# Kinetic Resolution of Cyclic Tertiary Alcohols with Lipase A from *Candida antarctica*

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## Abstract

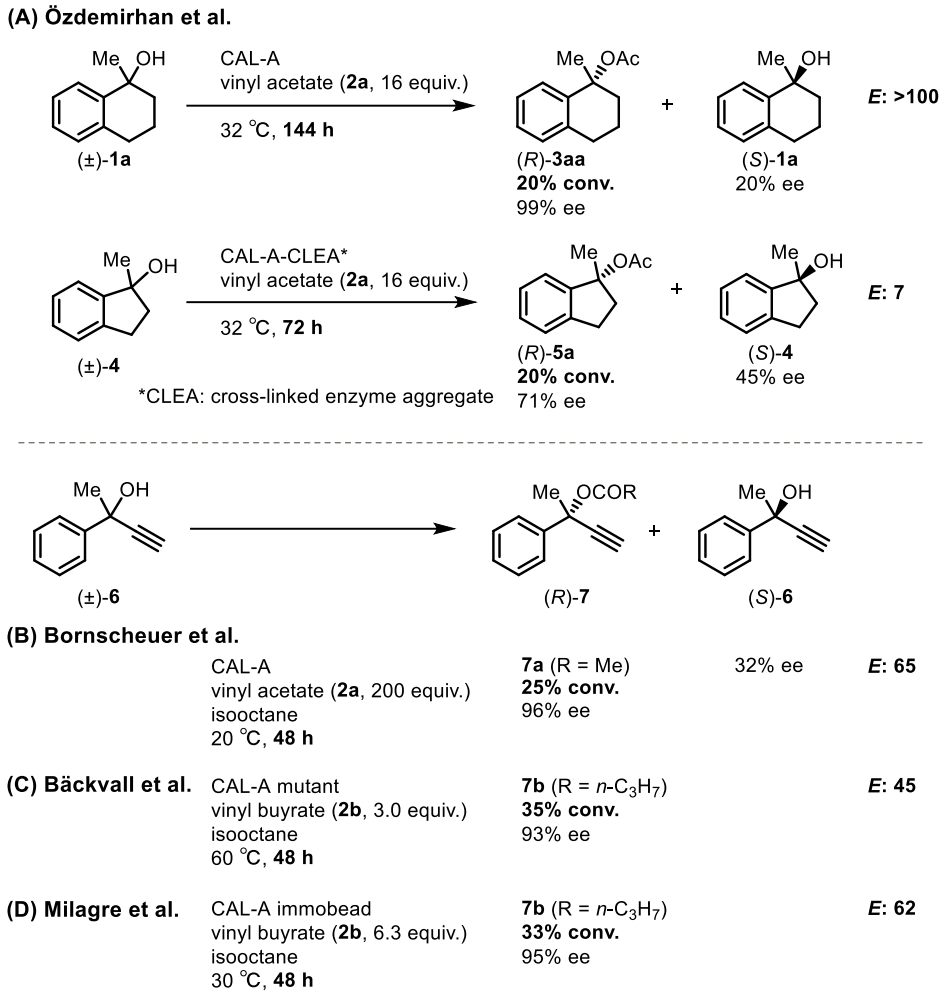
Enzyme-catalyzed acylative kinetic resolution (KR) and dynamic kinetic resolution (DKR) of racemic primary and secondary alcohols have been widely reported to produce esters with high enantiomeric purity. In contrast, similar KRs of tertiary alcohols have been reported for only a limited range of substrates and require prolonged reaction times of several days. To gain deeper insight into the substrate scope and increase the process efficiency, we examined the reaction conditions using commercially available immobilized lipase A from *Candida antarctica* and found that the addition of the heterogeneous, inorganic base sodium carbonate significantly increased the reaction rate while maintaining high enantioselectivity. The use of vinyl hexanoate as the acyl donor provided esters that were stable during chromatography purification. The optimized reaction conditions were then successfully applied to a range of cyclic tertiary alcohols containing tetralin, dihydroindene, chromane, and thiochromane skeletons having, in part, a substituent on the aromatic ring. In this study on the structure–reactivity relationship of enzymatic KR-type reactions, we achieved >30% conversion for various tertiary alcohols in 24 h at 25 °C, producing optically active esters with 88–99% ee.

## Introduction

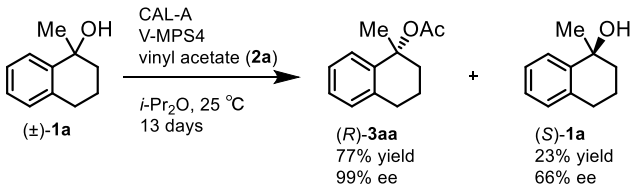
Tertiary alcohols and their derivatives are important substructures found in many natural products and synthetic drugs.[1] They are widely used as synthetic building blocks. Therefore, the synthesis of enantiomerically pure tertiary alcohols has received increasing attention over the past two decades in the fields of synthetic organic chemistry and biocatalysis; nonetheless, it still remains challenging.[1–3] By exploiting the excellent enantiomeric discrimination abilities of lipases and other hydrolytic enzymes, kinetic resolution (KR) and dynamic kinetic resolution (DKR) via esterification of racemic alcohols have been extensively studied. However, most of these reports describe the use of primary or secondary alcohols as substrates,[4,5] and to date, successful KR of tertiary alcohols by lipases has offered very limited substrate variation, as summarized in Scheme 1. This is mainly because of the bulkiness and steric rigidity of tertiary alcohols, which significantly reduce their reactivity with acylated lipase

intermediates. Therefore, the KR of tertiary alcohols by acylation reported thus far mostly requires prolonged reaction times of several days. Furthermore, in contrast to primary and secondary alcohols, the range of lipases suitable for tertiary alcohols is very limited. Thus far, only a few commercial lipases, such as lipase A from *Candida antarctica* (CAL-A), lipase from *Candida rugosa*, and lipase from *Burkholderia cepacia*, are applicable.[6–9] Namely, the KR of (±)-**1a** containing a tetralin skeleton reported by Özdemirhan et al. reached 20% conversion in 144 h, producing ester (*R*)-**3aa** (99% ee) with very high enantioselectivity (*E*[10]: >100). In contrast, the KR of (±)-**4** containing the less bulky dihydroindene moiety reached 20% conversion in 72 h, but the enantiomeric purity of ester (*R*)-**5a** (71% ee) and the enantioselectivity (*E*: 7) were low (Scheme 1A).[6] Bornscheuer et al. performed KR of tertiary propargylic alcohol (±)-**6** at 20 °C, in which the conversion reached 25% in 48 h, yielding ester (*R*)-**7a** with 96% ee (*E*: 65) (Scheme 1B).[7] Subsequently, Bäckvall et al. prepared CAL-A mutants, which improved the reactivity of the original lipase and reduced the reaction time of the KR of (±)-**6** to 48 h but at a higher temperature such as 60 °C (35% conv., *E*: 45) (Scheme 1C).[8] In 2023, another approach for improving the KR reaction rate of (±)-**6** via reaction engineering, such as the selection of better immobilization carriers for commercial CAL-A, was reported to give (*R*)-**7b** (33% conv., 95% ee, *E*: 62) in 48 h at 30 °C (Scheme 1D).[9] Although the enzymatic KR of esters derived from racemic tertiary alcohols via enantioselective hydrolysis has also been reported, most of the substrates are limited to esters of 1-arylpropargylic alcohols.[11]

We recently reported the first enzymatic DKR of (±)-**1a** affording the optically active ester (*R*)-**3aa** in 77% yield and with 99% ee,[12] in which enantioselective acylation with CAL-A proceeded simultaneously with the racemization of remaining (*S*)-**1a** by our original racemization catalyst V-MPS4[13] (Scheme 2). However, the reaction took 13 d and required the sequential addition of fresh CAL-A and V-MPS4. In addition, only one such example has been reported thus far. Since then, to improve the efficiency and substrate applicability of our DKR protocol, we have been studying two approaches in parallel: optimization of the reaction conditions and generation of improved CAL-A mutants.[14] Regarding the first approach, we herein report a substantial reactivity improvement and substrate scope expansion of the KR of tertiary alcohols using commercial CAL-A.




**Scheme 1.** Reported lipase-catalyzed KR of tertiary alcohols (±)-**1a**, (±)-**4** and (±)-**6**.



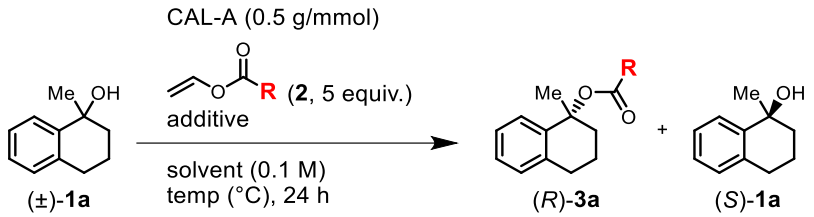

**Scheme 2.** CAL-A and V-MPS4 co-catalyzed DKR of (±)-**1a**.

## Results and Discussion

As benchmark experiments, the reaction conditions for the CAL-A-catalyzed KR of (±)-**1a** (0.12 mmol) were examined at 25 °C using diisopropyl ether and isooctane as solvents according to our previous DKR studies.[12] First, we investigated the effect of the alkyl chain length of vinyl esters on the biotransformation of (±)-**1a** (Table 1). Vinyl acetate (R = Me, **2a**), which was used in the previous DKR, produced (*R*)-**3aa** (30% yield) with very high enantioselectivity (*E* >100) in 24 h (entry 1). Under the same conditions, vinyl butyrate (R = *n*-$C_3H_7$, **2b**) and vinyl hexanoate (R = *n*-$C_5H_{11}$, **2c**) slightly increased the product yield, while maintaining high enantioselectivities (entries 2 and 3). In contrast, the

yield decreased to 21% when vinyl decanoate (R = *n*-$C_9H_{19}$, **2d**) was used (entry 4). In our parallel studies on the DKR of tertiary alcohols, the formation of alkenes (e.g., 4-methyl-1,2-dihydronaphthalene) from esters **3a** was sometimes observed in the presence of V-MPS4, but we found that such side reactions were significantly suppressed in esters such as hexanoate and decanoate.[15] Therefore, considering the stability of esters **3a** and the reaction rate, **2c** was selected as the best acyl donor for this purpose.[16] Using **2c**, we next examined similar KRs at higher temperatures (entries 5 and 6), in isooctane (entry 7), or with twice the amount of CAL-A (entry 8). However, no significant improvements were observed. In contrast, the addition of sodium carbonate (1 mol equiv.) to the conditions shown in entry 3 led to increased conversion (46%) in 24 h while maintaining high enantioselectivity (entry 9).[17] Accordingly, the condition of entry 9 was determined to be optimal.

**Table 1.** Optimization of reaction conditions for CAL-A-catalyzed KR of (±)-**1a**[a].




| Entry | R | Temp. (℃) | Additive | Solvent | Yield [%] of 3a[b] | Ee [%] of 1a | *E*[c] |
|---|---|---|---|---|---|---|---|
| **1** | Me (**2a**) | 25 | – | *i*-$Pr_2O$ | 30 (**3aa**) | 42 | >100 |
| **2** | *n*-$C_3H_5$ (**2b**) | 25 | – | *i*-$Pr_2O$ | 33 (**3ab**) | 49 | >100 |
| **3** | *n*-$C_5H_{11}$ (**2c**) | 25 | – | *i*-$Pr_2O$ | 36 (**3ac**) | 53 | >100 |
| **4** | *n*-$C_9H_{19}$ (**2d**) | 25 | – | *i*-$Pr_2O$ | 21 (**3ad**) | 26 | >100 |
| **5** | *n*-$C_5H_{11}$ (**2c**) | 35 | – | *i*-$Pr_2O$ | 28 (**3ac**) | 38 | >100 |
| **6** | *n*-$C_5H_{11}$ (**2c**) | 50 | – | *i*-$Pr_2O$ | 27 (**3ac**) | 37 | >100 |
| **7** | *n*-$C_5H_{11}$ (**2c**) | 25 | – | isooctane | 29 (**3ac**) | 41 | >100 |
| **8**[d] | *n*-$C_5H_{11}$ (**2c**) | 25 | – | *i*-$Pr_2O$ | 34 (**3ac**) | 52 | >100 |
| **9** | *n*-$C_5H_{11}$ (**2c**) | 25 | $Na_2CO_3$ (1 mol equiv.) | *i*-$Pr_2O$ | 45 (**3ac**) | 79 | >100 |
| **10** | *n*-$C_5H_{11}$ (**2c**) | 25 | *n*-$C_5H_{11}COONa$ (2 mol equiv.) | *i*-$Pr_2O$ | 48 (**3ac**) | 85 | >100 |
| **11** | *n*-$C_5H_{11}$ (**2c**) | 25 | *n*-$C_5H_{11}COOH$ (1 mol equiv.) | *i*-$Pr_2O$ | 29 (**3ac**) | 44 | >100 |

[a] The reaction of each entry was performed with (±)-**1a** (0.12 mmol) and other reagents under the conditions shown in the Table. [b] Calculated by the molar ratio of **1a** and **3a** determined by $^1$H NMR analysis of a crude product. [c] Calculated based on enantiomeric excess of 1a and conversion, i.e., the yield of **3a**, according to the reference method.[10] [d] CAL-A (1.0 g/mmol) was used.

To understand what improved the yield of (*R*)-**3ac** in the above-mentioned KR of (±)-**1a** in the presence of $Na_2CO_3$, we performed the KR of (±)-**1a** under the same conditions as entry 3 of Table 1 with some additives (entries 10 and 11). At the same time, the time course of the yield of (*R*)-**3ac** in the KR of entries 3, 9, 10 and 11 was also examined (Fig. 1). Fig. 1 indicated that the addition of $Na_2CO_3$ (entry 9) resulted in almost the same initial reaction rate as that of no additive (entry 3), and a higher initial reaction rate was observed with sodium *n*-hexanoate (entry 10). Between 2–24 h, the yields of **3ac** were always highest under the conditions with sodium *n*-hexanoate, followed by $Na_2CO_3$, and no additive, in that order. Interestingly, the yields of **3ac** obtained under the first two conditions reached almost the same, i.e. 48% and 45% yield, respectively after 24 h (Table 1, entries 9 and 10). In contrast, when adding *n*-hexanoic acid, the yield of **3ac** was always lower than without an additive throughout 24 h (entry 11). Another important observation is that little reaction progress was observed after 8 h both under conditions without and with *n*-hexanoic acid. These results indicate that hexanoic acid decreases the CAL-A activity. Considering the fact that the acylation rate of tertiary alcohols in KR is much lower than that of primary or secondary alcohols, it is suggested that during KR of tertiary alcohols, more vinyl *n*-hexanoate are hydrolyzed in the presence of water on the lipase surface to form *n*-hexanoic acids. Therefore, we speculate that *n*-hexanoic acid generated by the CAL-A-catalyzed hydrolysis of vinyl *n*-hexanoate, which occurred simultaneously with the CAL-A-catalyzed acylation of **1a**, diminishes the catalytic activity of CAL-A and, thus, reduces the acylation reaction rate. On the other hand, the addition of $Na_2CO_3$ to KR is thought to suppress the decrease in reactivity of CAL-A because *n*-hexanoic acid produced during the KR reaction is quenched by $Na_2CO_3$ to form sodium *n*-hexanoate. Furthermore, the initial reaction rate of KR was highest in the presence of sodium *n*-hexanoate, which itself may also contribute to increasing the reactivity of CAL-A.

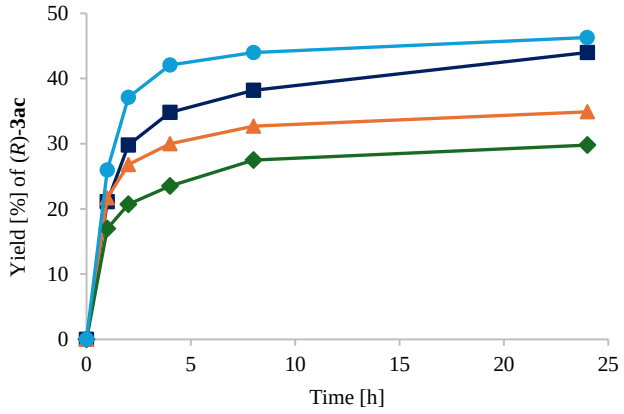
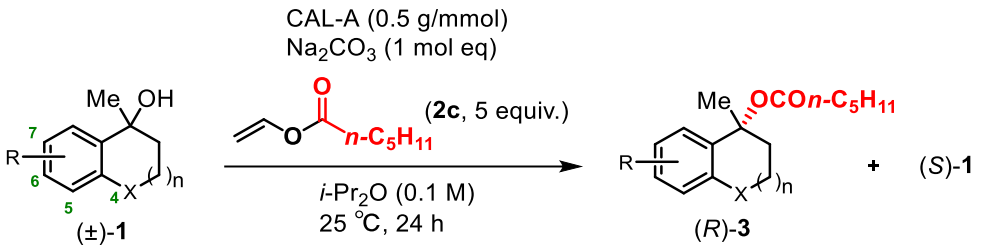


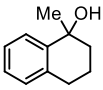
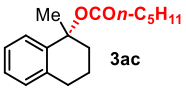
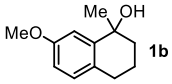
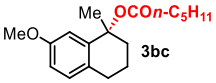
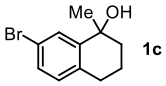
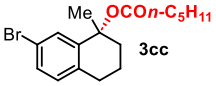
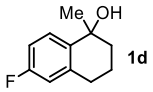
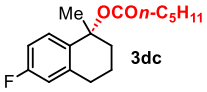
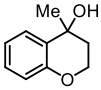
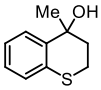
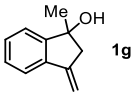

**Figure 1.** Time course of the yield of (*R*)-**3ac** in the KR of (±)-**1a** under the conditions given in Table 1, entries 3, 9, 10 and 11: (▲) without additive (entry 3), (■) with $Na_2CO_3$ (entry 9), (●) with *n*-$C_5H_{11}COONa$ (entry 10), (◆) with *n*-$C_5H_{11}COOH$ (entry 11). Each yield [%] of (*R*)-**3ac** was calculated based on the enantiomeric excesses of (*R*)-**3ac** and (*S*)-**1a**, respectively (see also footnote b in Table S1 in Supporting Information), and the enantiomeric excess of (*R*)-**3ac** and (*S*)-**1a** at each time was calculated from chiral HPLC analysis of an aliquot of the reaction solution.

Next, we studied the substrate scope under the optimal reaction conditions (Table 1, entry 9). Thus, KR of (±)-**1a** was performed again at an 0.18-mmol scale, and the products were purified via flash column chromatography using silica gel modified with aminopropyl groups (product name: Wakogel® 50NH2, FUJIFILM Wako Pure Chemical, Japan) to give (*R*)-**3ac** (R = *n*-$C_5H_{11}$, 44% yield, 99% ee) and (*S*)-**1a** (54% yield, 80% ee) (Table 2, entry 1), in which the yield and enantiomeric purity were almost the same as the results of entry 9 in Table 1. We found that the use of Wakogel® 50NH2 for the chromatography purification allowed the isolation of pure **3ac** without loss of material. In contrast, flash chromatography using ordinary silica gel caused gradual degradation of **3ac**, forming alkenes, owing to the acidity of the silica gel, and the contamination of the alkenes in **3ac** was unavoidable.

Under the same reaction and purification conditions, the KR of (±)-**1b**–**1d** each having a substituent at either the C6 or C7 position of tetralin afforded the esters (*R*)-**3bc**–**3dc** in 32%–39% isolated yields with excellent enantiomeric purity (97%–99% ee) (entries 2–4).[18] Similarly, (±)-**1e** and (±)-**1f**, in which the C4 carbon is replaced by a heteroatom such as oxygen or sulfur, produced (*R*)-**3ec** and (*R*)-**3fc** with 96% ee and 98% ee, respectively, although their yields were slightly reduced compared with **1a** (entries 5 and 6). Alcohol (±)-**1g** containing a dihydroindene skeleton reacted very fast even without sodium carbonate to give (*R*)-**3gc** (88% ee, *E*: 31) in 41% yield after only 4 h. This result suggests that the introduction of a substituent at the C3 position of dihydroindene increases enantioselectivity, because a similar KR of racemic 1-methyl-2,3-dihydro-1*H*-inden-1-ol (±)-**4** produced the ester (*R*)-**5** with lower enantioselectivity (*E*: 7) (Scheme 2A).[6]

**Table 2.** CAL-A-Catalyzed KR of various tertiary alcohols (±)-**1**.[a]




| Entry | (±)-1 | (*R*)-3 | (*R*)-3 Yield [%][b] | (*R*)-3 Ee [%] | (*S*)-1 Yield [%][b] | (*S*)-1 Ee [%] | *E* Value[c] |
|---|---|---|---|---|---|---|---|
| 1 |  **1a** |  **3ac** | 44 | 99 | 54 | 80 | >100 |
| 2 |  **1b** |  **3bc** | 34 | 99 | 65 | 52 | >100 |
| 3 |  **1c** |  **3cc** | 32 | 99 | 65 | 53 | >100 |
| 4 |  **1d** |  **3dc** | 39 | 97 | 60 | 65 | >100 |
| 5 |  **1e** |  **3ec** | 33 | 96 | 67 | 37 | 70 |
| 6 |  **1f** |  **3fc** | 31 | 98 | 69 | 50 | >100 |
| 7[d] |  **1g** |  **3gc** | 41 | 88 | 59 | 67 | 31 |

[a] The reaction of each entry was performed with (±)-**1** (0.12–0.19 mmol) and other reagents under the conditions shown in the Table.
[b] Isolated yield. [c] Calculated based on the enantiomeric excess of **1** and that of **3**. [d] Reaction was conducted for 4 h without $Na_2CO_3$.

According to the results in Table 3, the effects of structural variations on the reactivity (i.e., yield of **3**) and enantioselectivity (*E* value) were visualized by plotting **1a**–**1g** on a yield–*E* value graph (Fig. 2A). Some less-reactive alcohols (**1h**–**1l**) are shown in Fig. 2B. From these data, the following distinctive features were observed. (i) The substituents at the C6 and C7 positions of the tetralin skeleton had little effect on the reactivity, as **1b**–**1d** exhibited a conversion rate similar to that of **1a**. In contrast, the substituent at the C5 position had a major impact, as in **1h** containing a methoxy group at the C5 position, only 10% conversion was obtained, even after 48 h. (ii) Almost the same high reactivity and enantioselectivity as **1a** were observed for **1e** and **1f**, where the C4 carbon of **1a** was replaced by oxygen or sulfur. (iii) The bulkiness around the hydroxy group and the size of the cyclic alcohol moiety

significantly affected the reactivity. For example, the reactivity of **1g**, which has a five-membered ring, is higher than that of **1a**, which has a six-membered ring. However, the reaction did not proceed with **1i** with a seven-membered ring, **1j** with an additional benzene ring, and **1k** with an ethyl group. (iv) The nucleophilicity of the hydroxy group appeared to be important because acylation did not proceed for **1l** with an electron-withdrawing $CF_3$ group (instead of a methyl group, as in the case of most other examples) as a substituent at the quaternary carbon.

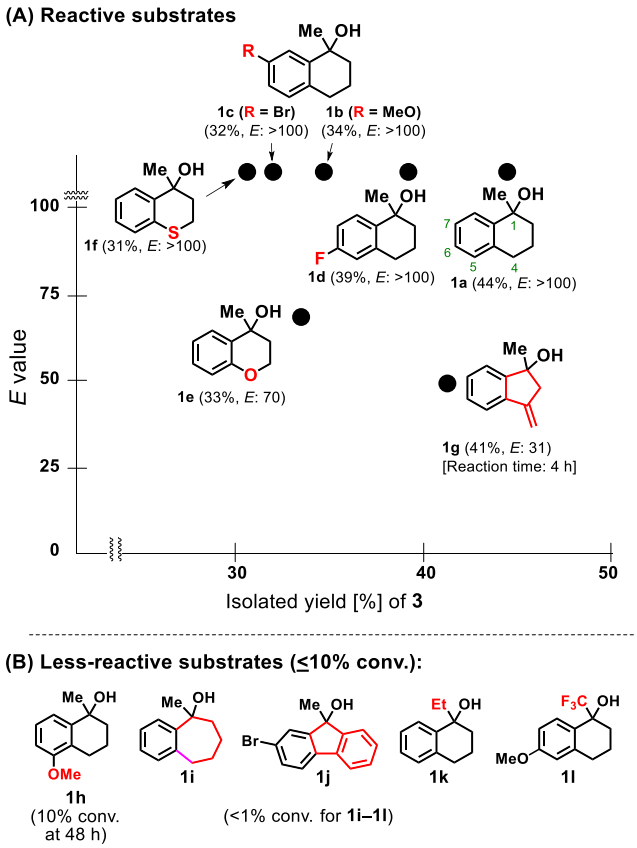



**Figure 2.** The influence of structural variations of tertiary alcohols **1** on reactivity (i.e., yield of **3**) and enantioselectivity (*E* value), in which the yield and *E* value in Table 2 are shown in parentheses. (A) Reactive substrates, (B) Less-reactive substrates.

## Conclusion

In this study, we improved the process for kinetic resolution (KR) of various tertiary alcohols using commercially available immobilized lipase A from *Candida antarctica* (CAL-A). The reaction rate was significantly increased by using vinyl hexanoate and sodium carbonate to obtain optically active esters (*R*)-**3** with up to 44% yield in only 24 h at 25 °C; thus, the reaction time was substantially reduced compared with previously reported results.[6] In addition, we found that six new tertiary alcohols, **1b**–**1g** were applicable to KR with CAL-A, and the enantiomeric purity of esters **3ac**–**3gc** was in the range of 88–99% ee. The *E* value was >30 for all these cases, which is notable because such high

enantioselectivity allows the production of esters with excellent enantiomeric purity when KR is applied to DKR. Simultaneously, we recognized the limitations of the substrate structure, which can be adapted to commercially available CAL-A. Future studies are underway to expand the substrate scope of this KR and apply it to the DKR in the presence of racemization catalysts for synthesizing optically active compounds in higher yields and with improved efficiency.

## Experimental Section

**General procedure for kinetic resolution of (±)-1**

Diisopropyl ether (0.1 M) was added to (±)-**1** (1.0 equiv.), CAL-A (0.5 g/mmol) and $Na_2CO_3$ (1.0 mol equiv.), followed by vinyl hexanoate (5.0 equiv.). The reaction mixture was stirred at 25 ºC for 4 h or 24 h. The resultant mixture was filtered through a Celite pad, and the filtrate was concentrated under reduced pressure. The crude residue was purified by flash column chromatography filled with Wakogel® 50NH2 to give (*R*)-**3** and (*S*)-**1**.

**Kinetic resolution of (±)-1a**

According to the general procedure, (*R*)-**3ac** (21 mg, 0.082 mmol, 44% yield) and (*S*)-**1a** (16 mg, 0.10 mmol, 54% yield) were obtained from (±)-**1a** (30 mg, 0.18 mmol).

**(*R*)-1-Methyl-1,2,3,4-tetrahydronaphthalen-1-yl hexanoate [(*R*)-3ac]**

A colorless oil; $[\alpha]^{23}_D$ = –25 (*c* 0.95, $CH_3OH$); its enantiomeric excess (99% ee) was determined by HPLC analysis at 25 ºC using a CHIRALPAK IJ-3 column (hexane/2-propanol = 98:2, 1 mL/min), UV detection 210 nm, retention time 4.6 min (*S*), 5.5 min (*R*). $^1$H NMR (400 MHz, $CD_3OD$) $\delta$ 7.36-7.28 (m, 1H), 7.16-7.08 (m, 2H), 7.07-7.03 (m, 1H), 2.85 (ddd, *J* = 16.4, 10.4, 5.2 Hz, 1H), 2.73 (dt, *J* = 16.4, 4.4 Hz, 1H), 2.57 (td, *J* = 12.8, 3.2 Hz, 1H), 2.25 (t, *J* = 7.2 Hz, 2H), 2.05 (dddd, *J* = 12.8, 6.0, 4.0, 1.2 Hz, 1H), 2.02-1.91 (m, 1H), 1.86-1.74 (m, 1H), 1.69 (s, 3H), 1.56 (quint., *J* =7.2 Hz, 2H), 1.38-1.22 (m, 4H), 0.90 (t, *J* = 7.2 Hz, 3H); $^{13}$C NMR (100 MHz, $CD_3OD$) $\delta$ 174.9, 141.5, 137.8, 129.7, 128.0, 127.1, 126.7, 82.6, 37.0, 35.7, 32.4, 30.6, 30.4, 25.9, 23.4, 22.2, 14.3; IR (neat) $\nu$ 1733 cm$^{-1}$; HRMS (EI) *m/z* calcd for $C_{17}H_{24}O_2$ [$M^{+\bullet}$]: 260.1776, found: 260.1774.

**(*S*)-1-Methyl-1,2,3,4-tetrahydronaphthalen-1-ol [(*S*)-1a]**

A colorless solid, mp 68-69 ºC; $[\alpha]^{29}_D$ = +28 (*c* 0.61, $CHCl_3$), lit.[6] ($[\alpha]^{26}_D$ = +7.9 (*c* 1.00, $CHCl_3$); its enantiomeric excess (80% ee) was determined by HPLC analysis at 25 ºC using a CHIRALPAK IJ-3 column (hexane/2-propanol = 98:2, 1 mL/min), UV detection 220 nm, retention time 8.3 min (*S*), 9.8 min (*R*). $^1$H NMR (400 MHz, $CD_3OD$) $\delta$ 7.54 (dd, *J* = 7.2, 1.2 Hz, 1H), 7.16 (td, *J* = 7.2, 1.6 Hz, 1H), 7.10 (td, *J* = 7.2, 1.6 Hz, 1H), 7.03 (dd, *J* = 7.2, 1.2 Hz, 1H), 2.86-2.68 (m, 2H), 2.01-1.86 (m, 3H), 1.86-1.73 (m, 1H), 1.50 (s, 3H).

**Kinetic resolution of (±)-1b**

According to the general procedure, (*R*)-**3bc** (15 mg, 0.052 mmol, 34% yield) and (*S*)-**1b** (20 mg, 0.10 mmol, 65% yield) were obtained from (±)-**1b** (30 mg, 0.16 mmol).

**(*R*)-7-Methoxy-1-methyl-1,2,3,4-tetrahydronaphthalen-1-yl hexanoate [(*R*)-3bc]**

A colorless oil; $[\alpha]^{23}_{D}$ = –53 (*c* 0.72, $CH_3OH$); its enantiomeric excess (99% ee) was determined by HPLC analysis at 25 ºC using a CHIRALPAK IC-3 column (hexane/2-propanol = 98:2, 1 mL/min), UV detection 254 nm, retention time 6.3 min (*S*), 7.5 min (*R*). $^1$H NMR (400 MHz, $CD_3OD$) $\delta$ 6.97 (d, *J* = 8.4 Hz, 1H), 6.85 (d, *J* = 2.8 Hz, 1H), 6.72 (dd, *J* = 8.4, 2.8 Hz, 1H), 3.74 (s, 3H), 2.77 (ddd, *J* = 16.0, 10.8, 4.8 Hz, 1H), 2.67 (dt, *J* = 16.0, 4.8 Hz, 1H), 2.53 (td, *J* = 12.8, 3.6 Hz, 1H), 2.26 (t, *J* = 7.2 Hz, 2H), 2.03 (dddd, *J* = 12.8, 6.0, 3.2, 1.6 Hz, 1H), 1.99-1.87 (m, 1H), 1.85-1.71 (m, 1H), 1.68 (s, 3H), 1.57 (quint., *J* = 7.2 Hz, 2H), 1.39-1.23 (m, 4H), 0.90 (t, *J* = 7.2 Hz, 3H); $^{13}$C NMR (100 MHz, $CD_3OD$) $\delta$ 174.5, 159.5, 142.5, 130.6, 129.9, 114.1, 111.6, 82.7, 56.6, 36.4, 35.6, 32.4, 30.5, 29.8, 25.9, 23.4, 22.4, 14.3; IR (neat) *v* 1731 cm$^{-1}$; HRMS (EI) *m/z* calcd for $C_{18}H_{26}O_3$ [$M^{+\bullet}$]: 290.1882, found: 290.1883.

**(*S*)-7-Methoxy-1-methyl-1,2,3,4-tetrahydronaphthalen-1-ol [(*S*)-1b]**

A colorless solid, mp 41-43 ºC; $[\alpha]^{27}_{D}$ = +23 (*c* 1.00, $CH_3OH$); its enantiomeric excess (52% ee) was determined by HPLC analysis at 25 ºC using a CHIRALPAK IA-3 column (hexane/2-propanol = 90:10, 1 mL/min), UV detection 220 nm, retention time 7.6 min (*S*), 9.1 min (*R*). $^1$H NMR (400 MHz, $CD_3OD$) $\delta$ 7.10 (d, *J* = 2.8 Hz, 1H), 6.95 (d, *J* = 8.4 Hz, 1H), 6.71 (dd, *J* = 8.4, 2.8 Hz, 1H), 3.77 (s, 3H), 2.79-2.61 (m, 2H), 1.98-1.85 (m, 3H), 1.84-1.70 (m, 1H), 1.49 (s, 3H).

**Kinetic resolution of (±)-1c**

According to the general procedure, (*R*)-**3cc** (14 mg, 0.040 mmol, 32% yield) and (*S*)-**1c** (20 mg, 0.081 mmol, 65% yield) were obtained from (±)-**1c** (30 mg, 0.12 mmol).

**(*R*)-7-Bromo-1-methyl-1,2,3,4-tetrahydronaphthalen-1-yl hexanoate [(*R*)-3cc]**

A colorless oil; $[\alpha]^{23}_{D}$ = –59 (*c* 0.68, $CH_3OH$); its enantiomeric excess (99% ee) was determined by HPLC analysis at 25 ºC using a CHIRALPAK IJ-3 column (hexane/2-propanol = 99:1, 0.5 mL/min), UV detection 254 nm, retention time 9.5 min (*S*), 10.7 min (*R*). $^1$H NMR (400 MHz, $CD_3OD$) $\delta$ 7.45 (d, *J* = 2.4 Hz, 1H), 7.26 (dd, *J* = 8.4, 2.4 Hz, 1H), 7.00 (d, *J* = 8.4 Hz, 1H), 2.85-2.66 (m, 2H), 2.52 (td, *J* = 12.4, 3.2 Hz, 1H), 2.27 (t, *J* = 7.2 Hz, 2H), 2.08-1.92 (m, 2H), 1.88-1.73 (m, 1H), 1.67 (s, 3H), 1.57 (quint., *J* = 7.2 Hz, 2H), 1.40-1.23 (m, 4H), 0.92 (t, *J* = 7.2 Hz, 3H); $^{13}$C NMR (100 MHz, $CD_3OD$) $\delta$ 174.4, 144.1, 137.1, 131.7, 131.0, 129.6, 120.5, 81.9, 36.3, 36.2, 32.4, 30.4, 30.0, 25.9, 23.4, 21.1, 14.3; IR (neat) *v* 1732 cm$^{-1}$; HRMS (EI) *m/z* calcd for $C_{17}H_{23}BrO_2$ [$M^{+\bullet}$]: 338.0881, Found: 338.0885.

**(*S*)-7-Bromo-1-methyl-1,2,3,4-tetrahydronaphthalen-1-ol [(*S*)-1c]**

A colorless oil; $[\alpha]^{27}_{D}$ = +20 (*c* 1.01, $CH_3OH$); its enantiomeric excess (53% ee) was determined by HPLC analysis at 25 ºC using a CHIRALPAK IA-3 column (hexane/2-propanol = 90:10, 1 mL/min),

UV detection 220 nm, retention time 5.5 min (*S*), 6.5 min (*R*). $^1$H NMR (400 MHz, $CD_3OD$) $\delta$ 7.68 (d, $J$ = 2.0 Hz, 1H), 7.25 (dd, $J$ = 8.0, 2.0 Hz, 1H), 6.98 (d, $J$ = 8.0 Hz, 1H), 2.81-2.65 (m, 2H), 2.00-1.87 (m, 3H), 1.86-1.72 (m, 1H), 1.48 (s, 3H).

**Kinetic resolution of (±)-1d**

According to the general procedure, (*R*)-**3dc** (18 mg, 0.065 mmol, 39% yield) and (*S*)-**1d** (18 mg, 0.10 mmol, 60% yield) were obtained from (±)-**1d** (30 mg, 0.17 mmol).

**(*R*)-6-Fluoro-1-methyl-1,2,3,4-tetrahydronaphthalen-1-yl hexanoate [(*R*)-3dc]**

A colorless oil; $[\alpha]^{23}_D$ = –21 (*c* 0.82, $CH_3OH$); its enantiomeric excess (97% ee) was determined by HPLC analysis at 15 ºC using two CHIRALPAK IJ-3 columns connected in series (hexane/2-propanol = 99:1, 0.3 mL/min), UV detection 265 nm, retention time 37.8 min (*S*), 40.4 min (*R*). $^1$H NMR (400 MHz, $CD_3OD$) $\delta$ 7.36 (dd, $J$ = 8.8, 6.0 Hz, 1H), 6.87 (td, $J$ = 8.8, 2.8 Hz, 1H), 6.79 (dd, $J$ = 9.6, 2.8 Hz, 1H), 2.85 (ddd, $J$ = 16.0, 10.8, 5.2 Hz, 1H), 2.74 (dt, $J$ = 16.0, 4.8 Hz, 1H), 2.54 (td, $J$ = 12.4, 3.2 Hz, 1H), 2.24 (t, $J$ = 7.6 Hz, 2H), 2.08-1.92 (m, 2H), 1.86-1.72 (m, 1H), 1.69 (s, 3H), 1.55 (quint., $J$ = 7.6 Hz, 2H), 1.38-1.22 (m, 4H), 0.90 (t, $J$ = 7.2 Hz, 3H); $^{13}$C NMR (100 MHz, $CD_3OD$) $\delta$ 174.5, 162.9 (d, $J_{C\text{-}F}$ = 244.4 Hz), 140.7 (d, $J_{C\text{-}F}$ = 6.7 Hz), 137.6 (d, $J_{C\text{-}F}$ = 2.9 Hz), 129.0 (d, $J_{C\text{-}F}$ = 8.6 Hz), 115.5 (d, $J_{C\text{-}F}$ = 20.1 Hz), 114.0 (d, $J_{C\text{-}F}$ = 21.1 Hz), 82.1, 36.4, 35.6, 32.4, 30.7, 30.2, 25.8, 23.4, 21.9, 14.3; $^{19}$F NMR (376 MHz, $CD_3OD$) $\delta$ –118.1 (td, $J$ = 9.6, 6.0 Hz); IR (neat) $\nu$ 1735 cm$^{-1}$; HRMS (EI) *m/z* calcd for $C_{17}H_{23}FO_2$ [$M^{+\bullet}$]: 278.1682, found: 278.1685.

**(*S*)-6-Fluoro-1-methyl-1,2,3,4-tetrahydronaphthalen-1-ol [(*S*)-1d]**

A colorless oil; $[\alpha]^{27}_D$ = +15 (*c* 0.98, $CH_3OH$); its enantiomeric excess (65% ee) was determined by HPLC analysis at 25 ºC using a CHIRALPAK IA-3 column (hexane/2-propanol = 95:5, 1 mL/min), UV detection 254 nm, retention time 7.6 min (*S*), 8.5 min (*R*). $^1$H NMR (400 MHz, $CD_3OD$) $\delta$ 7.56 (dd, $J$ = 8.8, 6.0 Hz, 1H), 6.89 (td, $J$ = 8.8, 2.8 Hz, 1H), 6.77 (dd, $J$ = 9.6, 2.8 Hz, 1H), 2.86-2.68 (m, 2H), 2.01-1.87 (m, 3H), 1.86-1.73 (m, 1H), 1.49 (s, 3H); $^{19}$F NMR (470 MHz, $CD_3OD$) $\delta$ –118.7 (td, $J$ = 9.6, 6.0 Hz).

**Kinetic resolution of (±)-1e**

According to the general procedure, (*R*)-**3ec** (16 mg, 0.060 mmol, 33% yield) and (*S*)-**1e** (20 mg, 0.12 mmol, 67% yield) were obtained from (±)-**1e** (30 mg, 0.18 mmol).

**(*R*)-4-Methylchroman-4-yl hexanoate [(*R*)-3ec]**

A colorless oil; $[\alpha]^{24}_D$ = +10 (*c* 0.62, $CH_3OH$); its enantiomeric excess (96% ee) was determined by HPLC analysis at 25 ºC using a CHIRALPAK IC-3 column (hexane/2-propanol = 98:2, 1 mL/min), UV detection 275 nm, retention time 4.7 min (*R*), 6.8 min (*S*). $^1$H NMR (400 MHz, $CD_3OD$) $\delta$ 7.45 (d, $J$ = 8.0, 1.6 Hz, 1H), 7.14 (ddd, $J$ = 8.0, 7.2, 1.6 Hz, 1H), 6.88 (td, $J$ = 7.2, 1.6 Hz, 1H), 6.76 (dd, $J$ = 8.0, 1.6 Hz, 1H), 4.29 (ddd, $J$ = 11.2, 8.0, 3.2 Hz, 1H), 4.17 (ddd, $J$ = 11.2, 8.0, 3.2 Hz, 1H), 2.64 (ddd, $J$ =

14.4, 8.0, 3.6 Hz, 1H), 2.28-2.16 (m, 3H), 1.85 (s, 3H), 1.56 (quint., $J$ = 7.2 Hz, 2H), 1.37-1.21 (m, 4H), 0.89 (t, $J$ = 7.2 Hz, 3H); $^{13}$C NMR (100 MHz, $CD_3OD$) $\delta$ 174.5, 155.4, 130.3, 128.6, 126.8, 121.3, 117.9, 77.8, 64.2, 36.3, 35.3, 32.3, 27.4, 25.8, 23.4, 14.3; IR (neat) $\nu$ 1732 cm$^{-1}$; HRMS (EI) *m/z* calcd for $C_{16}H_{22}O_3$ [$M^{+\bullet}$]: 262.1569, found: 262.1572.

**(*S*)-4-Methylchroman-4-ol [(*S*)-1e]**

A colorless solid, mp 99-102 ºC; $[\alpha]^{27}_D$ = –14 (*c* 0.88, $CH_3OH$); its enantiomeric excess (37% ee) was determined by HPLC analysis at 25 ºC using a CHIRALPAK OD-3 column (hexane/2-propanol = 95:5, 1 mL/min), UV detection 220 nm, retention time 8.2 min (*S*), 9.7 min (*R*). $^1$H NMR (400 MHz, $CD_3OD$) $\delta$ 7.48 (dd, $J$ = 8.0, 1.6 Hz, 1H), 7.11 (ddd, $J$ = 8.0, 7.6, 1.6 Hz, 1H), 6.88 (ddd, $J$ = 8.0, 7.6, 1.6 Hz, 1H), 6.73 (dd, $J$ = 8.0, 1.6 Hz, 1H), 4.26 (ddd, $J$ = 11.6, 7.6, 4.4 Hz, 1H), 4.18 (ddd, $J$ = 10.8, 6.0, 4.4 Hz, 1H), 2.10-1.97 (m, 2H), 1.57 (s, 3H).

