.1, 138.1, 163.7, 199.5. $^{19}$F NMR (376 MHz, $CDCl_3$, rt, δ/ppm): –120.3 (t, $J_{FH}$ = 18.0 Hz, 2F), –138.8 (d, $J_{FH}$ = 53.9 Hz, 2F). HRMS Calcd for $C_{20}H_{26}F_4O_2$ 374.1869, Found *m/z* 374.1864.

**(*Z*)-1-(4-(dimethylamino)phenyl)-6,6,7,7-tetrafluoro-2,3-dipropylhept-2-en-1-one (16ah)**

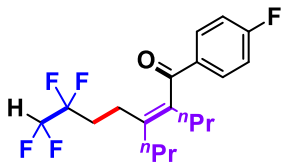



By following the general procedure ***B***, the reaction with 4-dimethylaminobenzaldehyde (**15h**: 74.5 mg, 0.50 mmol) was conducted to give **16ah** (63.1 mg, 33%) as colorless oil.

$^1$H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): 0.78 (t, $J_{HH}$ = 6.8 Hz, 3H), 0.94 (t, $J_{HH}$ = 7.0 Hz, 3H), 1.24–1.33 (m, 2H), 1.41–1.51 (m, 2H), 1.80–2.08 (m, 6H), 2.19 (t, $J_{HH}$ = 8.7 Hz, 2H), 2.96 (s, 6H), 5.52 (tt, $J_{HF}$ = 53.6, 3.4 Hz, 1H), 6.56 (d, $J_{HH}$ = 8.9 Hz, 2H), 7.71 (d, $J_{HH}$ = 8.9 Hz, 2H). $^{13}$C{$^1$H} NMR (100 MHz, $CDCl_3$, rt, δ/ppm): 14.1, 14.3, 21.7, 21.9,

24.1 (t, $J_{CF}$ = 4.7 Hz), 29.3 (t, $J_{CF}$ = 22.6 Hz), 32.3, 33.0, 39.9, 110.1 (tt, $J_{CF}$ = 250.5, 39.7 Hz), 110.7, 117.5 (tt, $J_{CF}$ = 247.5, 28.6 Hz), 124.5, 131.5, 134.7, 138.6, 153.6, 199.0. $^{19}$F NMR (376 MHz, $CDCl_3$, rt, δ/ppm): –120.4 (t, $J_{FH}$ = 17.7 Hz, 2F), –139.0 (d, $J_{FH}$ = 53.6 Hz, 2F). HRMS Calcd for $C_{21}H_{29}F_4NO$ 387.2185, Found *m/z* 387.2183.

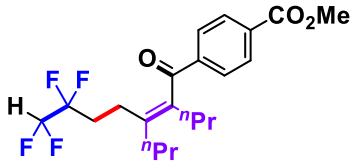
**(*Z*)-6,6,7,7-tetrafluoro-1-(4-fluorophenyl)-2,3-dipropylhept-2-en-1-one (16ai)**




By following the general procedure ***B***, the reaction with 4-fluorobenzaldehyde (**15i**: 52.5 μL, 0.50 mmol) was conducted to give **16ai** (83.1 mg, 47%) as colorless oil.

$^1$H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): 0.79 (t, $J_{HH}$ = 7.2 Hz, 3H), 0.94 (t, $J_{HH}$ = 7.2 Hz, 3H), 1.21–1.31 (m, 2H), 1.42–1.51 (m, 2H), 1.87–2.04 (m, 4H), 2.08 (t, $J_{HH}$ = 7.9 Hz, 2H), 2.19 (t, $J_{HH}$ = 8.6 Hz, 2H), 5.53 (tt, $J_{HF}$ = 54.8, 3.0 Hz, 1H), 7.01–7.06 (m, 2H), 7.80–7.83 (m, 2H). $^{13}$C{$^1$H} NMR (100 MHz, $CDCl_3$, rt, δ/ppm): 13.9, 14.2, 21.7, 21.9, 24.2 (t, $J_{CF}$ = 3.8 Hz), 29.2 (t, $J_{CF}$ = 22.6 Hz), 32.4, 32.5, 110.1 (tt, $J_{CF}$ = 249.3, 40.9 Hz), 115.8 (d, $J_{CF}$ = 21.7 Hz), 117.4 (tt, $J_{CF}$ = 245.1, 28.2 Hz), 131.7 (d, $J_{CF}$ = 9.3 Hz), 133.2 (d, $J_{CF}$ = 2.9 Hz), 137.4, 137.6, 165.9 (d, $J_{CF}$ = 255.5 Hz), 199.1. $^{19}$F NMR (376 MHz, $CDCl_3$, rt, δ/ppm): –108.1 (m, 1F), –120.2 (t, $J_{FH}$ = 17.1 Hz, 2F), –138.7 (d, $J_{FH}$ = 54.8 Hz, 2F). HRMS Calcd for $C_{19}H_{23}F_5O$ 362.1669, Found *m/z* 362.1664.

