Electronic Supplementary Information

Alcohol synthesis based on the S_N2 reactions of alkyl halides with squarate dianion

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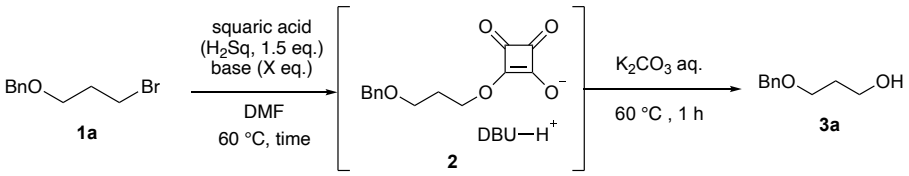
ESI-1. Optimization of base and solvent for the transformation of 1a into 3a

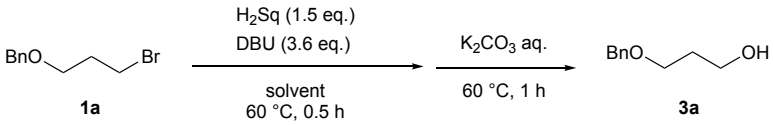
1. Screening of base



entry	base (X eq.)	time (h)	yield of alcohol **3a** (%)	recovery of **1a** (%)
1	Cs_2CO_3 (1.5)	5	26	73
2	pyridine (3.0)	5	20	60
3	Et_3N (3.0)	1	14[a]	20[a]
4	K_2CO_3 (1.5)	0.5	6	86
5	$NaHCO_3$ (3.0)	0.5	4	87
6	*i*-Pr_2NEt (3.0)	0.5	27	20
7	TMEDA (1.5)	0.5	7	43
8	KOH (3.0)	0.5	6	86
9	DBU (3.0)	0.5	89	–
10	DBU (3.6)	0.5	96	–

[a] NMR yield

2. Screening of solvent



entry	solvent	yield of alcohol **3a** (%)	recovery of **1a** (%)
1	THF	43	48
2	EtOH	54	38
3	acetone	20	–
4	DMSO	80	–
4	MeCN	82	–
5	DMF	96	–

ESI-2. General information

All reactions were carried out in flame- or oven-dried glassware under an argon atmosphere with dry solvents unless otherwise stated. The reactions heating to high temperatures were carried out using an oil bath unless otherwise stated. THF was distilled from sodium and benzophenone. Bis-tetra-*n*-propylammonium salt of squaric acid,[1] di-sodium salt of squaric acid,[2] compounds **1e**,[3] **1m**,[4] **1n**,[5] **1r**,[6] **1s**[7], **5**,[8] and **8**[9] were prepared by the known procedures. A salt, as shown entry 4 in Table 1, was prepared by squaric acid and diazabicyclo[5.4.0]undecene (DBU) as a 1:2 mol ratio. All other reagents and solvents were used as received from commercial sources without further purification.

All reaction were monitored by thin-layer chromatography which was performed by using Merck silica gel 60 F254 pre-coated plates (0.25 mm) and visualized with UV (254 nm) and stained with a solution of 2% anisaldehyde, 5% H_2SO_4 in ethanol or a solution of 10% phosphomolybdic acid in ethanol under heating at ca. 200 °C. Flash column chromatography was performed by using Kanto Silica Gel 60 N. IR spectra were recorded on JASCO FT/IR-4100 and the major absorbance bands are all reported in wavenumbers (cm^{-1}). Preparative TLC (PTLC) was performed by using Merck silica gel 60 F254 pre-coated plates (0.5 mm). HRMS were recorded on a JEOL JMS-T100GCV at Research Faculty of Agriculture, Hokkaido University for FD/FI method. NMR spectra were recorded on JEOL JNM-ECX-500 (500 MHz for ^1H and 126 MHz for ^{13}C) with residual $CHCl_3$ of chloroform-*d* or benzene of benzene-d_6 as internal reference (^1H NMR: 7.26 ppm for chloroform-*d*, 7.15 ppm for benzene-d_6,^{13}C NMR: 77.16 ppm for chloroform-*d,* 128.06 ppm for benzene-d_6). Chemical shift was reported in part per million (ppm) and signals of ^1H NMR spectra were expressed as follows: singlet (s), doublet (d), triplet (t), quartet (q), quintet (quint) and multiplet (m).

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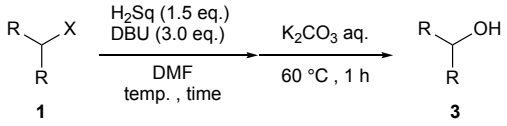
1. M. G. Topuzova, S. V. Kotov and T. M. Kolev, *Appl. Catal., A*, 2005, **281**, 157.
2. Q. Zhao, J. Wang, Y. Lu, Y. Li, G. Liang and J. Chen, *Angew. Chem. Int. Ed.*, 2016, **55**, 12528.
3. A. Itoh, T. Saito, K. Oshima and H. Nozaki, *Bull. Chem. Soc. Jpn.,* 1981, **54**, 1456.
4. S. G. Hegde, D. Beckwith, R. Doti and J. Wolinsky, *J. Org. Chem.*, 1985, **50**, 894.
5. M. Xuan, I. Paterson and S. M. Dalby, *Org. Lett.*, 2012, **14**, 5492.
6. H. Zhao, A. J. McMillan, T. Constantin, R. C. Mykura, F. Juliá, and D. Leonori, *J. Am. Chem. Soc.*, 2021, **143**, 14806.
7. I. Ryu, H. Matsubara, S. Yasuda, H. Nakamura, and D. P. Curran, *J. Am. Chem. Soc.*, 2002, **124**, 12946.
8. K. Zhao and R. R. Knowles, *J. Am. Chem. Soc.*, 2022, **144**, 137.
9. N. Saygili, R. J. Brown, P. Day, R. Hoelzl, P. Kathirgamanathan, E. R. Mageean, T. Ozturk, M. Pilkington, M. M. B. Qayyum, S. S. Turner, L. Vorwerg and J. D. Wallis, *Tetrahedron*, 2001, **57**, 5015.

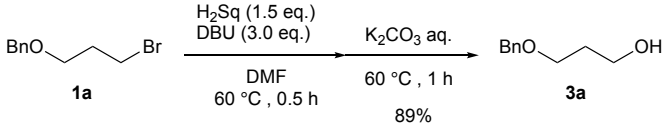
ESI-3. Experimental section

General synthetic procedure



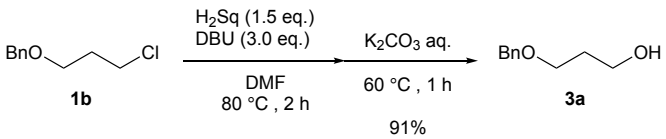
To a solution of **1** (1.0 eq.) and squaric acid (1.5 eq.) in DMF (ca. 0.5 M) was added DBU (3.0 eq.) at rt, and the reaction mixture was stirred at the optimized reaction temperature among 60–120 °C. After stirring for the reaction time corresponding to the substrate, 10% (w/w) K_2CO_3 aq. (1 mL) was added. After stirring for 1 h at 60 °C, brine was added to the reaction mixture, and the aqueous mixture was extracted with EtOAc for three times. The combined organic layers were dried over $MgSO_4$ and filtered. The filtrate was concentrated under reduced pressure to give a crude product. Purification of the crude product by silica gel column chromatography (hexane/EtOAc system) gave **3**. When the reaction protocol or the reaction conditions differed from the general procedure, the detailed information was mentioned in the procedures of each of synthesized compounds.

Synthesis of **3a** from bromide **1a**



According to the general procedure, the reaction of **1a** (45.9 mg, 200 μmol) and H_2Sq (34.2 mg, 300 μmol) in DMF (400 μL) with DBU (89.7 μL, 600 μmol) at 60 °C for 0.5 h, followed by the treatment of the mixture with 10% (w/w) K_2CO_3 aq. (1 mL) at 60 °C for 1 h afforded a crude product including **3a**. Purification of the crude product by silica gel column chromatography (hexane/EtOAc = 3/1) gave **3a** (29.6 mg, 178 μmol, 89%) as a colorless oil. The spectral data of **3a** was in good agreement with the literature data.[10]

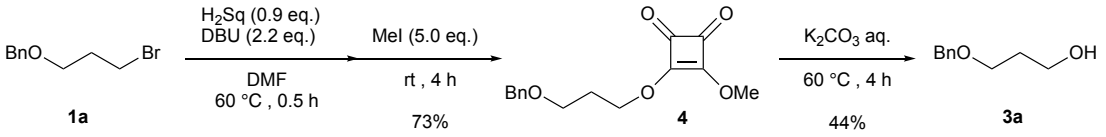
Synthesis of **3a** from chloride **1b**



According to the general procedure, the reaction of **1b** (37.6 mg, 204 μmol) and H_2Sq (34.7 mg, 304 μmol) in DMF (410 μL) with DBU (91.4 μL, 611 μmol) at 80 °C for 2 h, followed by the treatment of the mixture with 10% (w/w) K_2CO_3 aq. (1 mL) at 60 °C for 1 h afforded a crude product including **3a**. Purification of the crude product by silica gel column chromatography (hexane/EtOAc = 3/1) gave **3a** (30.6 mg, 184 μmol, 91%) as a colorless oil. The spectral data of **3a** was in good agreement with the literature data.[10]

10. L. V. Heumann and G. E. Keck, *Org. Lett.*, 2007, **9**, 1951.

Synthesis of **3a** from dialkyl squarate **4**

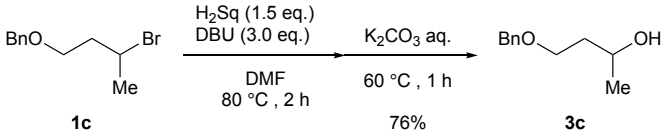


To a solution of **1a** (100 mg, 436 μmol) and H_2Sq (44.1 mg, 387 μmol) in DMF (870 μL) was added DBU (141 μL, 944 μmol). After stirring for 0.5 h at 60 °C, MeI (136 μL, 2.18 mmol) was added at 0 °C. After stirring for 4 h at rt, H_2O (1 mL) was added to the reaction mixture, and the aqueous mixture was extracted with EtOAc (5 mL × 3). The organic layer was dried over $MgSO_4$ and filtered. The filtrate was concentrated under reduced pressure to give a crude product, which was purified by silica gel column chromatography (hexane/EtOAc = 4/1) to give **4** (78.7 mg, 285 μmol, 73%) as a yellow oil.

A mixture of **4** (28.1 mg, 123 μmol) in 10% (w/w) K_2CO_3 aq. (1 mL) was stirred for 4 h at 60 °C. Then, the reaction mixture was extracted with EtOAc (1 mL × 3). The organic layer was dried over $MgSO_4$ and filtered. The filtrate was concentrated under reduced pressure to give a crude product, which was purified by silica gel column chromatography (hexane/EtOAc = 4/1) to give **3a** (8.9 mg, 53.5 μmol, 44%) as a colorless oil. The spectral data of **3a** was in good agreement with the literature data.[10]

Data for **4**: IR (ATR): 2961, 2866, 1812, 1732, 1601, 1476, 1454, 1395, 1361, 1340, 1100, 1026, 917, 823, 741, 700 cm^{-1}. ^1H NMR ($CDCl_3$, 500 MHz): δ = 7.37−7.23 (m, 5H), 4.79 (t, *J* = 6.0 Hz, 2H), 4.49 (s, 2H), 4.30 (s, 3H), 3.60 (t, *J* = 6.0 Hz, 2H), 2.09 (quint, *J* = 6.0 Hz, 2H). ^{13}C NMR ($CDCl_3$, 126 MHz): 189.30, 189.25, 184.5, 184.3, 138.1, 128.5 (2C), 127.9 (2C), 127.8, 73.2, 71.9, 65.7, 61.0, 30.2. HRMS (FD): *m*/*z* $[M]^+$ calcd for $C_{15}H_{16}O_5$: 276.0998; found: 276.0993.