**Kinetic resolution of (±)-1f**

According to the general procedure, (*R*)-**3fc** (14 mg, 0.051 mmol, 31% yield) and (*S*)-**1f** (21 mg, 0.12 mmol, 69% yield) were obtained from (±)-**1f** (30 mg, 0.17 mmol).

**(*R*)-4-Methylthiochroman-4-yl hexanoate [(*R*)-3fc]**

A colorless oil; $[\alpha]^{24}_D$ = –8.4 (*c* 0.69, $CH_3OH$); its enantiomeric excess (98% ee) was determined by HPLC analysis at 25 ºC using a CHIRALPAK IC-3 column (hexane/2-propanol = 98:2, 1 mL/min), UV detection 220 nm, retention time 6.0 min (*R*), 8.0 min (*S*). $^1$H NMR (400 MHz, $CD_3OD$) $\delta$ 7.42 (dd, $J$ = 7.6, 1.2 Hz, 1H), 7.11-6.99 (m, 3H), 3.18-3.02 (m, 2H), 2.85 (ddd, $J$ = 13.2, 9.6, 4.0 Hz, 1H), 2.36-2.22 (m, 3H), 1.74 (s, 3H), 1.78 (quint., $J$ = 7.2 Hz, 2H), 1.39-1.22 (m, 4H), 0.90 (t, $J$ = 7.2 Hz, 3H); $^{13}$C NMR (100 MHz, $CD_3OD$) $\delta$ 174.2, 138.1, 133.9, 128.5, 127.54, 127.47, 125.1, 80.4, 36.2, 34.9, 32.4, 29.1, 25.8, 24.3, 23.4, 14.3; IR (neat) $\nu$ 1735 cm$^{-1}$; HRMS (EI) *m/z* calcd for $C_{16}H_{22}O_2S$ [$M^{+\bullet}$]: 278.1341, found: 278.1347.

**(*S*)-4-Methylthiochroman-4-ol [(*S*)-1f]**

A colorless solid, mp 87-90 ºC; $[\alpha]^{27}_D$ = +17 (*c* 0.84, $CH_3OH$); its enantiomeric excess (50% ee) was determined by HPLC analysis at 25 ºC using a CHIRALPAK OD-3 column (hexane/2-propanol = 95:5, 1 mL/min), UV detection 254 nm, retention time 10.1 min (*S*), 11.7 min (*R*). $^1$H NMR (400 MHz, $CD_3OD$) $\delta$ 7.66-7.59 (m, 1H), 7.09-6.97 (m, 3H), 3.11-3.04 (m, 2H), 2.22-2.11 (m, 2H), 1.49 (s, 3H).

**Kinetic resolution of (±)-1g**

According to the general procedure, (*R*)-**3gc** (20 mg, 0.077 mmol, 41% yield) and (*S*)-**1g** (18 mg, 0.11 mmol, 59% yield) were obtained from (±)-**1g** (30 mg, 0.19 mmol).

**(*R*)-1-Methyl-3-methylene-2,3-dihydro-*1H*-inden-1-yl hexanoate [(*R*)-3gc]**

A colorless oil; $[\alpha]^{23}_D$ = –18 (*c* 0.94, $CH_3OH$); its enantiomeric excess (88% ee) was determined by

HPLC analysis at 25 ºC using a CHIRALPAK IG-3 column (hexane/2-propanol = 98:2, 0.5 mL/min), UV detection 254 nm, retention time 8.3 min (*S*), 8.9 min (*R*). $^1$H NMR (400 MHz, $CD_3OD$) $\delta$ 7.57-7.49 (m, 1H), 7.47-7.39 (m, 1H), 7.35-7.27 (m, 2H), 5.55 (t, $J$ = 2.4 Hz, 1H), 5.07 (t, $J$ = 2.0 Hz, 1H), 3.23 (dt, $J$ = 16.8, 2.4 Hz, 1H), 3.04 (dt, $J$ = 16.8, 2.4 Hz, 1H), 2.24 (td, $J$ = 7.8, 1.6 Hz, 2H), 1.68 (s, 3H), 1.56 (quint., $J$ = 7.4 Hz, 2H), 1.34-1.17 (m, 4H), 0.88 (t, $J$ = 6.8 Hz, 3H); $^{13}$C NMR (100 MHz, $CD_3OD$) $\delta$ 174.8, 148.9, 147.4, 140.9, 129.9, 129.8, 124.9, 121.5, 104.4, 87.8, 47.1, 35.9, 32.3, 26.5, 25.8, 23.4, 14.3; IR (neat) $\nu$ 1732 cm$^{-1}$; HRMS (EI) *m/z* calcd for $C_{17}H_{22}O_2$ [$M^{+\bullet}$]: 258.1620, found: 258.1616.

**(*S*)–1-Methyl-3-methylene-2,3-dihydro-*1H*-inden-1-ol [(*S*)-1g]**

A pale yellow solid, mp 88-90 ºC; $[\alpha]^{27}_D$ = +16 (*c* 0.72, $CH_3OH$); its enantiomeric excess (67% ee) was determined by HPLC analysis at 25 ºC using a CHIRALPAK IA-3 column (hexane/2-propanol = 95:5, 1 mL/min), UV detection 220 nm, retention time 8.0 min (*S*), 8.6 min (*R*). $^1$H NMR (400 MHz, $CD_3OD$) $\delta$ 7.54-7.47 (m, 1H), 7.45-7.39 (m, 3H), 7.34-7.25 (m, 2H), 5.52 (t, $J$ = 2.0 Hz, 1H), 5.05 (t, $J$ = 2.0 Hz, 1H), 2.88 (t, $J$ = 2.0 Hz, 1H), 1.50 (s, 3H).

## Acknowledgements

This work was supported by JSPS KAKENHI (Grant Numbers A21H026050 and T22KK00730) and Research Support Project for Life Science and Drug Discovery (Basis for Supporting Innovative Drug Discovery and Life Science Research (BINDS)) from AMED under Grant Number JP23ama121054. In addition, generous support from the Deutsche Forschungsgemeinschaft (DFG; Grant number: GR 3461/7-1) is gratefully acknowledged. S. H. thanks the Chugai Foundation for Innovative Drug Discovery Science for the scholarship.

## Conflict of Interests

The authors declare no conflict of interest.

**Keywords:** lipase • tertiary alcohol • kinetic resolution

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[16] Similar benchmark experiments for creating improved CAL-A mutants in our joint project were also simultaneously conducted, and vinyl butyrate, which showed the highest activity in KR, was selected as the most suitable acyl donor for this study targeting to maximize the mutant's activity. See Ref. 14 for the detail.

[17] We previously found that the addition of sodium carbonate significantly increased the reaction rate in the lipase-catalyzed enantioselective acylation of racemic BINOLs, see: G. A. I. Moustafa, K. Kasama, K. Higashio, S. Akai, *RSC Adv.* **2019**, *9*, 1165–1175.

[18] Since lipases tend to exhibit the same enantioselectivity on similar substrates, we inferred that the absolute configuration of all other esters **3bc**–**3gc** is also *R*.

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# Table of contents

## 1. General information

Infrared (IR) absorption spectra were recorded on a SHIMADZU IRAffinity-1S spectrophotometer. $^{1}H$ and $^{13}C$ NMR spectra were measured on a JEOL JNM-ECA500 ($^{1}H$: 500 MHz, $^{13}C$: 125 MHz), a JEOL JMN-ECS400 ($^{1}H$: 400 MHz, $^{13}C$: 100 MHz) and a JEOL JMN-ECS300 ($^{1}H$: 300 MHz, $^{13}C$: 75 MHz) instruments. Chemical shifts were reported in δ (ppm) relative to the residual nondeuterated solvent signal for $^{1}H$ ($CDCl_3$: $\delta$ = 7.26 ppm, methanol-$d_4$: δ = 3.31 ppm) and relative to the deuterated solvent signal for $^{13}C$ ($CDCl_3$: δ = 77.0 ppm, methanol-$d_4$: δ = 49.0 ppm). The high-resolution mass spectra (HRMS) were measured on a JEOL JMS-700 (EI) instruments at the Analytical Instrumentation Facility, Graduate School of Engineering, Osaka University. HPLC analysis was carried out using a JASCO LC-2000Plus system (HPLC pump: PU-2080, UV detector: MD-2018) equipped with a Daicel CHIRALPAK AD-3, IA-3, ID, IG or OD-3 with a size of 4.6 mm x 250 mm. Optical rotations were measured on a JASCO P-1020 polarimeter. Reagents and solvents were purchased from Tokyo Chemical Industry, Sigma-Aldrich, FUJIFILM Wako Pure Chemical, Nakalai Tesque, Kishida Chemical, and Combi Blocks, and used without further purification. Flash column chromatography was performed on silica gel 60N (particle size 40–50 μm) purchased from Kanto Chemical Co., Inc. Unless otherwise noted, the reactions were carried out in anhydrous solvents under argon atmosphere. Mesoporous silica (commercial name: TMPS-4R) was supplied by Taiyo Kagaku Co., Ltd. (Tokyo, Japan). Lipase AK "Amano" Conc. from *Pseudomonas fluorescens,* was supplied by Amano Enzyme Inc. (Aichi, Japan) and used for immobilization on Celite, whose procedure is shown below. *Candida antarctica* lipase B (CAL-B) immobilized on an organic polymer support (commercial name: Novozyme 435 or Chirazyme L-2 C4) was purchased from Roche Diagnostics K. K.

## 2. Preparation of VMPS4

VMPS4 was prepared according to the literature method.[1]

## 3. Preparation of immobilized Lipase AK and examination of its reactivity and enantioselectivity

### 3.1 Preparation of immobilized Lipase AK

**Method A:** Celite (3.0 g, Kishida) was put in a plastic bag. Then, water (100 mg) was sprayed with a mist and the mixture was mixed. The addition of water and mixing were repeated two more times. Lipase AK Conc. (1.0 g) was added to the above wet Celite, and the whole mixture was well mixed. The addition of Lipase AK Conc. and mixing were repeated two more times (a total 3.0 g of Lipase AK Conc. was used). The resulting powder was spread on a plastic plate and dried in air overnight. Then, the powder was put in a round-bottomed flask and vacuum dried (2 mmHg) for 24 h at room temperature.

Immobilization of Lipase AK Conc. on diatomite (3.0 g, Nacalai Tesque) was similarly conducted.

**Method B:** A carrier (0.25 g, Purolite Co.) was washed 4 times with 0.25 mL of potassium phosphate buffer (50 mM, pH 7.5). Lipase AK Conc. (20 mg) was dissolved in 1 mL of potassium phosphate buffer (50 mM, pH 7.5) and mixed with the washed carrier. The whole mixture was gently mixed with 80 rpm for 24 h at

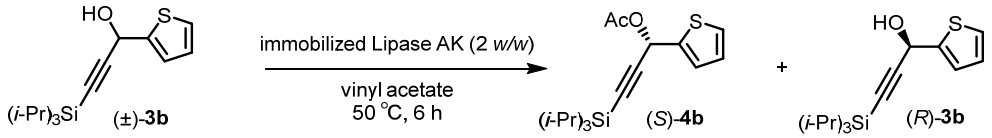
room temperature. The resultant mixture was filtered and the resulting material was washed with 1 mL of potassium phosphate buffer (10 mM, pH 7.5). Finally, the immobilized AK was dried overnight under vacuum (2 mmHg) at room temperature.

## 3.2. Analysis of the protein content of immobilized Lipase AK and examination of its reactivity and enantioselectivity

The amount of Lipase AK loaded in each immobilized Lipase AK was determined by a bicinchoninic acid assay kit, Takara Bio (see Table S1).

The catalytic activity and enantioselectivity of each immobilized AK were evaluated by kinetic resolution of (±)-**1b** at 50 ℃ for 6 h, and the results were summarized in Table S1. In terms of the conversion and E value, Lipase AK on Celite was found to be the best among all the immobilized Lipases examined (entries 1 and 2). Thereafter, Lipase AK immobilized on Celite (entry 1) was used for DKR.

**Table S1** Immobilization of Lipase AK and kinetic resolution of (±)-**3b** using immobilized Lipase AK



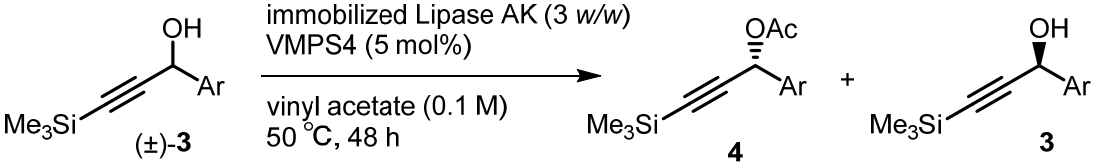

| | immobilization of Lipase AK | | | | | | KR of (±)-**3b** | | |
|---|---|---|---|---|---|---|---|---|---|
| emtry | carrier | type | immobilization method | carrier/Lipase (*w/w*) | enzyme loading (mg)[a] | immobilization yield (%) | conv.(%)[b] | ee (%) of (*R*)-**3b** | *E* value |
| 1 | Celite | absorption | A | 3:1 | 75 | 30 | 45 | 81 | >200 |
| 2 | Celite | absorption | A | 3:2 | 97 | 19 | 50 | 99 | >200 |
| 3 | Diatomaceous earth | absorption | A | 3:1 | 60 | 24 | 50 | 93 | 87 |
| 4 | ECR1090M[c] | absorption | B | 25:2 | 45 | 60 | 20 | 25 | 28 |
| 5 | ECR1030M[c] | absorption | B | 25:2 | 42 | 57 | 33 | 49 | 34 |
| 6 | ECR8806F[c] | absorption | B | 25:2 | 63 | 85 | 23 | 29 | 21 |
| 7 | ECR8204F[c] | covalent | B | 25:2 | 68 | 92 | 6 | 6 | 19 |
| 8 | ECR8285[c] | covalent | B | 25:2 | 66 | 89 | 46 | 83 | 53 |
| 9 | ECR8309F[c] | covalent | B | 25:2 | 44 | 59 | <1 | n.d. | n.d. |

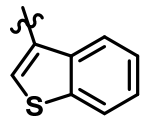
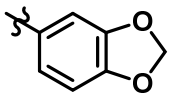
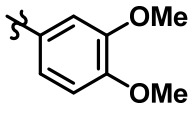
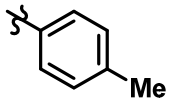
a) The amount of enzyme loaded in each 1 g of immobilized AK was determined by a bicinchoninic acid assay kit, Takara Bio Inc. b) The molar ratio of (*S*)-**4b** to the total of (*S*)-**4b** and (*R*)-**3b** determined by $^1$H NMR analysis of the crude product. c) Enzyme immobilization resins purchased from Purolite Co.

## 4. Examination of DKR conditions for (±)-3c-3f

Since the DKR of **3c-3f** by Method I resulted in low yields and other problems, further improvement of conditions was investigated and some typical results are summarized in Table S2.

**Table S2.** Examination of DKR conditions for **3c-3f**




| Ar | | Method[a] | NMR ratio (%) [isolated yield (%)] **4** | **3** |
|---|---|---|---|---|
|  | **3c** | I | 78 [-][f] | 16 |
| | | II[b] | 78 [65] | <5 |
| | | II[c] | 71 [66] | 19 |
| | | II[d] | 80 [66] | 16 |
|  | **3d** | I | 75 [-][f] | 6 |
| | | I[d,e] | 87 [64] | n.d. |
| | | II | 80 [50] | n.d. |
| | | II[d] | 93 [86] | n.d. |
|  | **3e** | I | 85 [-][f] | n.d. |
| | | I[d] | 93 [62] | n.d. |
| | | II | 87 [40] | n.d. |
| | | II[c] | 83 [65] | 15 |
| | | II[d] | 99 [64] | n.d. |
|  | **3f** | I | 36 [36] | 57 |
| | | II[b] | 64 [-][f] | 27 |
| | | III | 99 [72] | n.d. |

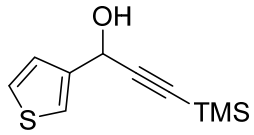
a) Method I: The reaction was conducted using immobilized Lipase AK (3 *w/w*) and VMPS4 (5 mol%) in vinyl acetate (0.1 M) at 50 ºC for 48 h. Method II: KR using vinyl acetate (2 eq) and immobilized Lipase AK (3 *w/w*) in $PhCF_3$ (0.1 M) was conducted at 50 ºC for 12 h. VMPS4 (1 mol%) was added and the mixture was stirred at 50 ºC for 36 h. Method III: KR using immobilized Lipase AK (3 *w/w*) in vinyl acetate (0.1 M) was conducted at 50 ºC for 12 h, and VMPS4 (5 mol%) was added. The mixture was stirred at 50 ºC for 12 h. Immobilized Lipase AK (3 *w/w*) and VMPS4 (5 mol%) were added again, and the whole mixture was stirred at 50 ºC for 24 h. b) Vinyl acetate was used as a solvent. c) 0.5 mol% of VMP4 was used. d) 1 mol% of VMP4 was used. e) $PhCF_3$ was used as a solvent. f) Not determined. n.d. = not detected.

## 5. Substrate syntheses

### 5.1 Preparation of racemic propargyl alcohols 3

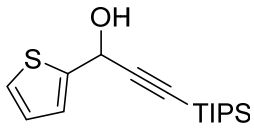
**The general procedure for the preparation of racemic propargyl alcohols 3:** Under argon atmosphere, $^{n}$BuLi (2.7 M in hexane, 1.05 equiv.) was added to a solution of trialkylsilylacetylene (1.1 equiv.) in anhydrous THF (0.1 M) at -78 ℃. After stirring for 10 min at the same temperature, the reaction mixture was warmed to 0 ℃ over a period of 10 min and stirred for another 10 min at 0 ℃. The solution was cooled to -78 ℃ before a solution of aryl aldehyde (1.0 equiv.) in THF was added. After stirring for 10 min at -78 ℃, the reaction mixture was warmed up to 0 ℃ over a period of 30 min and quenched with saturated aq. $NH_4Cl$. Two phases were separated, and the aqueous phase was extracted with $Et_2O$. The combined organic phases were washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by flash column chromatography to give (±)-**3**.

#### 1-(Thiophen-3-yl)-3-(trimethylsilyl)prop-2-yn-1-ol [(±)-3a]



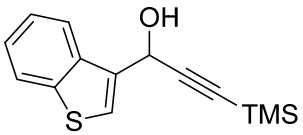

According to the general procedure for the preparation of racemic **3**, (±)-**3a** (0.45 g, 2.1 mmol) was obtained from thiophene-3-carbaldehyde (0.25 g, 2.2 mmol) in 96% yield; a colorless oil; $^1$H NMR data of the product (±)-**1a** were in agreement with those reported in the literature.[2]

#### 1-(Thiophen-2-yl)-3-(triisopropylsilyl)prop-2-yn-1-ol [(±)-3b]




According to the general procedure for the preparation of racemic **3**, (±)-**3b** (0.57 g, 1.9 mmol) was obtained from thiophene-3-carbaldehyde (0.25 g, 2.2 mmol) in 87% yield; a yellow oil; $^1$H NMR (400 MHz, $CDCl_3$) δ 7.30 (d, *J* = 5.0 Hz, 1H), 7.20 (d, *J* = 3.5 Hz, 1H), 6.99 (dd, *J* = 5.0, 3.5 Hz, 1H), 5.67 (d, *J* = 7.5 Hz, 1H), 2.33 (d, *J* = 7.5 Hz, 1H), 1.10 (s, 21H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 144.7, 126.7, 126.1, 125.7, 106.0, 87.6, 60.7, 18.6, 11.1; IR (neat): 3365, 2173 cm$^{-1}$. HRMS (MALDI) *m/z* calcd for $C_{16}H_{26}ONaSiS$ $[M+Na]^+$: 317.1366. Found: 317.1361.

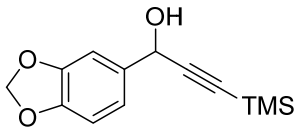
#### 1-(Benzo[*b*]thiophen-3-yl)-3-(trimethylsilyl)prop-2-yn-1-ol [(±)-3c]




According to the general procedure for the preparation of racemic **3**, (±)-**3c** (1.54 g, 5.9 mmol) was obtained

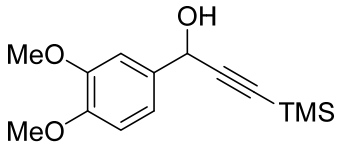
from benzo[*b*]thiophene-3-carbaldehyde (1.0 g, 6.2 mmol) in 96% yield; a colorless oil. $^{1}$H NMR (500 MHz, $CDCl_3$) δ 8.03 (dd, *J* = 7.0, 1.0 Hz, 1H), 7.87 (dd, *J* = 7.0, 1.0 Hz, 1H), 7.64 (brs, 1H), 7.43-7.36 (m, 2H), 5.76 (dd, *J* = 7.0, 1.0 Hz, 1H), 2.33 (d, *J* = 7.0 Hz, 1H), 0.24 (s, 9H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 141.1, 136.9, 135.1, 125.1, 124.8, 124.4, 123.0, 122.8, 104.1, 91.5, 60.4, -0.21; IR (NaCl): 3413 cm$^{-1}$; HRMS (EI) *m/z* calcd for $C_{14}H_{16}OSiS$ [$M^{+\bullet}$]: 260.0691. Found: 260.0688.

## 1-(Benzo[*d*][1,3]dioxol-5-yl)-3-(trimethylsilyl)prop-2-yn-1-ol [(±)-3d]



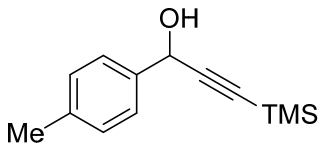

According to the general procedure for the preparation of racemic **3**, (±)-**3d** (1.80 g, 7.2 mmol) was obtained from benzo[*d*][1,3]dioxole-5-carbaldehyde (1.12 g, 7.5 mmol) in 97% yield; a colorless oil; $^{1}$H and $^{13}$C NMR data of the product (±)-**3d** were in agreement with those reported in the literature.[2]

## 1-(3,4-Dimethoxyphenyl)-3-(trimethylsilyl)prop-2-yn-1-ol [(±)-3e]



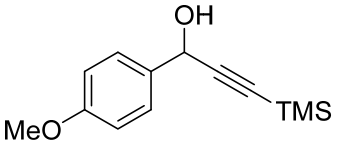

According to the general procedure for the preparation of racemic **3**, (±)-**3e** (1.53 g, 5.8 mmol) was obtained from 3,4-dimethoxybenzaldehyde (1.0 g, 6.0 mmol) in 96% yield; a colorless oil; $^{1}$H NMR (400 MHz, $CDCl_3$) δ 7.11-7.07 (m, 2H), 6.85 (d, *J* = 8.0 Hz, 1H), 5.40 (d, *J* = 6.0 Hz, 1H), 3.90 (s, 3H), 3.88 (s, 3H), 2.23 (d, *J* = 6.0 Hz, 1H), 0.20 (s, 9H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 149.0, 148.9, 132.9, 119.1, 110.8, 109.9, 105.0, 91.5, 64.8, 55.9, 55.7, -0.20; IR (NaCl): 3467 cm$^{-1}$; HRMS (EI) *m/z* calcd for $C_{14}H_{20}O_3Si$ [$M^{+\bullet}$]: 264.1182. Found: 264.1179.

## 1-(*p*-Tolyl)-3-(trimethylsilyl)prop-2-yn-1-ol [(±)-3f]




According to the general procedure for the preparation of racemic **3**, (±)-**3f** (1.67 g, 7.7 mmol) was obtained from 4-methylbezaldehyde (1.0 g, 8.3 mmol) in 92% yield; a colorless oil; $^{1}$H NMR data of the product (±)-**3f** were in agreement with those reported in the literature.[3]

### 1-(4-Methoxyphenyl)-3-(trimethylsilyl)prop-2-yn-1-ol [(±)-3g]



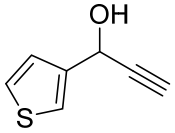

According to the general procedure for the preparation of racemic **3**, (±)-**3g** (0.84 g, 3.6 mmol) was obtained from 4-methoxybenzaldehyde (0.50 g, 3.7 mmol) in 98% yield; a colorless oil; $^1$H NMR data of the product (±)-**3g** were in agreement with those reported in the literature.[2]

## 5.2 Preparation of racemic propargyl alcohols 1

Alcohols (±)-**1b**[4], (±)-**1d**[4], (±)-**1e**[4], (±)-**1f**[4], and (±)-**1g**[4] were synthesized according to the literature methods. Alcohols (±)-**1a** and (±)-**1c** were synthesized according to the general procedure for the preparation of (±)-**1**.

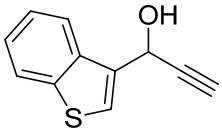
**A general procedure for the preparation of (±)-1:** To a crude reaction mixture containing (±)-**3**, prepared as described above, $Bu_4NF$ (a 1.0 M solution in THF, 1.5 equiv.) was added at 0 °C. The reaction mixture was stirred at 0 °C for 1 h and quenched with saturated aq. $NH_4Cl$. The aqueous phase was extracted with $Et_2O$ (3 x 20 mL), and the combined organic phases were washed with brine (50 mL), dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel) to give (±)-**1**.

### 1-(Thiophen-3-yl)prop-2-yn-1-ol [(±)-1a]




(±)-**1a** (0.29 g, 2.1 mmol) was obtained from thiophene-3-carbaldehyde (0.25 g, 2.2 mmol) in 95% yield; a colorless oil. $^1$H NMR data of the product (±)-**1a** were in agreement with those reported in the literature.[5]

### 1-(Benzo[b]thiophen-3-yl)prop-2-yn-1-ol [(±)-1c]




(±)-**2c** (0.14 g, 0.74 mmol) was obtained from benzo[b]thiophene-3-carbaldehyde (0.23 g, 1.1 mmol) in 96% yield; a colorless solid. $^1$H NMR data of the product (±)-**1c** were in agreement with those reported in the literature.[6]

## References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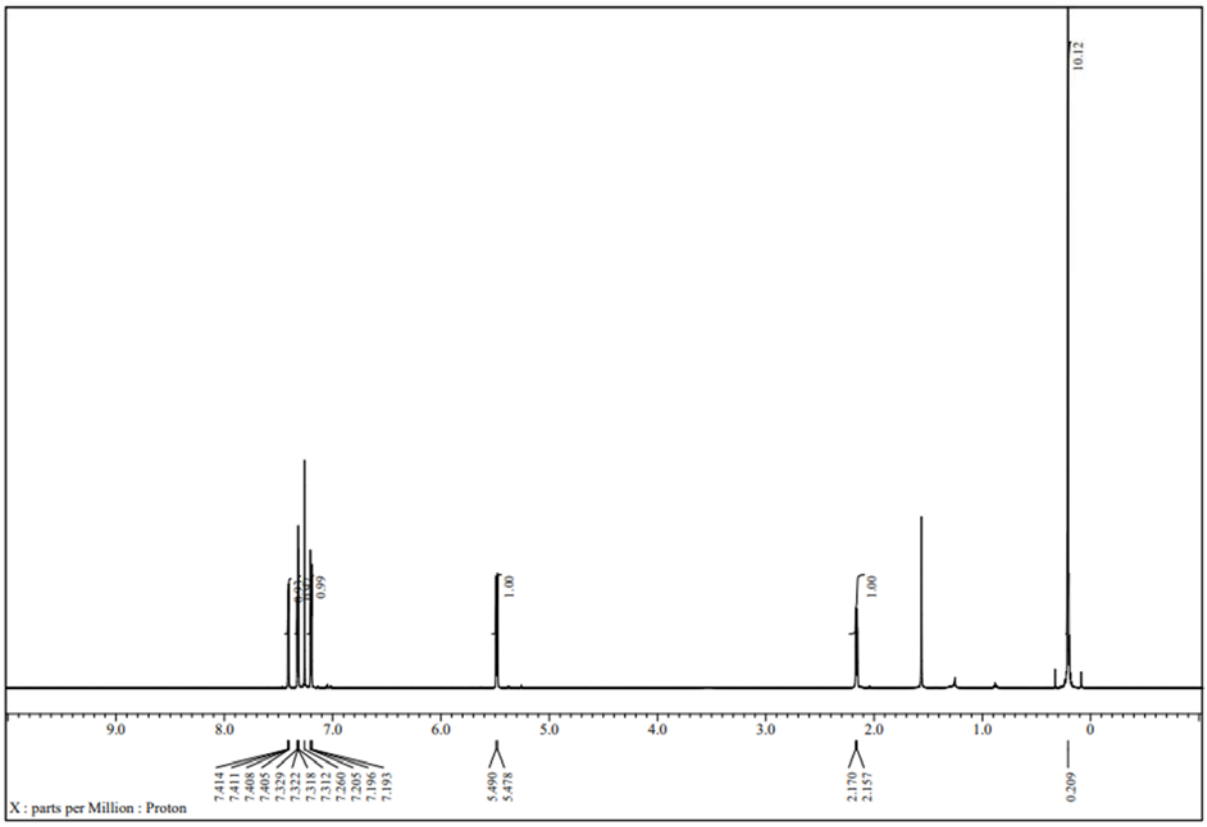
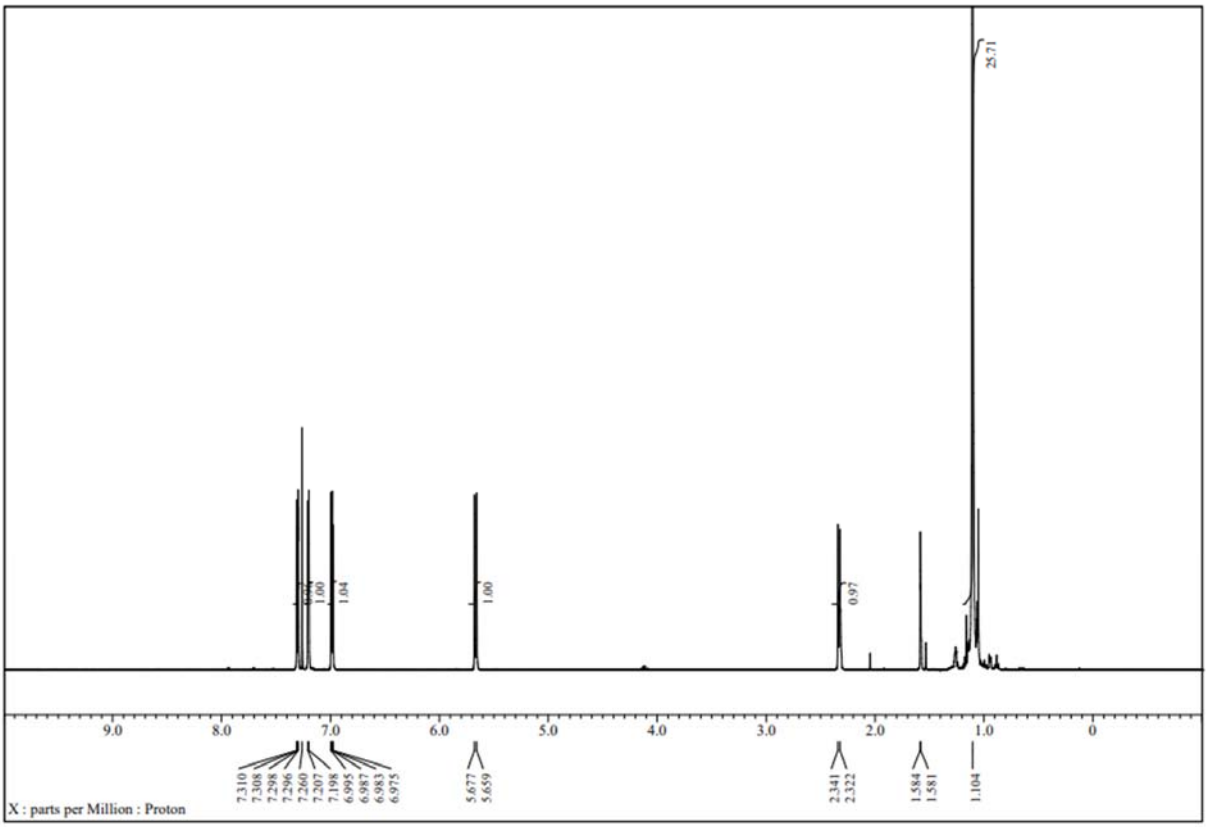
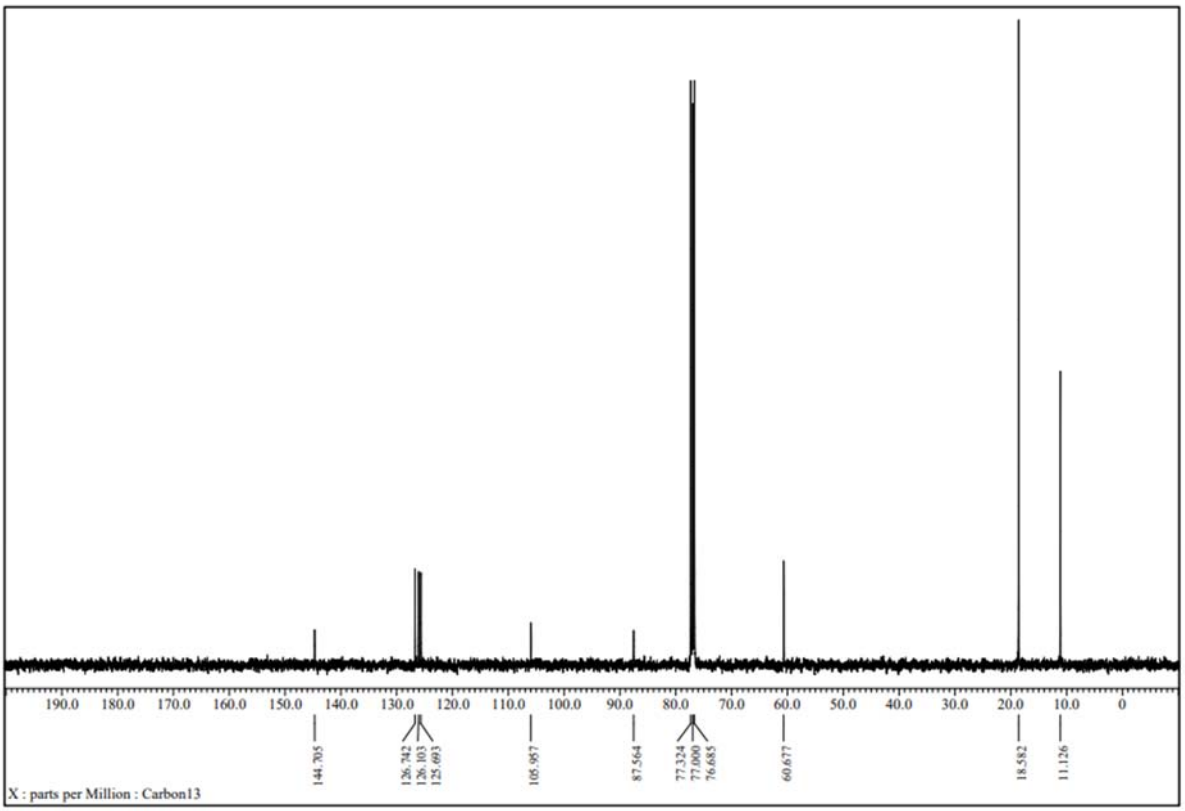
## 7. Spectra data

### 1-(Thiophen-3-yl)-3-(trimethylsilyl)prop-2-yn-1-ol [(±)-3a]

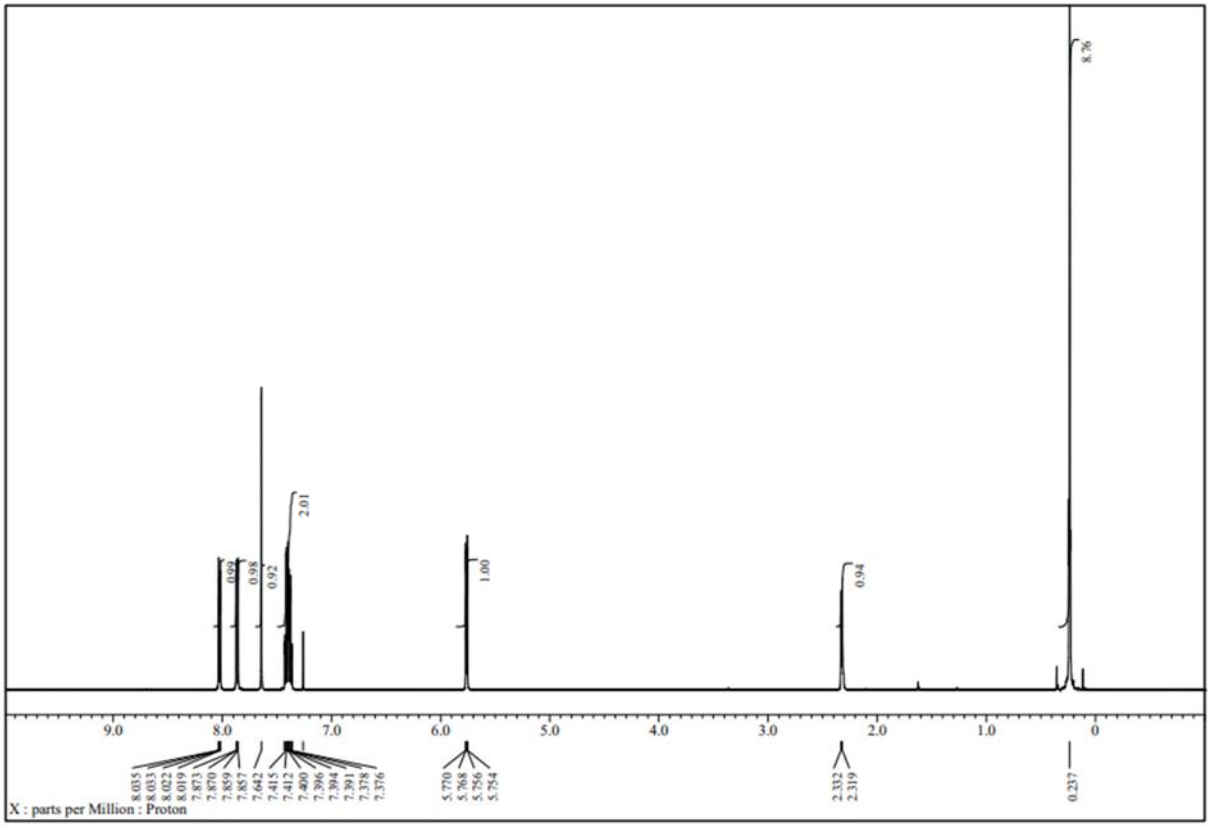


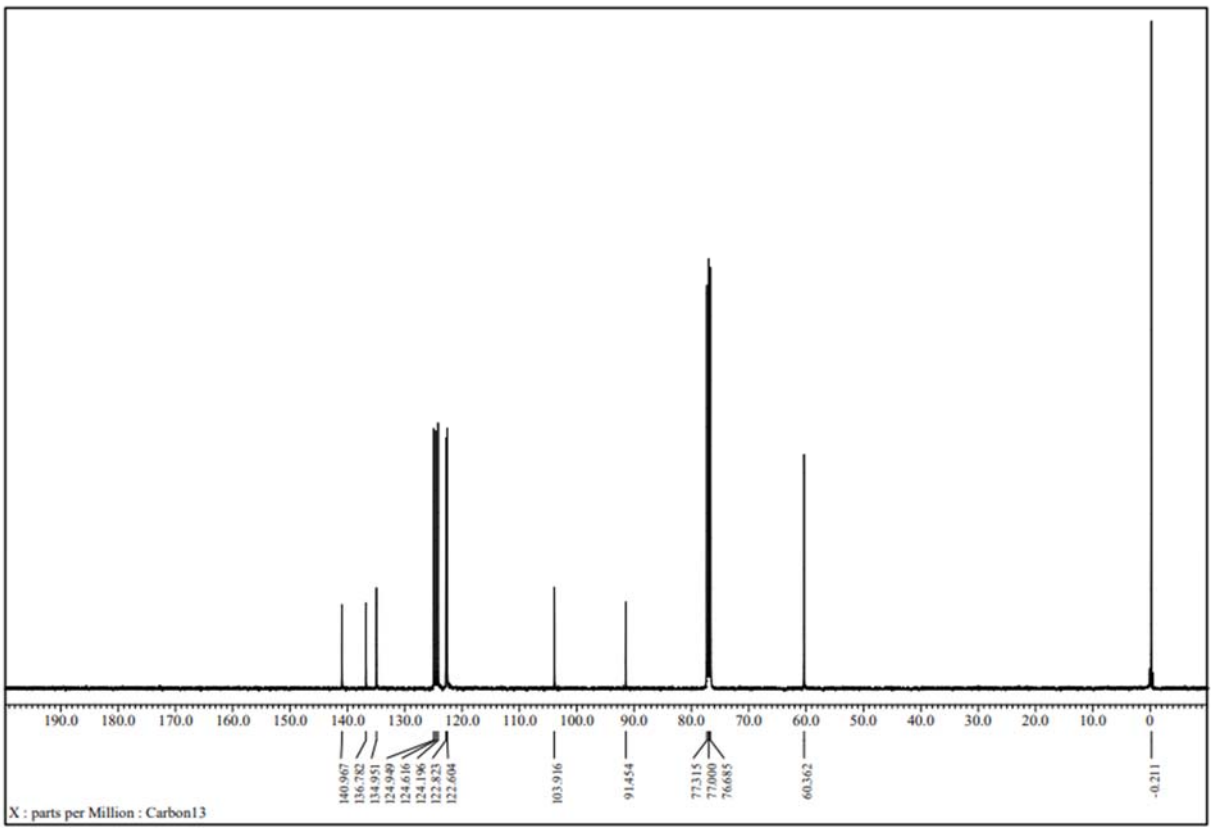
**1-(Thiophen-2-yl)-3-(triisopropylsilyl)prop-2-yn-1-ol [(±)-3b]**