**methyl-(*Z*)-4-(6,6,7,7-tetrafluoro-2,3-dipropylhept-2-enoyl)benzoate (16aj)**

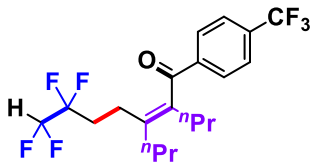



By following the general procedure ***C***, the reaction with methyl-4-formylbenzoate (**15j**: 82.1 mg, 0.50 mmol) was conducted to give **16aj** (142.2 mg, 71%) as colorless oil.

$^1$H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): 0.78 (t, $J_{HH}$ = 7.1 Hz, 3H), 0.95 (t, $J_{HH}$ = 7.6 Hz, 3H), 1.21–1.30 (m, 2H), 1.44–1.53 (m, 2H), 1.88–2.05 (m, 4H), 2.10 (t, $J_{HH}$ = 6.0 Hz, 2H), 2.21 (t, $J_{HH}$ = 8.0 Hz, 2H), 3.86 (s, 3H), 5.54 (t, $J_{HF}$ = 53.3 Hz, 1H), 7.83 (d, $J_{HH}$ =

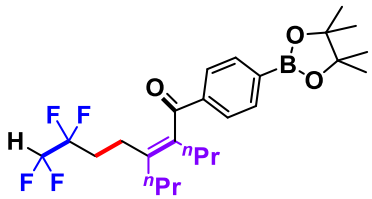
8.3 Hz, 2H), 8.04 (d, $J_{HH}$ = 8.3 Hz, 2H). $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$, rt, δ/ppm): 13.8, 14.2, 21.7, 21.9, 24.3 (t, $J_{CF}$ = 4.3 Hz), 29.2 (t, $J_{CF}$ = 22.3 Hz), 32.4, 32.6, 52.4, 110.1 (tt, $J_{CF}$ = 247.1, 40.4 Hz), 117.4 (tt, $J_{CF}$ = 244.7, 28.5 Hz), 128.9, 129.9, 133.9, 137.6, 138.5, 140.2, 166.2, 200.1. $^{19}F$ NMR (376 MHz, $CDCl_3$, rt, δ/ppm): –120.1 (t, $J_{FH}$ = 16.8 Hz, 2F), –138.7 (d, $J_{FH}$ = 53.3 Hz, 2F). HRMS Calcd for $C_{21}H_{26}F_4O_3$ 402.1818, Found *m/z* 402.1820.