Synthesis of **3c** from bromide **1c**



According to the general procedure, the reaction of **1c** (49.1 mg, 202 μmol) and H_2Sq (34.5 mg, 302 μmol) in DMF (400 μL) with DBU (90.6 μL, 606 μmol) at 80 °C for 2 h, followed by the treatment of the mixture with 10% (w/w) K_2CO_3 aq. (1 mL) at 60 °C for 1 h afforded a crude product including **3c**. Purification of the crude product by silica gel column chromatography (hexane/EtOAc = 3/1) gave **3c** (27.6 mg, 153 μmol, 76%) as a colorless oil. The spectral data of **3c** was in good agreement with the literature data.[11]

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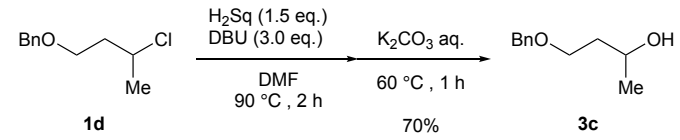
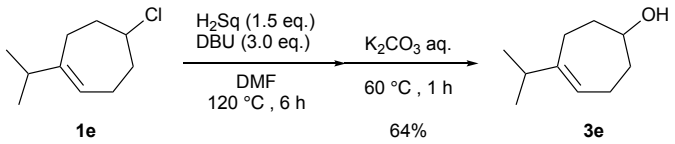
11. C. Cadot, P. I. Dalko, J. Cossy, C. Ollivier, R. Chuard, and P. Renaud, *J. Org. Chem*., 2002, **67**, 7193.

Synthesis of **3c** from chloride **1d**



According to the general procedure, the reaction of **1d** (39.6 mg, 199 μmol) and H_2Sq (34.1 mg, 299 μmol) in DMF (400 μL) with DBU (89.4 μL, 598 μmol) at 90 °C for 2 h, followed by the treatment of the mixture with 10% (w/w) K_2CO_3 aq. (1 mL) at 60 °C for 1 h afforded a crude product including **3c**. Purification of the crude product by silica gel column chromatography (hexane/EtOAc = 3/1) gave **3c** (25.1 mg, 139 μmol, 70%) as a colorless oil. The spectral data of **3c** was in good agreement with the literature data.[11]

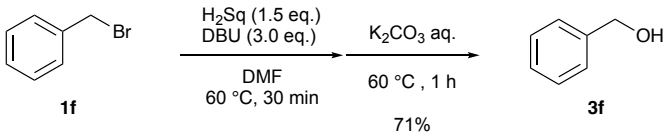
Synthesis of **3e** from chloride **1e**



According to the general procedure, the reaction of **1e** (18.4 mg, 107 μmol) and H_2Sq (18.1 mg, 159 μmol) in DMF (210 μL) with DBU (47.9 μL, 320 μmol) at 120 °C for 6 h, followed by the treatment of the mixture with 10% (w/w) K_2CO_3 aq. (1 mL) at 60 °C for 1 h afforded a crude product including **3e**. Purification of the crude product by silica gel column chromatography (hexane/EtOAc = 3/1) gave **3e** (10.5 mg, 68.1 μmol, 64%) as a colorless oil.

Data for **3e**: IR (ATR): 3342, 2957, 2927, 2853, 1463, 1361, 1293, 1035, 829 cm^{-1}. ^1H NMR ($CDCl_3$, 500 MHz): δ = 5.52 (t, *J* = 6.6 Hz, 1H), 3.81–3.75 (m, 1H), 2.24–2.13 (m, 3H), 1.96–1.87 (m, 4H), 1.34–1.26 (m, 2H), 0.97 (d, *J* = 6.9, 3H), 0.96 (d, *J* = 6.9, 3H). ^{13}C NMR ($CDCl_3$, 126 MHz): 150.1, 122.6, 74.8, 37.1, 35.9, 35.8, 24.5, 22.5, 21.4, 21.2. HRMS (FI): *m/z* $[M]^+$ calcd for $C_{10}H_{18}O$: 154.1358; found: 154.1365.

Synthesis of **3f** from bromide **1f**



According to the general procedure, the reaction of **1f** (34.3 mg, 200 μmol) and H_2Sq (34.2 mg, 301 μmol) in DMF (400 μL) with DBU (89.7 μL, 600 μmol) at 60 °C for 0.5 h, followed by the treatment of the mixture with 10% (w/w) K_2CO_3 aq. (1 mL) at 60 °C for 1 h afforded a crude product including **3f**. Purification of the crude product by silica gel column chromatography (hexane/EtOAc = 3/1) gave **3f** (15.4 mg, 142 μmol, 71%) as a colorless oil. The spectral data of **3f** was in good agreement with the literature data.[12]

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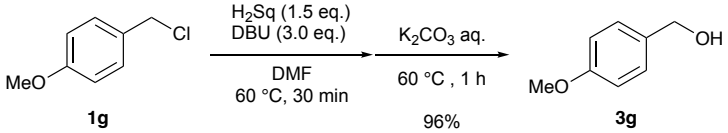
12. P. Bhattacharya, J. A. Krause, and H. Guan, *Organometallics*, 2011, **30**, 4720.

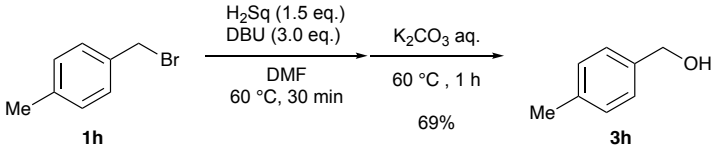
Synthesis of **3g** from chloride **1g**



1g **3g**

According to the general procedure, the reaction of **1g** (31.1 mg, 200 μmol) and H_2Sq (34.2 mg, 300 μmol) in DMF (400 μL) with DBU (89.7 μL, 600 μmol) at 60 °C for 0.5 h, followed by the treatment of the mixture with 10% (w/w) K_2CO_3 aq. (1 mL) at 60 °C for 1 h afforded a crude product including **3g**. Purification of the crude product by silica gel column chromatography (hexane/EtOAc = 3/1) gave **3g** (26.6 mg, 193 μmol, 96%) as a white solid. The spectral data of **3g** was in good agreement with the literature data.[12]

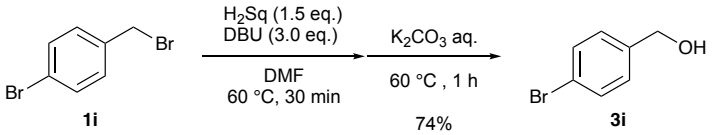
Synthesis of **3h** from bromide **1h**



1h **3h**

According to the general procedure, the reaction of **1h** (36.5 mg, 197 μmol) and H_2Sq (34.4 mg, 301 μmol) in DMF (400 μL) with DBU (89.7 μL, 600 μmol) at 60 °C for 0.5 h, followed by the treatment of the mixture with 10% (w/w) K_2CO_3 aq. (1 mL) at 60 °C for 1 h afforded a crude product including **3h**. Purification of the crude product by silica gel column chromatography (hexane/EtOAc = 3/1) gave **3h** (16.8 mg, 134 μmol, 69%) as a white solid. The spectral data of **3h** was in good agreement with the literature data.[12]

Synthesis of **3i** from bromide **1i**



1i **3i**

According to the general procedure, the reaction of **1i** (50.0 mg, 200 μmol) and H_2Sq (34.1 mg, 299 μmol) in DMF (400 μL) with DBU (89.7 μL, 600 μmol) at 60 °C for 0.5 h, followed by the treatment of the mixture with 10% (w/w) K_2CO_3 aq. (1 mL) at 60 °C for 1 h afforded a crude product including **3i**. Purification of the crude product by silica gel column chromatography (hexane/EtOAc = 3/1) gave **3i** (27.7 mg, 148 μmol, 74%) as a white solid. The spectral data of **3i** was in good agreement with the literature data.[13]

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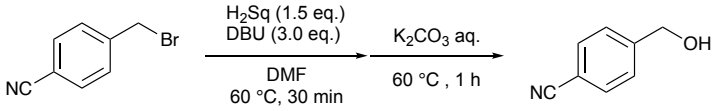
13. A. Harinath, J. Bhattacharjee, T. K. Panda, *Chem. Commun.*, 2019, **55**, 1386.

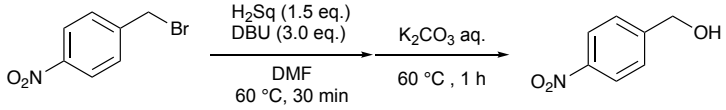
Synthesis of **3j** from bromide **1j**



1j **3j**

According to the general procedure, the reaction of **1j** (39.1 mg, 199 μmol) and H_2Sq (34.0 mg, 298 μmol) in DMF (400 μL) with DBU (89.7 μL, 600 μmol) at 60 °C for 0.5 h, followed by the treatment of the mixture with 10% (w/w) K_2CO_3 aq. (1 mL) at 60 °C for 1 h afforded a crude product including **3j**. Purification of the crude product by silica gel column chromatography (hexane/EtOAc = 2/1) gave **3j** (23.2 mg, 174 μmol, 87%) as a white solid. The spectral data of **3j** was in good agreement with the literature data.[14]

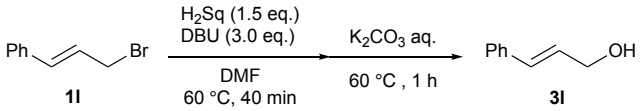
Synthesis of **3k** from bromide **1k**



1k **3k**

According to the general procedure, the reaction of **1k** (43.1 mg, 200 μmol) and H_2Sq (34.2 mg, 300 μmol) in DMF (400 μL) with DBU (89.7 μL, 600 μmol) at 60 °C for 0.5 h, followed by the treatment of the mixture with 10% (w/w) K_2CO_3 aq. (1 mL) at 60 °C for 1 h afforded a crude product including **3k**. Purification of the crude product by silica gel column chromatography (hexane/EtOAc = 2/1) gave **3k** (20.2 mg, 132 μmol, 66%) as a yellow solid. The spectral data of **3k** was in good agreement with the literature data.[13]

Synthesis of **3l** from bromide **1l**



1l **3l**

According to the general procedure, the reaction of **1l** (38.4 mg, 195 μmol) and H_2Sq (33.6 mg, 295 μmol) in DMF (390 μL) with DBU (87.5 μL, 585 μL) at 60 °C for 40 min, followed by the treatment of the mixture with 10% (w/w) K_2CO_3 aq. (1 mL) at 60 °C for 1 h afforded a crude product including **3l**. Purification of the crude product by silica gel column chromatography (hexane/EtOAc = 3/1) gave **3l** (14.8 mg, 110 μmol, 57%) as a white solid. The spectral data of **3l** was in good agreement with the literature data.[15]

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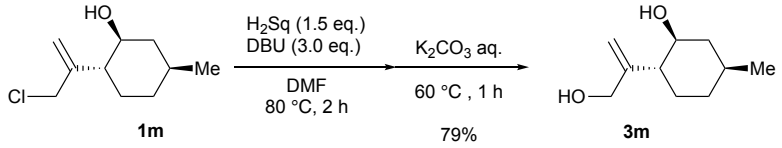
14. M. Zhao, W. Xie, and C. Cui, *Chem. Eur. J.*, 2014, **20**, 9259.