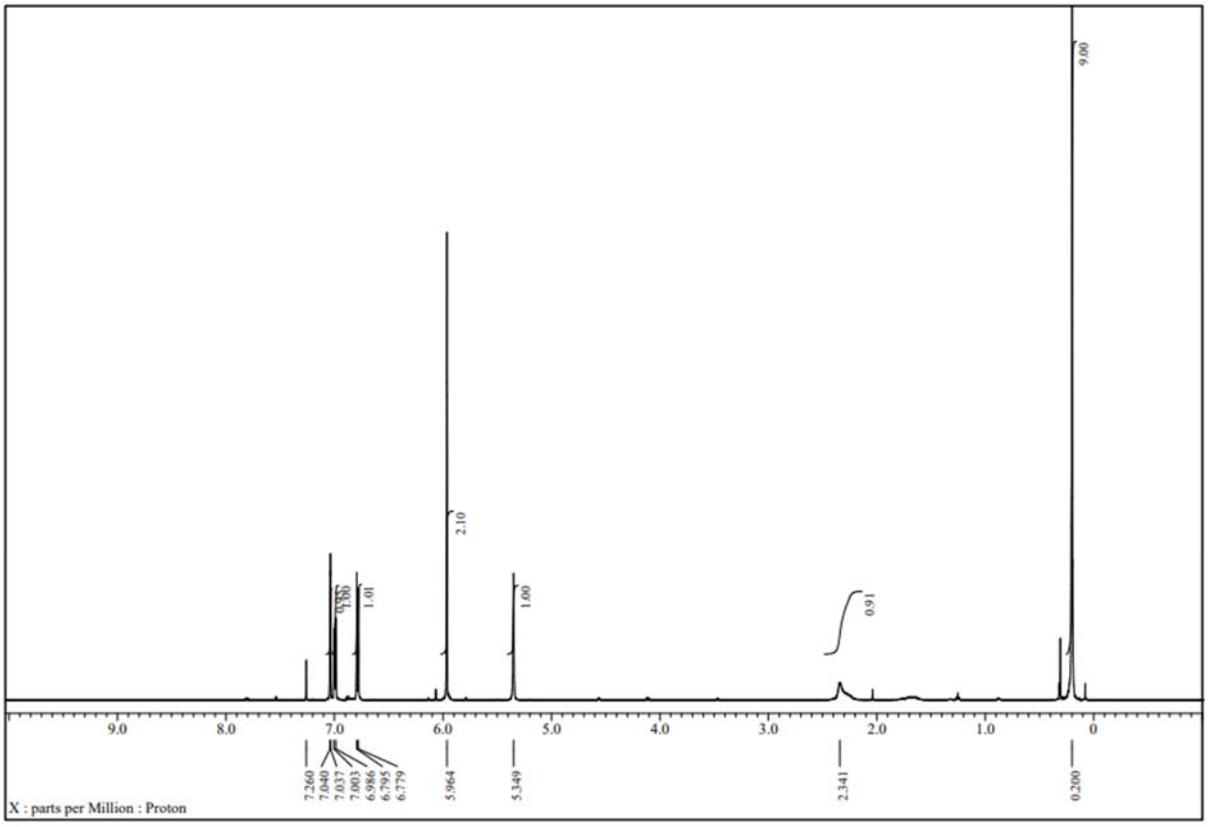



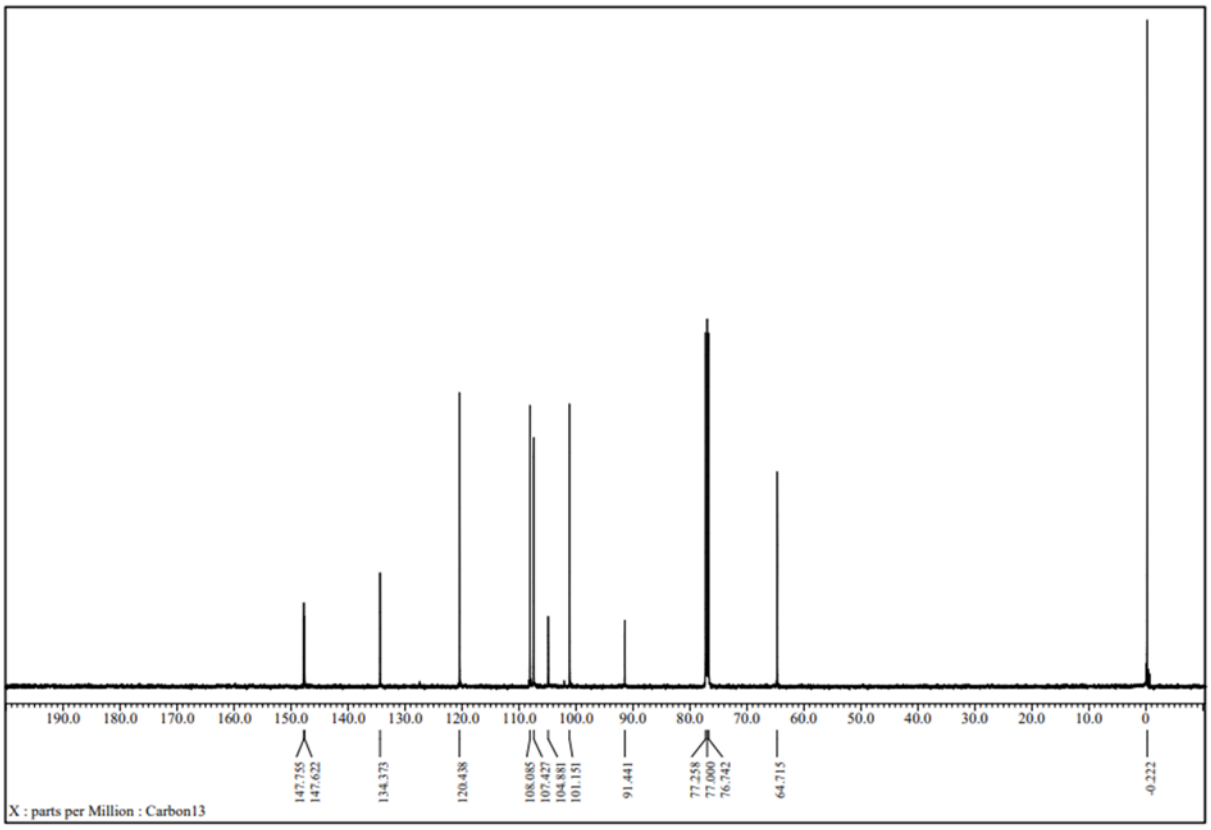
**1-(Benzo[b]thiophen-3-yl)-3-(trimethylsilyl)prop-2-yn-1-ol [(±)-3c]**



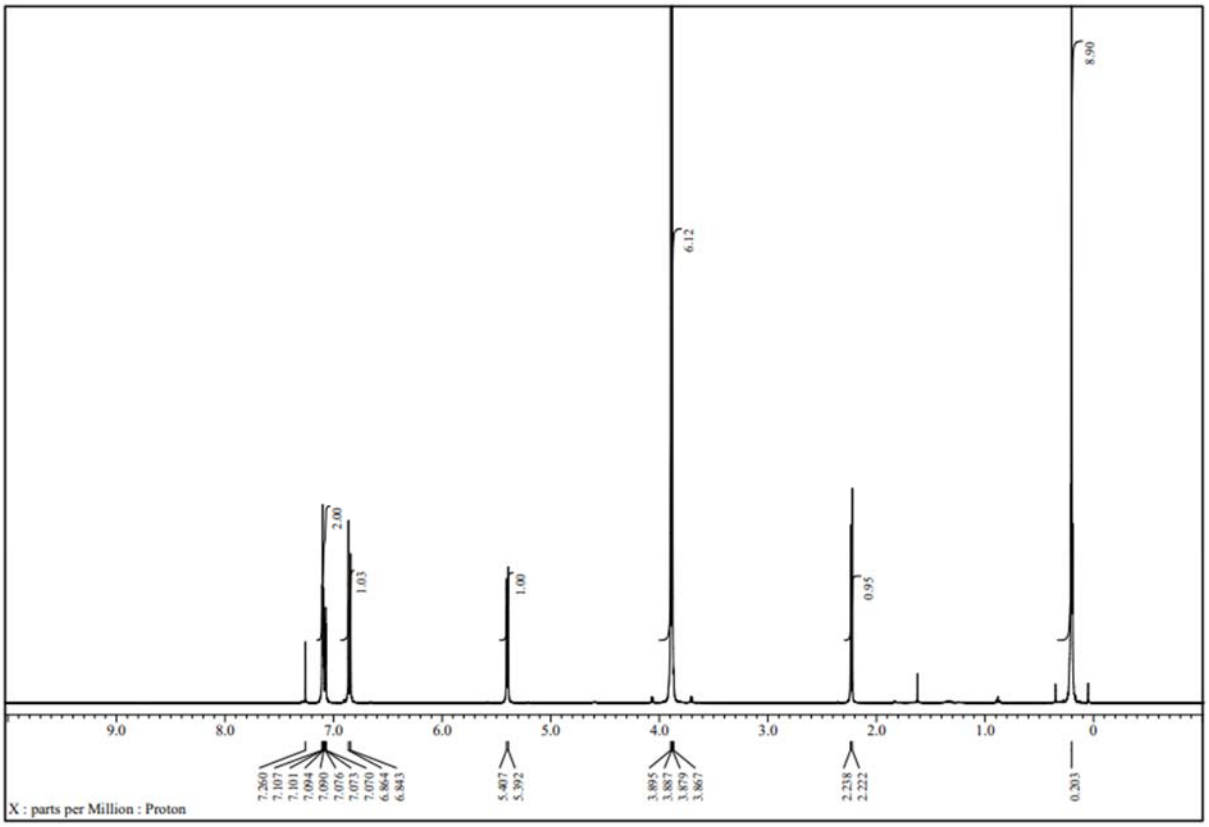



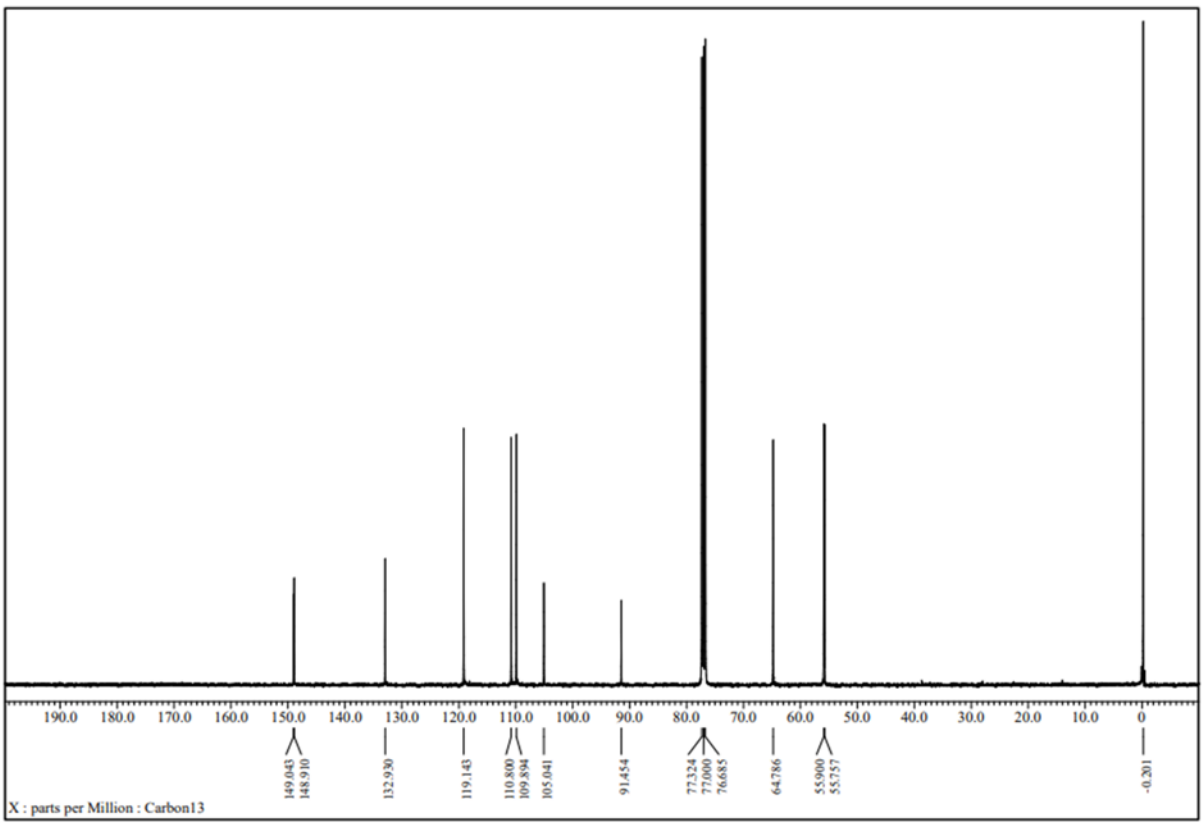
**1-(benzo[d][1,3]dioxol-5-yl)-3-(trimethylsilyl)prop-2-yn-1-ol [(±)-3d]**



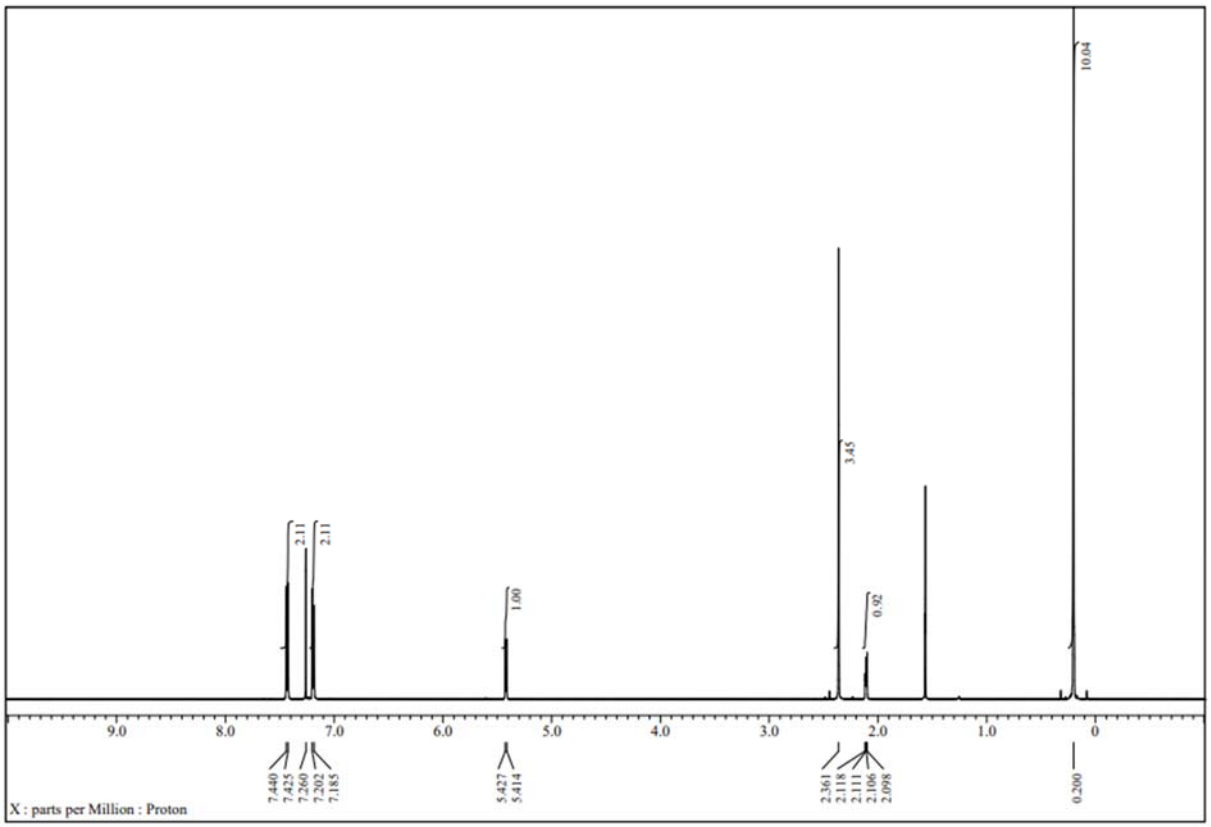



**1-(3,4-Dimethoxyphenyl)-3-(trimethylsilyl)prop-2-yn-1-ol [(±)-3e]**

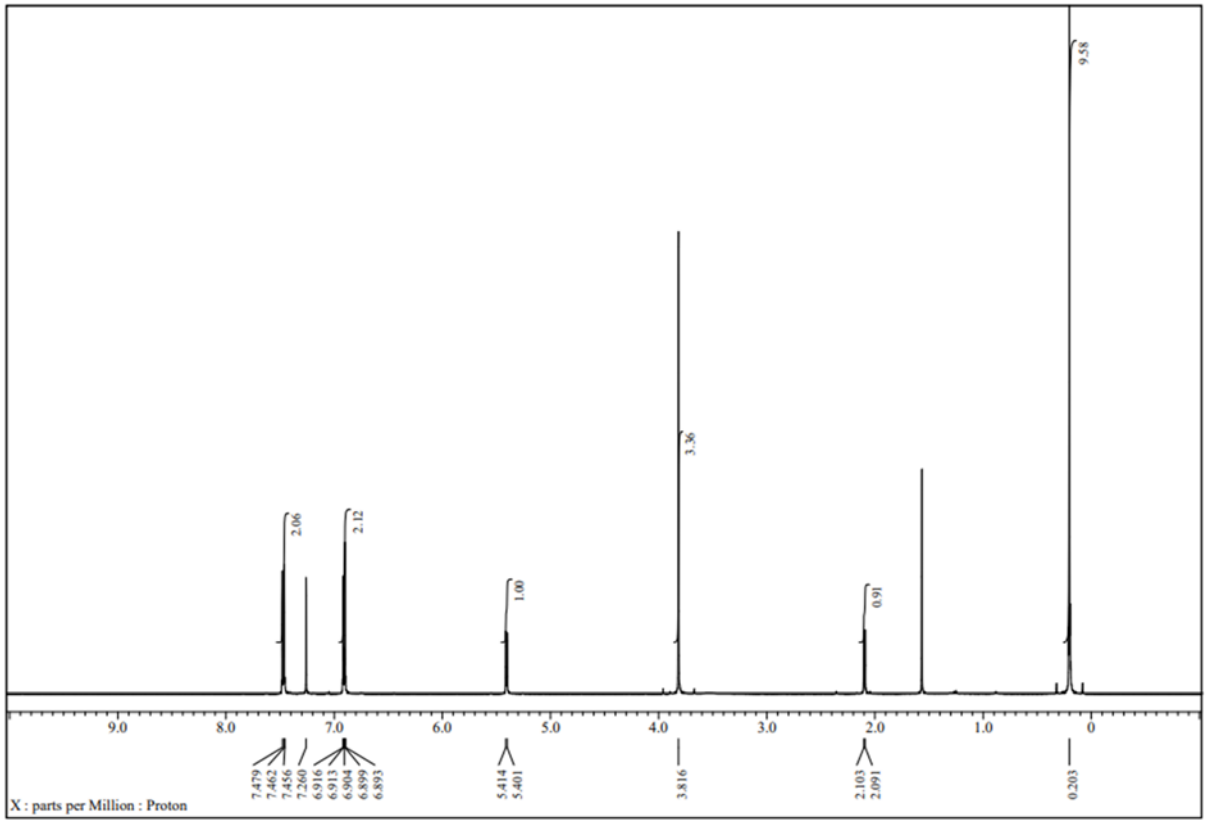


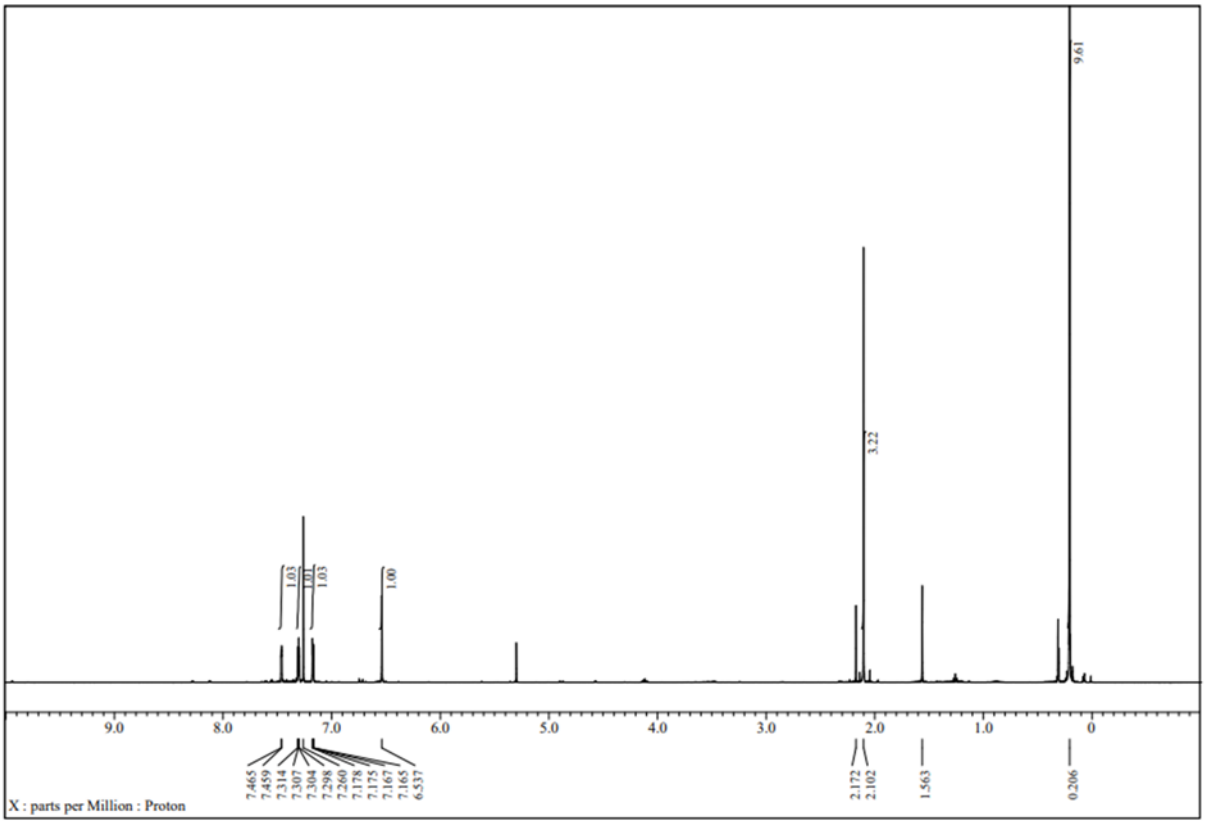
**1-(*p*-Tolyl)-3-(trimethylsilyl)prop-2-yn-1-ol [(±)-3f]**

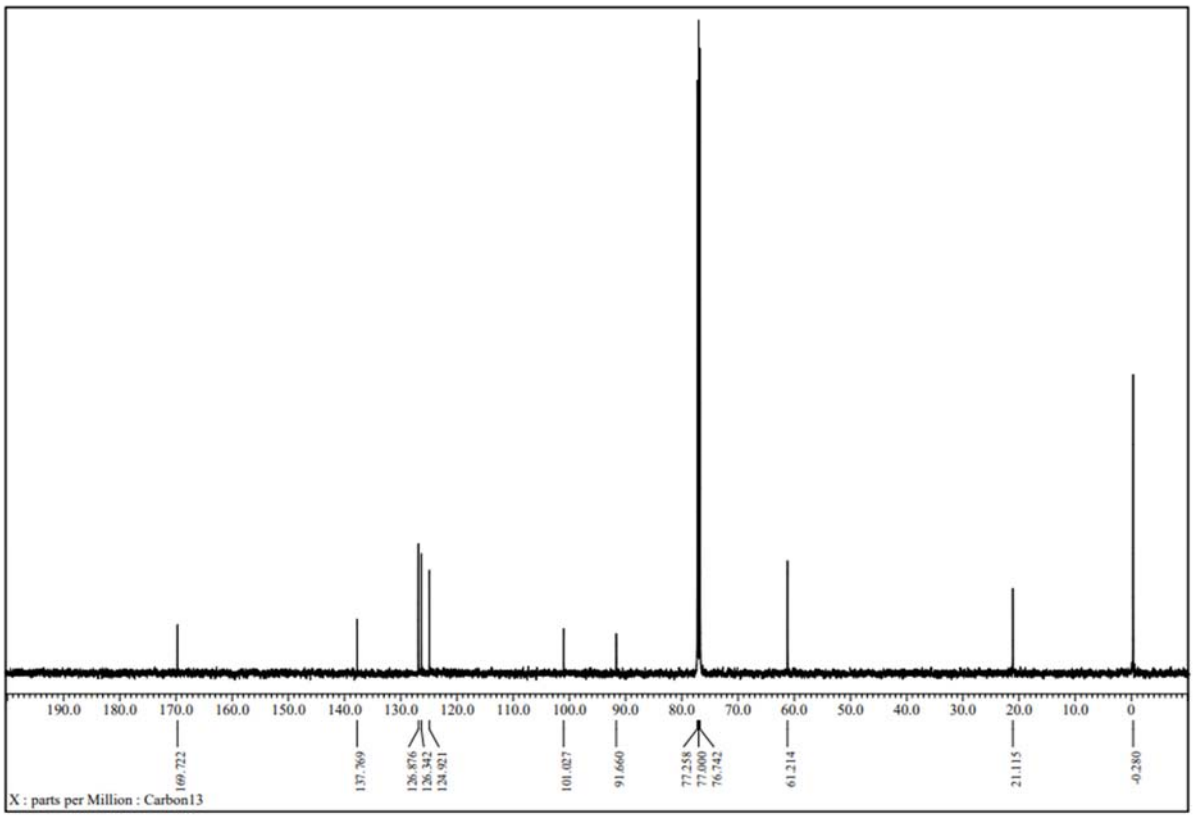


**1-(4-Methoxyphenyl)-3-(trimethylsilyl)prop-2-yn-1-ol [(±)-3g]**

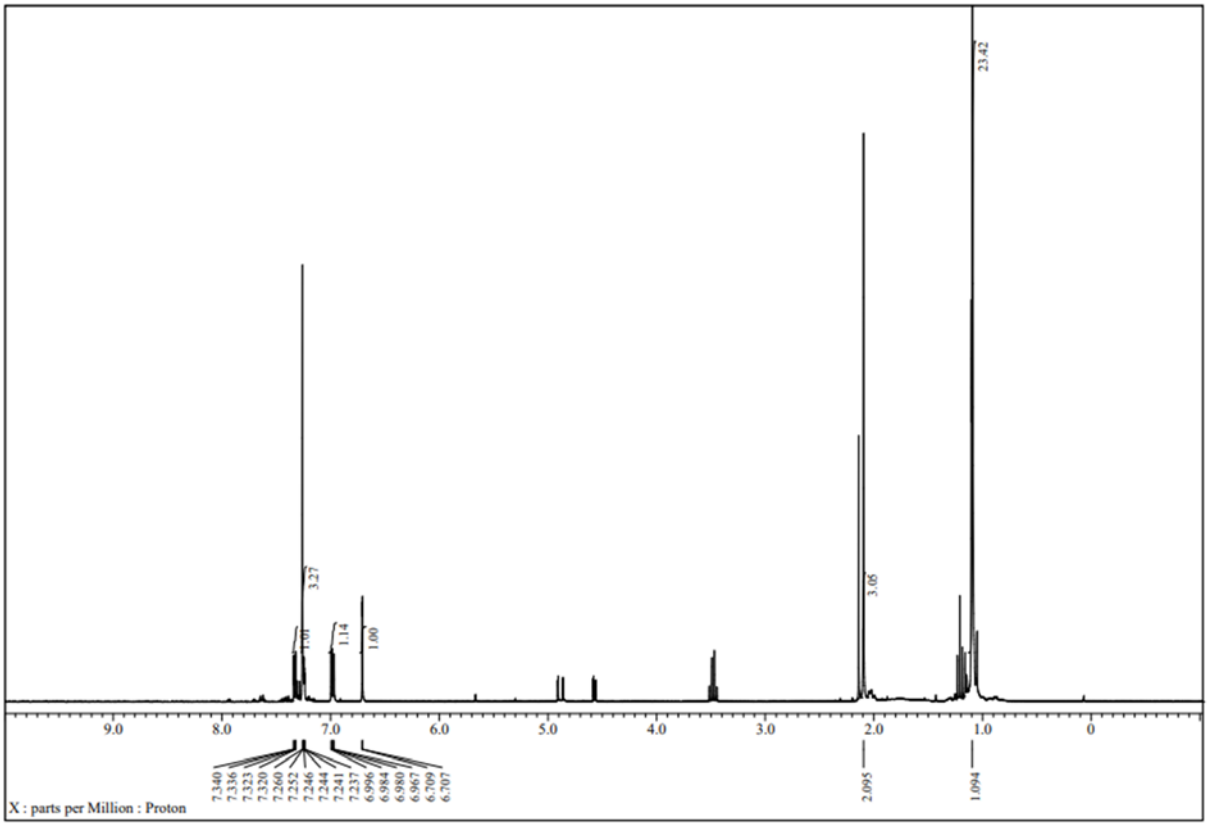


**(*S*)-1-(Thiophen-3-yl)-3-(trimethylsilyl)prop-2-yn-1-yl acetate [(*S*)-4a]**

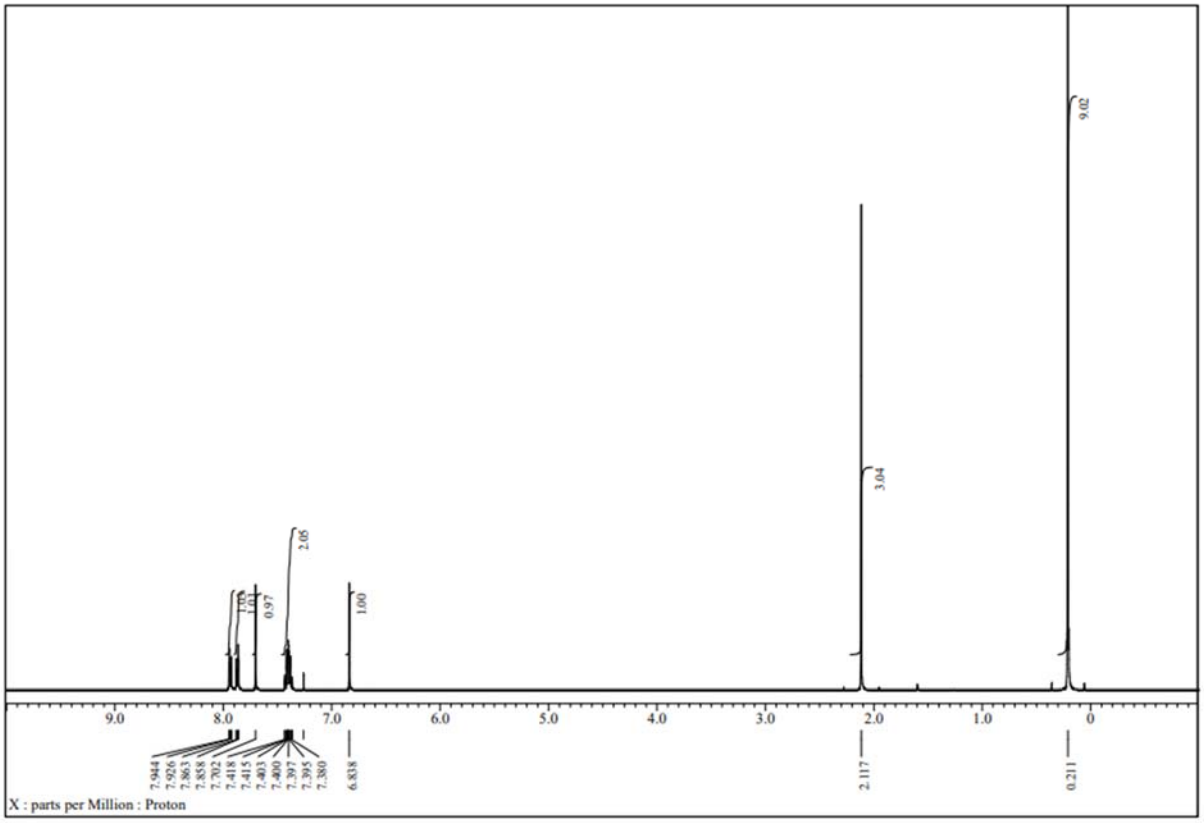


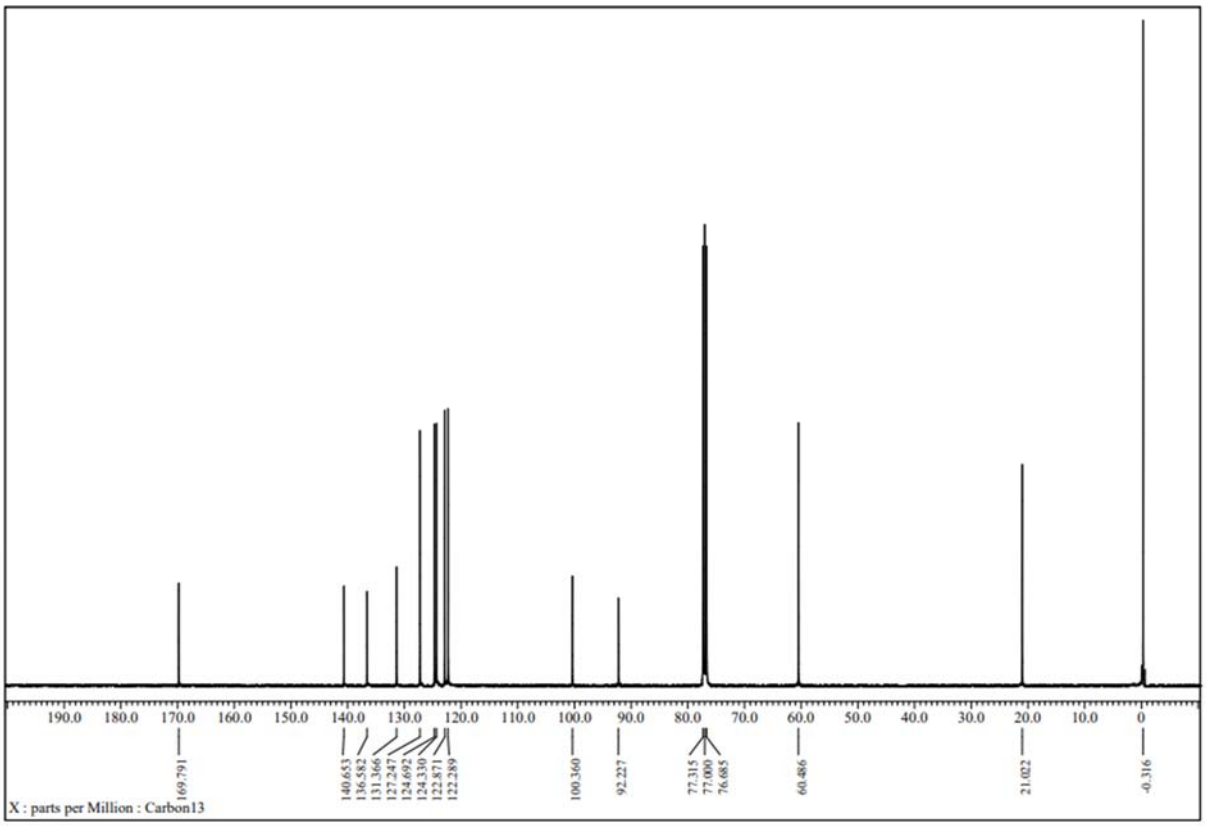



**(*S*)-1-(Thiophen-2-yl)-3-(triisopropylsilyl)prop-2-yn-1-yl acetate [(*S*)-4b]**

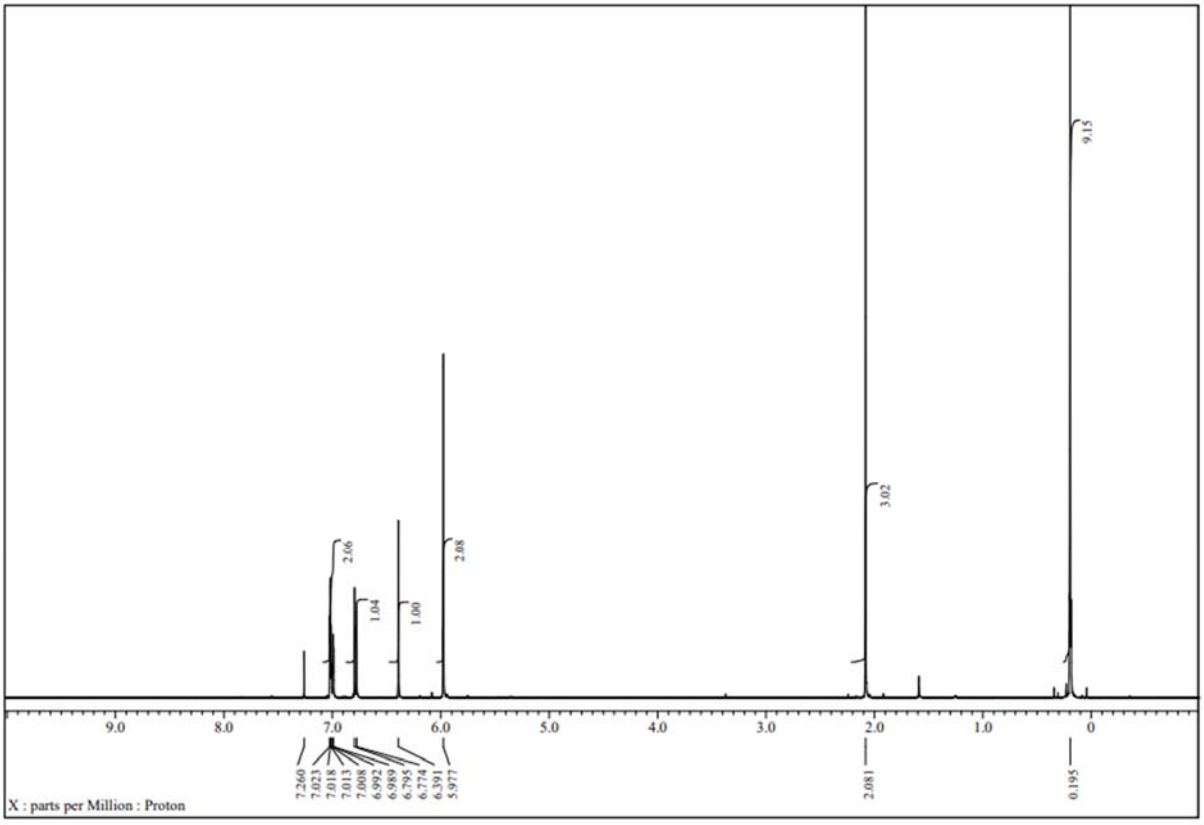


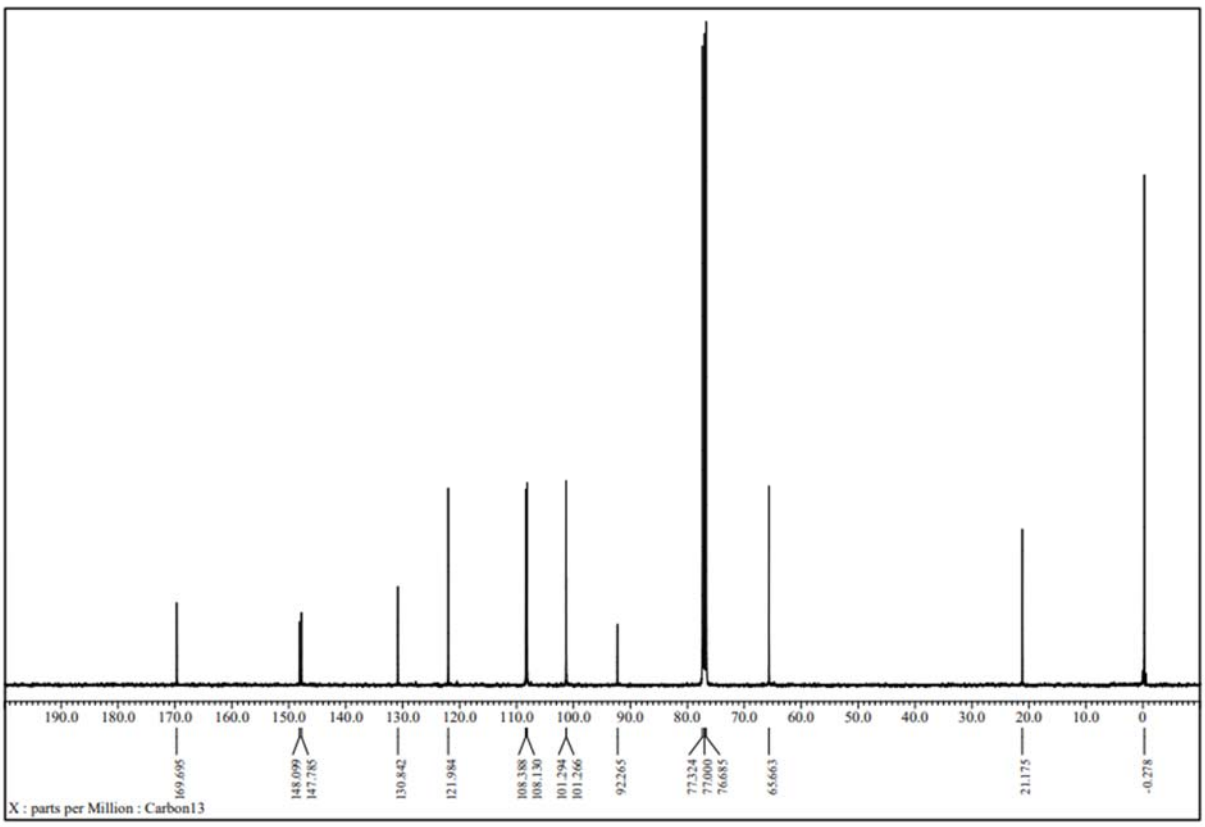
**(*S*)-1-(Benzo[b]thiophen-3-yl)-3-(trimethylsilyl)prop-2-yn-1-yl acetate [(*S*)-4c]**