**(*Z*)-6,6,7,7-tetrafluoro-2,3-dipropyl-1-(4-(trifluoromethyl)phenyl)hept-2-en-1-one (16ak)**




By following the general procedure ***B***, the reaction with 4-trifluoromethylbenzaldehyde (**15k**: 67.3 μL, 0.50 mmol) was conducted to give **16ak** (77.4 mg, 38%) as colorless oil. $^{1}H$ NMR (400 MHz, $CDCl_3$, rt, δ/ppm): 0.79 (t, $J_{HH}$ = 6.7 Hz, 3H), 0.95 (t, $J_{HH}$ = 7.2 Hz, 3H), 1.21–1.31 (m, 2H), 1.44–1.53 (m, 2H), 1.88–2.05 (m, 4H), 2.11 (t, $J_{HH}$ = 7.3 Hz, 2H), 2.21 (t, $J_{HH}$ = 8.2 Hz, 2H), 5.54 (tt, $J_{HF}$ = 54.0, 3.1 Hz, 1H), 7.65 (d, $J_{HH}$ = 8.0 Hz, 2H), 7.89 (d, $J_{HH}$ = 8.0 Hz, 2H). $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$, rt, δ/ppm): 13.8, 14.2, 21.7, 21.9, 24.3 (t, $J_{CF}$ = 3.6 Hz), 29.1 (t, $J_{CF}$ = 21.4 Hz), 32.3, 32.5, 110.1 (tt, $J_{CF}$ = 250.2, 41.3 Hz), 117.3 (tt, $J_{CF}$ = 246.5, 29.8 Hz), 125.8 (q, $J_{CF}$ = 3.8 Hz), 129.3, 134.5 (q, $J_{CF}$ = 32.7 Hz), 137.4, 138.8, 139.6, 199.6. Resonances attributable to the $CF_3$ moiety could not be detected due to multiple $^{13}C$–$^{19}F$ couplings. $^{19}F$ NMR (376 MHz, $CDCl_3$, rt, δ/ppm): –66.3 (s, 3F), –120.1 (t, $J_{FH}$ = 17.6 Hz, 2F), –138.6 (d, $J_{FH}$ = 54.0 Hz, 2F). HRMS Calcd for $C_{20}H_{23}F_7O$ 412.1637, Found *m/z* 412.1640.

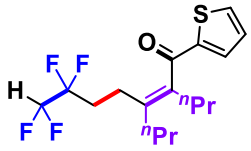
**(*Z*)-6,6,7,7-tetrafluoro-2,3-dipropyl-1-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)hept-2-en-1-one (16al)**



By following the general procedure ***B***, the reaction with 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzaldehyde (**15l**: 116.0 mg, 0.50 mmol) was conducted to give **16al** (136.3 mg, 58%) as colorless oil.

$^{1}$H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): 0.77 (t, $J_{HH}$ = 7.1 Hz, 3H), 0.93 (t, $J_{HH}$ = 7.4 Hz, 3H), 1.22–1.32 (m, 2H), 1.25 (s, 12H), 1.42–1.52 (m, 2H), 1.86–2.04 (m, 4H), 2.09 (t, $J_{HH}$ = 8.0 Hz, 2H), 2.19 (t, $J_{HH}$ = 7.0 Hz, 2H), 5.52 (tt, $J_{HF}$ = 54.2, 2.6 Hz, 1H), 7.76 (d, $J_{HH}$ = 7.6 Hz, 2H), 7.81 (d, $J_{HH}$ = 7.6 Hz, 2H). $^{13}$C{$^{1}$H} NMR (100 MHz, $CDCl_3$, rt, δ/ppm): 13.9, 14.2, 21.6, 21.9, 24.3 (t, $J_{CF}$ = 3.7 Hz), 24.8, 29.3 (t, $J_{CF}$ = 22.8 Hz), 32.5, 32.5, 84.1, 110.1 (tt, $J_{CF}$ = 246.7, 42.0 Hz), 117.4 (tt, $J_{CF}$ = 247.6, 30.0 Hz), 128.1, 135.0, 135.0, 137.4, 138.0, 138.7, 201.0. $^{19}$F NMR (376 MHz, $CDCl_3$, rt, δ/ppm): –120.2 (t, $J_{FH}$ = 17.9 Hz, 2F), –138.8 (d, $J_{FH}$ = 54.2 Hz, 2F). HRMS Calcd for $C_{25}H_{34}BF_4O_3$ 470.2615, Found *m/z* 470.2613.

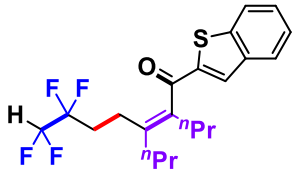
**(*Z*)-6,6,7,7-tetrafluoro-2,3-dipropyl-1-(thiophen-2-yl)hept-2-en-1-one (16am)**




By following the general procedure ***D***, the reaction with 2-thiophenecarboxaldehyde (**15m**: 45.9 μL, 0.50 mmol) was conducted to give **16am** (140.5 mg, 80%) as colorless oil.