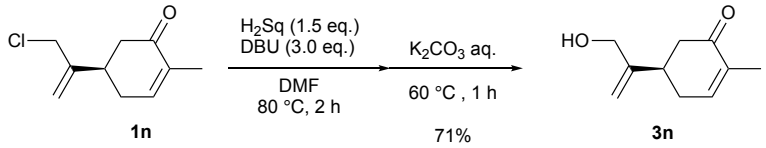
15. K. Zhu, M. P. Shaver, and S. P. Thomas, *Eur. J. Org. Chem.*, 2015, 2119.

Synthesis of **3m** from chloride **1m**



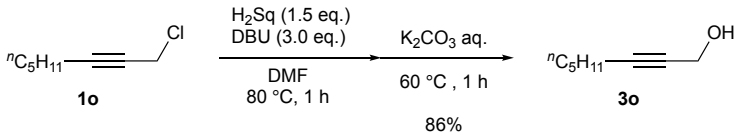
According to the general procedure, the reaction of **1m** (37.3 mg, 198 μmol) and H_2Sq (33.9 mg, 297 μmol) in DMF (400 μL) with DBU (88.7 μL, 593 μmol) at 80 °C for 2 h, followed by the treatment of the mixture with 10% (w/w) K_2CO_3 aq. (1 mL) at 60 °C for 1 h afforded a crude product including **3m**. Purification of the crude product by silica gel column chromatography (hexane/EtOAc = 1/2) gave **3m** (26.5 mg, 156 μmol, 79%) as a white solid. The spectral data of **3m** was in good agreement with the literature data.[16]

Synthesis of **3n** from chloride **1n**



According to the general procedure, the reaction of **1n** (39.0 mg, 211 μmol) and H_2Sq (35.9 mg, 315 μmol) in DMF (420 μL) with DBU (94.8 μL, 634 μmol) at 80 °C for 2 h, followed by the treatment of the mixture with 10% (w/w) K_2CO_3 aq. (1 mL) at 60 °C for 1 h afforded a crude product including **3n**. Purification of the crude product by silica gel column chromatography (hexane/EtOAc = 1/1) gave **3n** (24.8 mg, 149 μmol, 71%) as a yellow oil. The spectral data of **3n** was in good agreement with the literature data.[5]

Synthesis of **3o** from chloride **1o**



According to the general procedure, the reaction of **1o** (28.9 mg, 200 μmol) and H_2Sq (34.2 mg, 300 μmol) in DMF (400 μL) with DBU (89.7 μL, 600 μmol) at 80 °C for 1 h, followed by the treatment of the mixture with 10% (w/w) K_2CO_3 aq. (1 mL) at 60 °C for 1 h afforded a crude product including **3o**. Purification of the crude product by silica gel column chromatography (hexane/EtOAc = 3/1) gave **3o** (21.7 mg, 172 μmol, 86%) as a yellow oil. The spectral data of **3o** was in good agreement with the literature data.[17]

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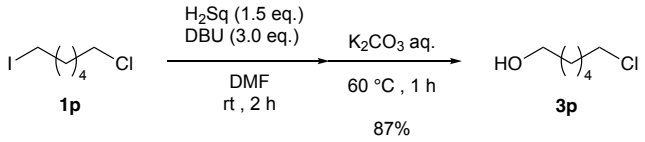
16. N. A. Clanton, N. A. Wilson, E. Ortiz, S. T. Blumberg, and D. E. Frantz, *Org. Lett.,* 2023, **25**, 277.

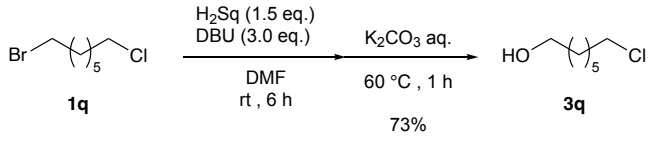
17. A. Gansäuer, C.-A. Fan, F. Keller, and J. Keil, *J. Am. Chem. Soc.,* 2007, **129**, 3484.

Synthesis of **3p** from iodochloride **1p**



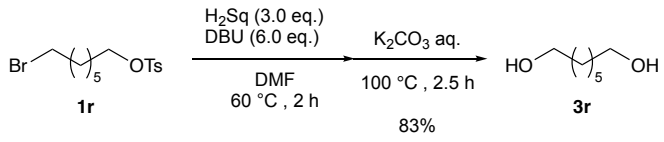
According to the general procedure, the reaction of **1p** (31.0 mg, 200 μmol) and H_2Sq (34.5 mg, 302 μmol) in DMF (400 μL) with DBU (89.7 μL, 600 μmol) at rt for 2 h, followed by the treatment of the mixture with 10% (w/w) K_2CO_3 aq. (1 mL) at 60 °C for 1 h afforded a crude product including **3p**. Purification of the crude product by silica gel column chromatography (hexane/EtOAc = 5/1) gave **3p** (23.9 mg, 175 μmol, 87%) as a pale yellow oil. The spectral data of **3p** was in good agreement with the literature data.[18]

Synthesis of **3q** from bromochloride **1q**



According to the general procedure, the reaction of **1q** (44.1 mg, 200 μmol) and H_2Sq (34.2 mg, 300 μmol) in DMF (400 μL) with DBU (89.7 μL, 600 μmol) at rt for 6 h, followed by the treatment of the mixture with 10% (w/w) K_2CO_3 aq. (1 mL) at 60 °C for 1 h afforded a crude product including **3q**. Purification of the crude product by silica gel column chromatography (hexane/EtOAc = 5/1) gave **3q** (21.9 mg, 145 μmol, 73%) as a pale yellow oil. The spectral data of **3q** was in good agreement with the literature data.[19]

Synthesis of **3r** from bromotosylate **1r**



According to the general procedure, a mixture of **1r** (74.0 mg, 212 μmol) and H_2Sq (72.6 mg, 637 μmol) in DMF (420 μL) was reacted with DBU (190 μL, 1.27 mmol) at 60 °C for 2 h, and the reaction mixture was treated with 10% (w/w) K_2CO_3 aq. (1 mL) at 100 °C for 2.5 h. Due to the high polarity of **3r**, the aqueous mixture was extracted with EtOAc (1 mL × 4) and THF (1 mL × 3). Purification of an obtained crude product including **3r** by silica gel column chromatography (hexane/EtOAc = 1/2) gave **3r** (23.2 mg, 175 μmol, 83%) as a colorless oil. The spectral data of **3r** was in good agreement with the literature data.[20]

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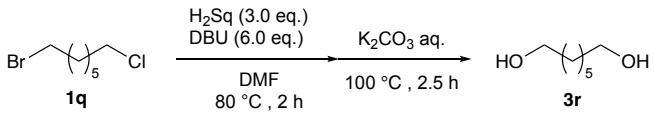
18. K. Matsuoka, N. Komami, M. Kojima, T. Mita, K. Suzuki, S. Maeda, T. Yoshino, and S. Matsunaga, *J. Am. Chem. Soc.* 2021, **143**, 103.

19. R. I. Khusnutdinov, N. A. Shchadneva, R. Yu. Burangulova, Z. S. Muslimov, and U. M. Dzhemilev, *Russ. J. Org. Chem.*, 2006, **42**, 1615.

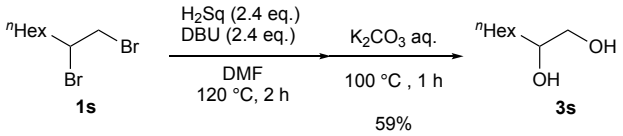
20. L. Wu, I. Fleischer, R. Jackstell, I. Profir, R. Franke, and M. Beller, *J. Am. Chem. Soc.*, 2013, **135**, 14306.

Synthesis of **3r** from bromochloride **1q**



According to the general procedure, a mixture of **1q** (44.1 mg, 200 μmol) and H_2Sq (68.6 mg, 601 μmol) in DMF (400 μL) was reacted with DBU (170 μL, 1.27 mmol) at 80 °C for 2 h, and the reaction mixture was treated with 10% (w/w) K_2CO_3 aq. (1 mL) at 100 °C for 2.5 h. Due to the high polarity of **3r**, the aqueous mixture was extracted with THF (1 mL × 5) Purification of an obtained crude product including **3r** by silica gel column chromatography (hexane/EtOAc = 1/2) gave **3r** (22.5 mg, 170 μmol, 85%) as a colorless oil. The spectral data of **3r** was in good agreement with the literature data.[20]

Synthesis of **3s** from dibromide **1s**



Note: When this reaction was conducted according to the general procedure, an E2 reaction triggered by DBU occurred preferentially; thus, the following protocol was performed.

To a solution of H_2Sq (57.5 mg, 504 μmol) in DMF (210 μL) was added DBU (75.5 μL, 505 μmol) and the mixture was stirred for 5 min at 120 ℃. Then, a solution of **1s** (57.2 mg, 210 μmol) in DMF (210 μL) was added to the reaction mixture. After stirring for 2 h at 120 ℃, to the reaction mixture was added 10%(w/w) K_2CO_3 aq (1 mL). After stirring for 1 h at 100 °C, the reaction was quenched with brine (1 mL), and the mixture was extracted with EtOAc (1 mL × 3). The organic layer was dried over $MgSO_4$ and filtered. The filtrate was concentrated under reduced pressure to give a crude product including **3s**, which was purified by silica gel column chromatography (hexane/EtOAc = 1/1) to give **3s** (18.0 mg, 123 μmol, 59%) as a pale yellow oil. The spectral data of **3s** was in good agreement with the literature data.[21]

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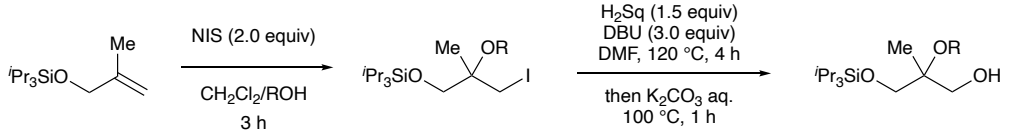
21. Q. Yao, *Org. Lett.* 2002, **4**, 2197.

Synthesis of alcohol **7** from alkene **5**



5

6a: R = Me (84%)
6b: R = Bn (79%)
6c: R = propargyl (82%)

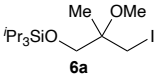
7a: R = Me (94%)
7b: R = Bn (82%)
7c: R = propargyl (90%)

General procedure of synthesis of ether 6 and 7

To a solution of **5** in a mixture of CH_2Cl_2 and ROH (ca. 1:1. 0.24 M) was added NIS (2.0 eq.) at rt. After stirring for 3 h, the reaction was quenched with 10% $Na_2S_2O_3$ aq. (1 mL). The mixture was extracted with diethyl ether for three times, and the combined organic layers were dried over $MgSO_4$ and filtered. The filtrate was concentrated under reduced pressure to give a crude product, which was purified by silica gel column chromatography to give **6**.