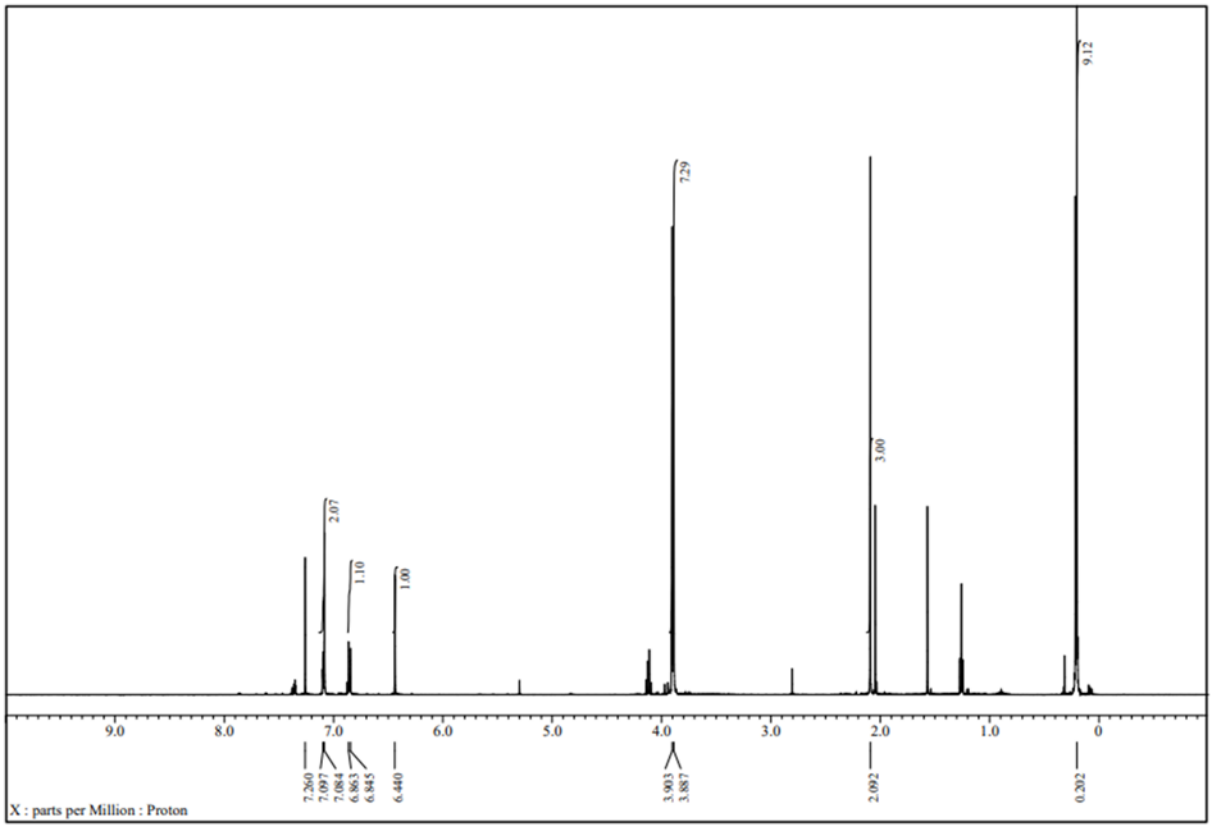



**(*R*)-1-(Benzo[d][1,3]dioxol-5-yl)-3-(trimethylsilyl)prop-2-yn-1-yl acetate [(*R*)-4d]**

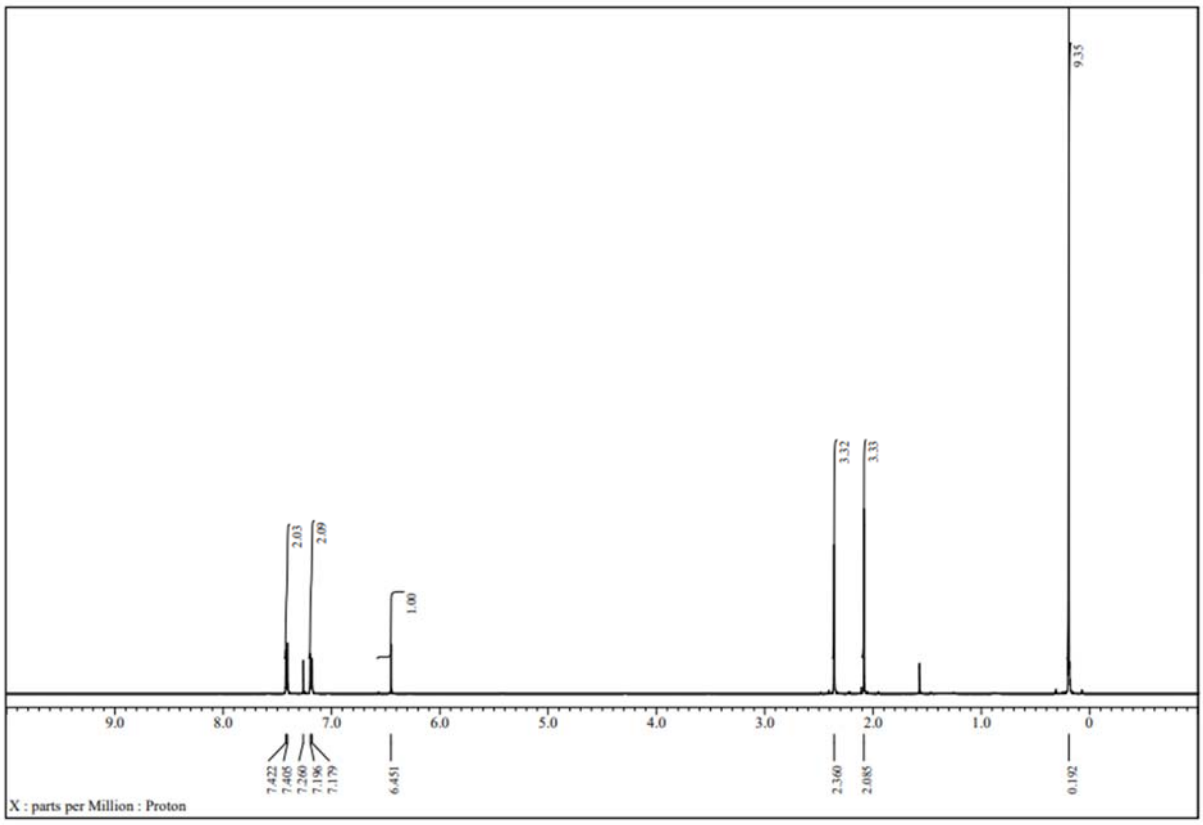


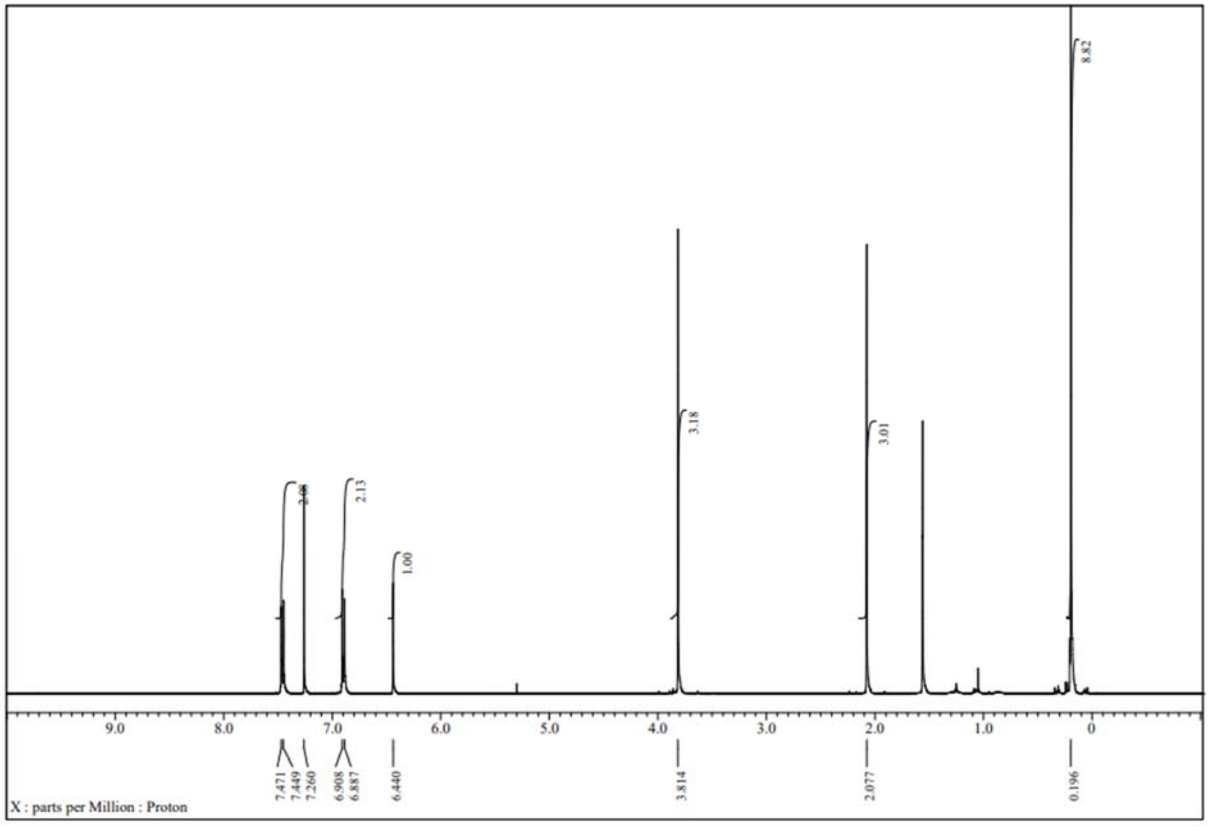
**(*R*)-1-(3,4-Dimethoxyphenyl)-3-(trimethylsilyl)prop-2-yn-1-yl acetate [(*R*)-4e]**



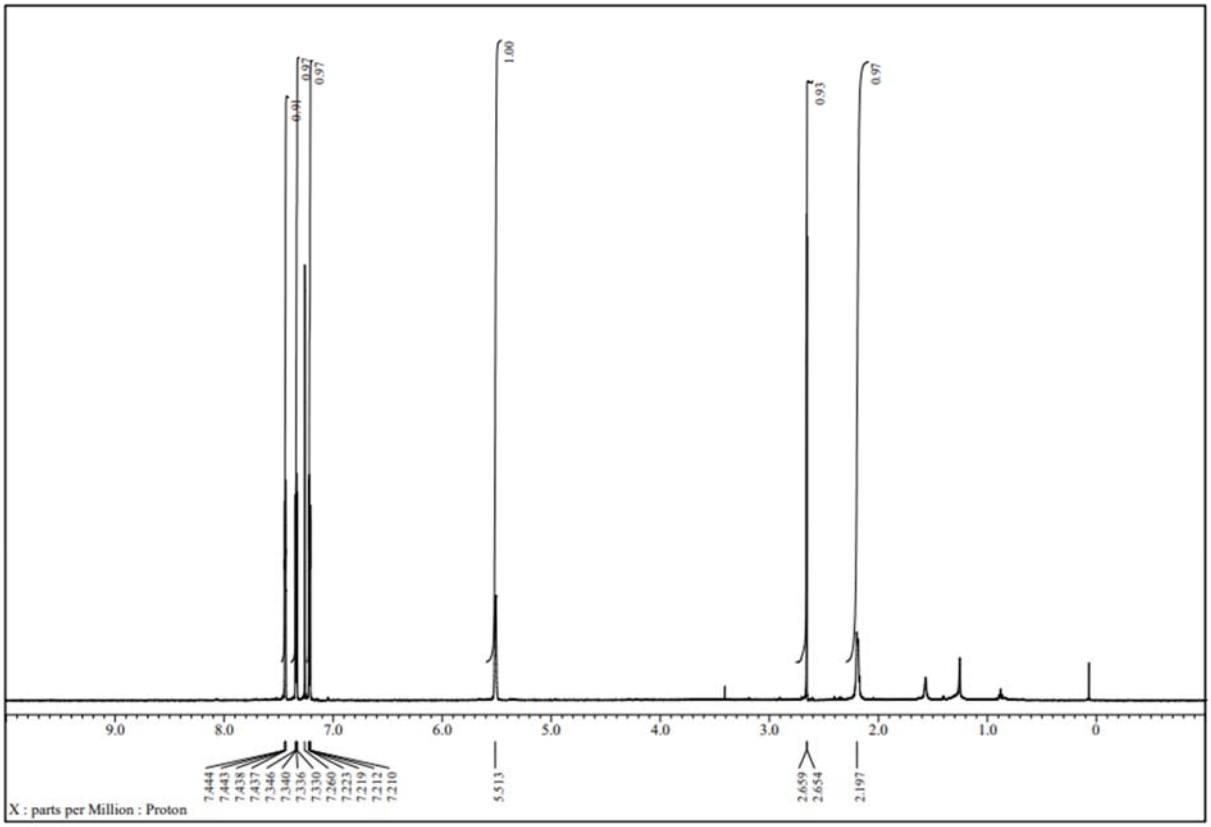

**(*R*)-1-(*p*-Tolyl)-3-(trimethylsilyl)prop-2-yn-1-yl acetate [(*R*)-4f]**

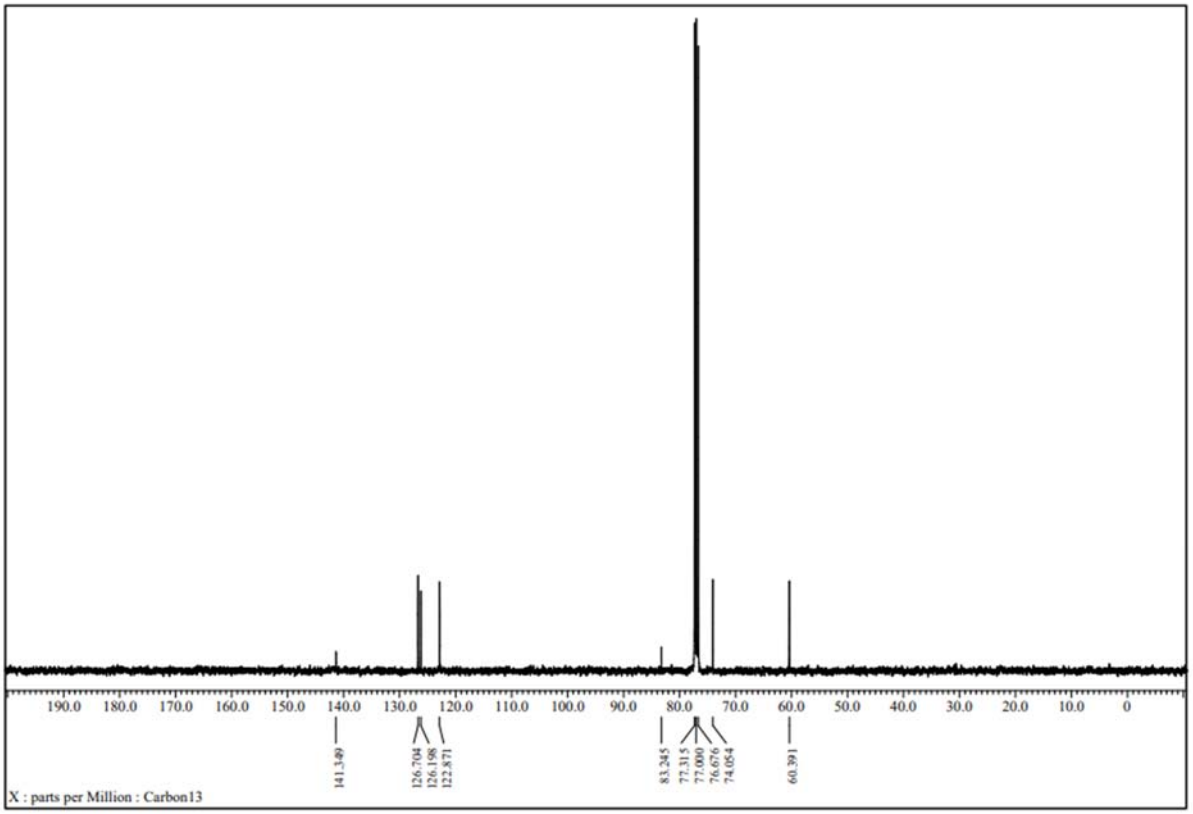


**(*R*)-1-(4-Methoxyphenyl)-3-(trimethylsilyl)prop-2-yn-1-yl acetate [(*R*)-4g]**



**(*S*)-1-(Thiophen-3-yl)prop-2-yn-1-ol [(*S*)-1a]**



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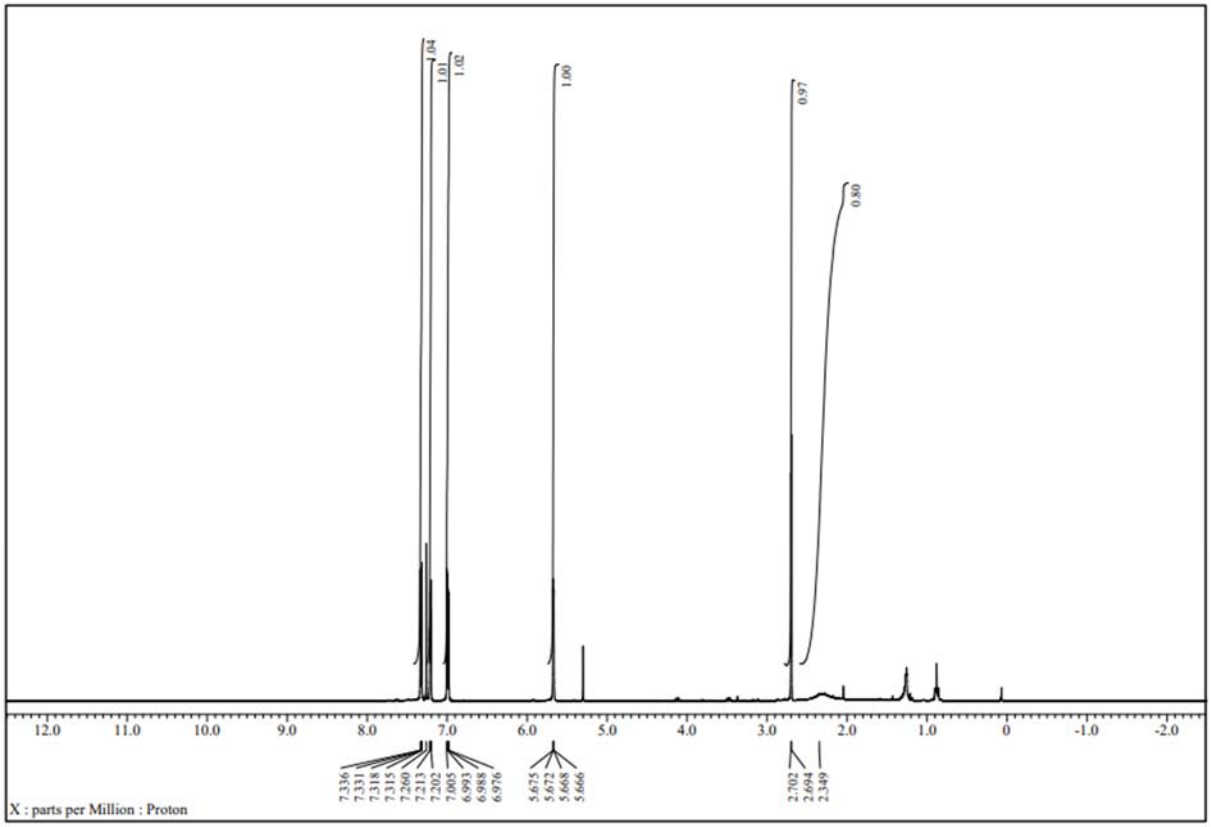
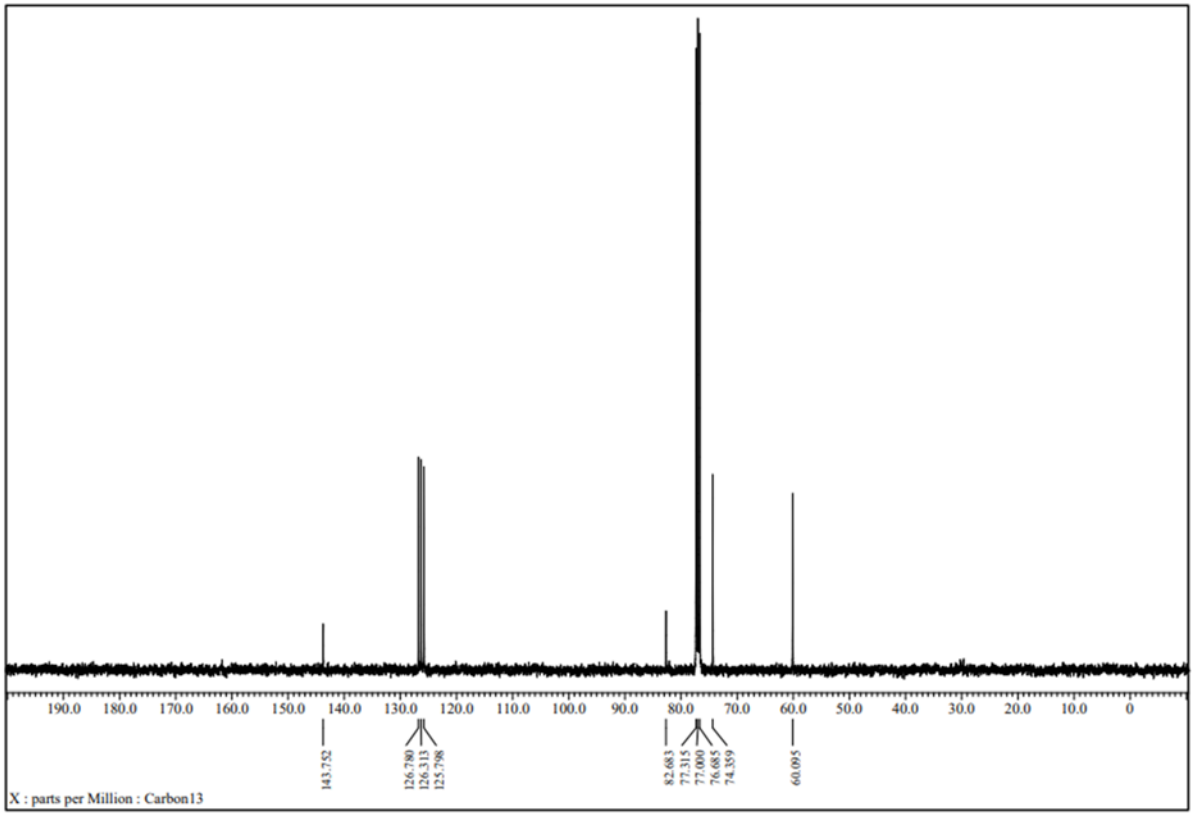
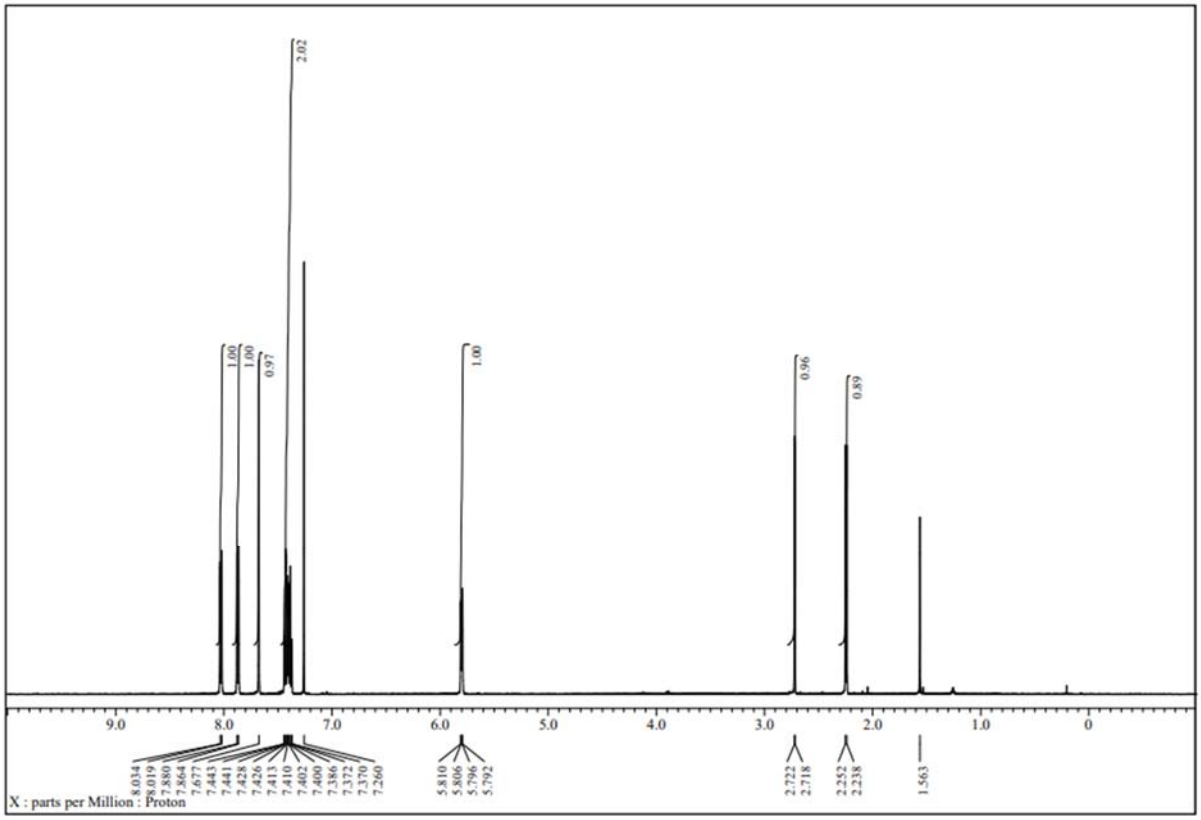
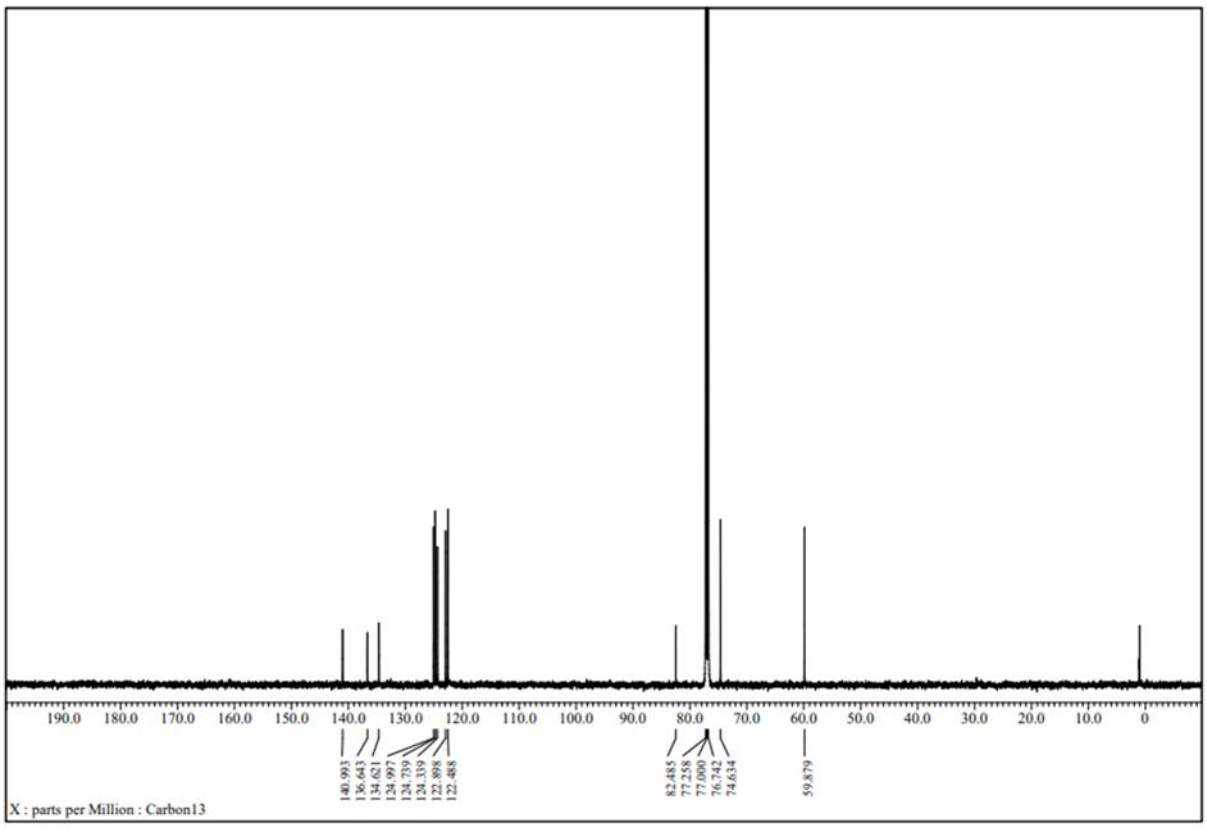


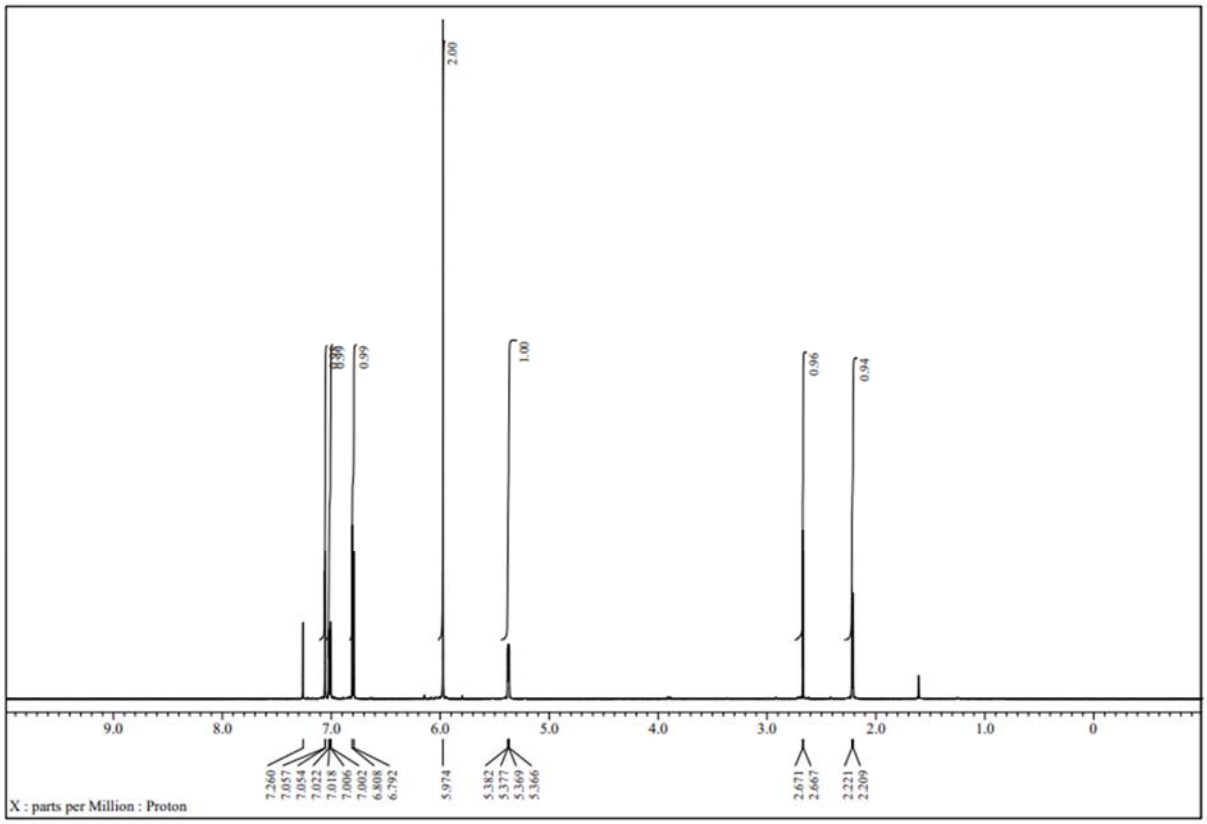



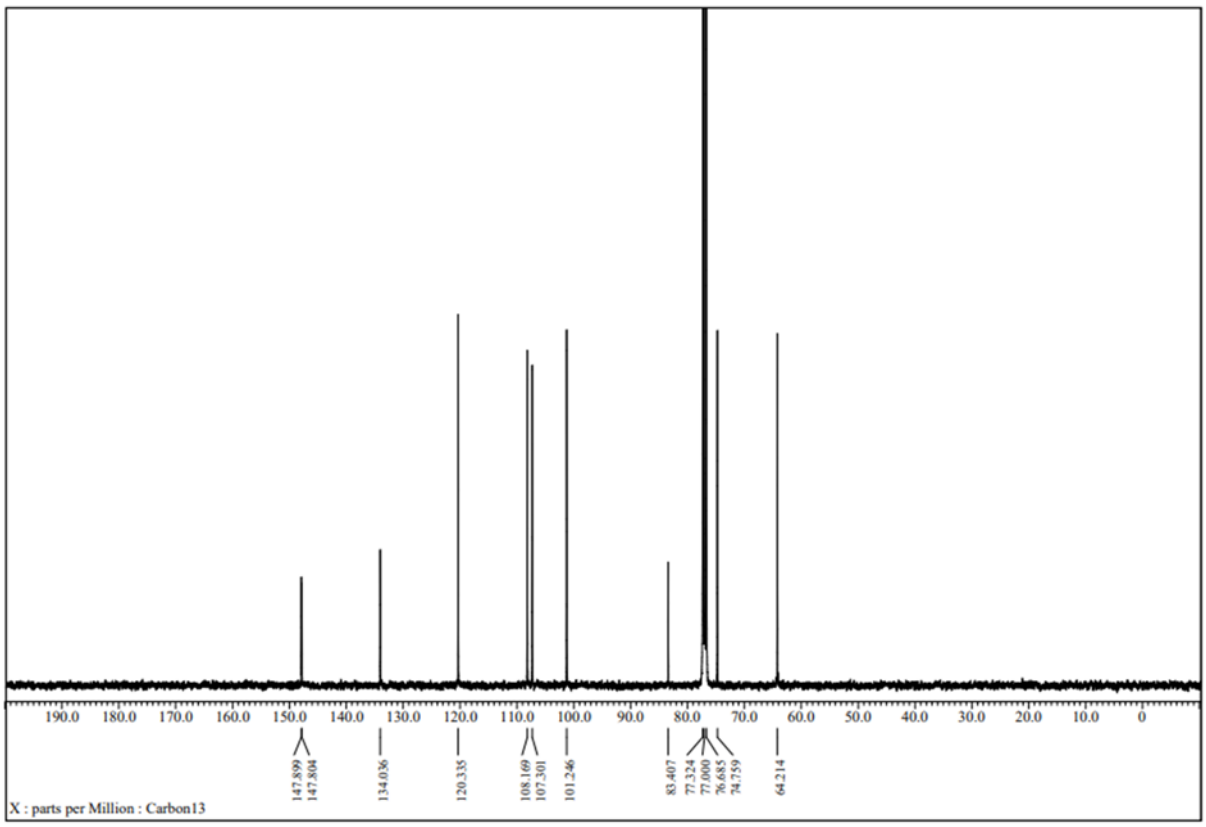
**(*S*)-1-(Benzo[b]thiophen-3-yl)prop-2-yn-1-ol [(*S*)-1c]**



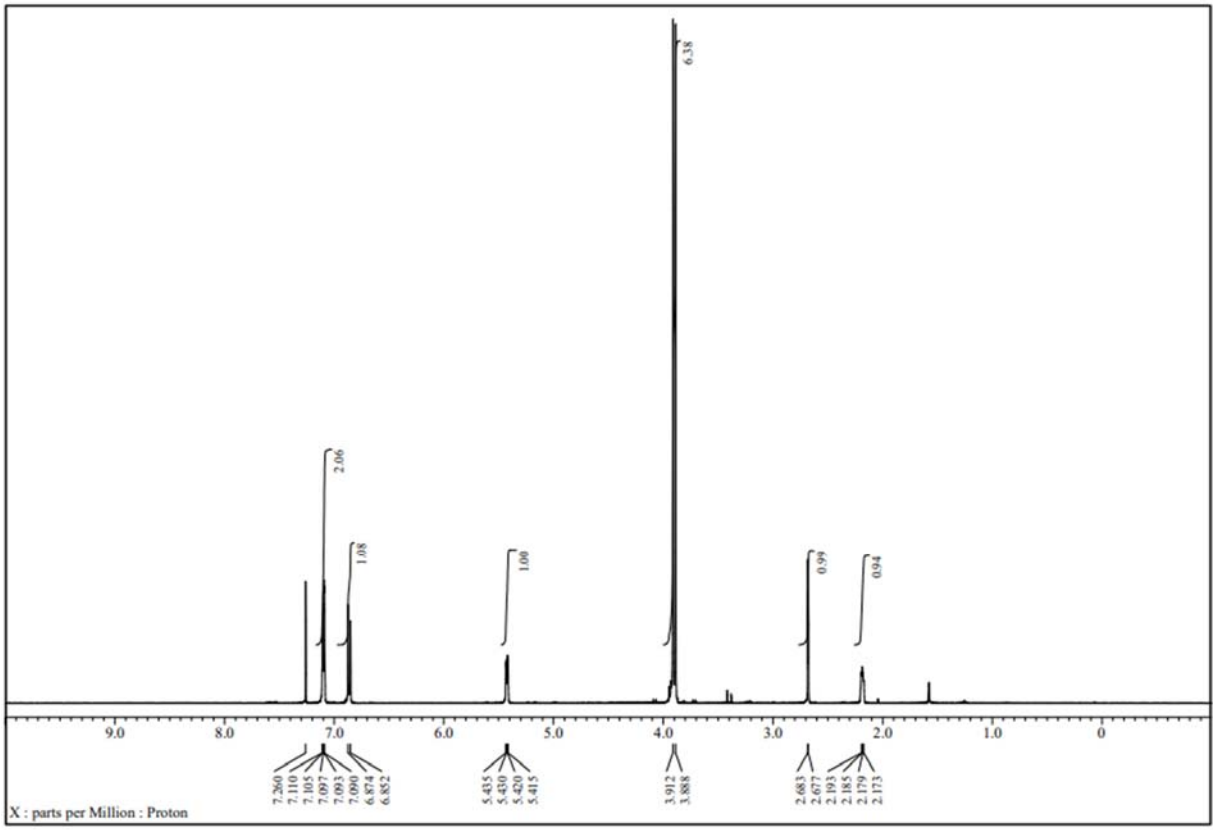



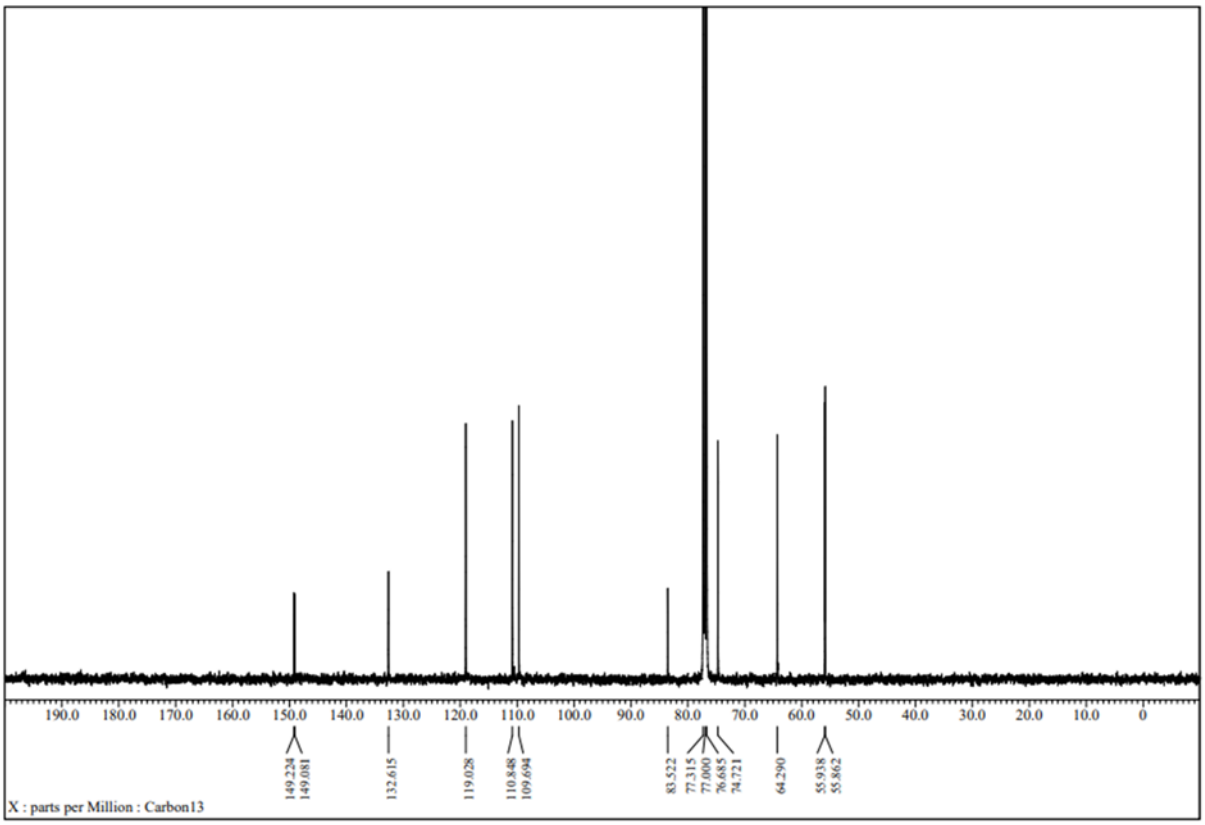
**(*S*)-1-(Benzo[d][1,3]dioxol-5-yl)prop-2-yn-1-ol [(*S*)-1d]**