$^{1}$H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): 0.81 (t, $J_{HH}$ = 6.8 Hz, 3H), 0.93 (t, $J_{HH}$ = 7.2 Hz, 3H), 1.27–1.37 (m, 2H), 1.41–1.50 (m, 2H), 1.87–2.00 (m, 2H), 2.05–2.12 (m, 4H), 2.25 (t, $J_{HH}$ = 7.7 Hz, 2H), 5.54 (tt, $J_{HF}$ = 53.6, 2.9 Hz, 1H), 7.03 (dd, $J_{HH}$ = 4.3, 4.3 Hz, 1H), 7.50 (d, $J_{HH}$ = 4.3 Hz, 1H), 7.58 (d, $J_{HH}$ = 4.3 Hz, 1H). $^{13}$C{$^{1}$H} NMR (100 MHz, $CDCl_3$, rt, δ/ppm): 13.9, 14.2, 21.6, 22.0, 24.3 (t, $J_{CF}$ = 4.3 Hz), 29.3 (t, $J_{CF}$ = 21.6 Hz), 32.2, 32.8, 110.1 (tt, $J_{CF}$ = 248.7, 40.3 Hz), 117.4 (tt, $J_{CF}$ = 245.8, 28.6 Hz), 128.1, 133.5, 134.4, 136.9, 138.1, 144.4, 193.1. $^{19}$F NMR (376 MHz, $CDCl_3$, rt, δ/ppm): –120.2 (t, $J_{FH}$ = 17.5 Hz, 2F), –138.7 (d, $J_{FH}$ = 53.6 Hz, 2F). HRMS Calcd for $C_{17}H_{22}F_4OS$ 350.1327, Found *m/z* 350.1330.

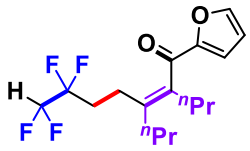
**(*Z*)-1-(benzo[b]thiophen-2-yl)-6,6,7,7-tetrafluoro-2,3-dipropylhept-2-en-1-one (16an)**



By following the general procedure ***D***, the reaction with benzo[b]thiophene-2-carboxaldehyde (**15n**: 81.1 mg, 0.50 mmol) was conducted to give **16an** (160.2 mg, 81%) as colorless oil.

$^{1}$H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): 0.80 (t, $J_{HH}$ = 7.2 Hz, 3H), 0.95 (t, $J_{HH}$ = 7.2 Hz, 3H), 1.28–1.38 (m, 2H), 1.43–1.52 (m, 2H), 1.89–2.02 (m, 2H), 2.08 (t, $J_{HH}$ = 8.0 Hz, 2H), 2.11–2.15 (m, 2H), 2.28 (t, $J_{HH}$ = 8.2 Hz, 2H), 5.51 (tt, $J_{HF}$ = 53.4, 3.4 Hz, 1H), 7.28 (dd, $J_{HH}$ = 6.9, 7.5 Hz, 1H), 7.34 (dd, $J_{HH}$ = 7.5, 7.5 Hz, 1H), 7.71 (s, 1H), 7.74 (d, $J_{HH}$ = 7.5 Hz, 1H), 7.76 (d, $J_{HH}$ = 6.9 Hz, 1H). $^{13}$C{$^{1}$H} NMR (100 MHz, $CDCl_3$, rt, δ/ppm): 13.9, 14.2, 21.7, 22.1, 24.5 (t, $J_{CF}$ = 3.9 Hz), 29.4 (t, $J_{CF}$ = 22.8 Hz), 32.4, 32.8, 110.1 (tt, $J_{CF}$ = 249.7, 40.4 Hz), 117.4 (tt, $J_{CF}$ = 246.4, 28.7 Hz), 123.0, 125.0, 126.0, 127.5, 130.7, 137.6, 137.8, 139.0, 143.0, 143.8, 194.7. $^{19}$F NMR (376 MHz, $CDCl_3$, rt, δ/ppm): –120.2 (t, $J_{FH}$ = 17.3 Hz, 2F), –138.8 (d, $J_{FH}$ = 53.4 Hz, 2F). HRMS Calcd for $C_{21}H_{24}F_4OS$ 400.1484, Found *m/z* 400.1487.