To a solution of **6** (1.0 eq.) and H_2Sq (1.5 eq.) in DMF (0.5 M) was added DBU (3.0 eq.) at rt, and the reaction mixture was stirred at 120 °C. After stirring for 4 h, the reaction mixture was added 10% K_2CO_3 aq. (1 mL) at 100 °C, and the mixture was further stirred for 1 h at the same temperature. The reaction was quenched with brine (1 mL), and the aqueous mixture was extracted with EtOAc (1 mL × 3). The combined organic layers were dried over $MgSO_4$ and filtered. The filtrate was concentrated under reduced pressure to give a crude product, which was purified by silica gel column chromatography to give **7**.

Synthesis of ether **6a**

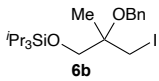


6a

According to the general procedure, the reaction of **5** (61.0 mg, 267 μmol) in MeOH (530 μL, 13.1 mmol) and CH_2Cl_2 (530 μL) with NIS (122 mg, 542 μmol) at rt for 3 h afforded a crude product including **6a**. Purification of the crude product by silica gel column chromatography (hexane/EtOAc = 20/1) gave **6a** (86.1 mg, 223 μmol, 84%) as a colorless oil.

Data for **6a**: IR (ATR): 2941, 2892, 2865, 1462, 1201, 1119, 882, 809, 682 cm^{-1}. ^1H NMR ($CDCl_3$, 500 MHz): δ = 3.76 (d, *J* = 9.7 Hz, 1H), 3.54 (d, *J* = 9.7 Hz, 1H), 3.51 (d, *J* = 10.3 Hz, 1H), 3.33 (d, *J* = 10.3 Hz, 1H), 3.27 (s, 3H), 1.36 (s, 3H), 1.19−1.06 (m, 21H). ^{13}C NMR ($CDCl_3$, 126 MHz): δ = 75.6, 67.7, 50.0, 19.2, 18.2 (6C), 13.3, 12.0 (3C). HRMS (FI): *m*/*z* $[M + H]^+$ calcd for $C_{14}H_{32}IO_2Si$: 387.1216; found: 387.1203.

Synthesis of ether **6b**



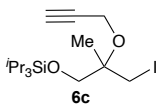
6b

According to the general procedure, the reaction of **5** (47.8 mg, 209 μmol) in BnOH (420 μL, 4.04 mmol) and CH_2Cl_2 (530 μL) with NIS (94.3 mg, 419 μmol) at rt for 3 h afforded a crude product including **6b**. Purification of the crude product by silica gel column chromatography (hexane/EtOAc = 100/1) gave **6b** (76.0 mg, 164 μmol, 79%) as a colorless oil.

Data for **6b**: IR (ATR): 2942, 2890, 2865, 1462, 1383, 1183, 1115, 1070, 882, 814, 736, 683 cm^{-1}. ^1H NMR ($CDCl_3$, 500 MHz): δ = 7.41–7.26 (m, 5H), 4.54 (d, *J* = 10.9 Hz, 1H), 4.48 (d, *J* = 10.9 Hz, 1H), 3.85 (d, *J* = 9.8 Hz, 1H), 3.63 (d, *J* = 9.8 Hz, 1H), 3.62 (d, *J* = 10.9 Hz, 1H), 3.45 (d, *J* = 10.9 Hz, 1H), 1.47 (s, 3H),

1.25–1.07 (m, 21H). ^{13}C NMR ($CDCl_3$, 126 MHz): δ = 138.7, 128.4 (2C), 127.9 (2C), 127.6, 76.0, 68.2, 64.5, 20.2, 18.2 (6C), 13.7, 12.0 (3C). HRMS (FI): *m*/*z* $[M + H]^+$ calcd for $C_{20}H_{36}IO_2Si$: 463.1529; found: 463.1548.

Synthesis of ether **6c**

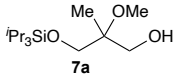


6c

According to the general procedure, the reaction of **5** (113 mg, 494 μmol) in propargyl alcohol (990 μL, 17.1 mmol) and CH_2Cl_2 (990 μL) with NIS (222 mg, 987 μmol) at rt for 3 h afforded a crude product including **6c**. Purification of the crude product by silica gel column chromatography (hexane/EtOAc = 30/1) gave **6c** (166.9 mg, 407 μmol, 82%) as a colorless oil.

Data for **6c**: IR (ATR): 3310, 2942, 2892, 2866, 2364, 1462, 1382, 1180, 1114, 1070, 996, 882, 798, 683 cm^{-1}. ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 4.24 (d, *J* = 14.9 Hz, 1H), 4.19 (d, *J* = 14.9 Hz, 1H), 3.81 (d, *J* = 9.7 Hz, 1H), 3.64 (d, *J* = 9.7 Hz, 1H), 3.50 (d, *J* = 10.9 Hz, 1H), 3.35 (d, *J* = 10.9 Hz, 1H), 2.41 (s, 1H), 1.43 (s, 3H), 1.29–0.94 (m, 21H). ^{13}C NMR ($CDCl_3$, 126 MHz): δ = 80.8, 77.0, 73.8, 68.0, 51.3, 20.2, 18.1 (6C), 12.8, 11.2 (3C). HRMS (FD): *m*/*z* $[M]^+$ calcd for $C_{16}H_{31}IO_2Si$: 411.1216; found: 411.1216.

Synthesis of alcohol **7a**

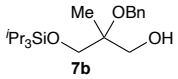


7a

According to the general procedure, **6a** (77.6 mg, 201 μmol) and H_2Sq (34.3 mg, 301 μmol) in DMF (400 μL) with DBU (90.2 μL, 603 μmol) at 120 °C for 4 h, followed by the treatment of the mixture with 10% K_2CO_3 aq. (1 mL) at 100 °C for 1 h afforded a crude product including **7a**. Purification of the crude product by silica gel column chromatography (hexane/EtOAc = 5/1) gave **7a** (51.9 mg, 188 μmol, 94%) as a colorless oil.

Data for **7a:** IR (ATR): 3459, 2942, 2866, 1464, 1109, 1069, 882, 805, 681 cm^{-1}. ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 3.77 (d, *J* = 9.7 Hz, 1H), 3.65–3.55 (m, 3H), 3.30 (s, 3H), 2.27 (t, *J* = 6.0 Hz, 1H), 1.15 (s, 3H), 1.14–0.86 (m, 21H). ^{13}C NMR ($CDCl_3$, 126 MHz): δ = 77.2, 67.1, 65.6, 50.1, 18.1 (6C), 16.9, 12.0 (3C). HRMS (FD): *m*/*z* $[M + H]^+$ calcd for $C_{14}H_{33}O_3Si$: 277.2199; found: 277.2212.

Synthesis of alcohol **7b**

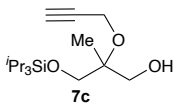


7b

According to the general procedure, **6b** (103 mg, 223 μmol) and H_2Sq (38.3 mg, 336 μmol) in DMF (450 μL) with DBU (100 μL, 669 μmol) at 120 °C for 4 h, followed by the treatment of the mixture with 10% K_2CO_3 aq. (1 mL) at 100 °C for 1 h afforded a crude product including **7b**. Purification of the crude product by silica gel column chromatography (hexane/EtOAc = 5/1) gave **7b** (64.7 mg, 184 μmol, 82%) as a colorless oil.

Data for **7b**: IR (ATR): 3473, 2942, 2866, 1463, 1385, 1109, 1065, 882, 804, 736, 682 cm^{-1}. ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 7.34–7.23 (m, 5H), 4.57 (s, 2H), 3.85 (d, *J* = 9.7 Hz, 1H), 3.70 (d, *J* = 9.7 Hz, 1H), 3.70 (d, *J* = 11.5 Hz, 1H), 3.65 (d, *J* = 11.5 Hz, 1H), 1.27 (s, 3H), 1.17–0.99 (m, 21H). ^{13}C NMR ($CDCl_3$, 126 MHz): δ = 139.2, 128.5 (2C), 127.6 (2C), 127.5, 77.9, 67.6, 66.3, 64.7, 18.1 (6C), 17.7, 12.0 (3C). HRMS (FD): *m*/*z* $[M + H]^+$ calcd for $C_{20}H_{37}O_3Si$: 353.2512; found: 353.2527.

Synthesis of alcohol **7c**

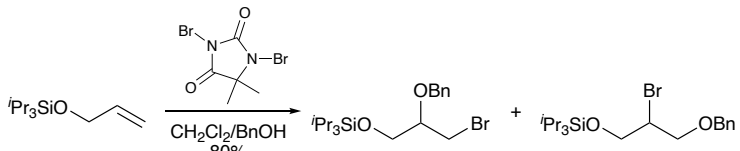


7c

According to the general procedure, **6c** (81.8 mg, 200 μmol) and H_2Sq (34.2 mg, 300 μmol) in DMF (400 μL) with DBU (89.6 μL, 599 μmol) at 120 °C for 4 h, followed by the treatment of the mixture with 10% K_2CO_3 aq. (1 mL) at 100 °C for 1 h afforded a crude product including **7c**. Purification of the crude product by silica gel column chromatography (hexane/EtOAc = 5/1) gave **7c** (53.8 mg, 180 μmol, 90%) as a colorless oil.

Data for **7c**: IR (ATR): 3447, 3311, 2941, 2866, 2359, 1463, 1385, 1108, 1063, 881, 804, 681 cm^{-1}. ^1H NMR ($CDCl_3$, 500 MHz): δ = 4.28 (d, *J* = 15.8 Hz, 1H), 4.24 (d, *J* = 15.8 Hz, 1H), 3.80 (d, *J* = 10.3 Hz, 1H), 3.67–3.58 (m, 3H), 2.42 (t, *J* = 2.3 Hz, 1H), 2.25 (t, *J* = 6.3 Hz, 1H), 1.23 (s, 3H), 1.14–0.86 (m, 21H). ^{13}C NMR ($CDCl_3$, 126 MHz): δ = 81.4, 79.0, 73.7, 67.5, 65.9, 51.3, 18.1 (6C), 17.4, 11.9 (3C). HRMS (FI): *m*/*z* $[M]^+$ calcd for $C_{16}H_{32}O_3Si$: 300.2121; found: 300.2112.

Synthesis of a 1.8:1 mixture of bromide **9** and **10**

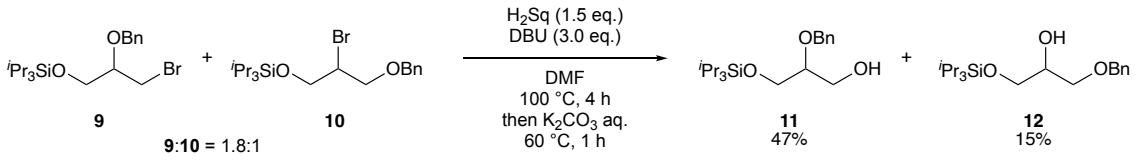


8 **9** **10**

To a solution of **8** (187 mg, 871 μmol) in $(CH_2Cl)_2$ (870 μL) and BnOH (870 μL) was added 1,3-dibromo-5,5-dimethylhydantoin (150 mg, 523 μmol). After stirring for 4 h at rt, the reaction was quenched with saturated NH_4Cl aq. (2 mL), and the mixture was extracted with diethyl ether (1 mL × 3). The organic layer was dried ($MgSO_4$) and filtered. The filtrate was concentrated under reduced pressure to give crude product. To remove excess BnOH, the crude product was roughly purified by silica gel column chromatography (hexane/EtOAc = 20/1) to give an impure product including **9** and **10**. The mixture was further purified by silica gel column chromatography (hexane/EtOAc = 100/1) to give an inseparable mixture of **9** and **10** (139 mg) as a pale yellow oil and a mixture of two desired products and benzaldehyde dibenzylacetal (157 mg). The impure product was purified by PTLC (0.05 mm, hexane/EtOAc = 10/1) to give an inseparable mixture of **9** and **10** (140 mg). The total amount of the obtained mixture of **9** and **10** were 279 mg (696 μmol, 80%, **9**:**10** = 1.8:1).