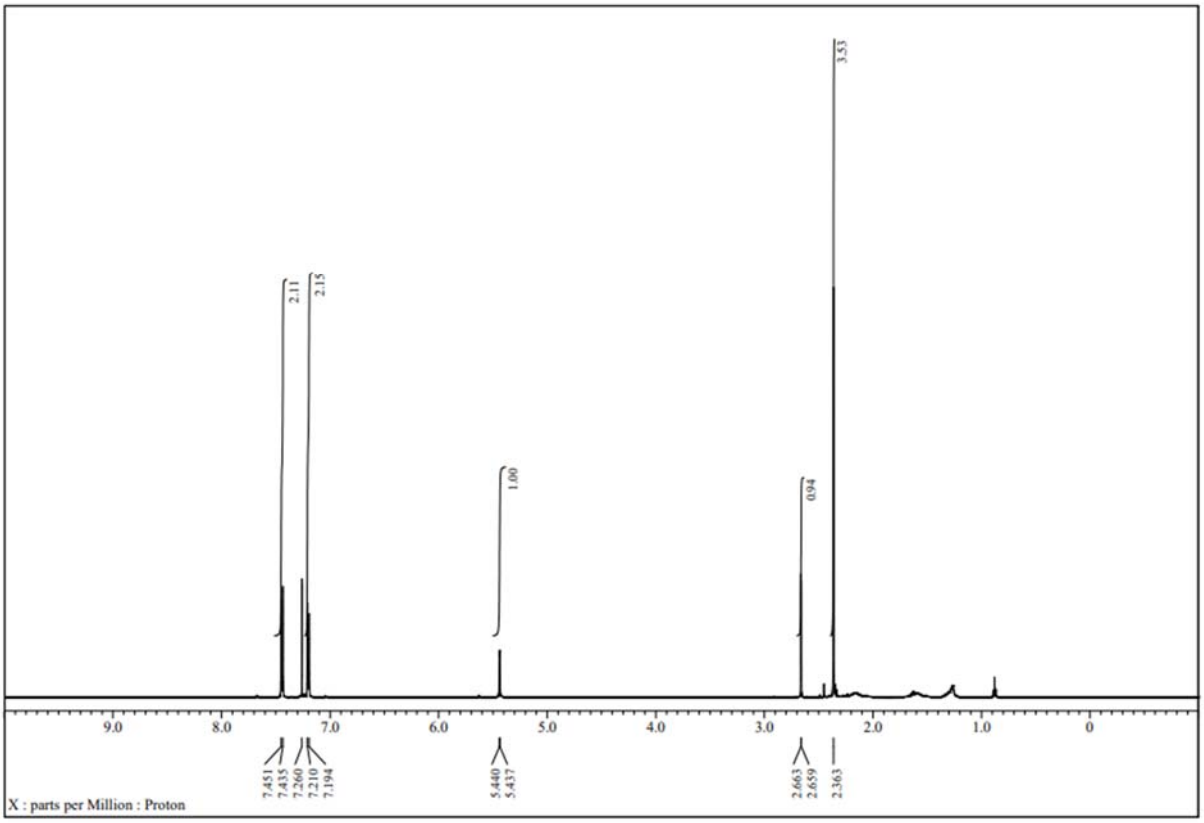



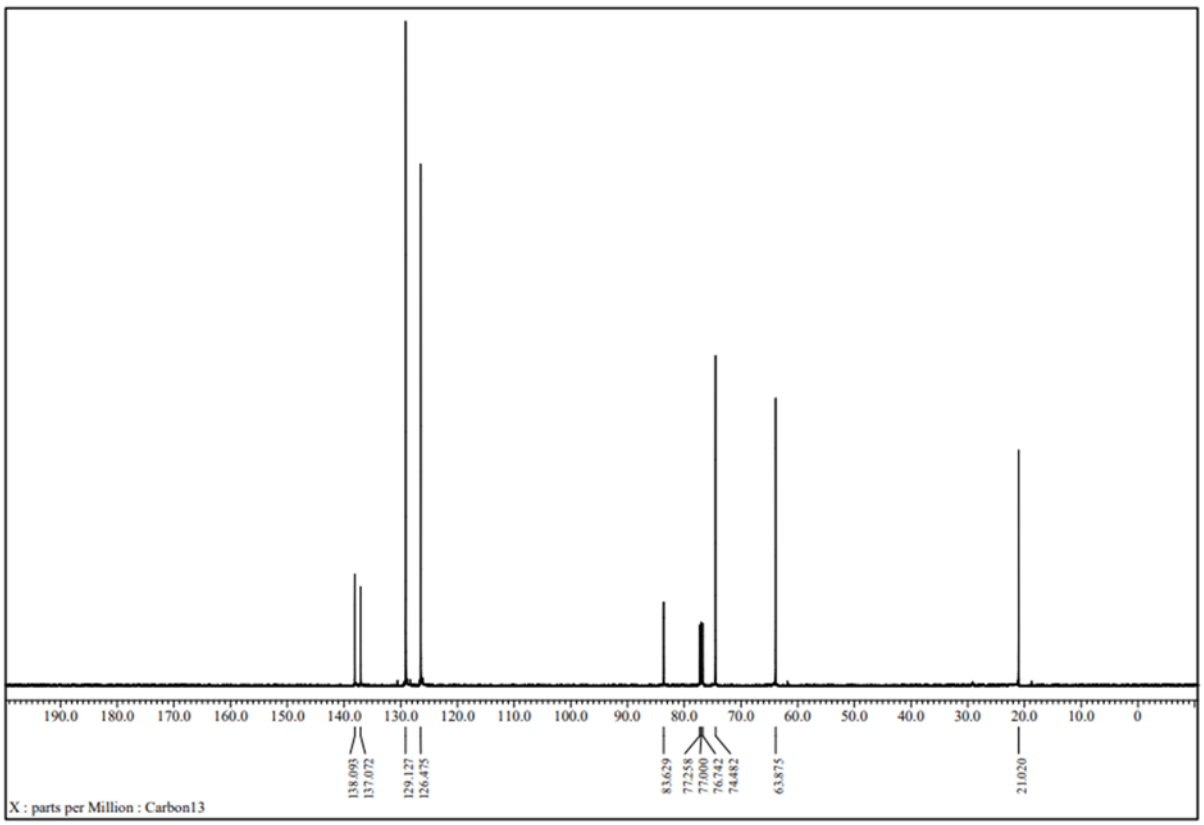
**(*S*)-1-(3,4-Dimethoxyphenyl)prop-2-yn-1-ol [(*S*)-1e]**



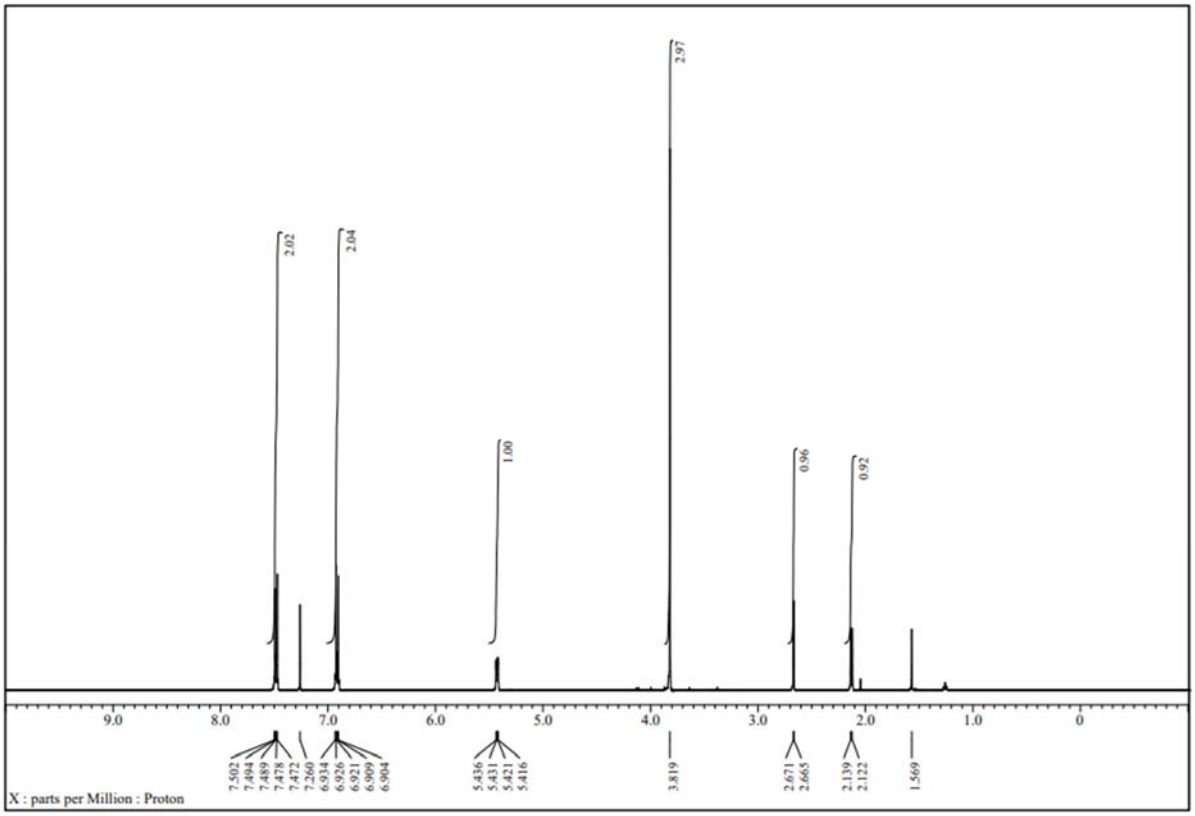



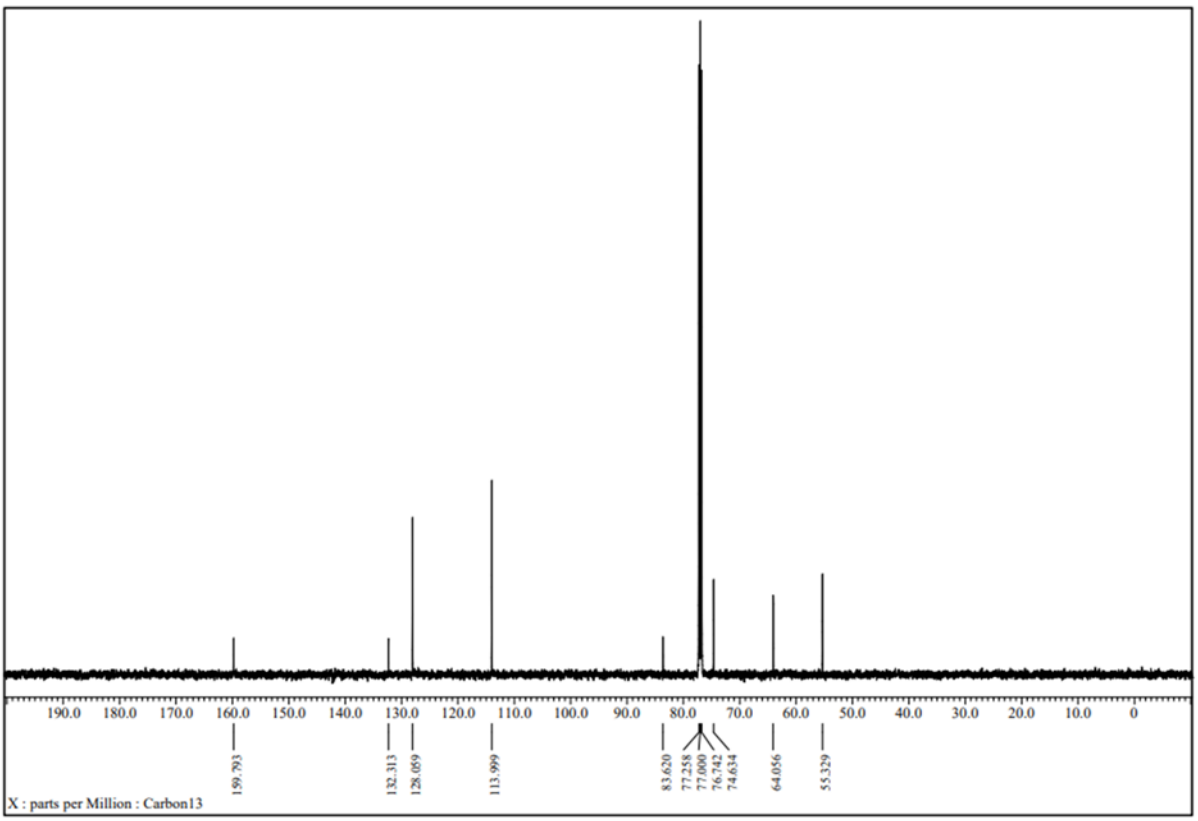
**(*S*)-1-(*p*-Tolyl)prop-2-yn-1-ol [(*S*)-1f]**



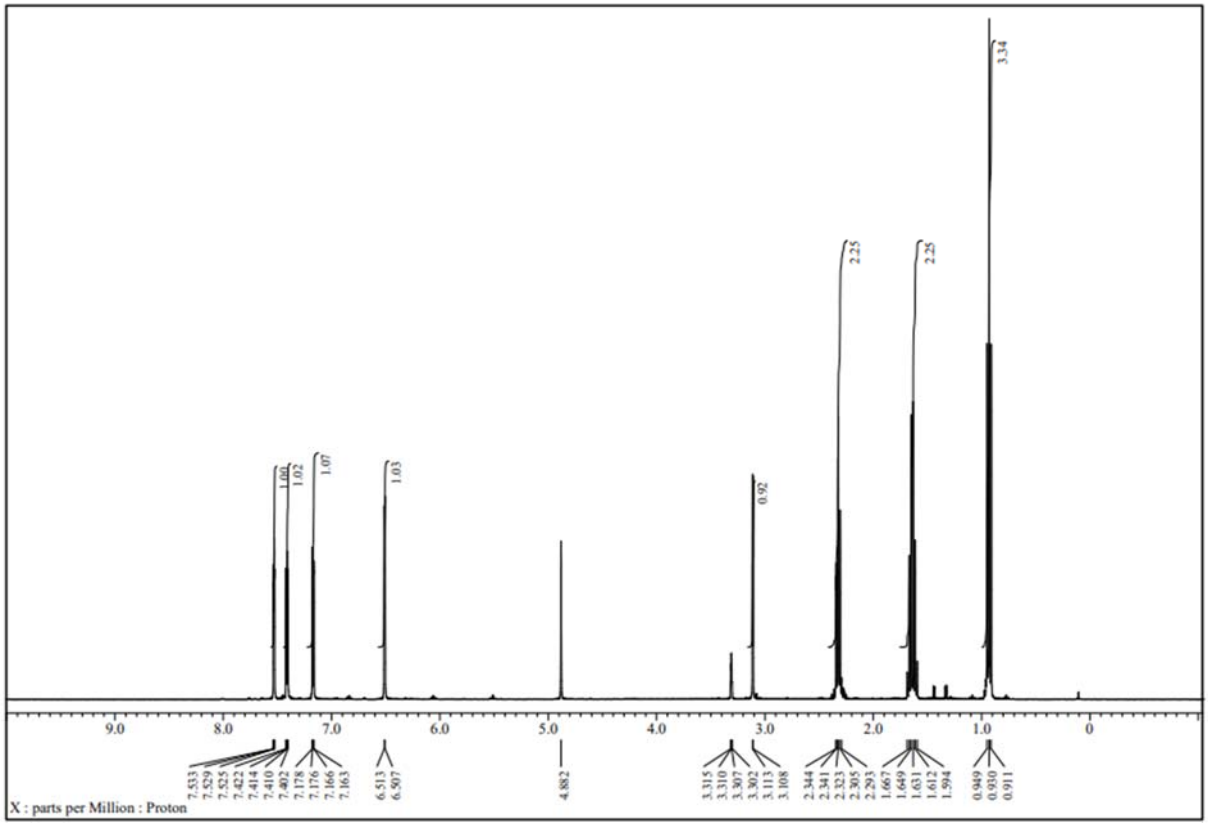



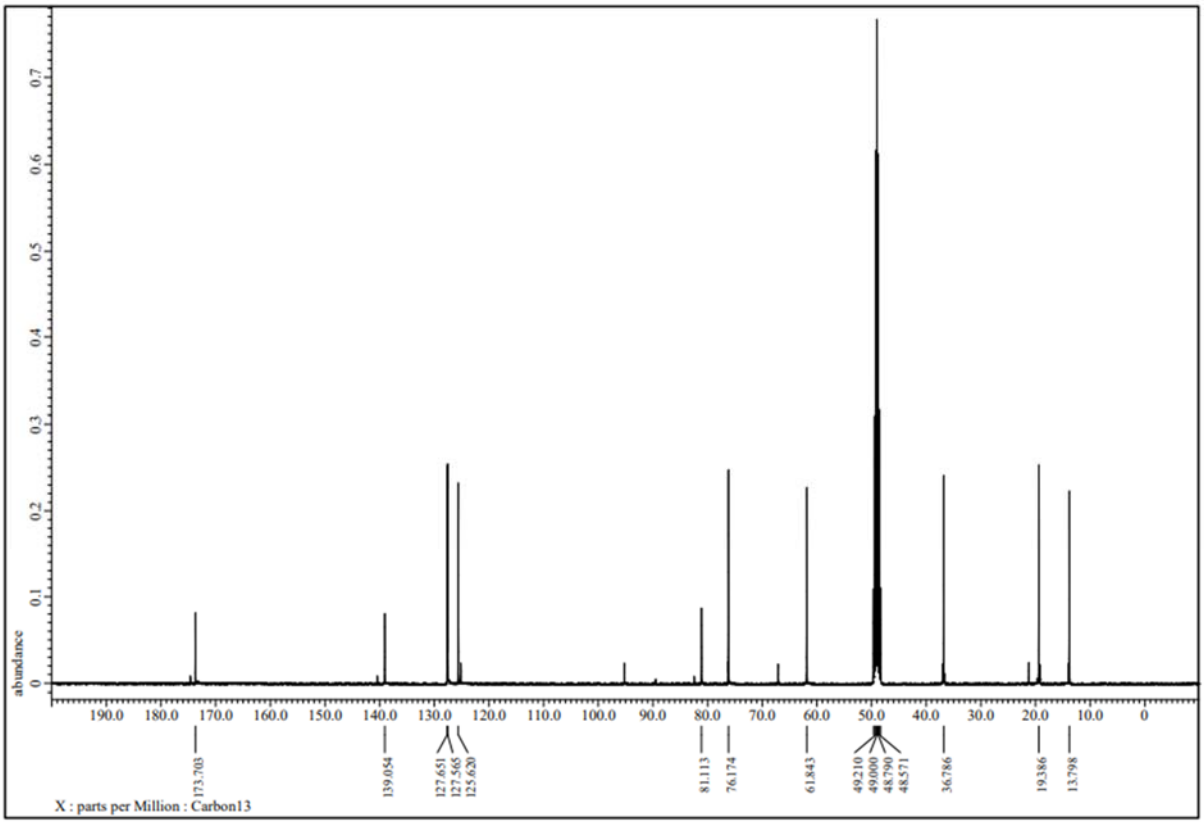
**(*S*)-1-(4-Methoxyphenyl)prop-2-yn-1-ol [(*S*)-1g]**



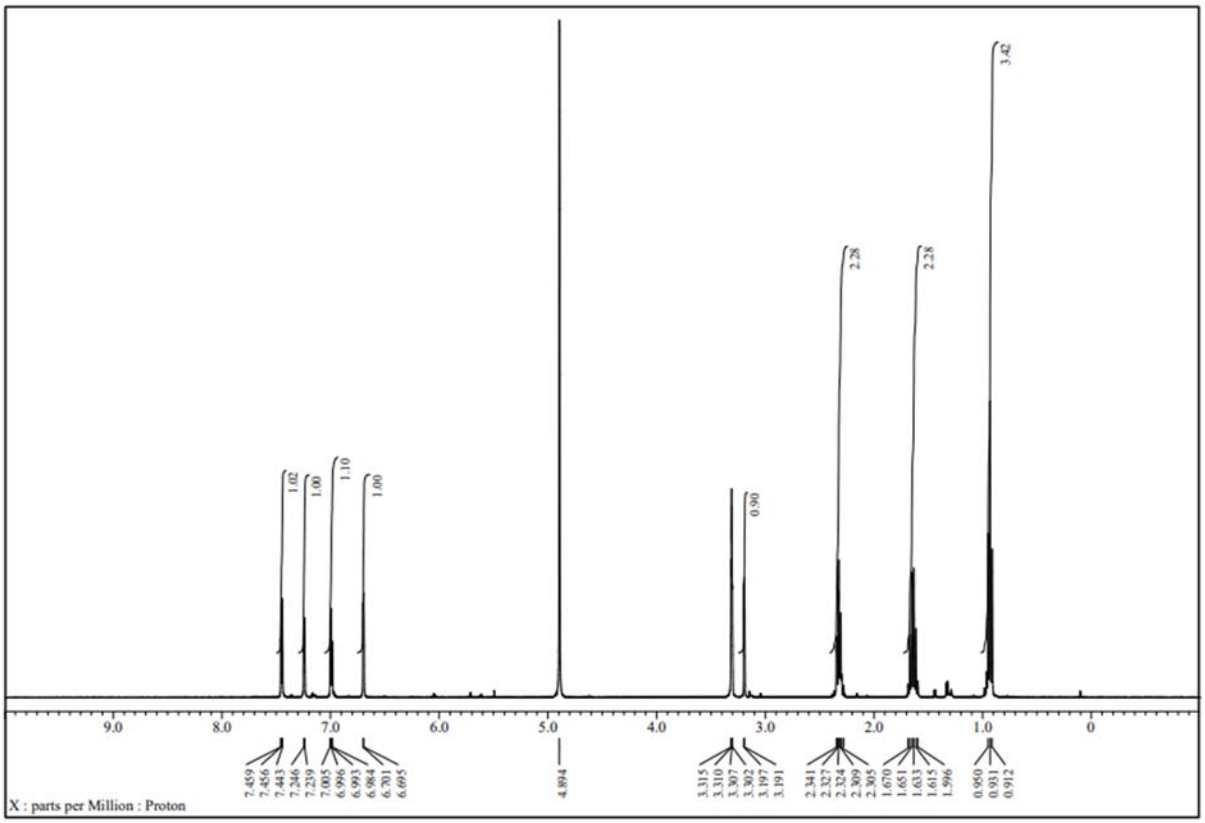



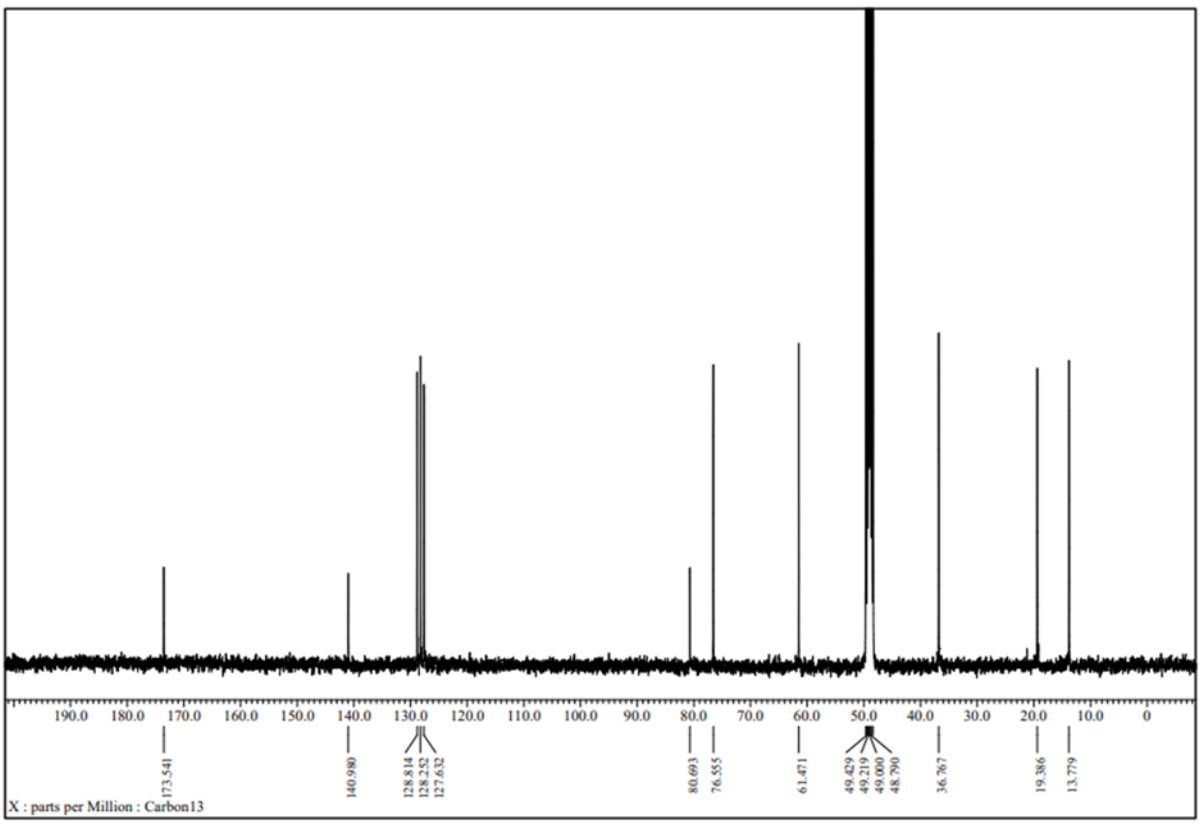
**(*R*)-1-(Thiophen-3-yl)prop-2-yn-1-yl butyrate [(*R*)-2a]**



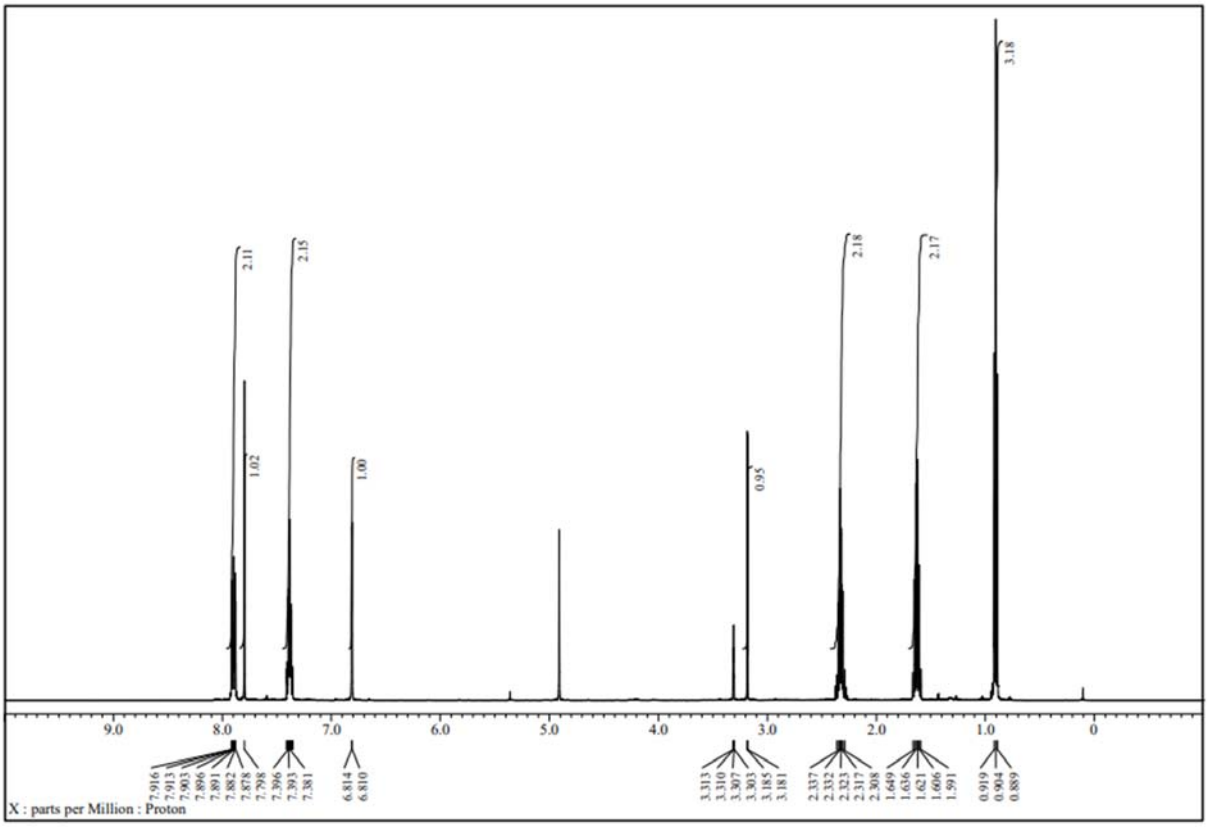



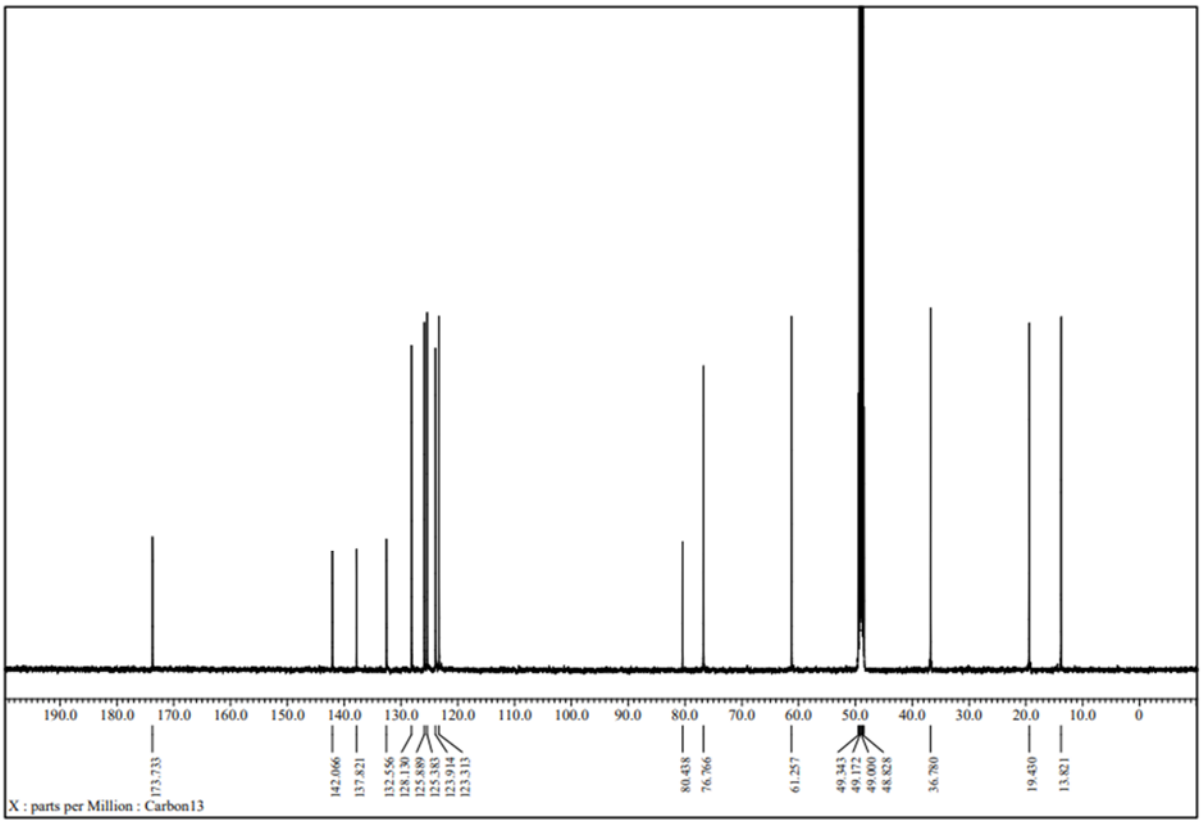
**(*R*)-1-(Thiophen-2-yl)prop-2-yn-1-yl butyrate [(*R*)-2b]**



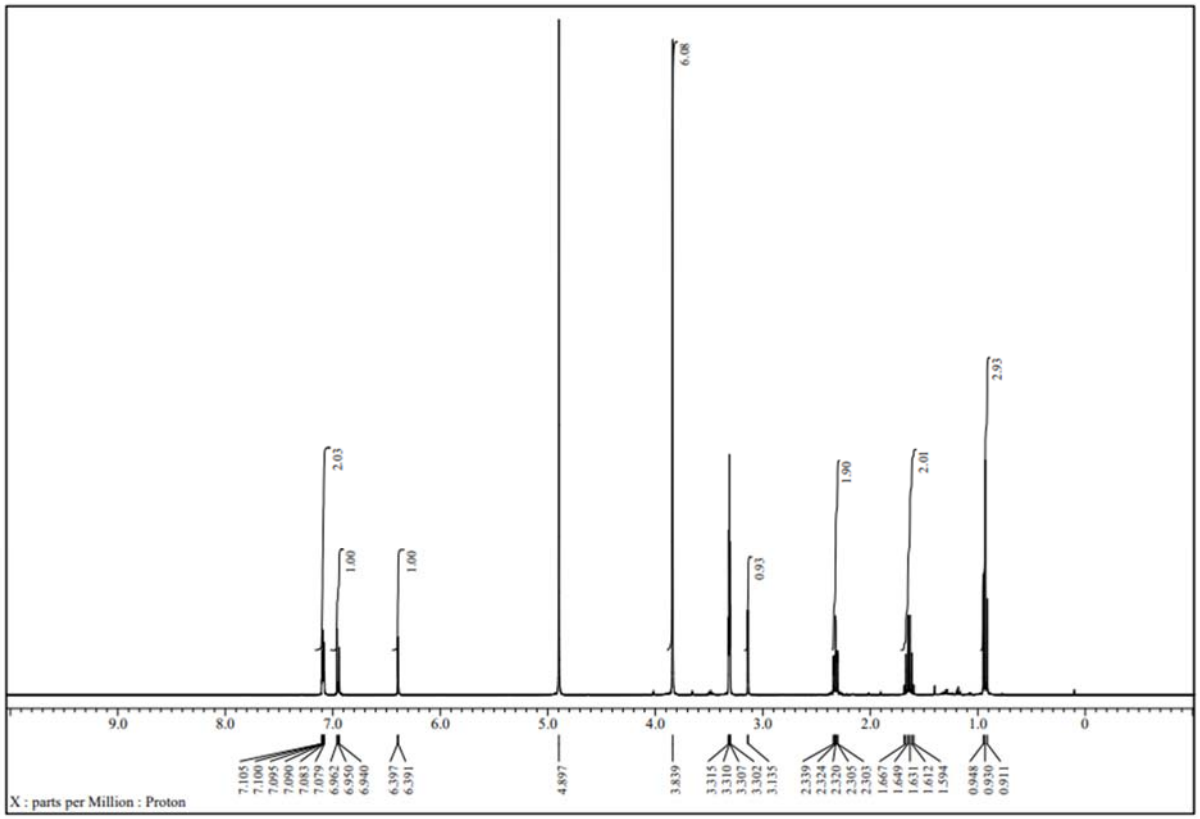



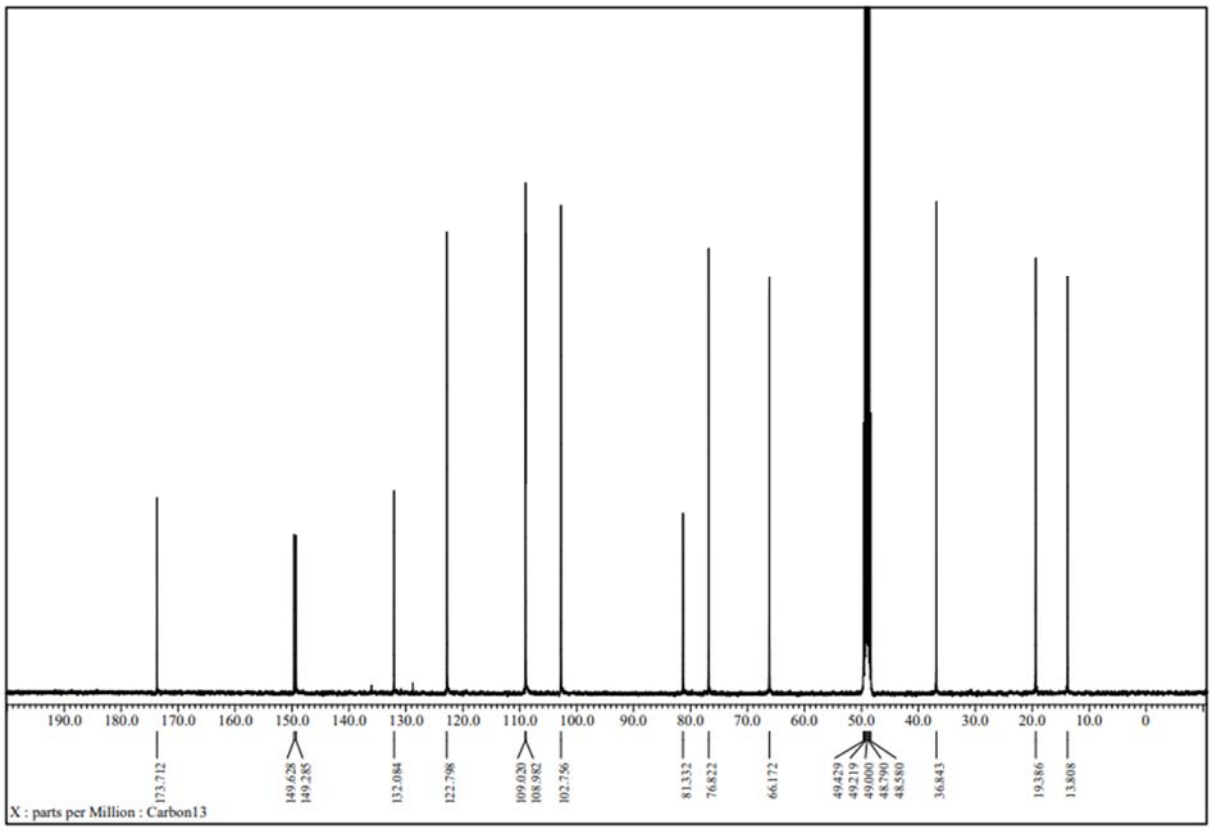
**(*R*)-1-(Benzo[b]thiophen-3-yl)prop-2-yn-1-yl butyrate [(*R*)-2c]**



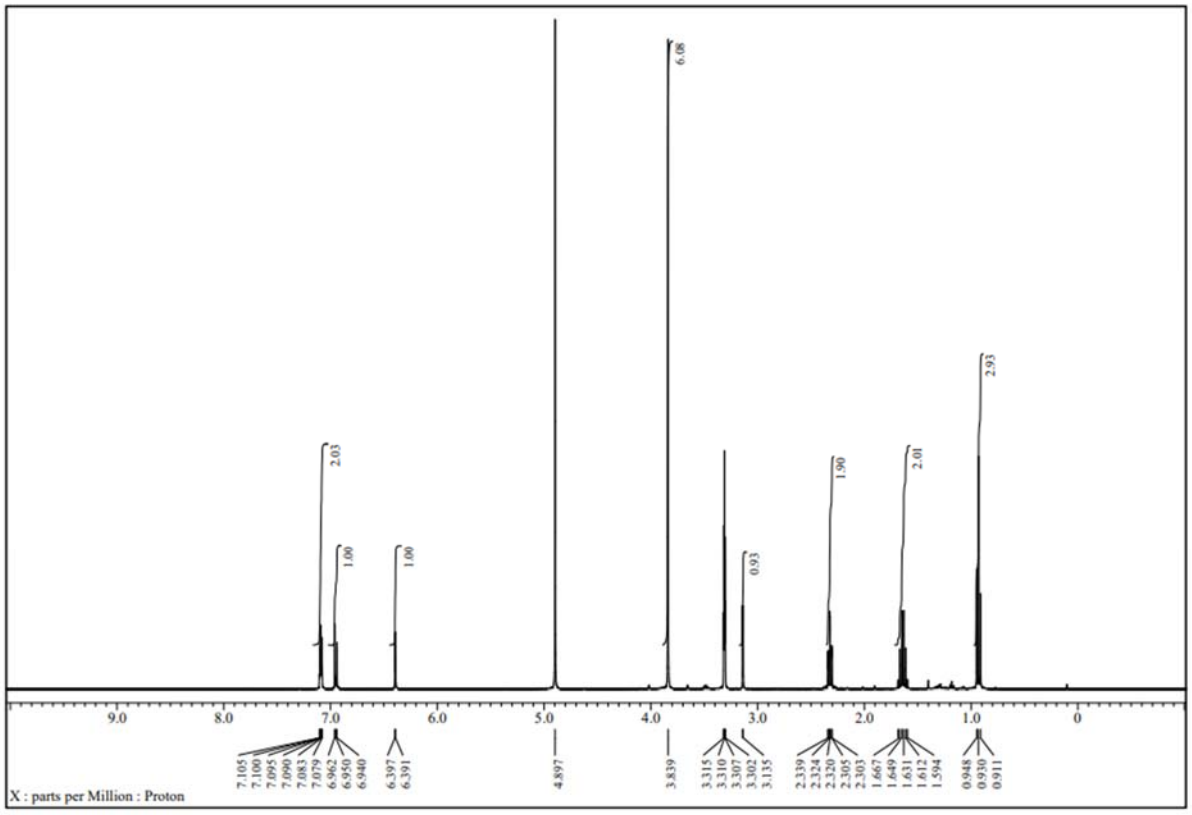



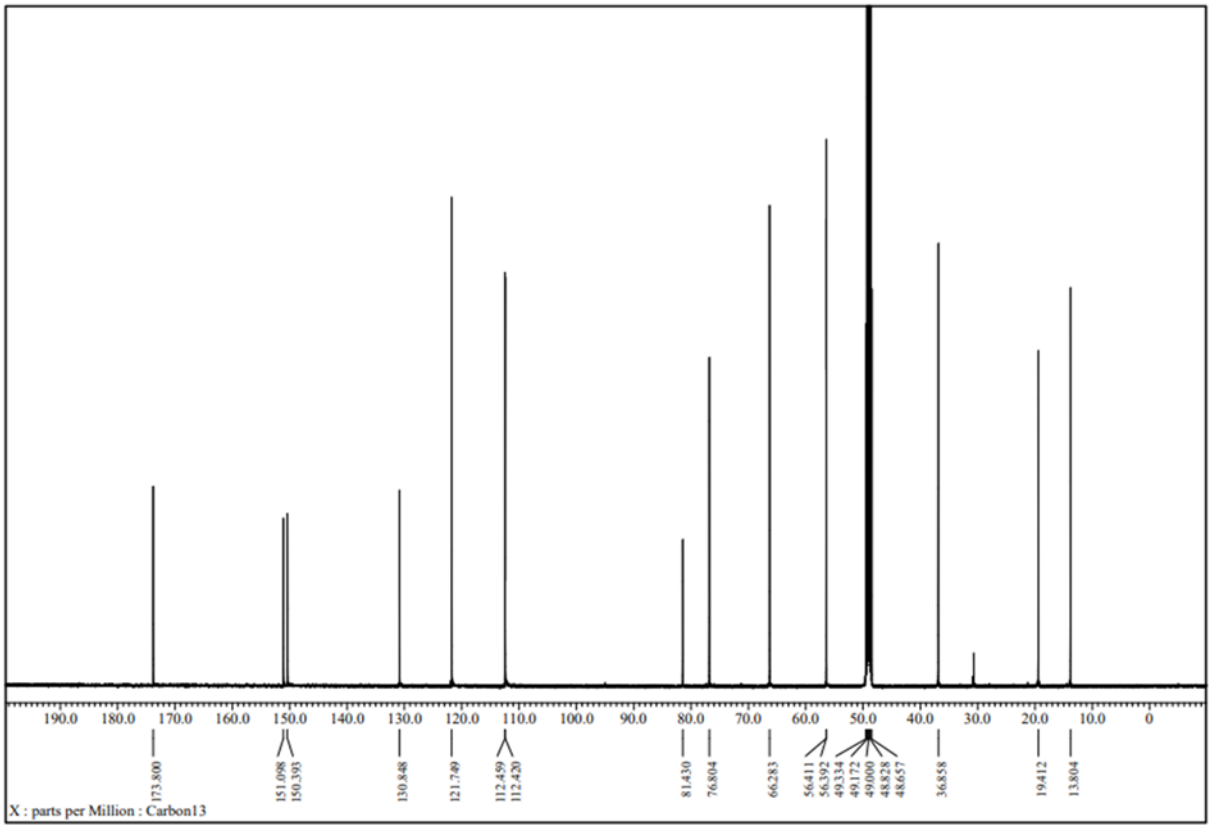
**(*R*)-1-(Benzo[d][1,3]dioxol-5-yl)prop-2-yn-1-yl butyrate [(*R*)-2d]**