**(*Z*)-6,6,7,7-tetrafluoro-1-(furan-2-yl)-2,3-dipropylhept-2-en-1-one (16ao)**

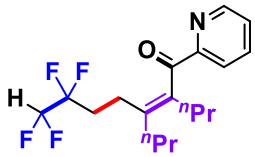


By following the general procedure ***D***, the reaction with 2-thiophenecarboxaldehyde (**15o**: 41.4 μL, 0.50 mmol) was conducted to give **16ao** (126.1 mg, 76%) as colorless oil.

$^{1}$H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): 0.86 (t, $J_{HH}$ = 7.2 Hz, 3H), 0.97 (t, $J_{HH}$ = 7.8 Hz, 3H), 1.31–1.40 (m, 2H), 1.45–1.54 (m, 2H), 1.93–2.17 (m, 6H), 2.30 (t, $J_{HH}$ = 7.6 Hz, 2H), 5.63 (tt, $J_{HF}$ = 54.2, 2.9 Hz, 1H), 6.51 (br, 1H), 7.07 (br, 1H), 7.59 (br, 1H). $^{13}$C{$^{1}$H} NMR (100 MHz, $CDCl_3$, rt, δ/ppm): 13.8, 14.0, 21.4, 21.9, 24.1 (t, $J_{CF}$ = 3.8

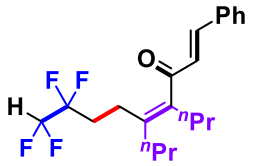
Hz), 29.2 (t, $J_{CF}$ = 21.9 Hz), 32.3, 32.4, 110.0 (tt, $J_{CF}$ = 249.2, 40.7 Hz), 112.2, 117.4 (tt, $J_{CF}$ = 246.9, 29.3 Hz), 119.2, 137.3, 137.9, 147.1, 152.7, 188.3. $^{19}$F NMR (376 MHz, $CDCl_3$, rt, δ/ppm): –120.4 (t, $J_{FH}$ = 17.3 Hz, 2F), –138.8 (d, $J_{FH}$ = 54.2 Hz, 2F). HRMS Calcd for $C_{17}H_{22}F_4O_2$ 334.1556, Found *m/z* 334.1560.

**(*Z*)-6,6,7,7-tetrafluoro-2,3-dipropyl-1-(pyridin-2-yl)hept-2-en-1-one (16ap)**



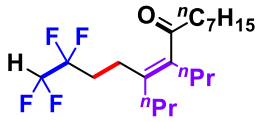

By following the general procedure ***B***, the reaction with 2-pyridinecarboxaldehyde (**15p**: 53.5 mg, 0.50 mmol) was conducted. After redundant TFE and ethylene were purged from the reactor, the reaction mixture was exposed to air to quench the catalyst. Tetradecane (10.0 μL, as an internal standard) was added to the reaction mixture. GC analysis revealed that the target compound **16ap** was not obtained.

**(*1E,4Z*)-8,8,9,9-tetrafluoro-1-phenyl-4,5-dipropylnona-1,4-dien-3-one (16aq)**




By following the general procedure ***B***, the reaction with *trans*-cinnamaldehyde (**15q**: 62.7 μL, 0.50 mmol) was conducted to give **16aq** (100.0 mg, 54%) as colorless oil.
$^1$H NMR (400 MHz, $CDCl_3$, rt, δ/ppm): 0.95 (t, $J_{HH}$ = 6.9 Hz, 3H), 1.06 (t, $J_{HH}$ = 7.5 Hz, 3H), 1.39–1.49 (m, 2H), 1.51–1.62 (m, 2H), 1.88–2.15 (m, 4H), 2.19 (t, $J_{HH}$ = 7.4 Hz, 2H), 2.35 (t, $J_{HH}$ = 7.6 Hz, 2H), 5.71 (t, $J_{HF}$ = 53.1 Hz, 1H), 6.83 (d, $J_{HF}$ = 17.1 Hz, 1H), 7.39–7.63 (m, 6H). $^{13}$C{$^1$H} NMR (100 MHz, $CDCl_3$, rt, δ/ppm): 14.0, 14.2, 21.7, 22.1, 24.3 (t, $J_{CF}$ = 3.3 Hz), 29.4 (t, $J_{CF}$ = 22.2 Hz), 32.2, 32.7, 110.2 (tt, $J_{CF}$ = 250.2, 40.5 Hz), 117.6 (tt, $J_{CF}$ = 245.6, 29.4 Hz), 126.8, 128.3, 128.9, 130.6, 134.5, 137.6, 138.6, 145.1, 200.2. $^{19}$F NMR (376 MHz, $CDCl_3$, rt, δ/ppm): –120.0 (t, $J_{FH}$ = 18.7 Hz, 2F), –138.6 (d, $J_{FH}$ = 53.1 Hz, 2F). HRMS Calcd for $C_{21}H_{26}F_4O$ 370.1920, Found *m/z* 370.1920.