NMR data of a 1.8:1 mixture of **9** and **10**: ^1H NMR ($CDCl_3$, 500 MHz): δ = 7.39−7.26 (m, 5H), 4.71 (d, *J* = 11.5 Hz, 0.64H), 4.64 (d, *J* = 11.5 Hz, 1H, 0.64H), 4.59 (s, 0.72H), 4.12 (dddd, *J* = 6.5, 5.8, 5.3, 4.5 Hz, 0.36H), 4.03−3.94 (m, 0.72H), 3.88 (dd, *J* = 10.3, 5.3 Hz, 0.36H), 3.84−3.74 (m, 1.28 + 0.36H), 3.70–3.61 (m, 1.28H), 3.54 (dd, *J* = 10.4 , 4.8 Hz, 0.64H), 1.15−0.96 (m, 21H). ^{13}C NMR ($CDCl_3$, 126 MHz): 138.2, 138.0, 128.5 (4C), 128.0 (2C), 127.9, 127.8 (3C), 78.9, 73.4, 72.4 70.9, 64.6, 63.7, 52.4, 33.1, 18.1 (12C), 12.1 (3C), 12.0 (3C).

Synthesis of alcohol **11** and **12**

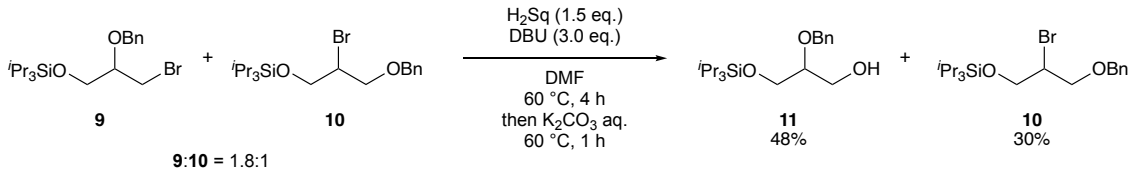


To a solution of H_2Sq (32.5 mg, 285 μmol) in DMF (180 μL) was added DBU (85.1 μL, 569 μmol), and the mixture was stirred at 100 °C for 5 minutes. Then, a 1.8:1 mixture of **9** and **10** (76.2 mg, 190 μmol) in DMF (180 μL) was added to the reaction mixture. After stirring for 4 h at 100 °C, 10% K_2CO_3 aq. (1 mL) was added to the reaction mixture, and the mixture was further stirred for 1 h at 60 °C. The reaction was quenched with brine (1 mL), and the mixture was filtered though a Celite pad to remove insoluble solids. The filtrate was extracted with Et_2O (1 mL × 3). The organic layer was dried ($MgSO_4$) and filtered. The filtrate was concentrated under reduced pressure to give a crude product, which was purified by silica gel column chromatography (hexane/EtOAc = 15/1) to give **11** (30.0 mg, 88.7 μmol, 47%) as a pale yellow oil and **12** (9.6 mg, 28.4 μmol, 15%) as a pale yellow oil.

Data for **11**: IR (ATR): 3442, 2942, 2866, 1463, 1105, 1068, 882, 683 cm^{-1}. ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 7.39−7.26 (m, 5H), 4.71 (d, *J* = 11.5 Hz, 1H), 4.63 (d, *J* = 11.5 Hz, 1H), 3.86 (dd, *J* = 10.5, 5.0 Hz, 1H), 3.82−3.74 (m, 2H), 3.69 (dd, *J* = 11.5, 5.0 Hz, 1H), 3.61 (dd, *J* = 10.5, 5.0 Hz, 1H), 1.15−0.98 (m, 21H). ^{13}C NMR ($CDCl_3$, 126 MHz): 138.5, 128.6 (2C), 127.9 (3C), 79.6, 72.4, 63.9, 63.2, 18.1 (6C), 12.0 (3C). HRMS (FI): *m*/*z* $[M + H]^+$ calcd for $C_{19}H_{35}O_3Si$: 339.2356; found: 339.2351.

Data for **12**: IR (ATR): 2943, 2866, 1456, 1104 cm^{-1}. ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 7.37−7.26 (m, 5H), 4.56 (s, 2H), 3.90−3.84 (m, 1H), 3.79−3.69 (m, 2H), 3.57 (dd, *J* = 9.5, 5.0 Hz, 1H), 3.53 (d, *J* = 9.5, 6.0 Hz, 1H), 1.15−0.98 (m, 21H). ^{13}C NMR ($CDCl_3$, 126 MHz): 138.2, 128.5 (2C), 127.9 (2C), 127.8, 73.6, 71.1, 71.0, 64.4, 18.1 (6C), 12.0 (3C). HRMS (FI): *m*/*z* $[M + H]^+$ calcd for $C_{19}H_{35}O_3Si$: 339.2356; found: 339.2355.

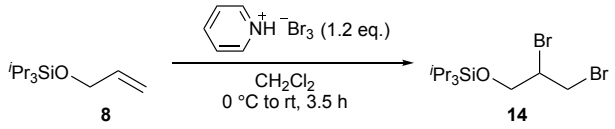
Synthesis of alcohol **11** and recovery of bromide **10**



To a solution of H_2Sq (20.4 mg, 179 μmol) in DMF (120 μL) was added DBU (53.5 μL, 358 μmol), and the mixture was stirred at 100 °C for 5 minutes. Then, a solution of a 1.8:1 mixture of **9** and **10** (111 mg, 0.276 mmol) in DMF (120 μL) was added to the reaction mixture. After stirring for 2 h at 60 °C, 10% K_2CO_3 aq. (1 mL) was added to the reaction mixture, and the mixture was further stirred for 1 h at 60 °C. The reaction was quenched with brine (1 mL), and the mixture was filtered through a Celite pad to remove insoluble solids. The filtrate was extracted with Et_2O (1 mL × 3). The organic layer was dried ($MgSO_4$) and filtered. The filtrate was concentrated under reduced pressure to give a crude product, which was purified by silica gel column chromatography (hexane/EtOAc = 30/1 to 10/1) to give **11** (19.2 mg, 56.7 μmol, 48%) as a pale yellow oil and **10** (14.4 mg, 35.9 μmol, 30%) as a pale yellow oil.

Data for **10**: IR (ATR): 3446, 2942, 2866, 1457, 1100, 882, 773, 682 cm^{-1}. ^1H NMR ($CDCl_3$, 500 MHz): δ = 7.39−7.26 (m, 5H), 4.59 (s, 2H), 4.12 (dddd, *J* = 6.5, 5.8, 5.3, 4.5 Hz, 1H), 4.03−3.94 (m, 2H), 3.88 (dd, *J* = 10.3, 5.3 Hz, 1H), 3.77 (dd, *J* = 10.3, 5.8 Hz, 1H), 1.15−0.96 (m, 21H). ^{13}C NMR ($CDCl_3$, 126 MHz): 138.0, 128.5 (2C), 127.8 (3C), 73.4, 70.9, 64.6, 52.4, 18.1 (6C), 12.1 (3C). HRMS (FD): *m*/*z* $[M + H]^+$ calcd for $C_{19}H_{34}BrO_2Si$: 401.1511; found: 401.1499.

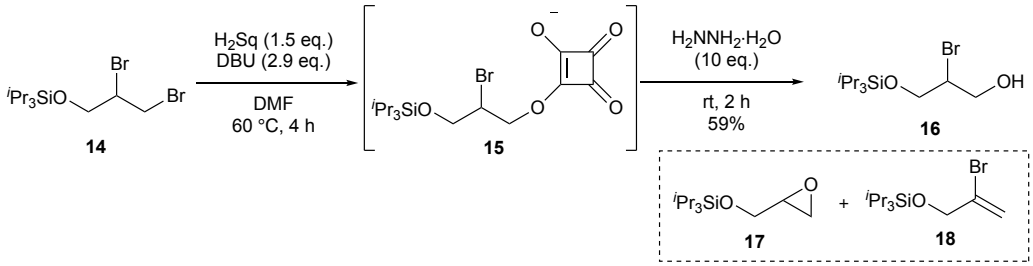
Synthesis of dibromide **14**



To a solution of **8** (627 mg, 2.92 mmol) in CH_2Cl_2 (8.9 mL) was added pyridinium tribromide (1.12 g, 3.51 mmol) at 0 °C, and the reaction mixture was stirred for 2.5 h at rt. After strring for 1 h at 0 °C, the reaction was quenched with 10 % $NaHSO_3$ aq. (5 mL). The mixtue was diluted with hexane (10 mL), and the organic layer was washed with water (10 mL × 3). The organic layer was dried over $MgSO_4$, and filtered. The filtrate was concentrated under reduced pressure to give **14** (1.07 g, 2.85 mmol, 98%) as a colorless oil.

Data for **14**: IR (ATR): 2943, 2866, 1459, 1142, 1068, 995, 930,882, 774, 684 cm^{-1}. ^1H NMR ($CDCl_3$, 500 MHz): δ = 4.24−4.12 (m, 2H), 4.01 (dd, *J* = 10.5, 4.8 Hz, 1H), 3.90 (dd, *J* = 10.0, 8.3 Hz, 1H), 3.79 (dd, *J* = 10.5, 4.5 Hz, 1H), 1.19−0.98 (m, 21H). ^{13}C NMR ($CDCl_3$, 126 MHz): 64.7, 52.1, 33.0, 18.1 (6C), 12.1 (3C). HRMS (FD): *m*/*z* $[M + H]^+$ calcd for $C_{12}H_{27}Br_2OSi$: 373.0198; found: 373.0207.

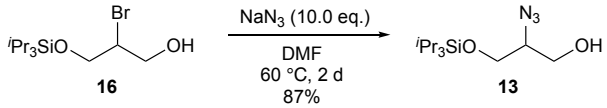
Synthesis of bromohydrin **16**



To a solution of H_2Sq (30.8 mg, 277 μmol) in DMF (180 μL) was added DBU (79.3 μL, 531 μmol). After stirring for 5 min at 60 °C, a solution of **14** (69.0 mg, 184 μmol) in DMF (180 μL) was added to the reaction mixture. After stirring for 4 h at 60 °C, $H_2NNH_2{\cdot}H_2O$ (89.4 μL, 1.84 mmol) was added to the reaction mixture at 0 °C. After stirring for 2 h at rt, the reaction was quenched with brine (1 mL). After the mixture was filtered through a Celite pad, the filtrate was extracted with EtOAc (1 mL × 3). The combined organic layers were dried over $MgSO_4$ and filtered. The filtrate was concentrated under reduced pressure to give a crude product, which was purified by silica gel column chromatography (hexane/ethyl acetate = 30/1 to 10/1) to give **16** (33.8 mg, 109 μmol, 59%) as a colorless oil. Byproducts **17** (2.0 mg, 8.68 μmol, 5%) and **18** (10.3 mg, 35.1 μmol, 19%) was also isolated through this purification.