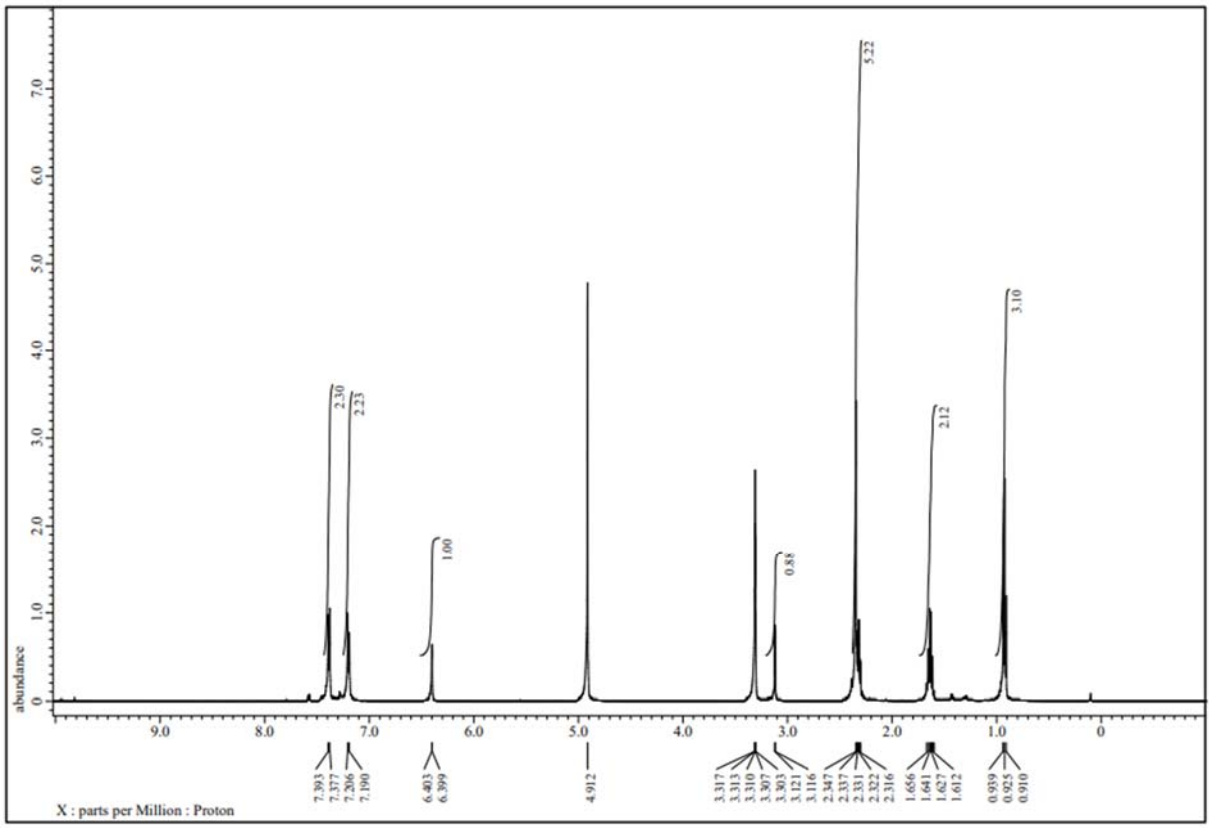



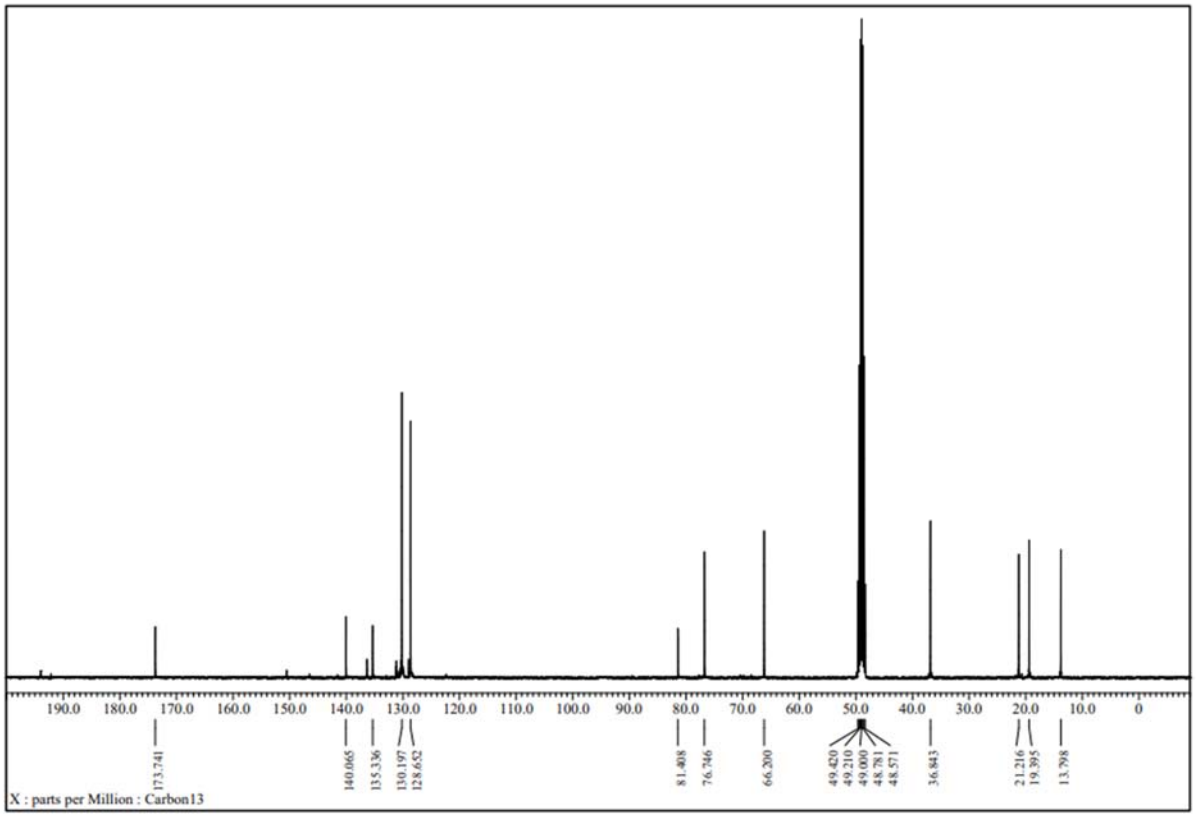
**(*R*)-1-(3,4-Dimethoxyphenyl)prop-2-yn-1-yl butyrate [(*R*)-2e]**



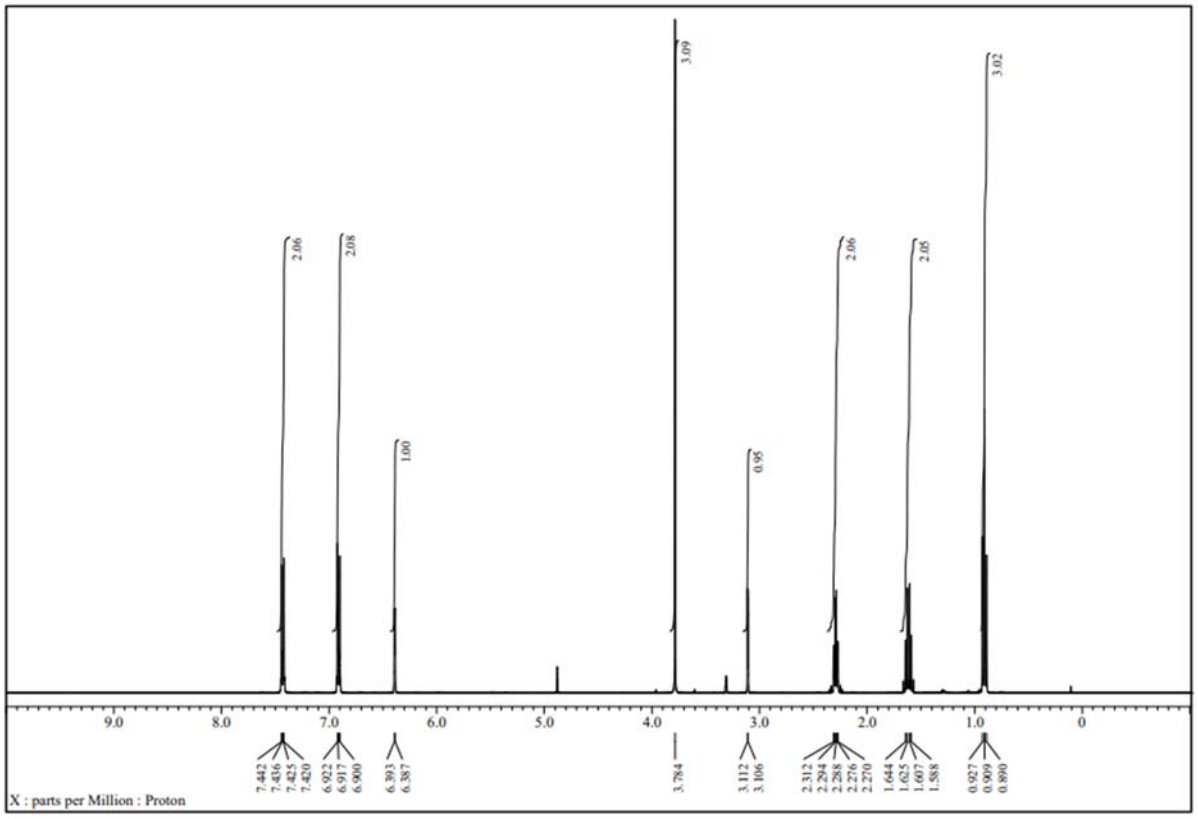



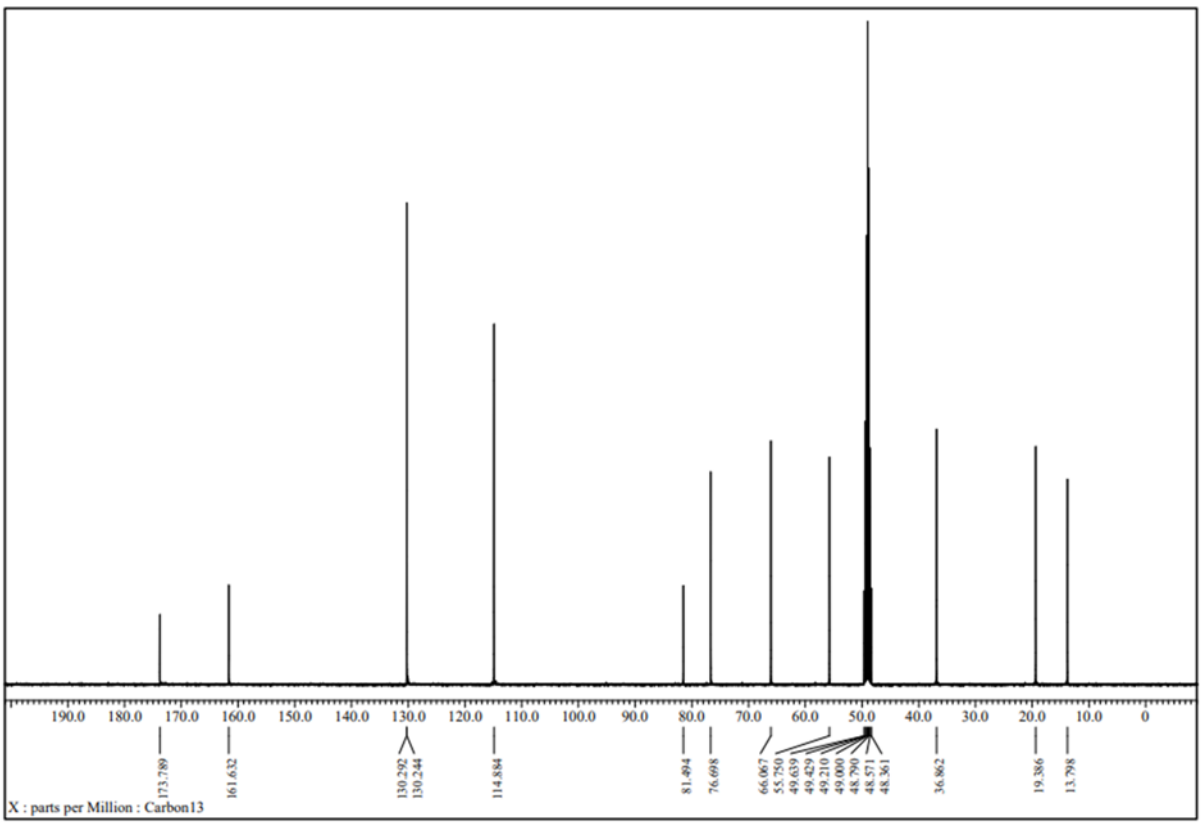
**(*R*)-1-(*p*-Tolyl)prop-2-yn-1-yl butyrate [(*R*)-2f]**



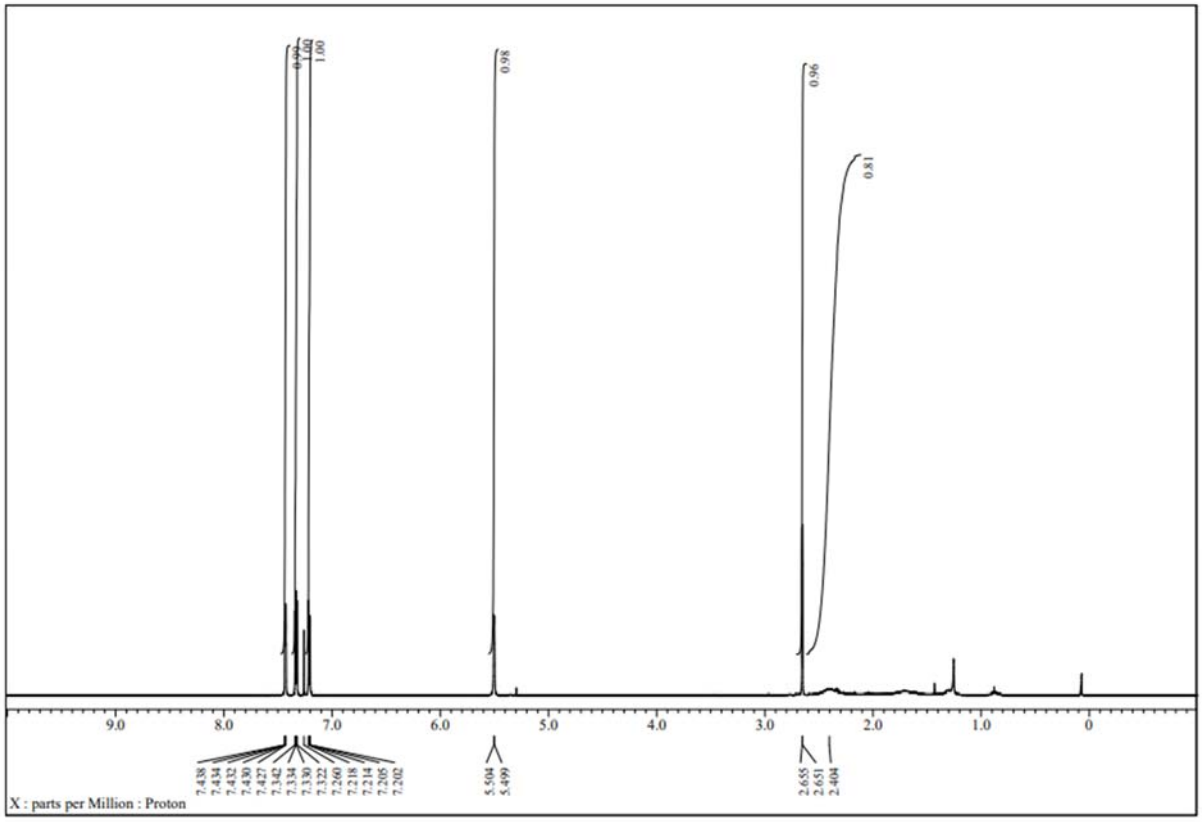



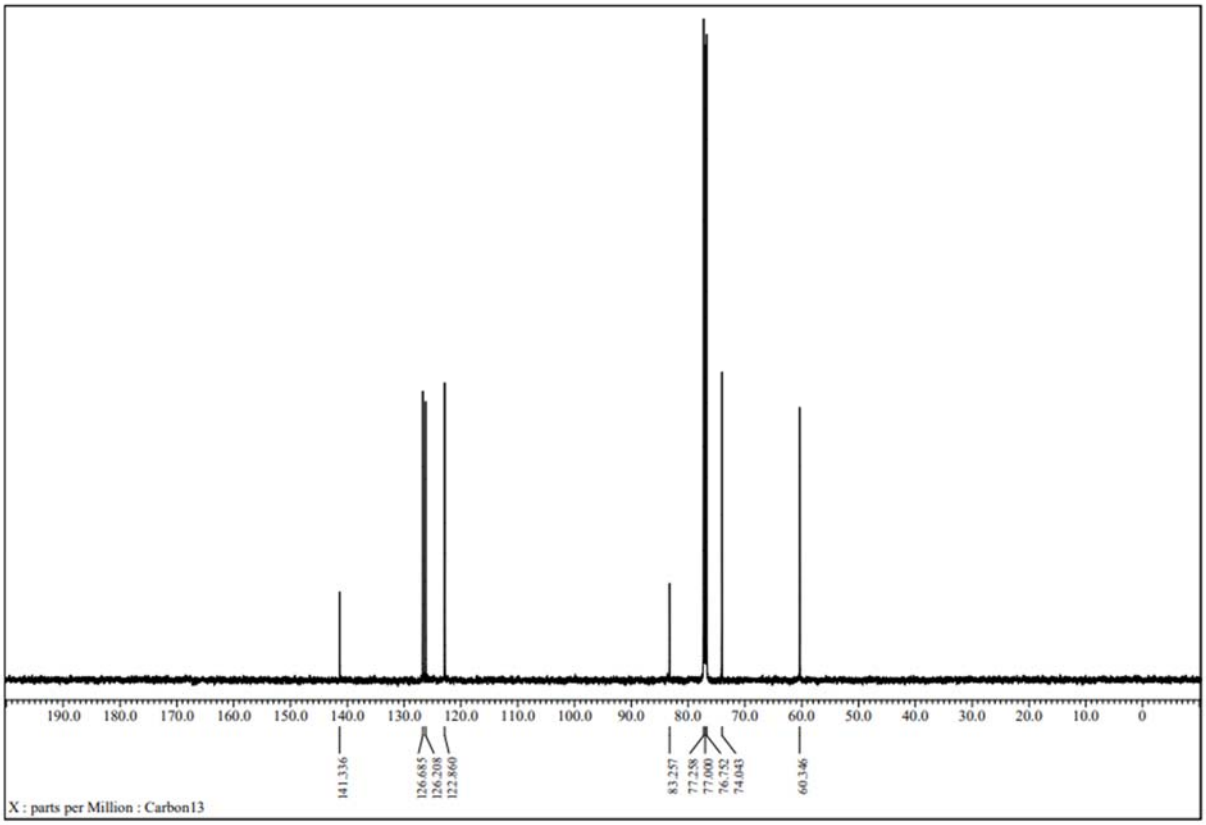
**(*R*)-1-(4-Methoxyphenyl)prop-2-yn-1-yl butyrate [(*R*)-2g]**



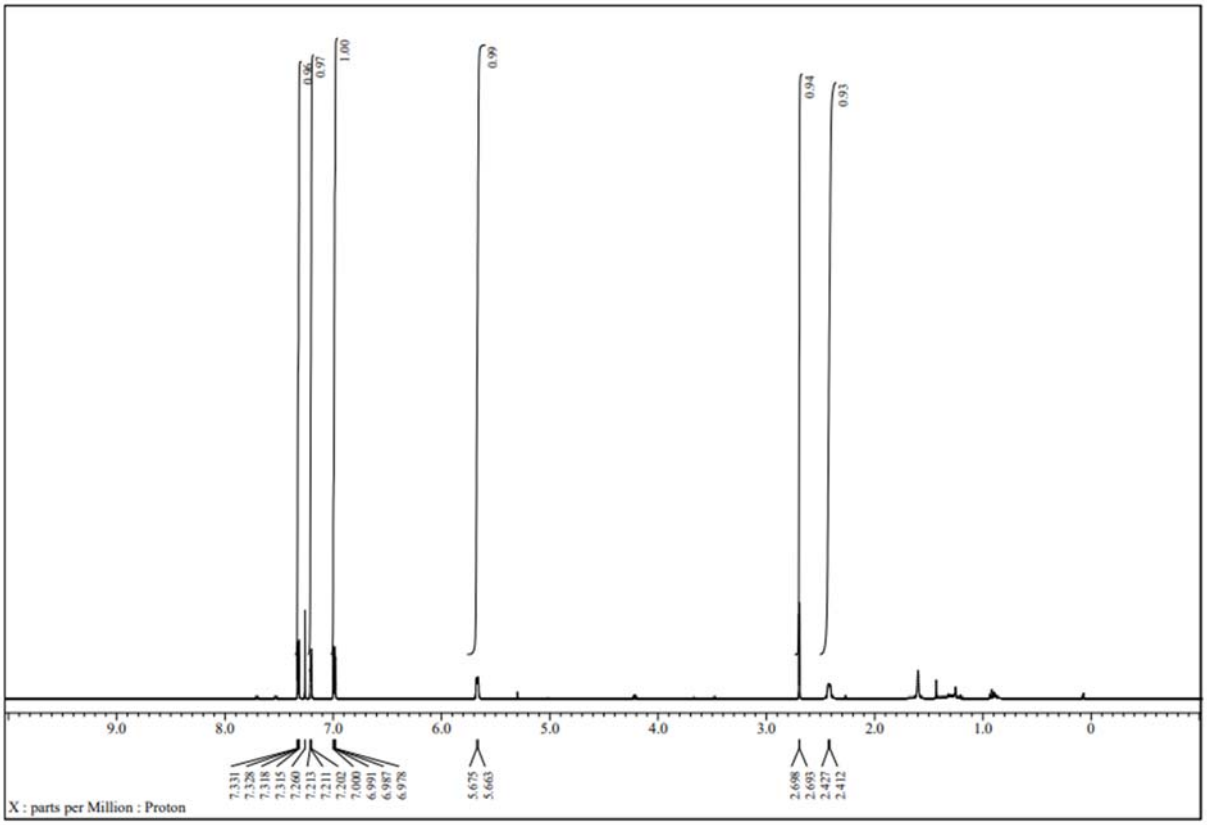



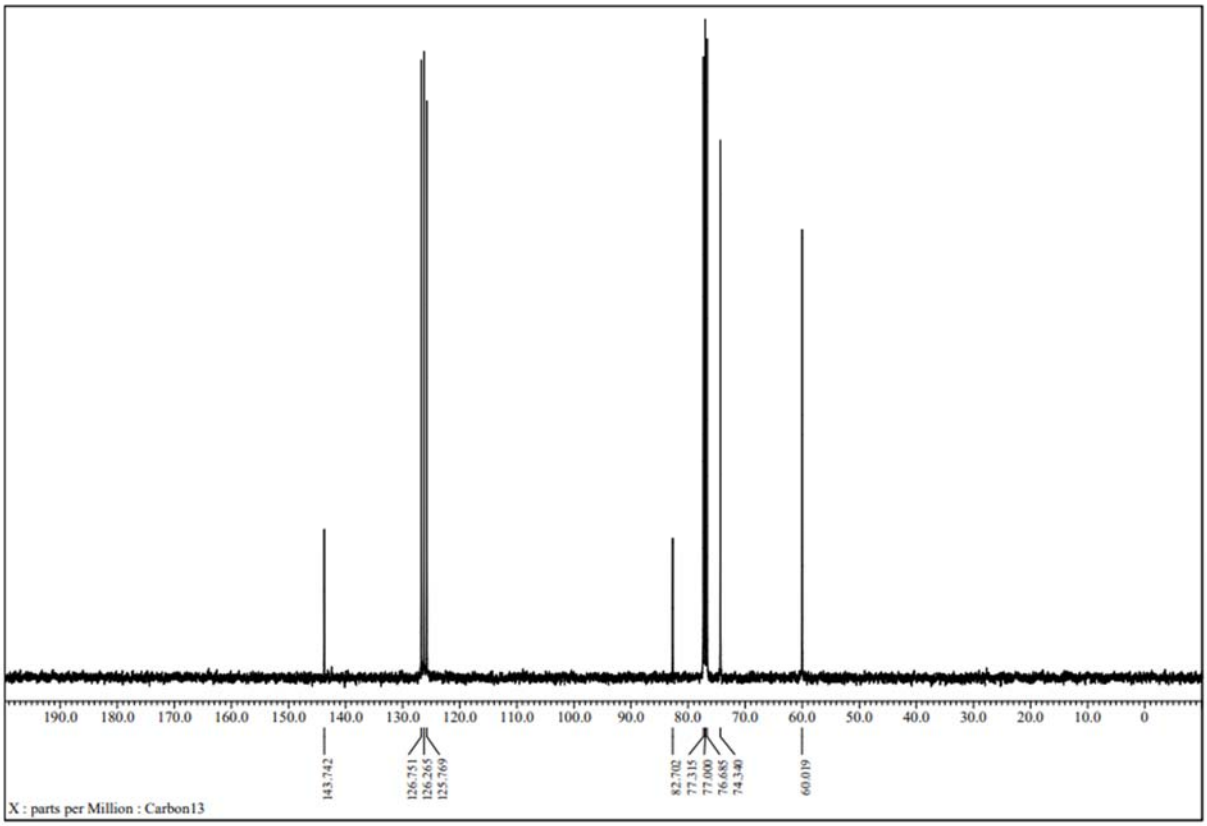
**(*R*)-1-(Thiophen-3-yl)prop-2-yn-1-ol [(*R*)-1a]**



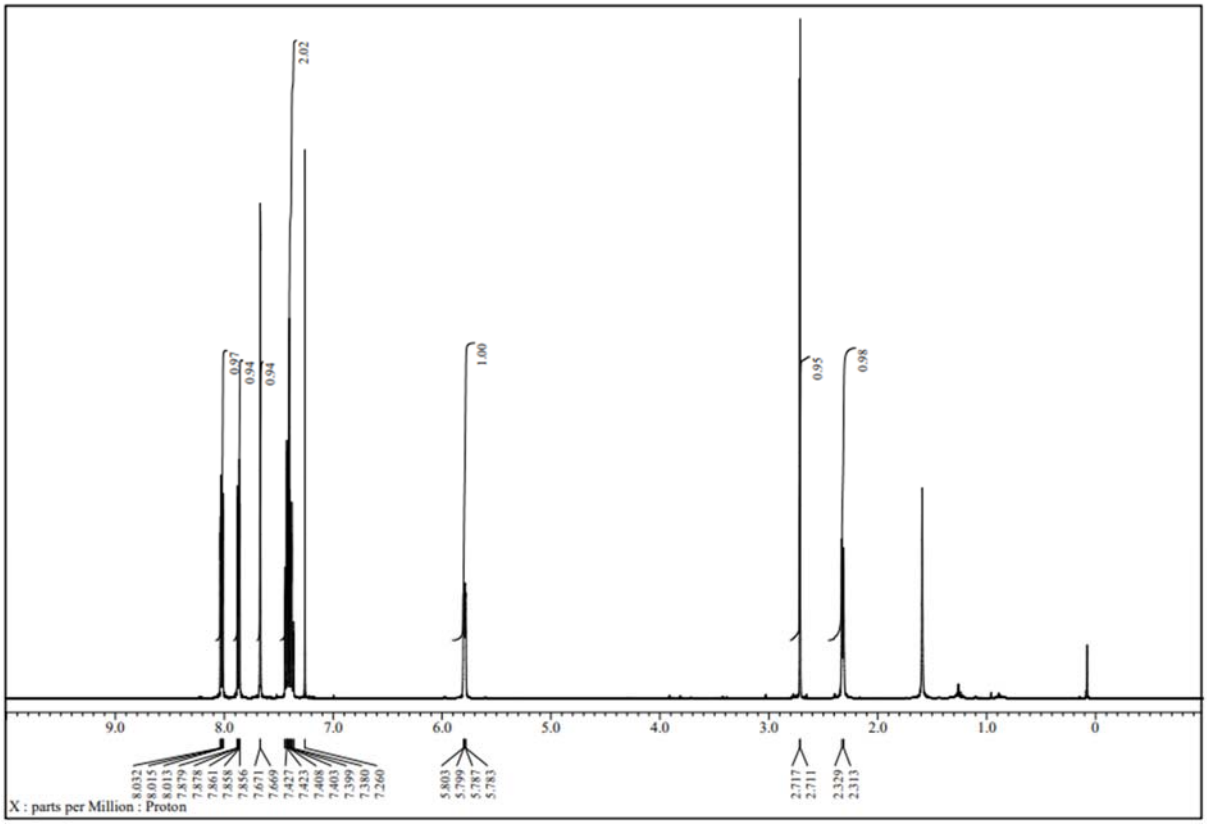



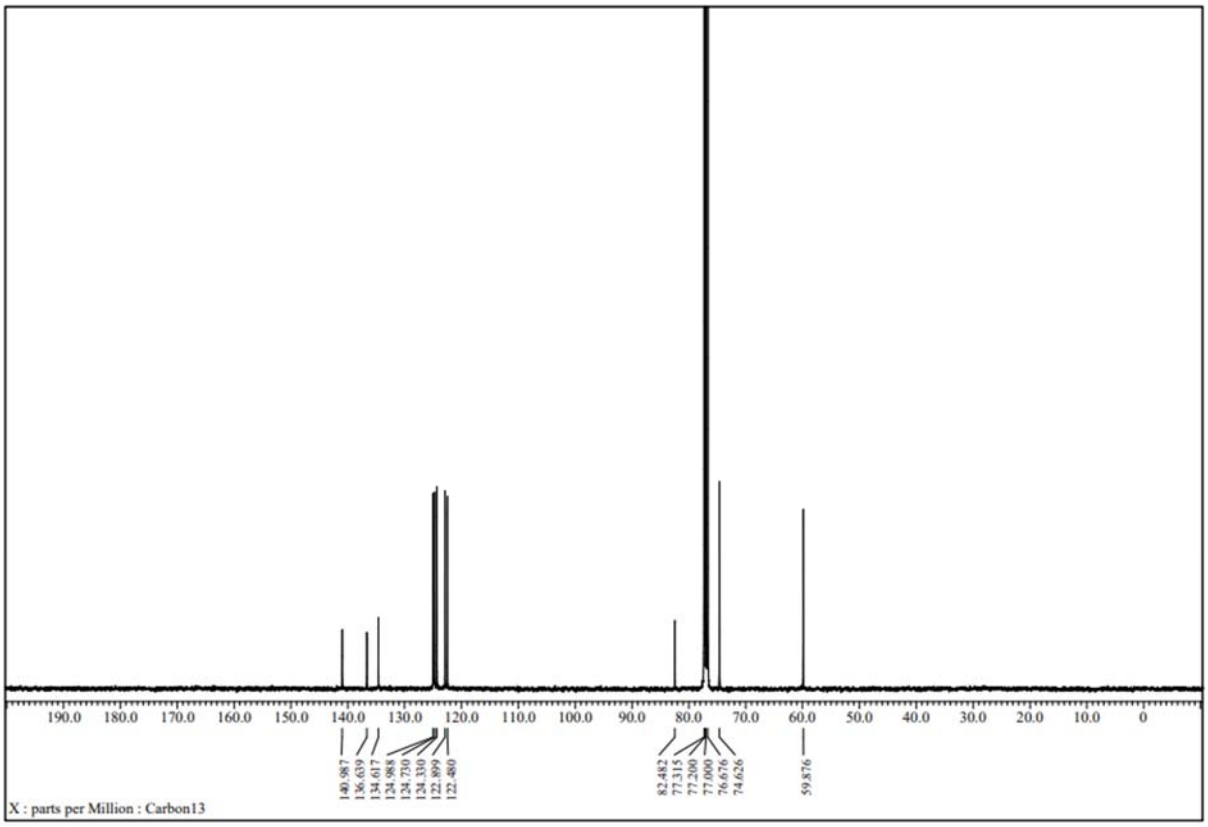
**(*R*)-1-(Thiophen-2-yl)prop-2-yn-1-ol [(*R*)-1b]**



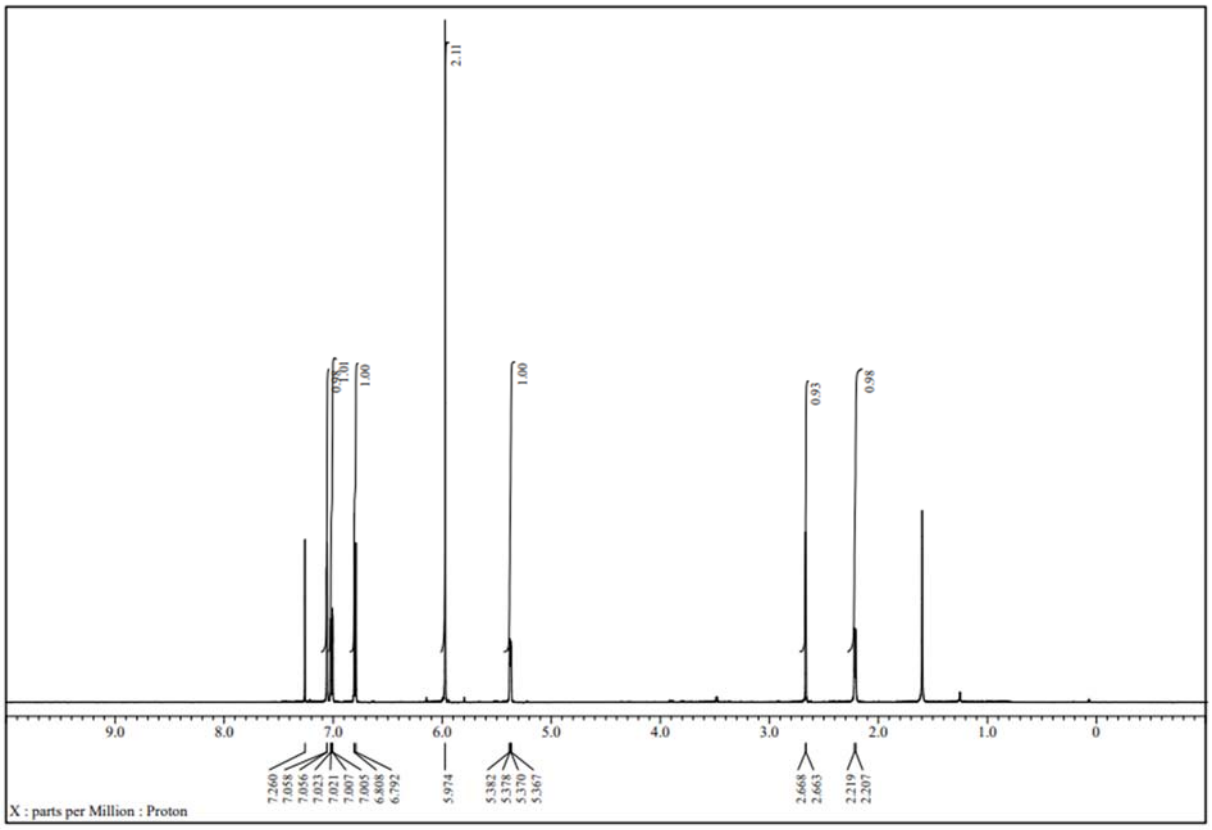



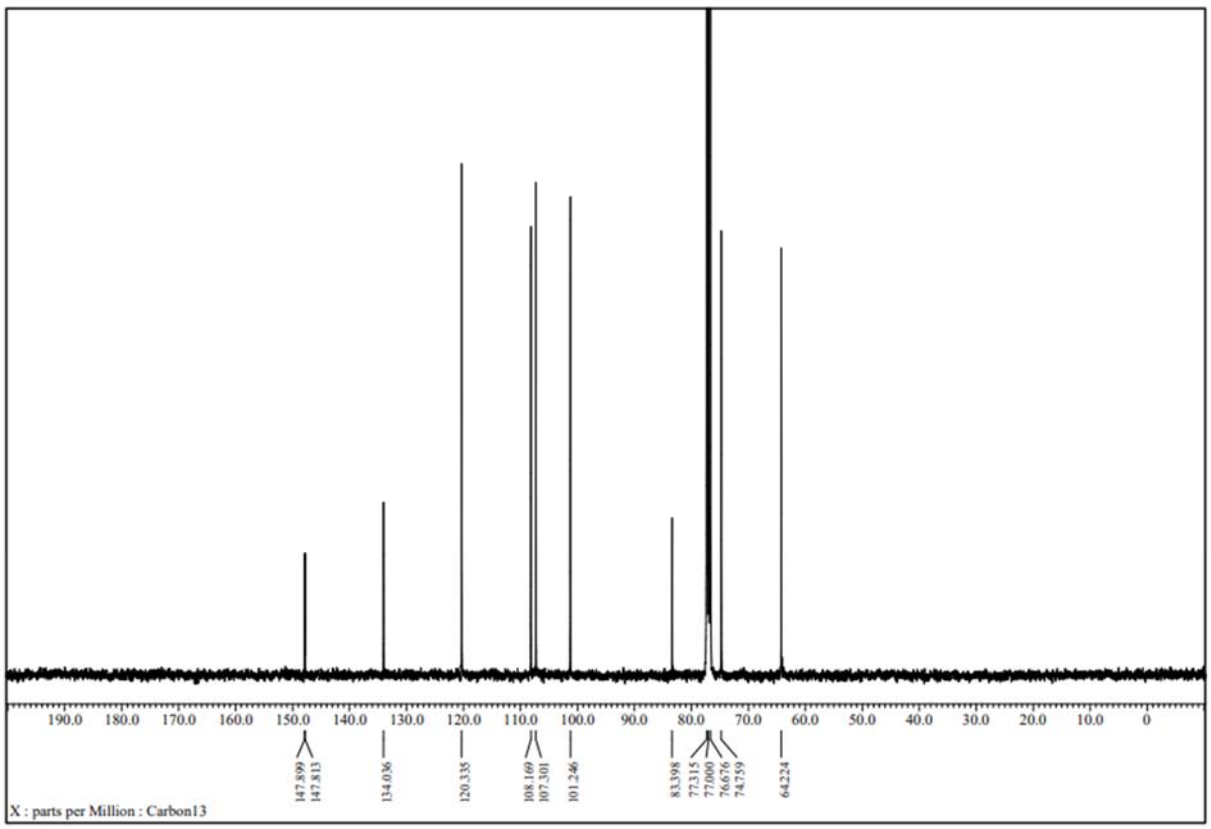
**(*R*)-1-(Benzo[b]thiophen-3-yl)prop-2-yn-1-ol [(*R*)-1c]**