**(*Z*)-1,1,2,2-tetrafluoro-5,6-dipropyltetradec-5-en-7-one (16ar)**



By following the general procedure ***B***, the reaction with octanal (**15r**: 77.8 μL, 0.50 mmol) was conducted. After redundant TFE and ethylene were purged from the reactor, the reaction mixture was exposed to air to quench the catalyst. Tetradecane (10.0 μL, as an internal standard) was added to the reaction mixture. GC analysis revealed that the target compound **16ar** was not obtained.

**Stoichiometric reaction of 1, 9a, and 15a (Scheme 4.6)**

A toluene solution (25 mL) of **1** (355.5 mg, 0.50 mmol), **9a** (145.0 μL, 1.0 mmol), and **15a** (115.0 μL, 1.0 mmol) was transferred into a sealed tube reactor, and the reaction mixture was stirred at 100 °C for 24 h. All volatiles were then removed under reduced pressure, and the crude product was purified by silica gel column chromatography. Further purification was conducted by recycle HPLC, giving **16aa** (135.1 mg, 75%) as colorless oil.

**Isolation of 18 (Scheme 4.7)**

A toluene solution (5.0 mL) of **17** (162.0 mg, 0.30 mmol)[S1] and **9q** (74.4 μL, 0.60 mmol) was transferred into a sealed tube, and the reaction mixture was thermostated at 40℃ for 24 h. All volatiles were removed under reduced pressure, and then residue was washed with hexane, affording **18** (84.4 mg, 44%) as yellow solid. Single crystals for X-ray diffraction analysis were prepared by recrystallization from toluene/pentane at room temperature.

$^{1}$H NMR (400 MHz, $C_6D_6$, rt, δ/ppm): 1.03 (t, $J_{HH}$ = 7.7 Hz, 3H), 1.07–2.27 (m, 36H), 1.91 (s, 3H), 2.54–2.66 (m, 1H), 2.92–3.06 (m, 1H), 3.11 (d, $J_{HH}$ = 2.7 Hz, 1H), 4.05 (dd, $J_{HH}$ = 4.2, 11.5 Hz, 1H), 7.08–7.10 (m, 2H), 7.14–7.17 (m, 3H). $^{13}$C{$^{1}$H} NMR (100 MHz, $C_6D_6$, rt, δ/ppm): 13.6, 22.4, 26.5, 27.8, 30.3 (d, $J_{CP}$ = 14.9 Hz), 30.9 (d, $J_{CP}$ = 5.0 Hz), 35.4 (d, $J_{CP}$ = 16.2 Hz), 42.0 (t, $J_{CF}$ = 24.7 Hz), 46.0, 63.2, 104.9, 126.3, 125.3, 128.1, 128.4, 144.1, 162.5 (d, $J_{CP}$ = 36.3 Hz). Resonances attributable to the $CF_2CF_2$ moiety could not be detected due to multiple $^{13}$C–$^{19}$F couplings. $^{31}$P{$^{1}$H} NMR

(162 MHz, $C_6D_6$, rt, δ/ppm): 31.3 (dd, $J_{PF}$ = 17.2, 28.4 Hz, 1P). $^{19}F$ NMR (376 MHz, $C_6D_6$, rt, δ/ppm): –96.6 (dm, $J_{FF}$ = 279.3 Hz, 1F), –99.6 (dd, $J_{FF}$ = 279.3, $J_{FP}$ = 28.4 Hz, 1F), –106.0 (dd, $J_{FF}$ = 239.4, $J_{FH}$ = 24.3 Hz, 1F), –119.1 (ddd, $J_{FF}$ = 239.4, $J_{FH}$ = 16.8, 24.3 Hz, 1F). Anal. Calcd for $C_{35}H_{51}F_4NiP$: C, 65.95; H, 8.06. Found: C, 67.15; H, 7.88.