Data for **16**: IR (ATR): 3404, 2943, 2866, 1463, 1102, 881, 791, 684 cm^{-1}. ^1H NMR ($CDCl_3$, 500 MHz): δ = 4.17−4.11 (m, 1H), 4.05 (dd, *J* = 10.5, 4.5 Hz, 1H), 4.02−3.90 (m, 3H), 2.36 (t, *J* = 6.6 Hz, 1H), 1.17−0.96 (m, 21H). ^{13}C NMR ($CDCl_3$, 126 MHz): 66.0, 65.4, 54.7, 18.0 (6C), 12.0 (3C). HRMS (FI): *m*/*z* $[M + H]^+$ calcd for $C_{12}H_{28}BrO_2Si$: 311.1042; found: 311.1041.

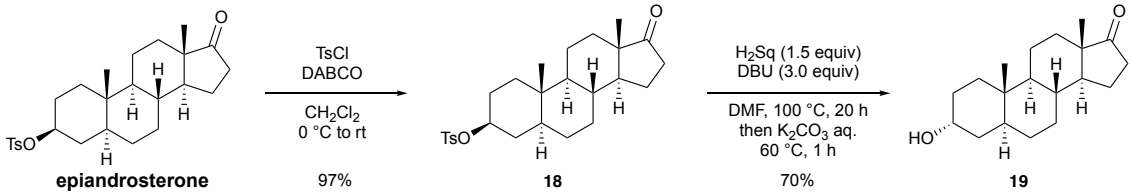
Synthesis of azidoalcohol **13**



To a solution of **16** (29.8 mg, 95.7 μmol) in DMF (480 μL) was added NaN_3 (62.2 mg, 957 μmol). After stirring for 2 d at 60 °C, the reaction was quenched with brine (1 mL), and the mixture was extracted with EtOAc (1 mL × 3). The combined organic layers were dried over $MgSO_4$ and filtered. The filtrate was concentrated under reduced pressure to give a crude product, which was purified by silica gel column chromatography (hexane/ethyl acetate = 10/1) to give **13** (22.7 mg, 83.0 μmol, 87%) as a colorless oil.

Data for **13**: IR (ATR): 3392, 2943, 2892, 2867, 2095, 1463, 1270, 1123, 1028, 882, 774, 684 cm^{-1}. ^1H NMR ($CDCl_3$, 500 MHz): δ = 3.89 (d, *J* = 5.7 Hz, 2H), 3.78 (ddd, *J* = 11.2, 6.0, 4.7 Hz, 1H), 3.69 (dt, *J* = 11.2, 6.0 Hz, 1H), 3.58 (ddd, *J* = 6.0, 5.7, 4.7 Hz, 1H), 1.96 (t, *J* = 6.0 Hz, 1H), 1.19−0.99 (m, 21H). ^{13}C NMR ($CDCl_3$, 126 MHz): 64.5, 64.4, 62.9, 18.0 (6C), 12.0 (3C). HRMS (FI): *m*/*z* $[M + H]^+$ calcd for $C_{12}H_{28}N_3O_2Si$: 274.1951; found: 274.1942.

Synthesis of tosylate (**18**) and androsterone (**19**)



Synthesis of tosylate (**18**)

To a solution of epiandrosterone (600 mg, 2.07 mmol) and DABCO (600 mg, 5.35 mmol) in CH_2Cl_2 (6 mL) was added TsCl (600 mg, 3.15 mmol) at 0 °C. After stirring for 1 h at rt, the reaction was quenched with sat. $NaHCO_3$ aq. (6 mL), and the aqueous mixture was extracted with CH_2Cl_2 for three times. The combined organic layers were dried over $MgSO_4$ and filtered. The filtrate was concentrated under reduced pressure to give a crude product, which was purified by silica gel column chromatography (hexane/EtOAc = 5/1) to give tosylate **18** (581 mg, 2.00 mmol, 97%) as a white solid.

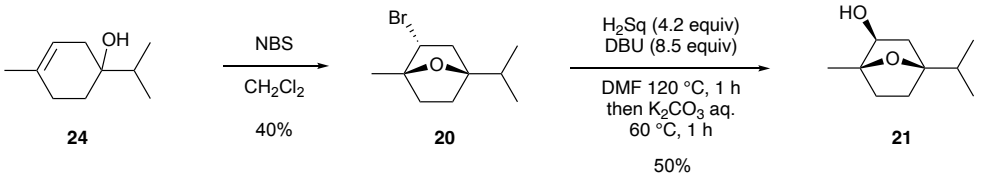
Data for **18**: mp 166–167 °C (recrystallized from Et_2O, colorless needle). IR (ATR): 2937, 2860, 1738, 1360, 1175, 930 cm^{-1}. ^1H NMR ($CDCl_3$, 500 MHz): δ = 7.79 (d, *J* = 8.0 Hz, 2H), 7.33 (d, *J* = 8.0 Hz, 2H), 4.44–4.38 (m, 1H), 2.47–2.40 (m, 4H), 2.09–2.02 (m, *J* = 9.5 Hz, 1H), 1.93–1.88 (m, 1H), 1.78–1.75 (m, 3H), 1.69 (dt, *J* = 13.4, 3.6 Hz, 1H), 1.65–1.44 (m, 6H), 1.32–1.17 (m, 5H), 1.12–1.07 (m, 1H), 0.97–0.88 (m, 2H), 0.85 (d, *J* = 11.5 Hz, 3H), 0.81 (s, 3H), 0.64 (td, J = 11.3, 3.6 Hz, 1H). ^{13}C NMR ($CDCl_3$, 126 MHz): δ = 221.2, 144.4, 134.6, 129.7 (2C), 127.6 (2C), 82.1, 54.1, 51.2, 47.7, 44.7, 36.7, 35.8, 35.3, 34.9, 34.8, 31.4, 30.7, 28.2, 28.0, 21.7, 21.6, 20.4, 13.8, 12.1. HRMS (FD): *m*/*z* $[M]^+$ calcd for $C_{26}H_{36}O_4S$: 444.2334; found: 444.2319.

Synthesis of androsterone (**19**)

According to the general procedure for the synthesis of **7** from **6**, the reaction of **18** (89.4 mg, 202 μmol) with a mixture of H_2Sq (34.2 mg, 300 μmol) and DBU (89.6 μL, 600 μmol)) in DMF (1 mL) at 100 °C for 20 h, followed by the treatment of the mixture with 10% K_2CO_3 aq. (2 mL) at 60 °C for 1 h afforded a crude product including **19**. Purification of the crude product by silica gel column chromatography (hexane/EtOAc = 5/1) gave **19** (40.6 mg, 140 μmol, 70%) as a white solid.

Data for **19**: mp 185–188 °C (recrystallized from hexane, colorless needle). IR (ATR): 3433, 2854, 1735, 1450, 1370, 1059, 1027, 1000, 731 cm^{-1}. ^1H NMR ($CDCl_3$, 500 MHz): δ = 4.04 (t, *J* = 2.6 Hz, 1H), 2.45–2.39 (m, 1H), 2.10–2.02 (m, 1H), 1.95–1.90 (m, 1H), 1.78 (qd, *J* = 6.4, 3.4 Hz, 2H), 1.71–1.17 (m, 16H), 1.01 (qd, *J* = 12.3, 4.9 Hz, 1H), 0.85 (s, 3H), 0.80–0.77 (m, 3H). ^{13}C NMR ($CDCl_3$, 126 MHz): δ = 221.5, 66.4, 54.4, 51.5, 47.8, 39.1, 36.2, 35.8, 35.7, 35.0, 32.1, 31.5, 30.8, 29.0, 28.2, 21.7, 20.0, 13.8, 11.2. HRMS (FD): *m*/*z* $[M]^+$ calcd for $C_{19}H_{30}O_2$: 290.2246; found: 290.2232.

Synthesis of bromide (**20**) and alcohol (**21**)



24 **20** **21**

Synthesis of bromide (**20**)

To a solution of NBS (801 mg, 4.50 mmol) in CH_2Cl_2 (10.0 mL) was added **24**[22] (500 μL, 3.05 mmol). After stirring for 1.5 h at rt, the reaction was quenched with sat. $NaHCO_3$ aq., and the aqueous mixture was extracted with hexane for three times. The combined organic layers were dried over $MgSO_4$ and filtered. The filtrate was concentrated under reduced pressure to give a crude product, which was purified by silica gel column chromatography (hexane/EtOAc= 35/1) to give **20** (281 mg, 1.21 mmol, 40%) as a colorless oil.

Data for **20**: IR (ATR): 2960, 2874, 1467, 1384, 831, 671 cm^{-1}. ^1H NMR ($CDCl_3$, 500 MHz): δ = 3.86 (qd, *J* = 5.3, 2.3 Hz, 1H), 2.56–2.51 (m, 1H), 2.35–2.30 (m, 1H), 2.03–1.98 (m, 1H), 1.73 (dd, *J* = 12.9, 4.9 Hz, 1H), 1.67–1.63 (m, 2H), 1.56–1.52 (m, 1H), 1.44 (s, 3H), 0.96 (d, *J* = 6.9 Hz), 0.96 (d, *J* = 6.9 Hz), 0.94 (d, *J* = 6.9 Hz). ^{13}C NMR ($CDCl_3$, 126 MHz): δ = 90.4, 85.9, 53.6, 43.7, 33.1, 32.7, 32.0, 18.8, 17.8, 17.6. HRMS (FD): *m*/*z* $[M]^+$ calcd for $C_{10}H_{17}BrO$: 232.0463; found: 232.0467.

Synthesis of alcohol (**21**)

According to the general procedure for the synthesis of **3** from **1**, the reaction of **20** (44.1 mg, 189 μmol) and H_2Sq (91.2 mg, 800 μmol) in DMF (400 μL) with DBU (240 μL, 1.71 mmol) at 120 °C for 1 d, followed by the treatment of the mixture with 10% (w/w) K_2CO_3 aq. (1 mL) at 60 °C for 1 h afforded a crude product including **21**. Purification of the crude product by silica gel column chromatography (hexane/EtOAc= 4/1) gave **21** (16.1 mg, 94.5 μmol, 50%) as a white solid.

Data for **21**: mp. 61–64 °C (recrystallized from $CDCl_3$, colorless needle). IR (ATR): 3260, 2964, 1460, 1115, 1053 cm^{-1}. ^1H NMR ($CDCl_3$, 500 MHz): δ = 3.74 (dd, *J* = 7.7, 7.7 Hz, 1H), 2.09–2.04 (m, 2H), 1.69–1.36 (m, 9H), 0.97 (d, *J* = 6.9 Hz, 3H), 0.95 (d, *J* = 6.9 Hz, 3 H). ^{13}C NMR (C_6D_6, 126 MHz): 88.1, 85.5, 76.8, 45.8, 33.2, 33.0, 32.5, 18.3, 18.2, 16.6. HRMS (FD): *m*/*z* $[M]^+$ calcd for $C_{10}H_{18}O_2$: 170.1307; found: 170.1313.