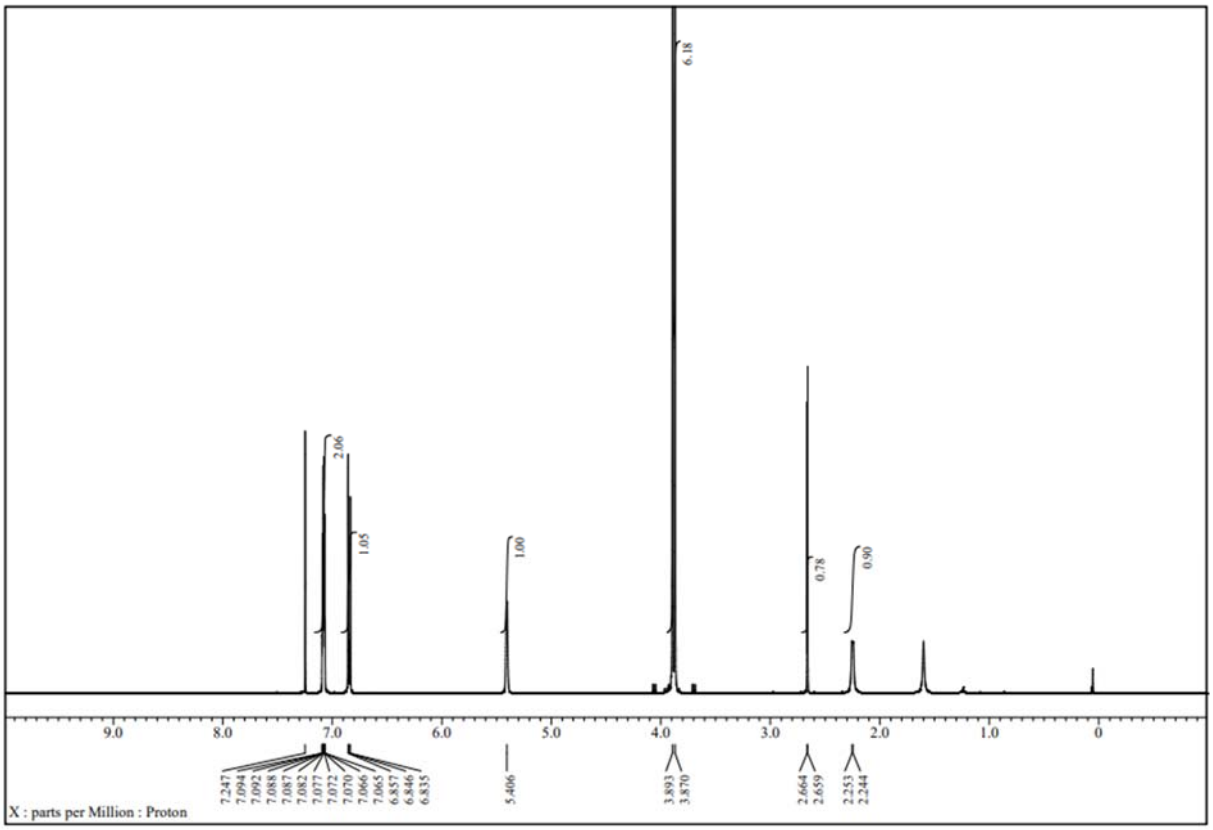



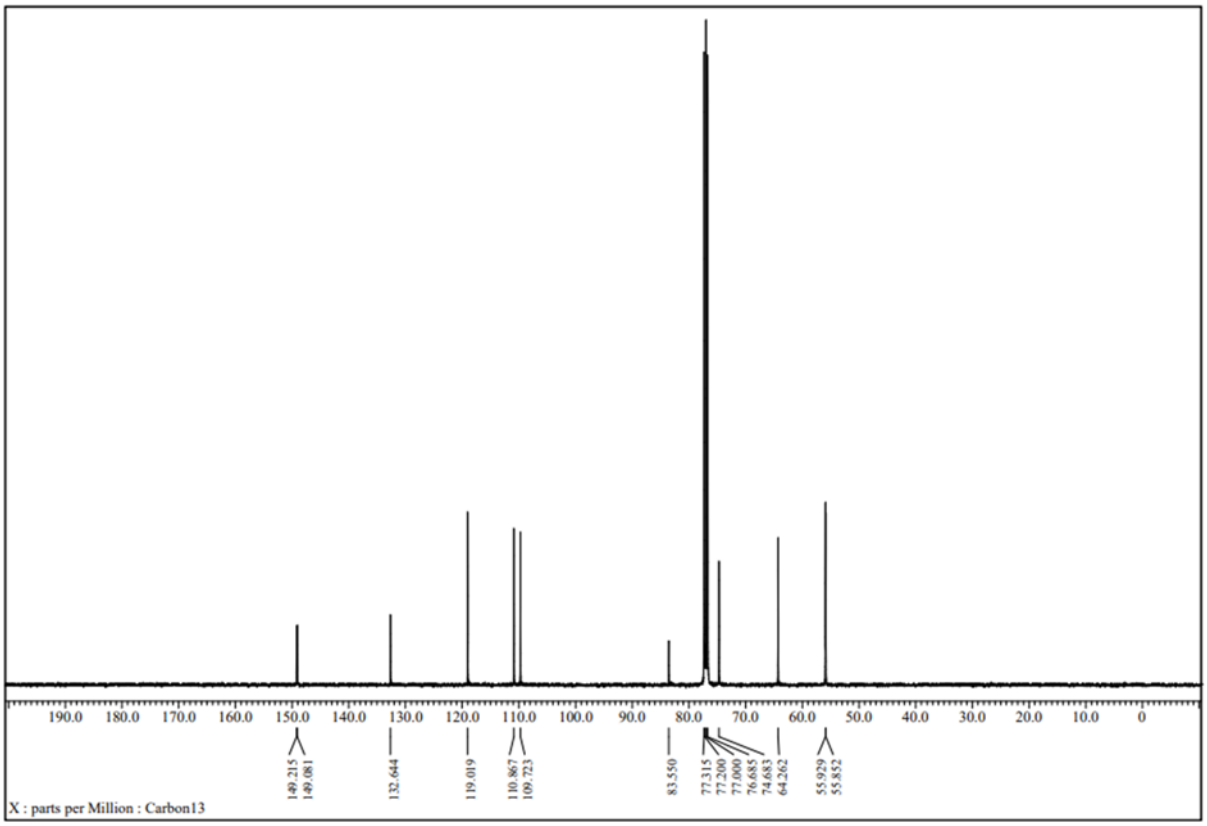
**(*R*)-1-(Benzo[d][1,3]dioxol-5-yl)prop-2-yn-1-ol [(*R*)-1d]**



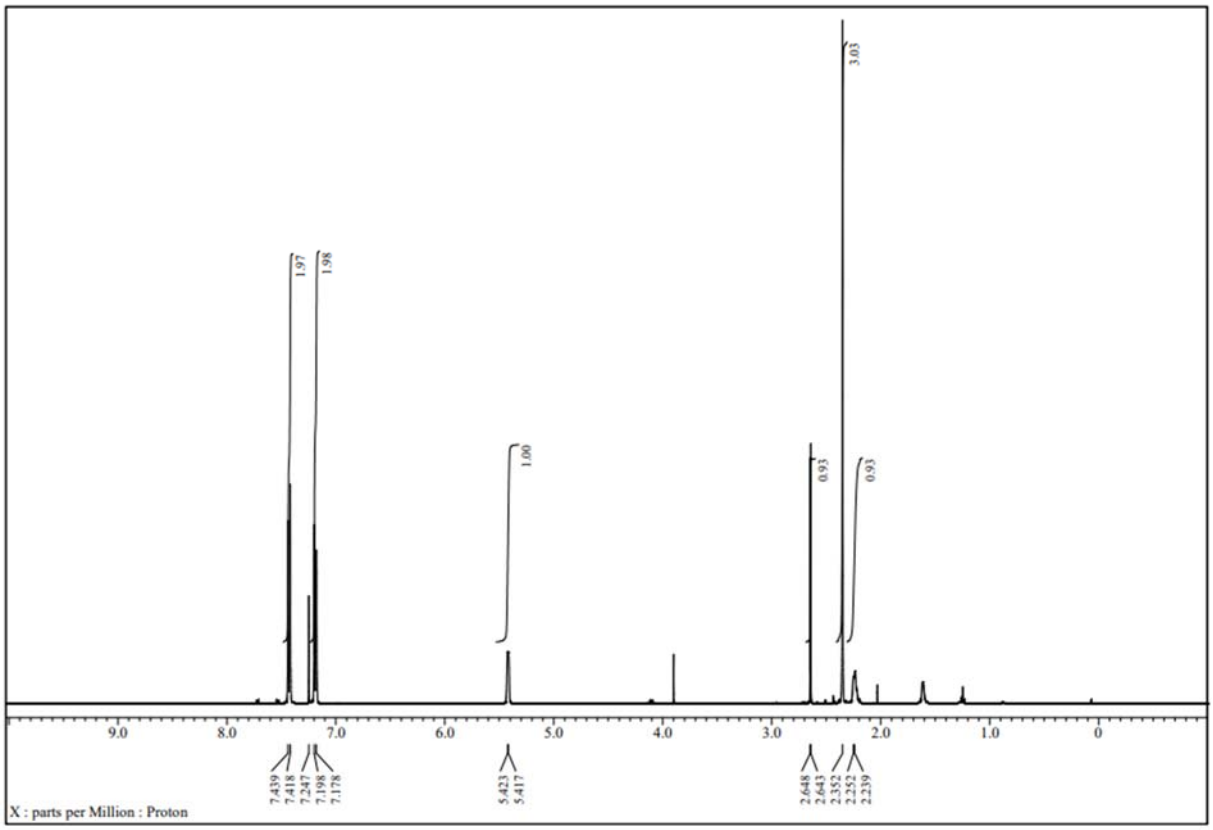



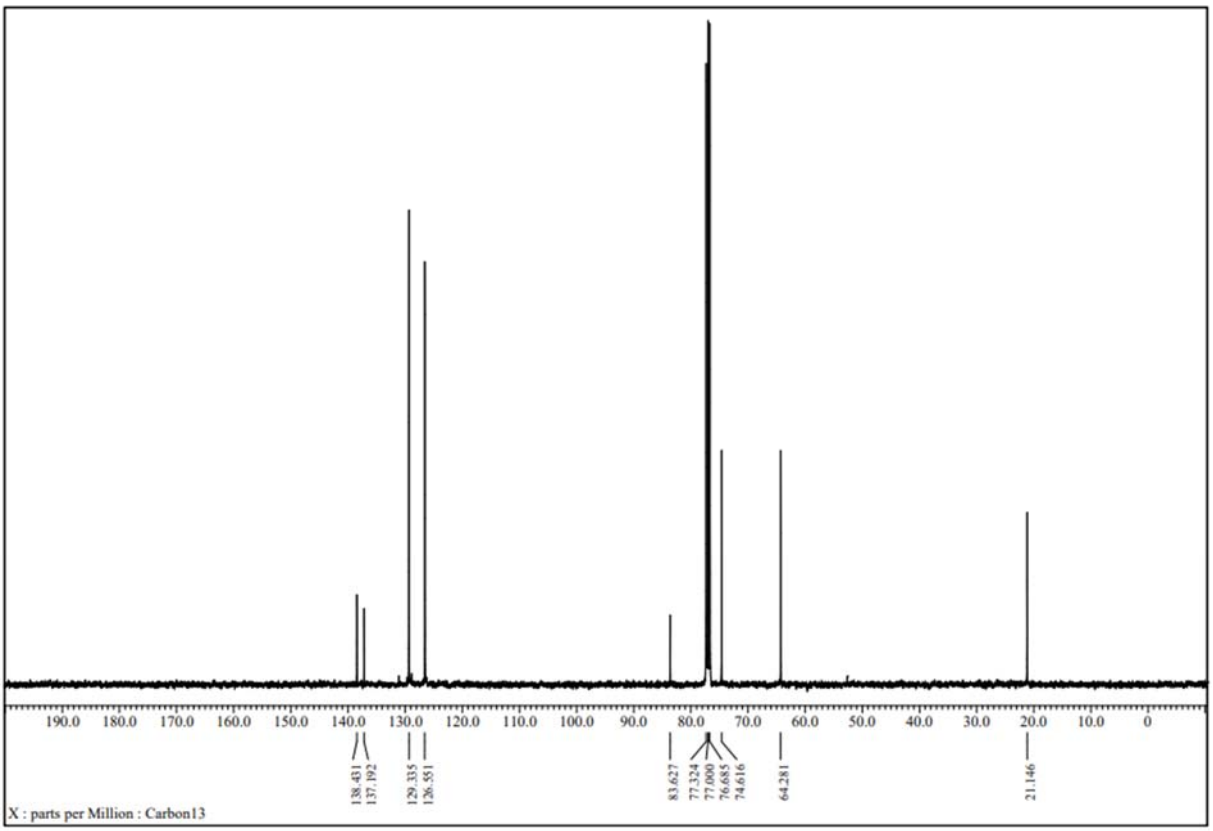
**(*R*)-1-(3,4-Dimethoxyphenyl)prop-2-yn-1-ol [(*R*)-1e]**



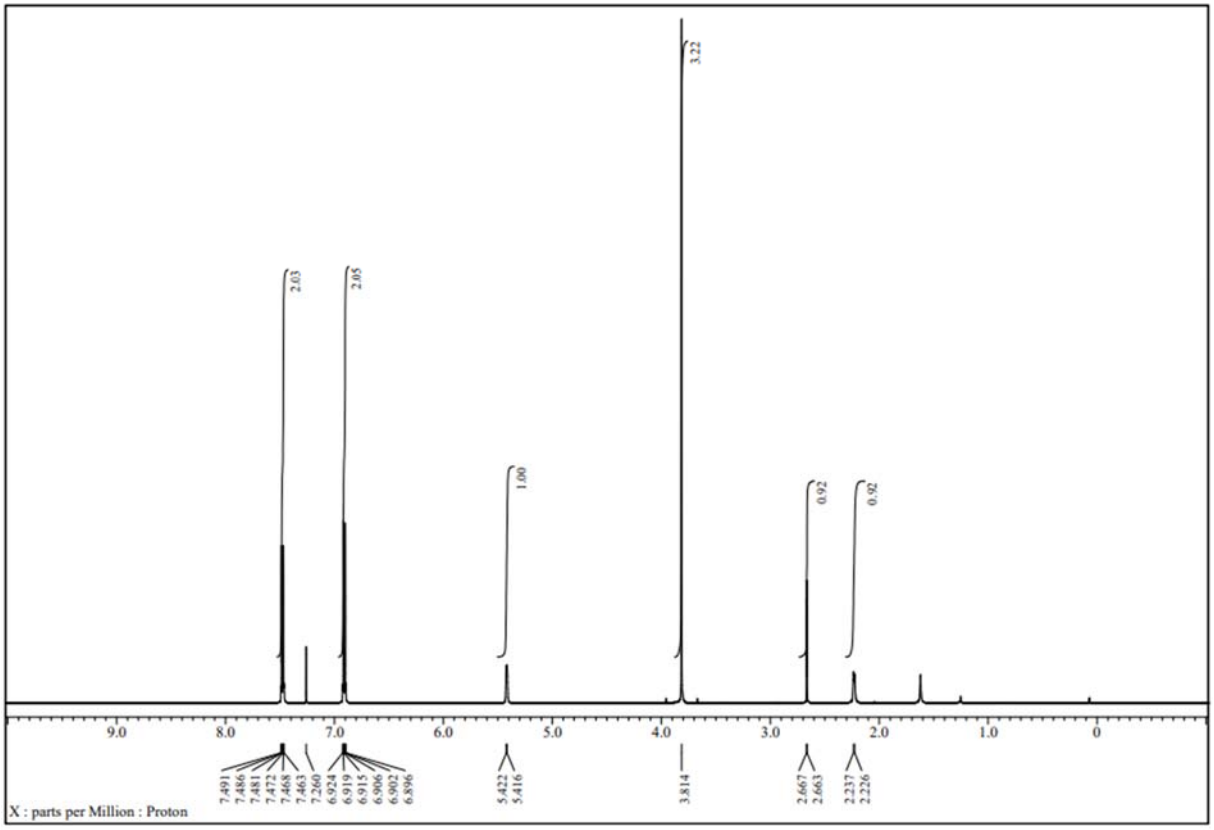



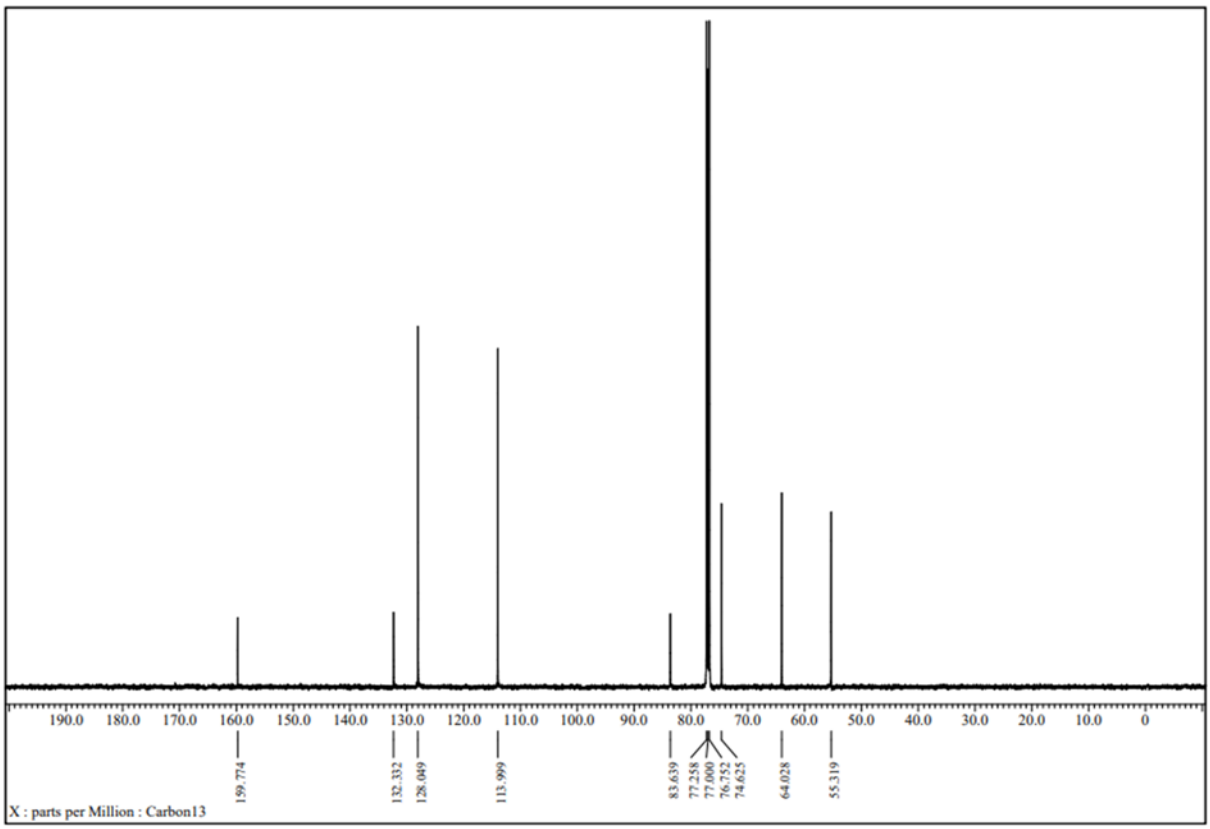
**(*R*)-1-(*p*-Tolyl)prop-2-yn-1-ol [(*R*)-1f]**



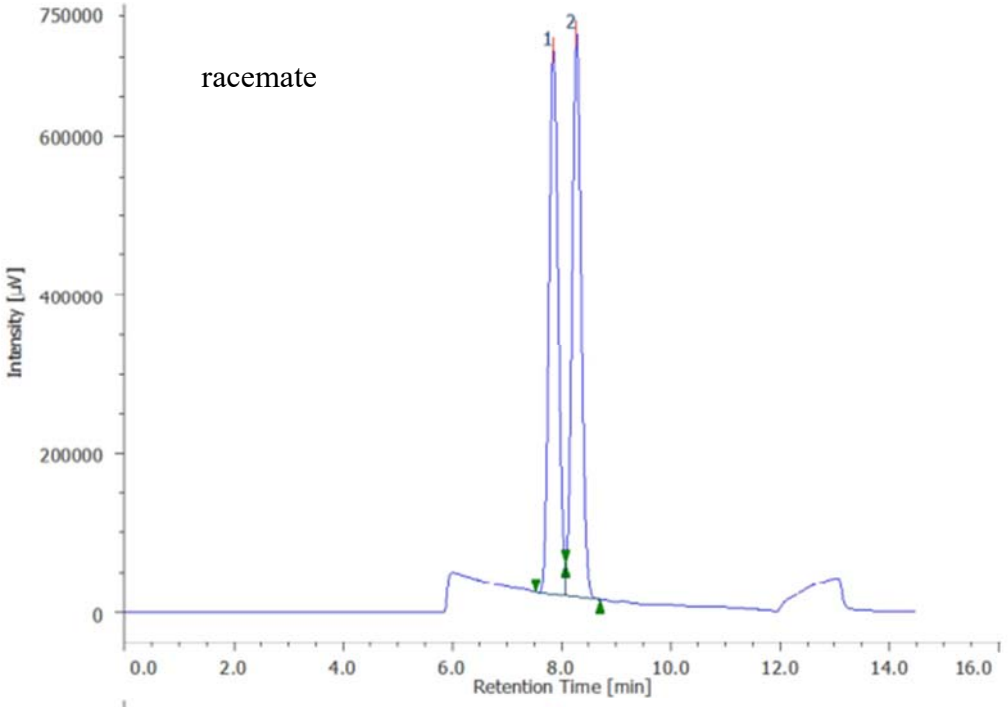
**(*R*)-1-(4-Methoxyphenyl)prop-2-yn-1-ol [(*R*)-1g]**

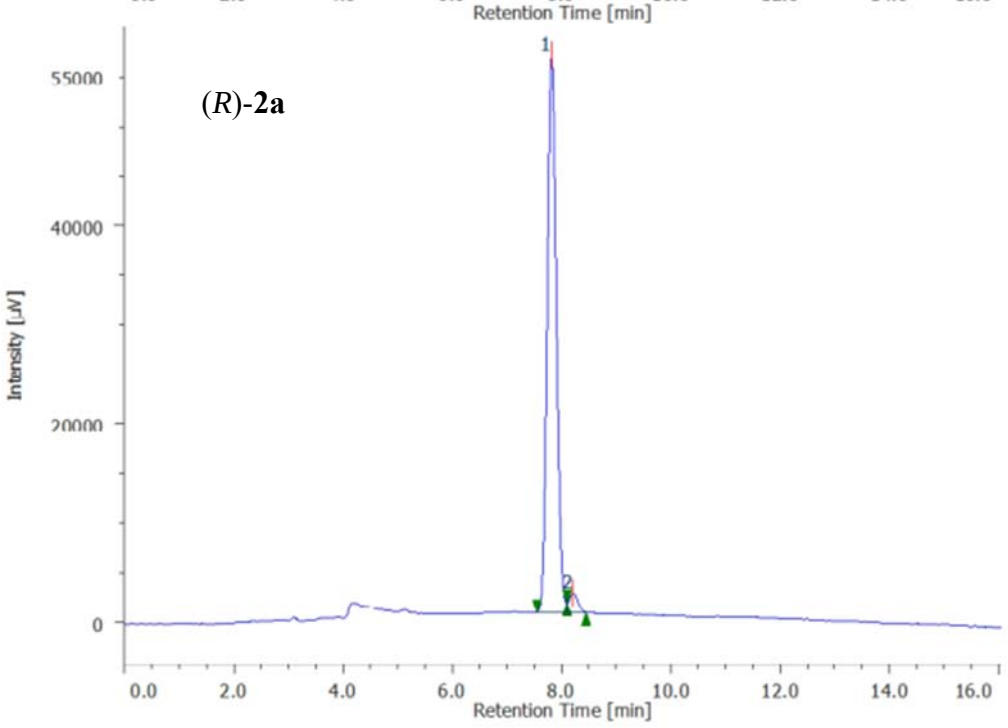


## 8. HPLC data

### (*R*)-1-(Thiophen-3-yl)prop-2-yn-1-yl butyrate [(*R*)-2a]



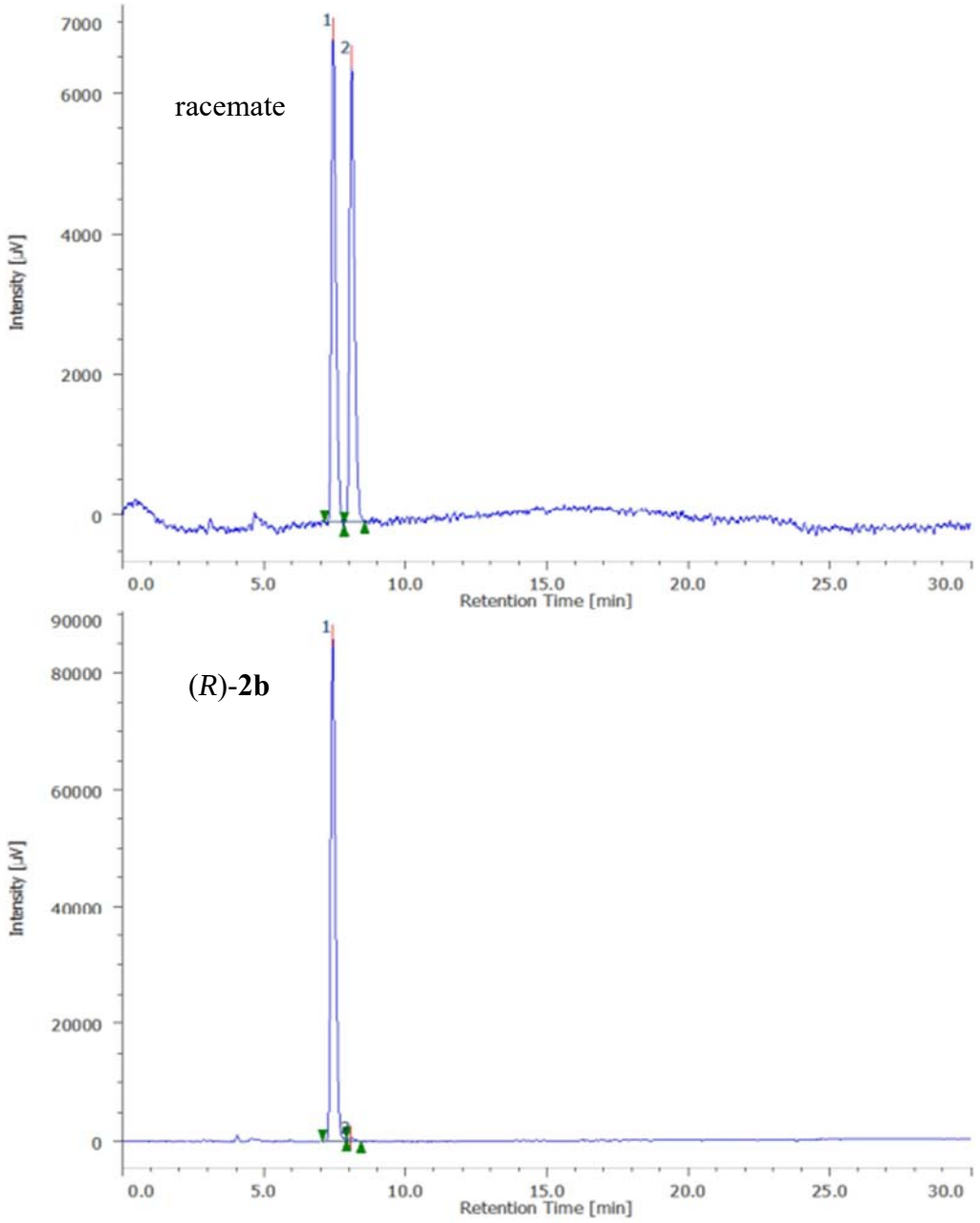

racemate

| # | Peak Name | CH | tR [min] | Area [μV·sec] | Height [μV] | Area% | Height% | Quantity | NTP | Resolution | Symmetry Factor | Warning |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Unknown | 9 | 7.850 | 8178407 | 684801 | 49.816 | 49.143 | N/A | 9705 | 1.360 | N/A | |
| 2 | Unknown | 9 | 8.273 | 8238986 | 708691 | 50.184 | 50.857 | N/A | 11738 | N/A | N/A | |

(*R*)-**2a**

| # | Peak Name | CH | tR [min] | Area [μV·sec] | Height [μV] | Area% | Height% | Quantity | NTP | Resolution | Symmetry Factor | Warning |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Unknown | 9 | 8.290 | 661779 | 45794 | 100.000 | 100.000 | N/A | 7755 | N/A | 1.351 | |

**(*R*)-1-(Thiophen-2-yl)prop-2-yn-1-yl butyrate [(*R*)-2b]**



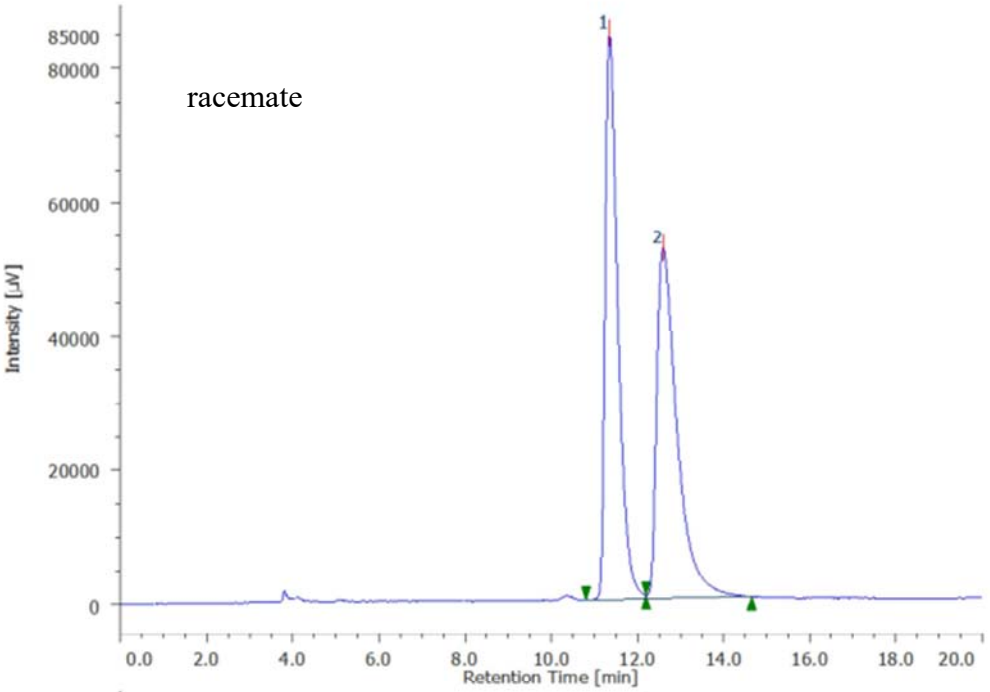

racemate

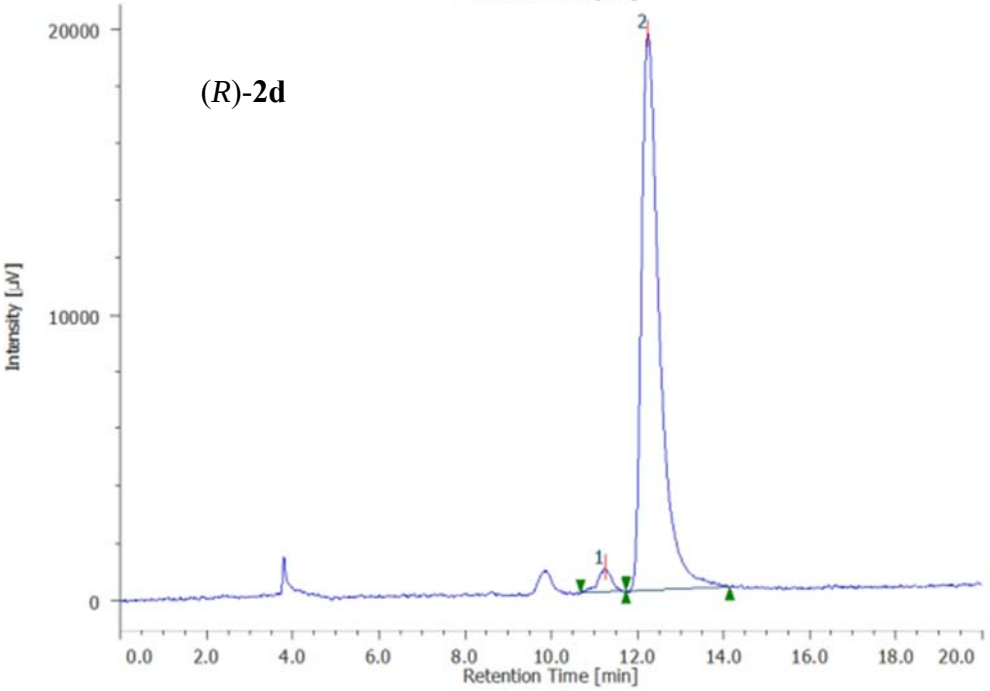
| # | Peak Name | CH | tR [min] | Area [μV·sec] | Height [μV] | Area% | Height% | Quantity | NTP | Resolution | Symmetry Factor | Warning |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Unknown | 6 | 7.440 | 76951 | 6986 | 49.772 | 51.409 | N/A | 10746 | 2.198 | 1.391 | |
| 2 | Unknown | 6 | 8.090 | 77656 | 6603 | 50.228 | 48.591 | N/A | 11180 | N/A | 1.404 | |

(*R*)-**2b**

| # | Peak Name | CH | tR [min] | Area [μV·sec] | Height [μV] | Area% | Height% | Quantity | NTP | Resolution | Symmetry Factor | Warning |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Unknown | 6 | 7.420 | 997991 | 86140 | 99.195 | 99.376 | N/A | 9636 | N/A | 1.325 | |
| 2 | Unknown | 6 | 8.067 | 8104 | 541 | 0.805 | 0.624 | N/A | N/A | N/A | N/A | |

**(*R*)-1-(Benzo[d][1,3]dioxol-5-yl)prop-2-yn-1-yl butyrate [(*R*)-2d]**



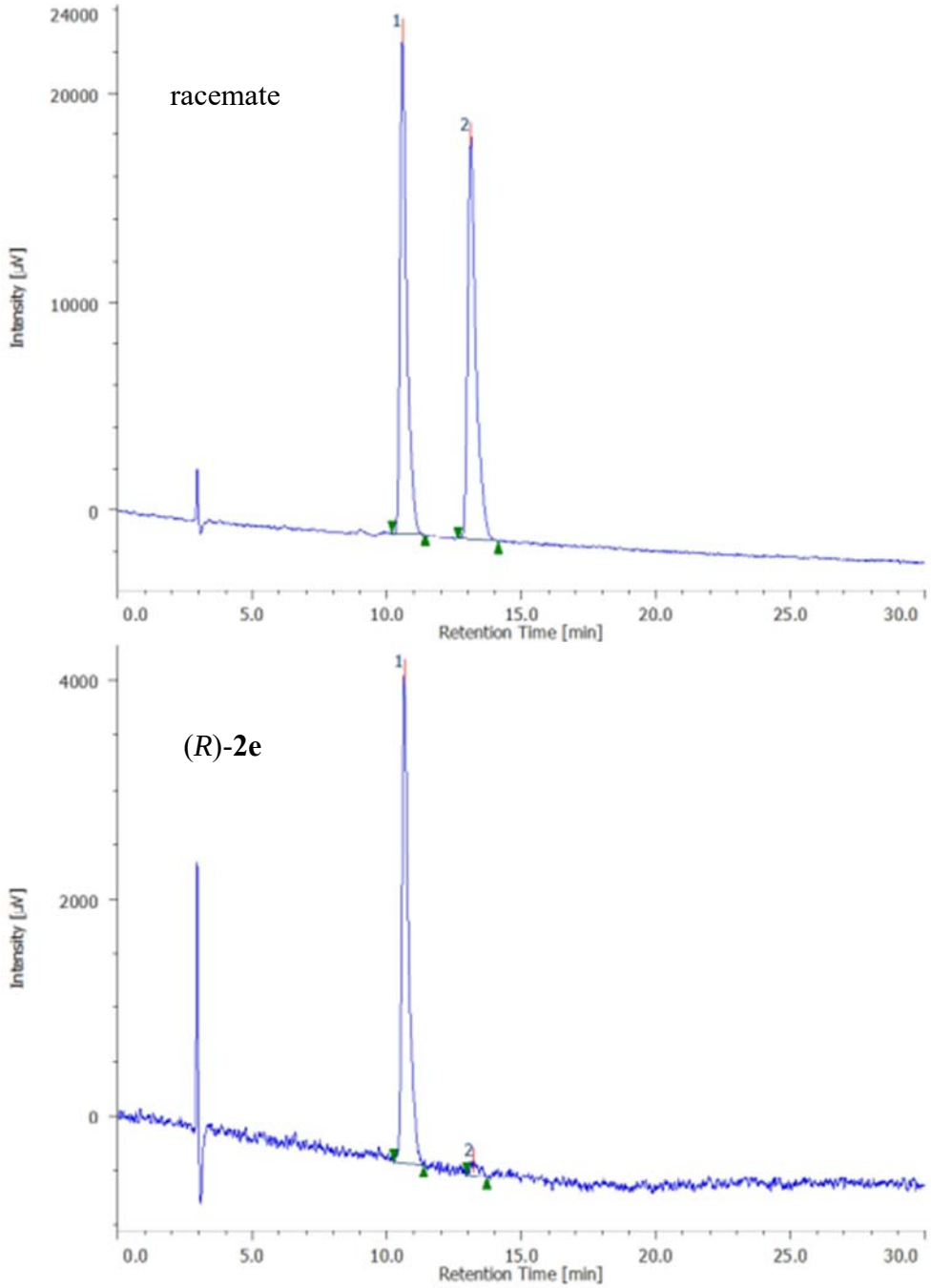

racemate

| # | Peak Name | CH | tR [min] | Area [μV·sec] | Height [μV] | Area% | Height% | Quantity | NTP | Resolution | Symmetry Factor | Warning |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Unknown | 5 | 11.350 | 1731760 | 84406 | 50.276 | 61.771 | N/A | 7476 | 1.879 | 1.809 | |
| 2 | Unknown | 5 | 12.597 | 1712759 | 52237 | 49.724 | 38.229 | N/A | 3910 | N/A | 2.155 | |

(*R*)-**2d**

| # | Peak Name | CH | tR [min] | Area [μV·sec] | Height [μV] | Area% | Height% | Quantity | NTP | Resolution | Symmetry Factor | Warning |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Unknown | 5 | 11.240 | 18643 | 878 | 3.165 | 4.314 | N/A | 7234 | 1.617 | 0.838 | |
| 2 | Unknown | 5 | 12.240 | 570366 | 19483 | 96.835 | 95.686 | N/A | 4736 | N/A | 1.841 | |

**(*R*)-1-(3,4-Dimethoxyphenyl)prop-2-yn-1-yl butyrate [(*R*)-2e]**



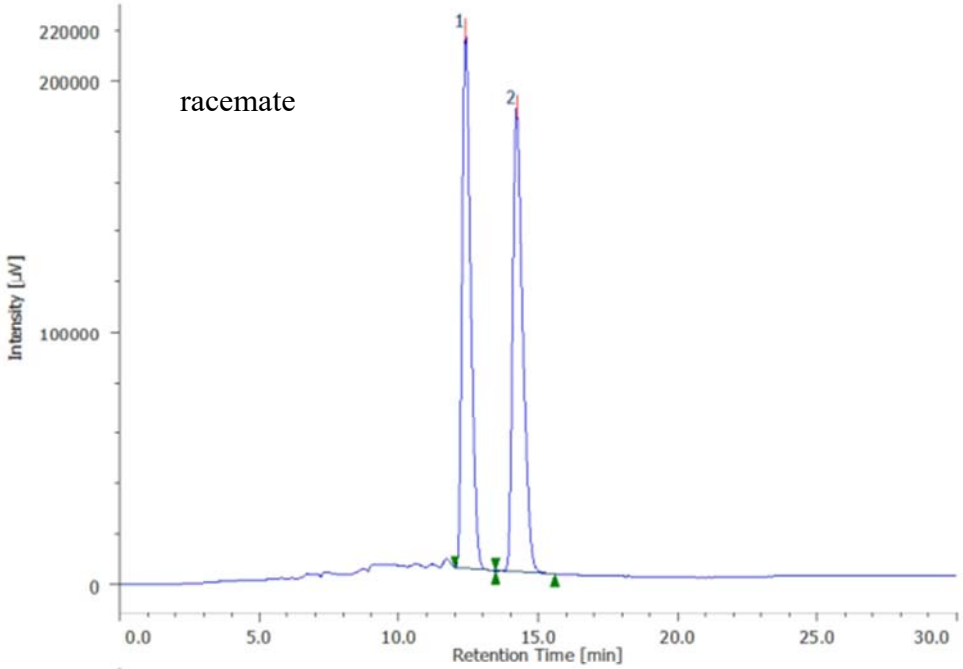

racemate

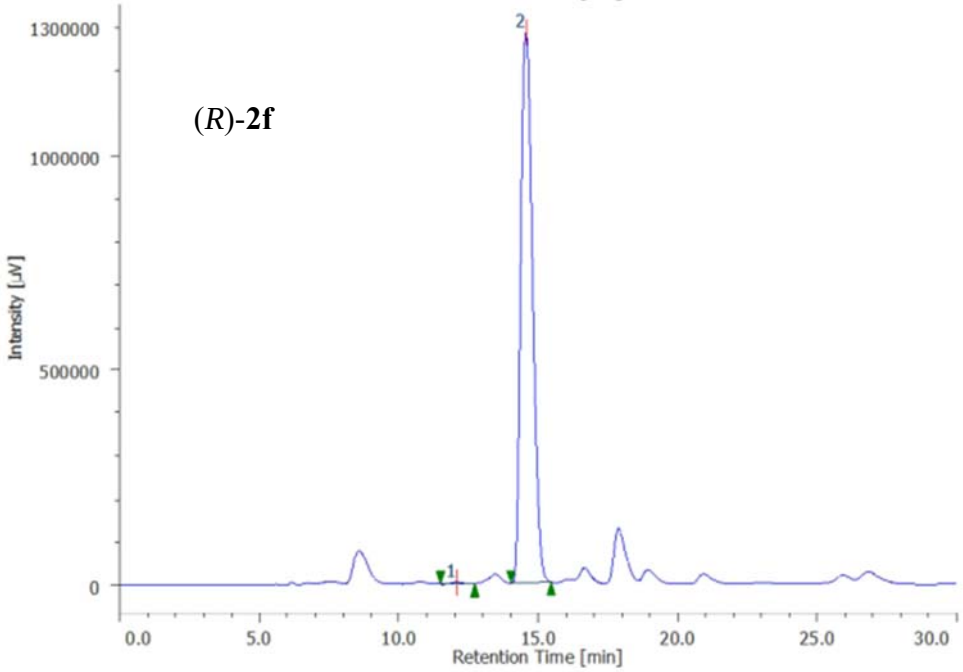
| # | Peak Name | CH | tR [min] | Area [μV·sec] | Height [μV] | Area% | Height% | Quantity | NTP | Resolution | Symmetry Factor | Warning |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Unknown | 5 | 10.577 | 406822 | 24042 | 49.773 | 55.353 | N/A | 11210 | 5.663 | 1.708 | |
| 2 | Unknown | 5 | 13.110 | 410530 | 19392 | 50.227 | 44.647 | N/A | 11113 | N/A | 1.670 | |

(*R*)-**2e**

| # | Peak Name | CH | tR [min] | Area [μV·sec] | Height [μV] | Area% | Height% | Quantity | NTP | Resolution | Symmetry Factor | Warning |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Unknown | 5 | 10.650 | 77007 | 4504 | 96.104 | 96.976 | N/A | 11369 | 4.242 | 1.634 | |
| 2 | Unknown | 5 | 13.233 | 3122 | 140 | 3.896 | 3.024 | N/A | 4151 | N/A | 1.354 | |