**Stoichiometric reaction of 18 with 15k (Scheme 4.7)**

To a $C_6D_6$ solution (0.5 mL) of **18** (19.1 mg, 0.03 mmol) and $PCy_3$ (8.4 mg, 0.03 mmol) was added *α,α,α*-trifluorotoluene (5.0 μL, as an internal standard) and **15k** (8.0 μL, 0.06 mmol). The solution was transferred into a sealed NMR tube. The reaction was monitored at 100 °C by means of $^{19}F$ NMR spectroscopy. After 24 h, a desired cross-tetramer (**19qk**) was obtained in 76% yield.

**Stoichiometric reaction of 18 with Ethylene (Scheme 4.7)**

To a $C_6D_6$ solution (0.5 mL) of **18** (19.1 mg, 0.03 mmol) and $PCy_3$ (8.4 mg, 0.03 mmol) was added *α,α,α*-trifluorotoluene (5.0 μL, as an internal standard). The solution was transferred into a pressure-tight NMR tube and ethylene (5.0 atm) was charged into the reactor. The reaction was monitored at 100 °C by means of $^{19}F$ NMR spectroscopy. After 24 h, a desired cross-tetramer (**14q**) was not obtained at all.

**References for Experimental Section**

S1 M. Ohashi, Y. Ueda, S. Ogoshi, *Angew. Chem. Int. Ed.* **2017**, *56*, 2435.

# Conclusion

Described in this thesis were the studies on cross-oligomerization reactions via oxidative cyclization of tetrafluoroethylene and ethylene with nickel. The studies enable efficient and straightforward formations of a variety of cross-oligomers with $CF_2CF_2H$. The partially fluorinated nickelacycles were found to play crucial roles in the transformation reactions.

In chapter 2, the Ni(0)-catalyzed co-trimerization reaction of TFE and ethylene was described. The five-membered nickelacycle intermediate generated by the oxidative cyclization of TFE and ethylene was isolated and the structure was unambiguously determined by X-ray diffraction analysis. Furthermore, Michael addition of this nickelacycle toward α,β-unsaturated carbonyl compound was also achieved.

In chapters 3 and 4, the Ni(0)-catalyzed three- or four-component cross-tetramerizations of TFE with various unsaturated compounds were described. These are the first examples of unprecedentedly high selective cross-tetramerizations using three or four different unsaturated compounds. Except for our works, the transition-metal-catalyzed cross-tetramerization have not been known at all, most likely due to potential side reactions that generate e.g. homo-coupling products. The transition-metal-catalyzed homo-tetramerization, such as tetramerization of ethylene to 1-octene, have only been reported.

It should be emphasized that efficient and general synthetic methods of the compounds with $CF_2CF_2H$ have not yet been developed. In addition, the application of $CF_2CF_2H$-containing compounds has not been studied as fully as expected. Thus, the studies in this thesis will provide new strategies of the synthesis of such compounds. I believe that these studies will give a significant development for the utility of $CF_2CF_2H$-based compounds in the next decades thanks to the availability of unprecedented derivatives.

# List of Publications

1. 2,2,3,3-Tetrafluoronickelacyclopentanes Generated via the Oxidative Cyclization of Tetrafluoroethylene and Simple Alkenes: A Key Intermediate in Nickel-Catalyzed C-C Bond-Forming Reactions
   M. Ohashi, T. Kawashima, T. Taniguchi, K. Kikushima, S. Ogoshi
   *Organometallics* **2015**, *34*, 1604–1607.
2. Nickel-Catalyzed Formation of 1,3-Dienes via a Highly Selective Cross-Tetramerization of Tetrafluoroethylene, Styrenes, Alkynes, and Ethylene
   T. Kawashima, M. Ohashi, S. Ogoshi
   *J. Am. Chem. Soc.* **2017**, *139*, 17795–17798.
3. Selective Catalytic Formation of Cross-Tetramers from Tetrafluoroethylene, Ethylene, Alkynes, and Aldehydes via Nickelacycles as Key Reaction Intermediates
   T. Kawashima, M. Ohashi, S. Ogoshi
   *J. Am. Chem. Soc.* **2018**, *140*, 17423–17427.