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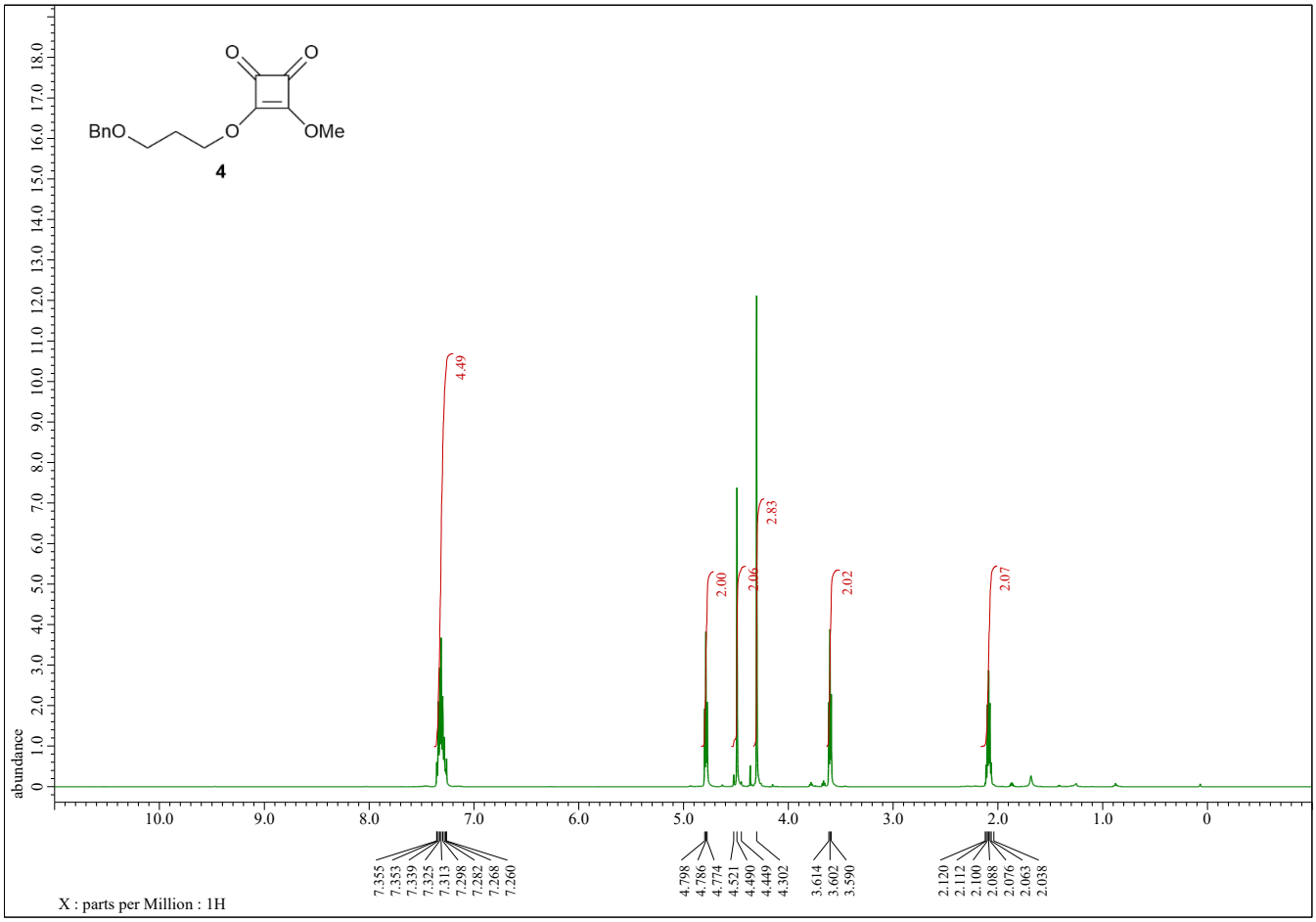
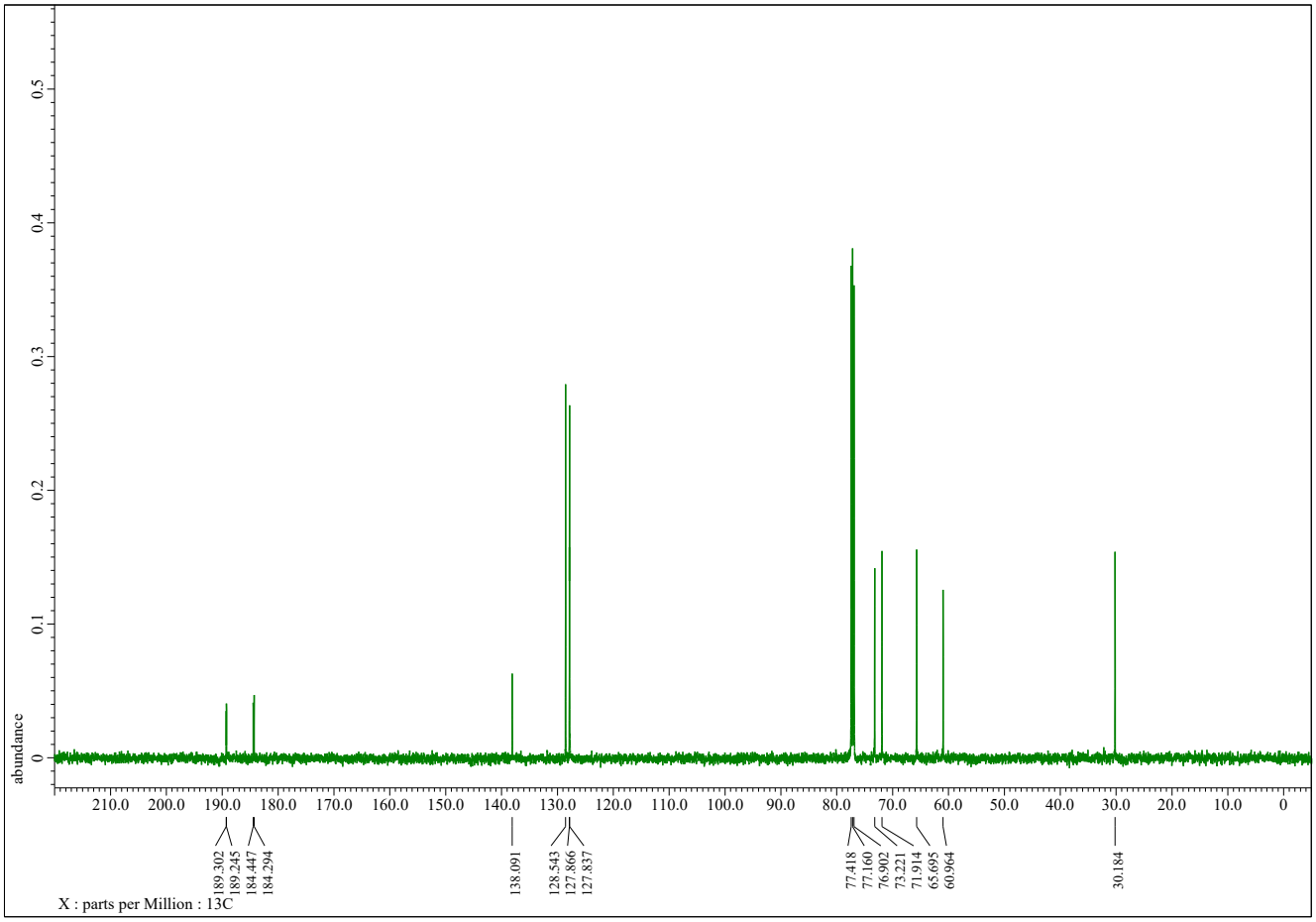
22. R. M. Carman, and B. N. Venzke, *Aust. J. Chem.,*1973, **26**, 2235.