**(*R*)-1-(*p*-Tolyl)prop-2-yn-1-yl butyrate [(*R*)-2f]**



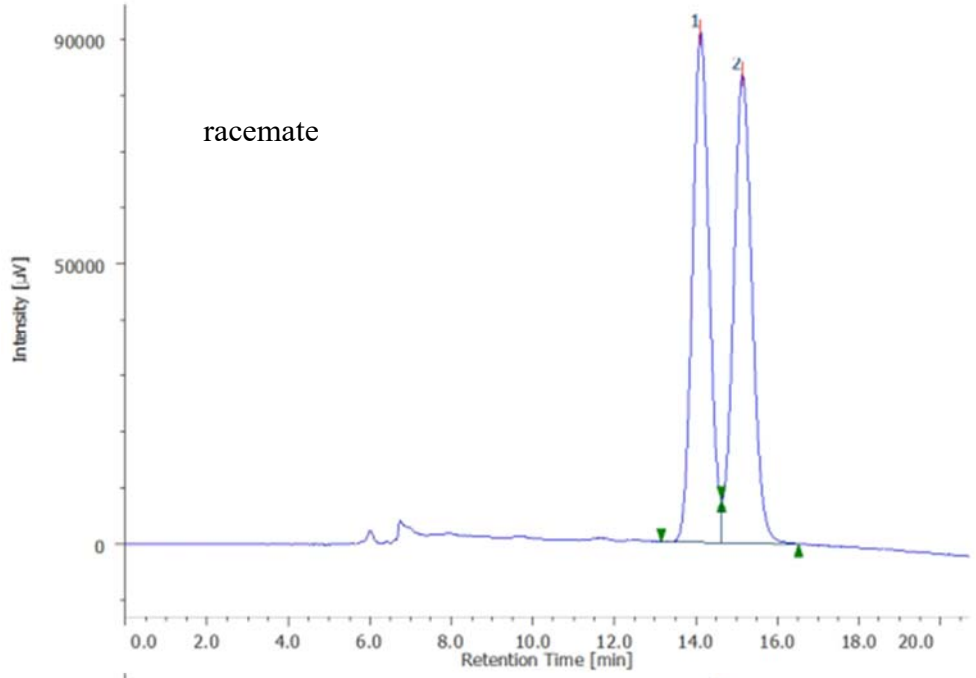

racemate

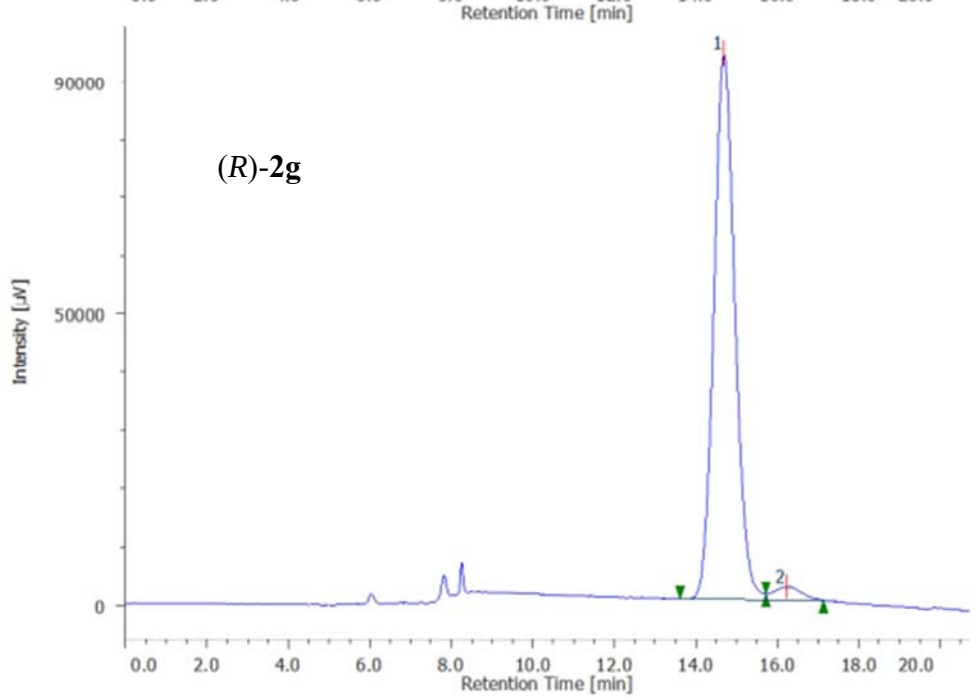
| # | Peak Name | CH | tR [min] | Area [μV·sec] | Height [μV] | Area% | Height% | Quantity | NTP | Resolution | Symmetry Factor | Warning |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Unknown | 6 | 12.390 | 4546746 | 213133 | 49.622 | 53.598 | N/A | 7812 | 3.029 | 1.388 | |
| 2 | Unknown | 6 | 14.220 | 4615989 | 184517 | 50.378 | 46.402 | N/A | 7636 | N/A | 1.457 | |

(*R*)-**2f**

| # | Peak Name | CH | tR [min] | Area [μV·sec] | Height [μV] | Area% | Height% | Quantity | NTP | Resolution | Symmetry Factor | Warning |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Unknown | 6 | 12.073 | 105528 | 4501 | 0.275 | 0.349 | N/A | 5186 | 3.380 | 1.021 | |
| 2 | Unknown | 6 | 14.560 | 38245957 | 1283472 | 99.725 | 99.651 | N/A | 5238 | N/A | 1.262 | |

**(*R*)-1-(4-Methoxyphenyl)prop-2-yn-1-yl butyrate [(*R*)-2g]**



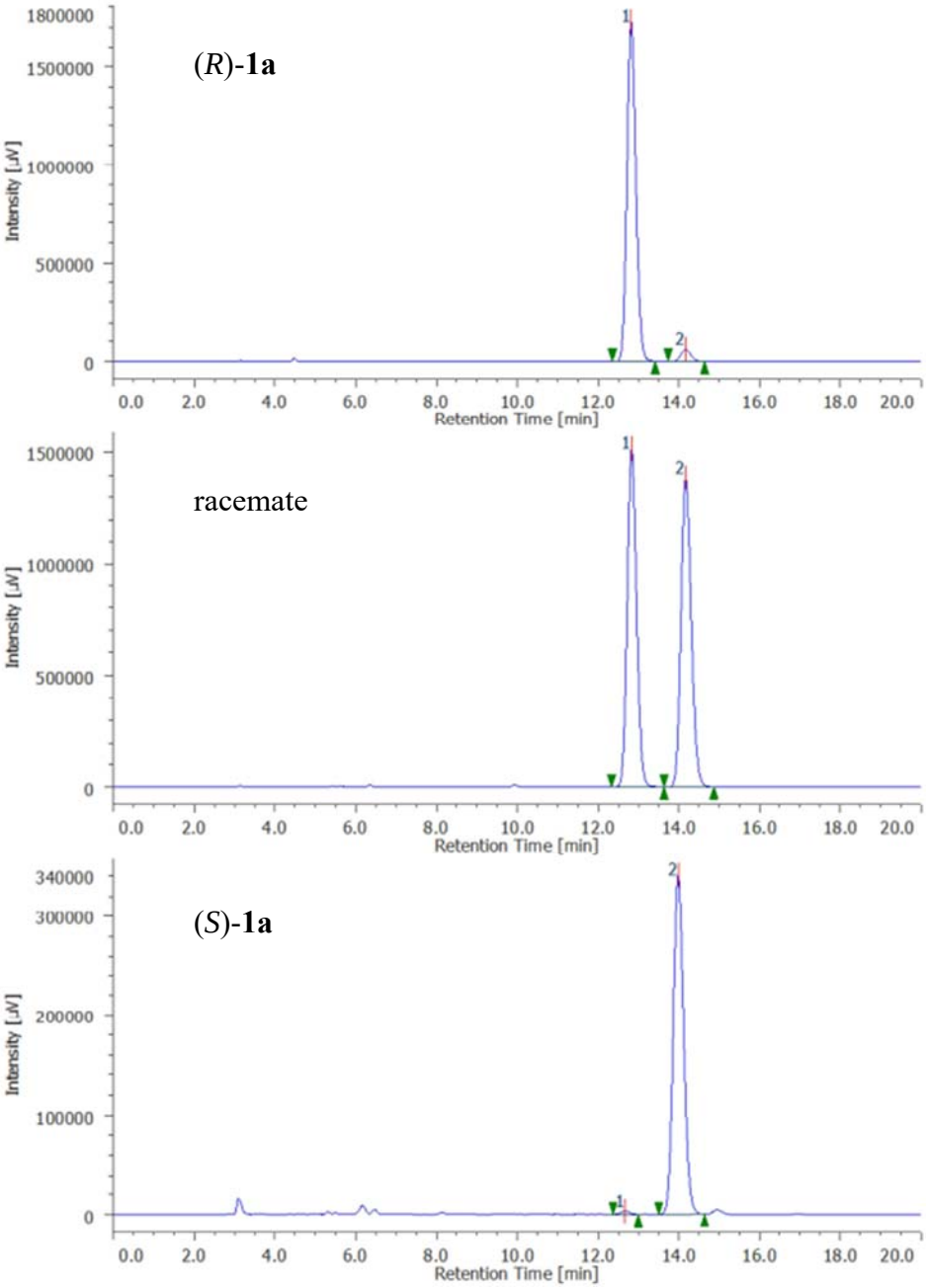

racemate

| # | Peak Name | CH | tR [min] | Area [μV·sec] | Height [μV] | Area% | Height% | Quantity | NTP | Resolution | Symmetry Factor | Warning |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Unknown | 6 | 14.117 | 2570554 | 90959 | 49.252 | 52.176 | N/A | 5777 | 1.318 | N/A | |
| 2 | Unknown | 6 | 15.143 | 2648587 | 83371 | 50.748 | 47.824 | N/A | 5462 | N/A | N/A | |

(*R*)-**2g**

| # | Peak Name | CH | tR [min] | Area [μV·sec] | Height [μV] | Area% | Height% | Quantity | NTP | Resolution | Symmetry Factor | Warning |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Unknown | 6 | 14.687 | 3357346 | 93604 | 96.855 | 97.603 | N/A | 3979 | 1.318 | 1.111 | |
| 2 | Unknown | 6 | 16.217 | 109014 | 2299 | 3.145 | 2.397 | N/A | 2158 | N/A | N/A | |

**1-(Thiophen-3-yl)prop-2-yn-1-ol [1a]**




(*R*)-**1a**

| # | Peak Name | CH | tR [min] | Area [μV·sec] | Height [μV] | Area% | Height% | Quantity | NTP | Resolution | Symmetry Factor | Warning |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Unknown | 6 | 12.817 | 26645426 | 1724202 | 96.374 | 96.694 | N/A | 15959 | 3.171 | 1.124 | |
| 2 | Unknown | 6 | 14.170 | 1002651 | 58954 | 3.626 | 3.306 | N/A | 15854 | N/A | 1.065 | |

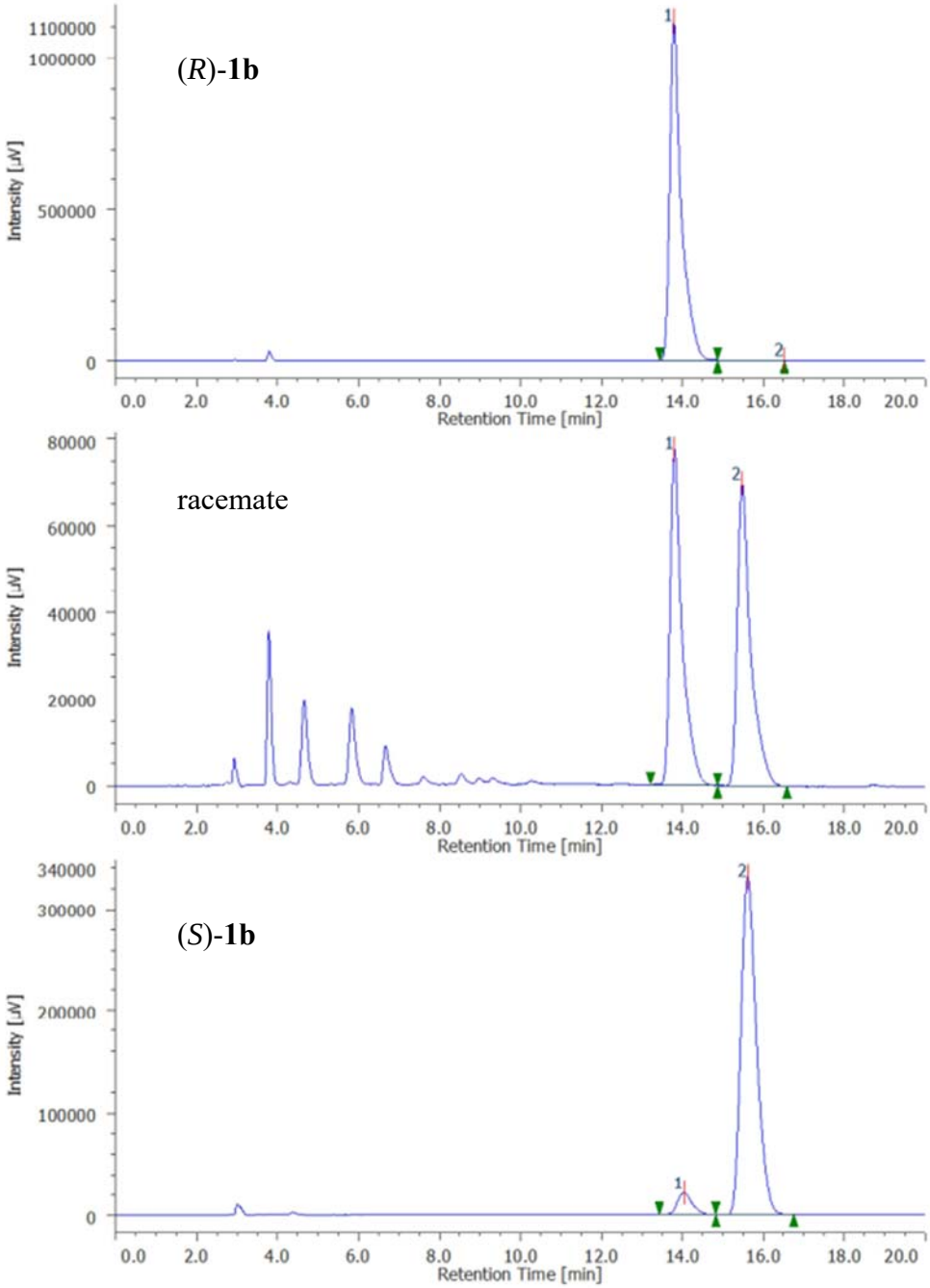
racemate

| # | Peak Name | CH | tR [min] | Area [μV·sec] | Height [μV] | Area% | Height% | Quantity | NTP | Resolution | Symmetry Factor | Warning |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Unknown | 6 | 12.827 | 24348785 | 1512702 | 49.908 | 52.204 | N/A | 14705 | 3.027 | 1.128 | |
| 2 | Unknown | 6 | 14.167 | 24438329 | 1384993 | 50.092 | 47.796 | N/A | 14880 | N/A | 1.165 | |

(*S*)-**1a**

| # | Peak Name | CH | tR [min] | Area [μV·sec] | Height [μV] | Area% | Height% | Quantity | NTP | Resolution | Symmetry Factor | Warning |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Unknown | 6 | 12.663 | 49537 | 3182 | 0.804 | 0.929 | N/A | 14458 | 2.962 | 1.076 | |
| 2 | Unknown | 6 | 13.983 | 6109798 | 339476 | 99.196 | 99.071 | N/A | 14011 | N/A | 1.101 | |

**1-(Thiophen-2-yl)prop-2-yn-1-ol [1b]**




(*R*)-**1b**

| # | Peak Name | CH | tR [min] | Area [μV·sec] | Height [μV] | Area% | Height% | Quantity | NTP | Resolution | Symmetry Factor | Warning |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Unknown | 6 | 13.787 | 22380922 | 1116438 | 100.000 | 99.998 | N/A | 14526 | 7.031 | 1.804 | |
| 2 | Unknown | 6 | 16.510 | −77 | 19 | N/A | 0.002 | N/A | 42809 | N/A | 0.525 | |

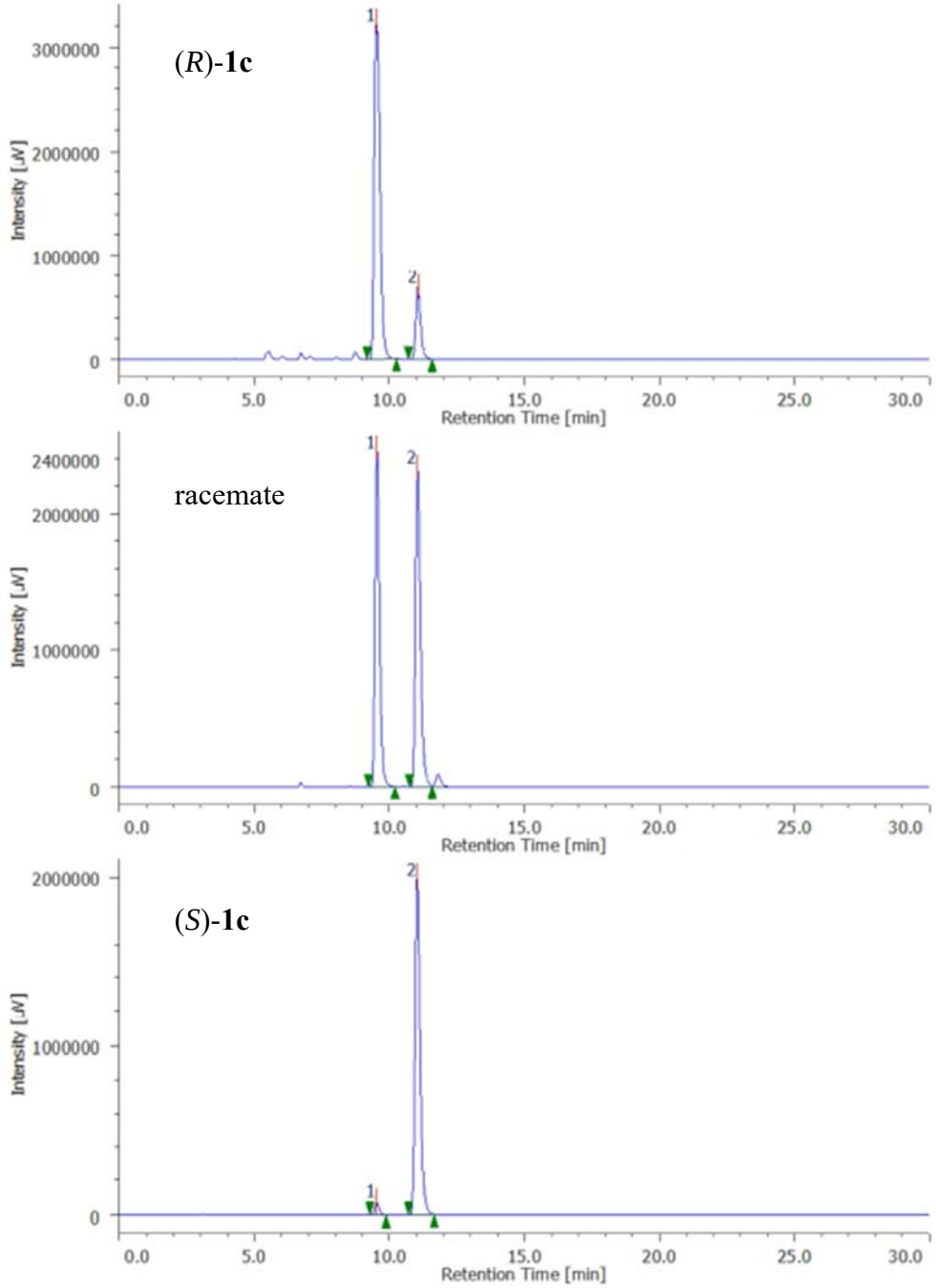
racemate

| # | Peak Name | CH | tR [min] | Area [μV·sec] | Height [μV] | Area% | Height% | Quantity | NTP | Resolution | Symmetry Factor | Warning |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Unknown | 6 | 13.803 | 1607626 | 77349 | 50.052 | 52.596 | N/A | 13131 | 3.306 | 1.742 | |
| 2 | Unknown | 6 | 15.477 | 1604287 | 69712 | 49.948 | 47.404 | N/A | 13477 | N/A | 1.767 | |

(*S*)-**1b**

| # | Peak Name | CH | tR [min] | Area [μV·sec] | Height [μV] | Area% | Height% | Quantity | NTP | Resolution | Symmetry Factor | Warning |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Unknown | 6 | 14.033 | 525225 | 21233 | 5.654 | 6.049 | N/A | 7624 | 2.373 | 1.235 | |
| 2 | Unknown | 6 | 15.613 | 8763657 | 329768 | 94.346 | 93.951 | N/A | 8133 | N/A | 1.298 | |

**1-(Benzo[b]thiophen-3-yl)prop-2-yn-1-ol [1c]**




(*R*)-**1c**

| # | Peak Name | CH | tR [min] | Area [μV·sec] | Height [μV] | Area% | Height% | Quantity | NTP | Resolution | Symmetry Factor | Warning |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Unknown | 5 | 9.537 | 1772202 | 164729 | 99.046 | 99.178 | N/A | 19843 | 5.385 | 1.325 | |
| 2 | Unknown | 5 | 11.087 | 17073 | 1366 | 0.954 | 0.822 | N/A | 20949 | N/A | 1.140 | |

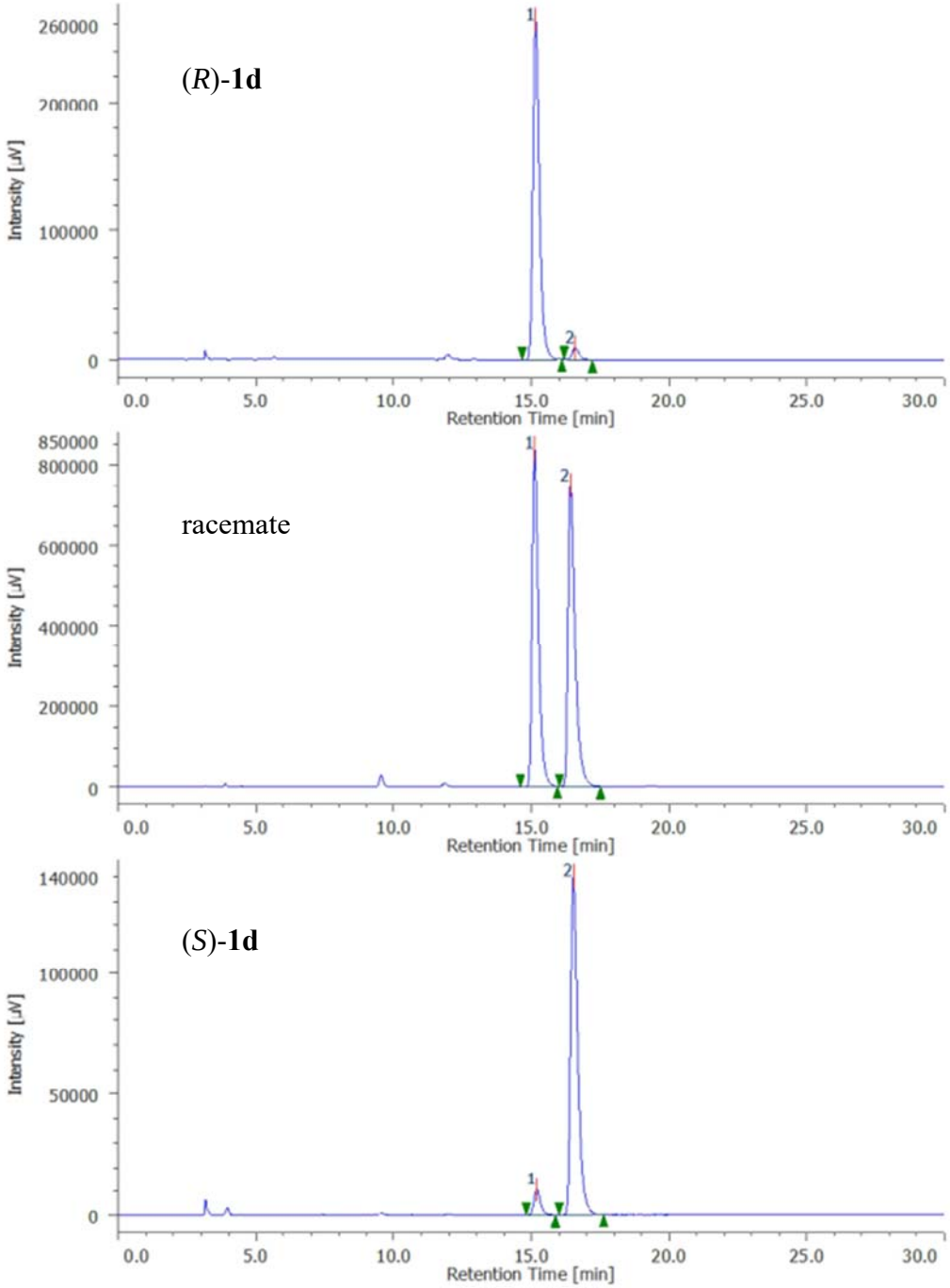
racemate

| # | Peak Name | CH | tR [min] | Area [μV·sec] | Height [μV] | Area% | Height% | Quantity | NTP | Resolution | Symmetry Factor | Warning |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Unknown | 5 | 9.530 | 8269471 | 779048 | 49.899 | 53.106 | N/A | 20917 | 5.349 | 1.365 | |
| 2 | Unknown | 5 | 11.037 | 8303029 | 687911 | 50.101 | 46.894 | N/A | 21479 | N/A | 1.395 | |

(*S*)-**1c**

| # | Peak Name | CH | tR [min] | Area [μV·sec] | Height [μV] | Area% | Height% | Quantity | NTP | Resolution | Symmetry Factor | Warning |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Unknown | 5 | 9.527 | 174527 | 15584 | 2.694 | 2.985 | N/A | 17766 | 5.010 | 1.257 | |
| 2 | Unknown | 5 | 11.027 | 6305018 | 506587 | 97.306 | 97.015 | N/A | 19671 | N/A | 1.327 | |

**1-(Benzo[d][1,3]dioxol-5-yl)prop-2-yn-1-ol [1d]**




(*R*)-**1d**

| # | Peak Name | CH | tR [min] | Area [μV·sec] | Height [μV] | Area% | Height% | Quantity | NTP | Resolution | Symmetry Factor | Warning |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Unknown | 6 | 15.157 | 4345961 | 263006 | 96.563 | 96.739 | N/A | 21136 | 3.316 | 1.387 | |
| 2 | Unknown | 6 | 16.593 | 154705 | 8865 | 3.437 | 3.261 | N/A | 21587 | N/A | 1.291 | |

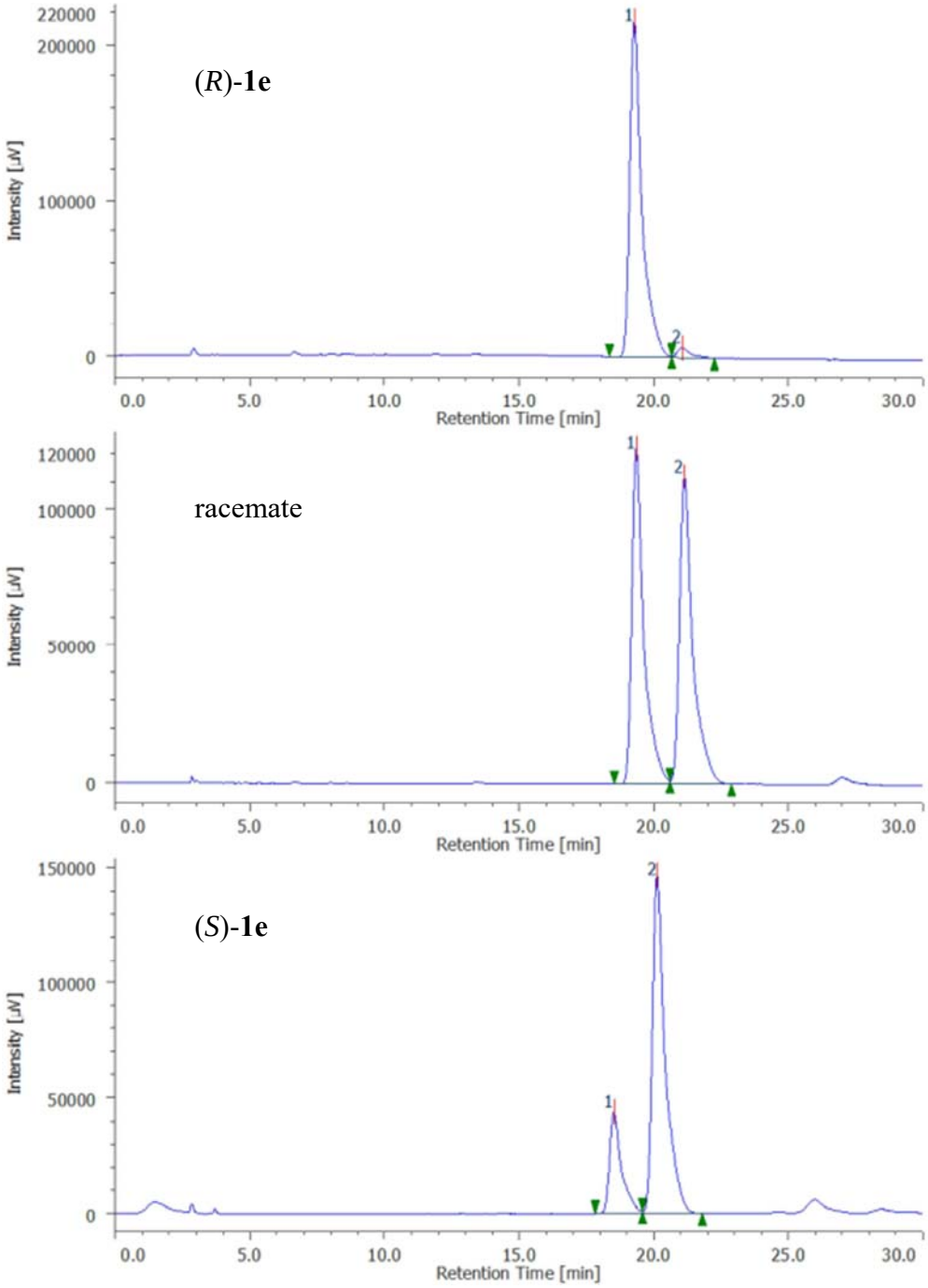
racemate

| # | Peak Name | CH | tR [min] | Area [μV·sec] | Height [μV] | Area% | Height% | Quantity | NTP | Resolution | Symmetry Factor | Warning |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Unknown | 6 | 15.120 | 13328290 | 836979 | 49.894 | 52.811 | N/A | 22893 | 3.097 | 1.503 | |
| 2 | Unknown | 6 | 16.420 | 13384902 | 747891 | 50.106 | 47.189 | N/A | 22076 | N/A | 1.774 | |

(*S*)-**1d**

| # | Peak Name | CH | tR [min] | Area [μV·sec] | Height [μV] | Area% | Height% | Quantity | NTP | Resolution | Symmetry Factor | Warning |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Unknown | 6 | 15.200 | 176671 | 10751 | 6.517 | 7.141 | N/A | 21465 | 3.051 | 1.276 | |
| 2 | Unknown | 6 | 16.523 | 2534182 | 139796 | 93.483 | 92.859 | N/A | 21115 | N/A | 1.548 | |

**1-(3,4-Dimethoxyphenyl)prop-2-yn-1-ol [1e]**




(*R*)-**1e**

| # | Peak Name | CH | tR [min] | Area [μV·sec] | Height [μV] | Area% | Height% | Quantity | NTP | Resolution | Symmetry Factor | Warning |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Unknown | 6 | 19.280 | 6861843 | 215277 | 97.133 | 97.262 | N/A | 11146 | 2.342 | 1.772 | |
| 2 | Unknown | 6 | 21.050 | 202560 | 6061 | 2.867 | 2.738 | N/A | 11498 | N/A | N/A | |

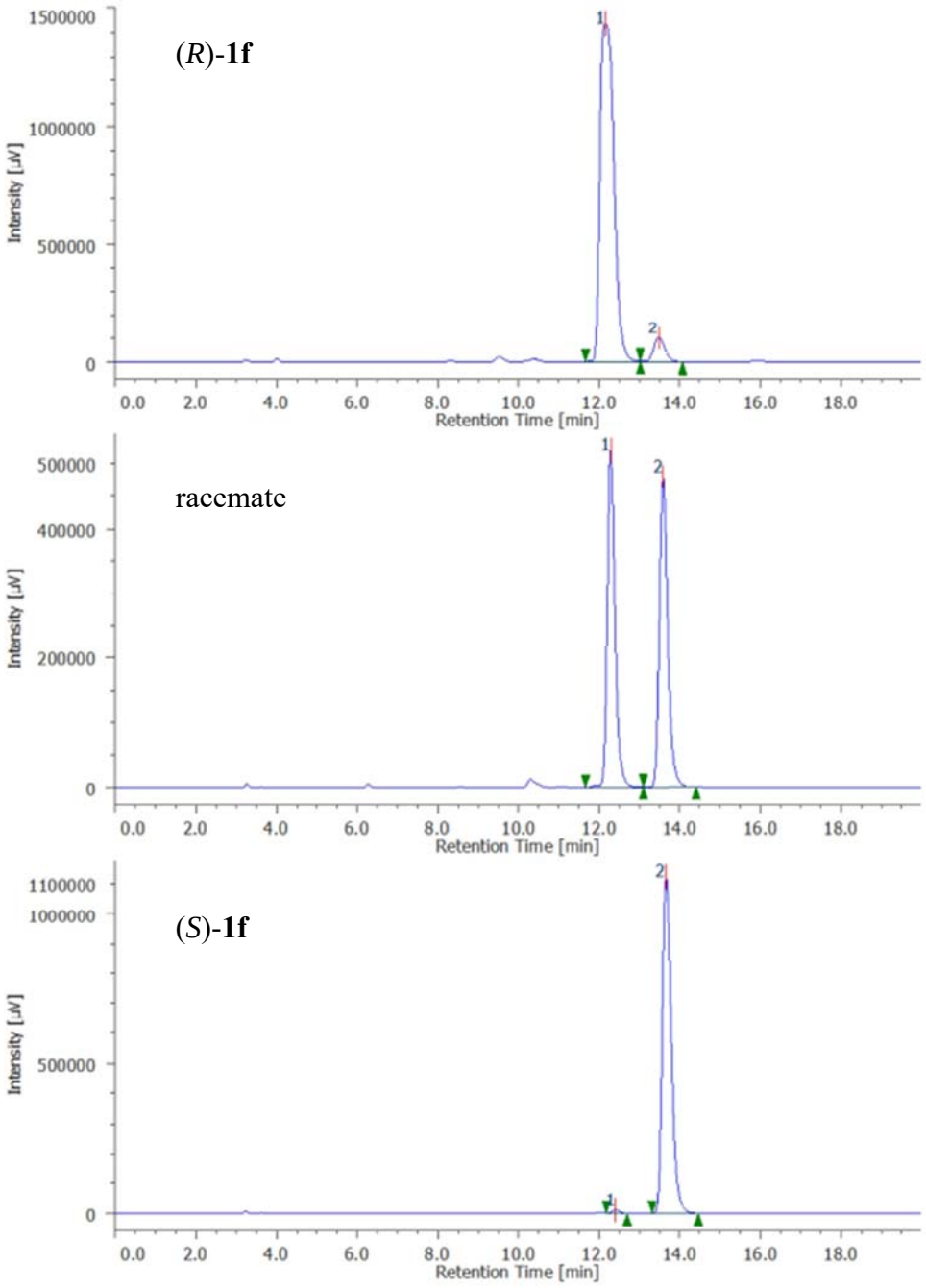
racemate

| # | Peak Name | CH | tR [min] | Area [μV·sec] | Height [μV] | Area% | Height% | Quantity | NTP | Resolution | Symmetry Factor | Warning |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Unknown | 6 | 19.350 | 3834021 | 121966 | 49.856 | 52.106 | N/A | 11634 | 2.394 | 1.809 | |
| 2 | Unknown | 6 | 21.143 | 3856148 | 112108 | 50.144 | 47.894 | N/A | 11618 | N/A | 1.759 | |

(*S*)-**1e**

| # | Peak Name | CH | tR [min] | Area [μV·sec] | Height [μV] | Area% | Height% | Quantity | NTP | Resolution | Symmetry Factor | Warning |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Unknown | 6 | 18.520 | 1355291 | 43981 | 21.942 | 23.069 | N/A | 10975 | 2.207 | 1.746 | |
| 2 | Unknown | 6 | 20.127 | 4821376 | 146672 | 78.058 | 76.931 | N/A | 11430 | N/A | 1.741 | |

**1-(*p*-Tolyl)prop-2-yn-1-ol [1f]**




(*R*)-**1f**

| # | Peak Name | CH | tR [min] | Area [μV·sec] | Height [μV] | Area% | Height% | Quantity | NTP | Resolution | Symmetry Factor | Warning |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Unknown | 6 | 12.157 | 34464606 | 1431468 | 94.677 | 93.475 | N/A | 5658 | 2.306 | 1.418 | |
| 2 | Unknown | 6 | 13.480 | 1937702 | 99923 | 5.323 | 6.525 | N/A | 11438 | N/A | 1.189 | |

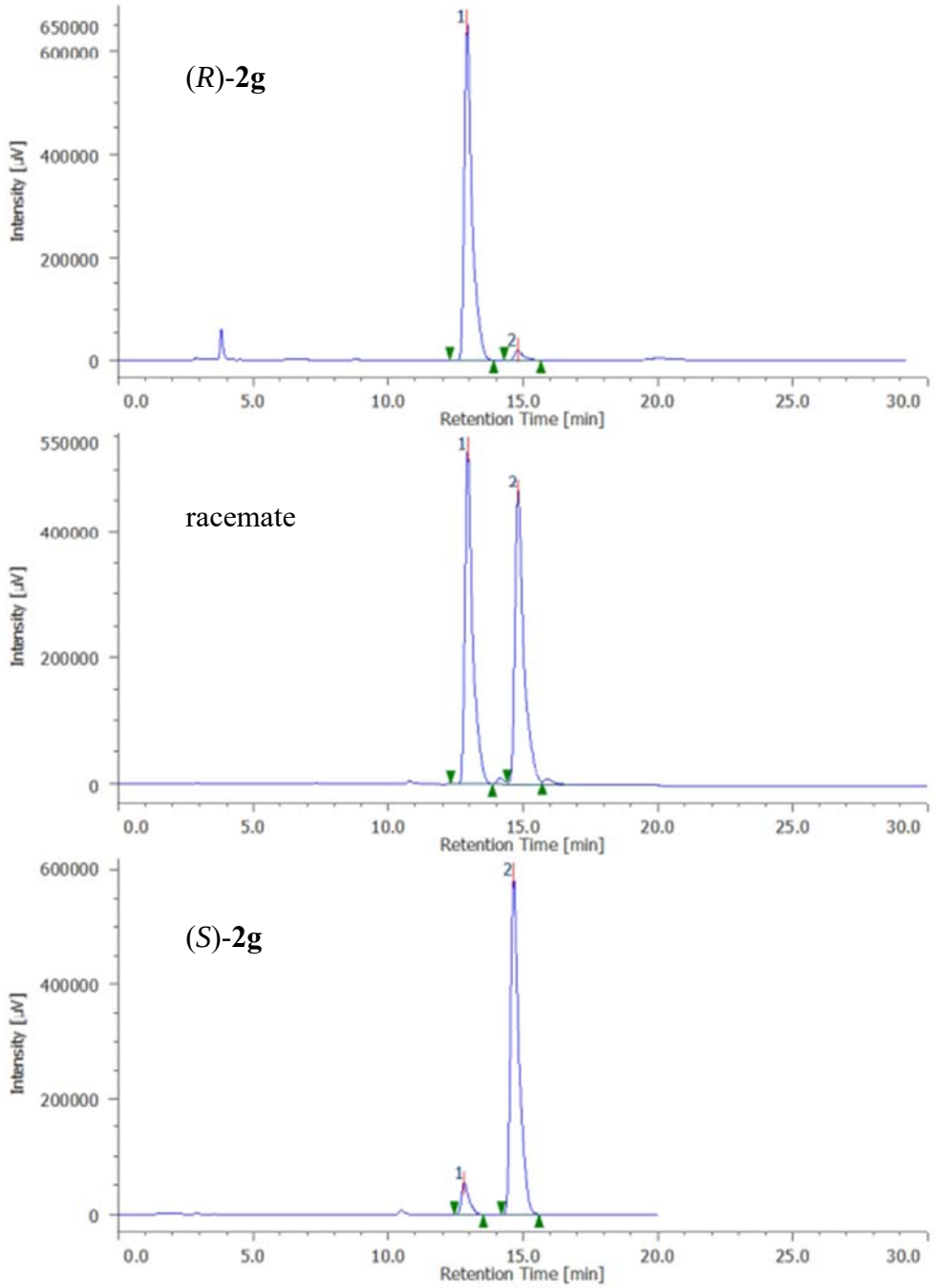
racemate

| # | Peak Name | CH | tR [min] | Area [μV·sec] | Height [μV] | Area% | Height% | Quantity | NTP | Resolution | Symmetry Factor | Warning |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Unknown | 6 | 12.287 | 6881566 | 518252 | 50.114 | 52.022 | N/A | 21607 | 3.737 | 1.280 | |
| 2 | Unknown | 6 | 13.587 | 6850260 | 477973 | 49.886 | 47.978 | N/A | 22371 | N/A | 1.289 | |

(*S*)-**1f**

| # | Peak Name | CH | tR [min] | Area [μV·sec] | Height [μV] | Area% | Height% | Quantity | NTP | Resolution | Symmetry Factor | Warning |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Unknown | 6 | 12.407 | 139558 | 11365 | 0.790 | 1.005 | N/A | 22235 | 3.399 | 1.169 | |
| 2 | Unknown | 6 | 13.657 | 17515499 | 1119681 | 99.210 | 98.995 | N/A | 18224 | N/A | 1.369 | |

**1-(4-Methoxyphenyl)prop-2-yn-1-ol [2g]**




(*R*)-**2g**

| # | Peak Name | CH | tR [min] | Area [μV·sec] | Height [μV] | Area% | Height% | Quantity | NTP | Resolution | Symmetry Factor | Warning |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Unknown | 6 | 12.923 | 12992887 | 654935 | 96.911 | 97.225 | N/A | 12641 | 3.853 | 1.752 | |
| 2 | Unknown | 6 | 14.800 | 414179 | 18691 | 3.089 | 2.775 | N/A | 13108 | N/A | 1.714 | |

racemate

| # | Peak Name | CH | tR [min] | Area [μV·sec] | Height [μV] | Area% | Height% | Quantity | NTP | Resolution | Symmetry Factor | Warning |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Unknown | 6 | 12.947 | 10435837 | 529868 | 49.689 | 53.289 | N/A | 12860 | 3.836 | 1.755 | |
| 2 | Unknown | 6 | 14.823 | 10566311 | 464456 | 50.311 | 46.711 | N/A | 12778 | N/A | 1.740 | |

(*S*)-**2g**

| # | Peak Name | CH | tR [min] | Area [μV·sec] | Height [μV] | Area% | Height% | Quantity | NTP | Resolution | Symmetry Factor | Warning |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Unknown | 6 | 12.820 | 1047782 | 54695 | 7.471 | 8.475 | N/A | 11978 | 3.648 | 1.580 | |
| 2 | Unknown | 6 | 14.650 | 12976580 | 590690 | 92.529 | 91.525 | N/A | 11891 | N/A | 1.595 | |