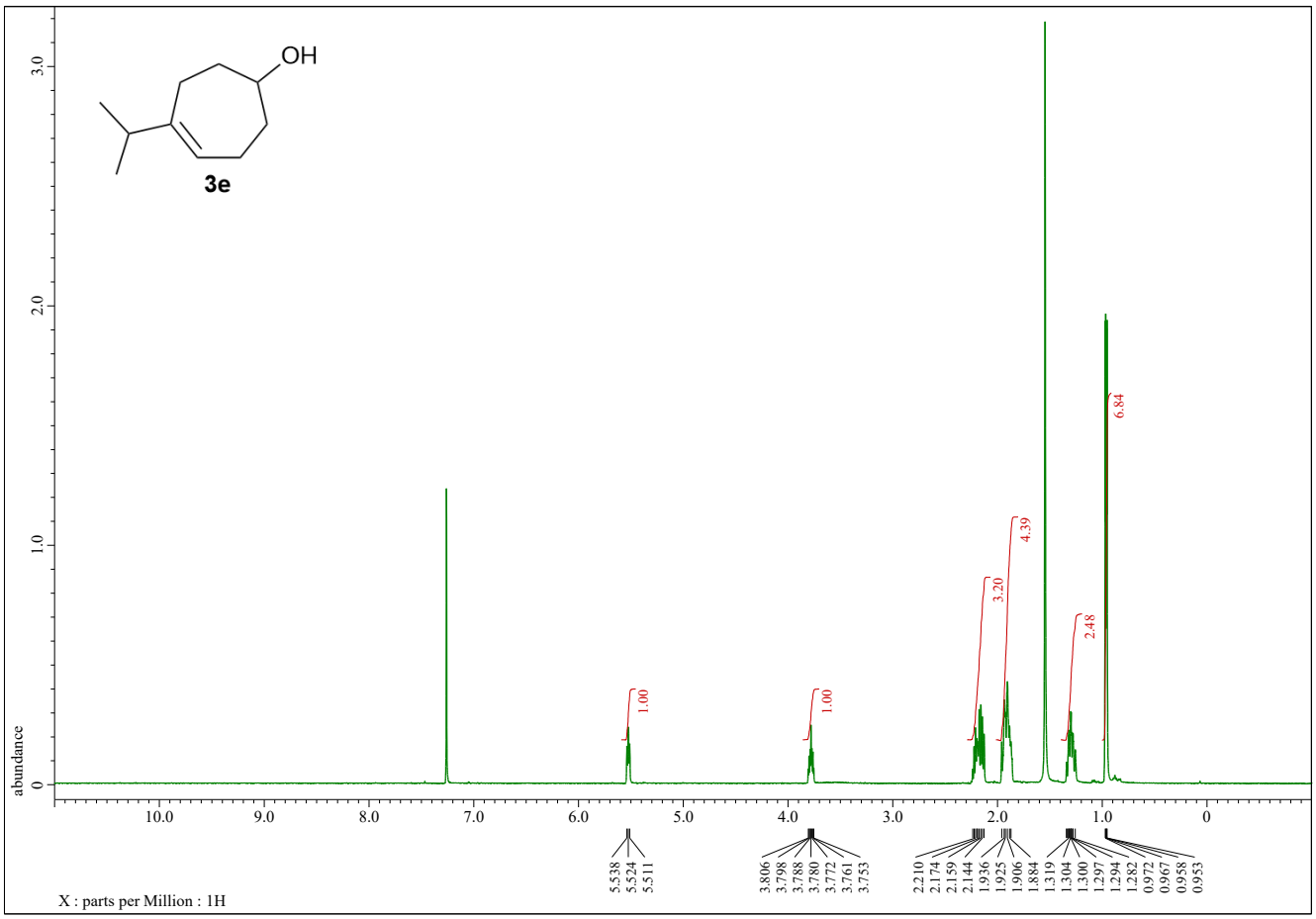
ESI-4 NMR spectra of novel compounds

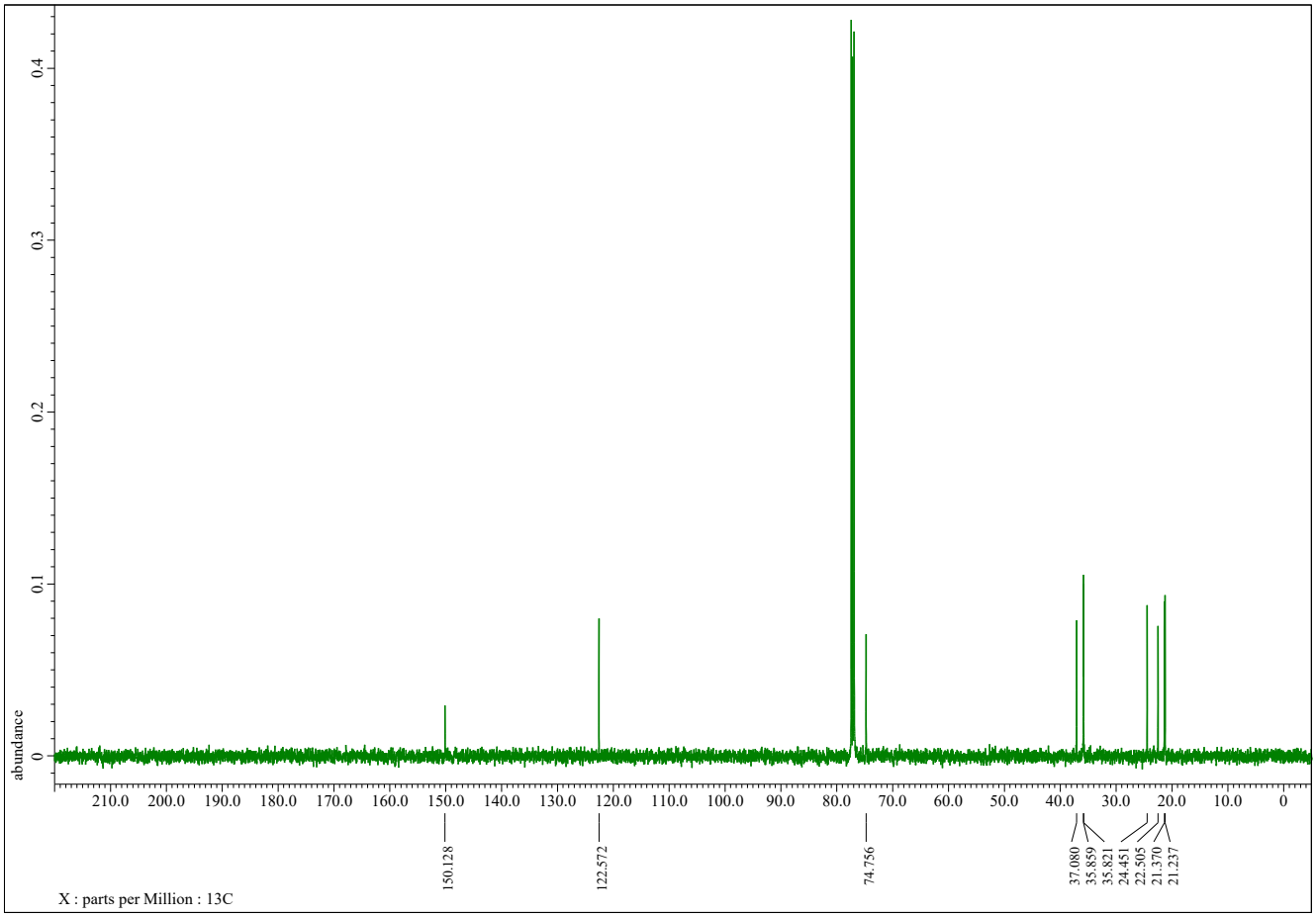
$^{1}H/^{13}C$ NMR spectra of methyl alkyl ester **4** (500/126 MHz, $CDCl_3$)



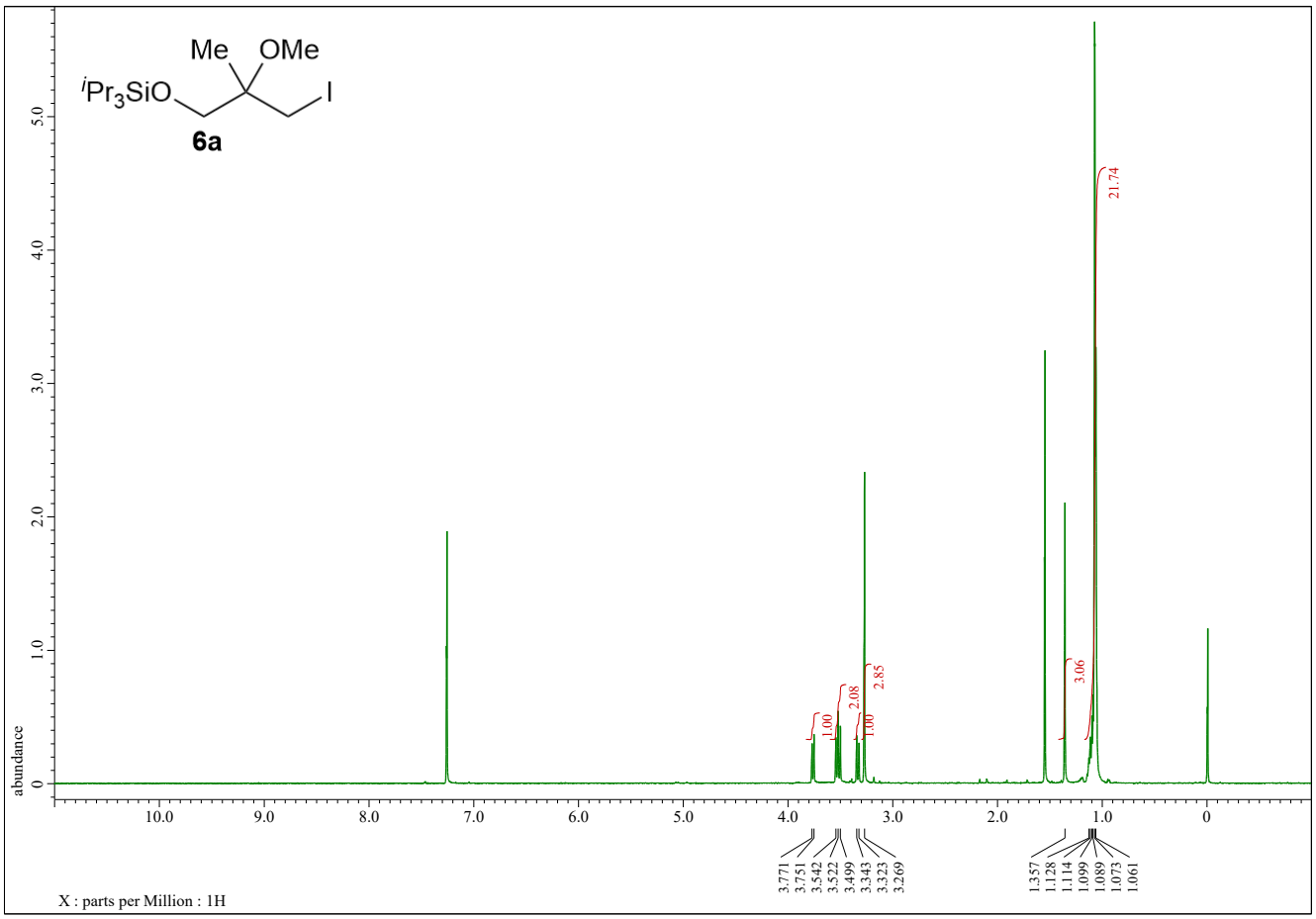


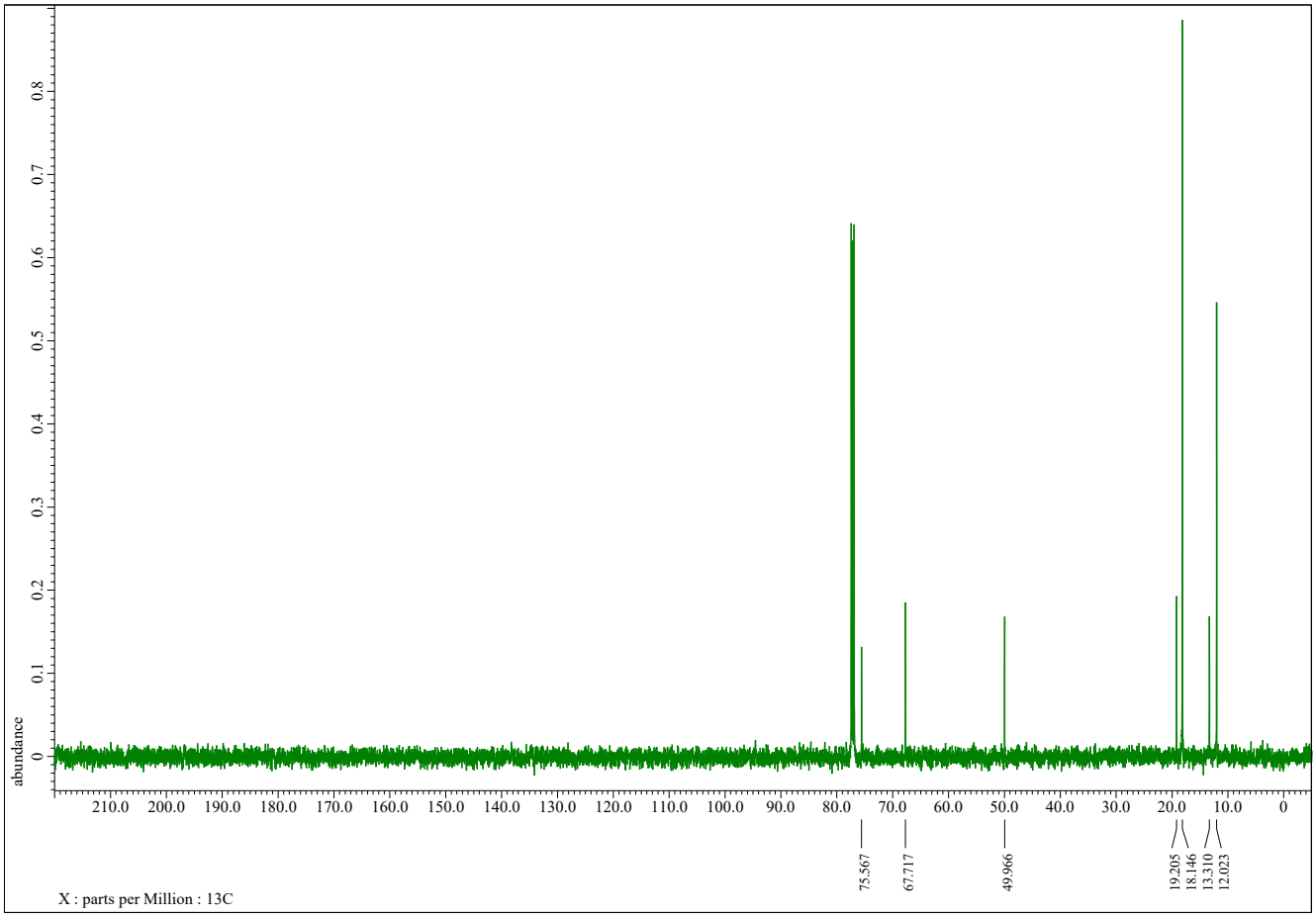
$^{1}H/^{13}C$ NMR spectra of alcohol **3e** (500/126 MHz, $CDCl_3$)



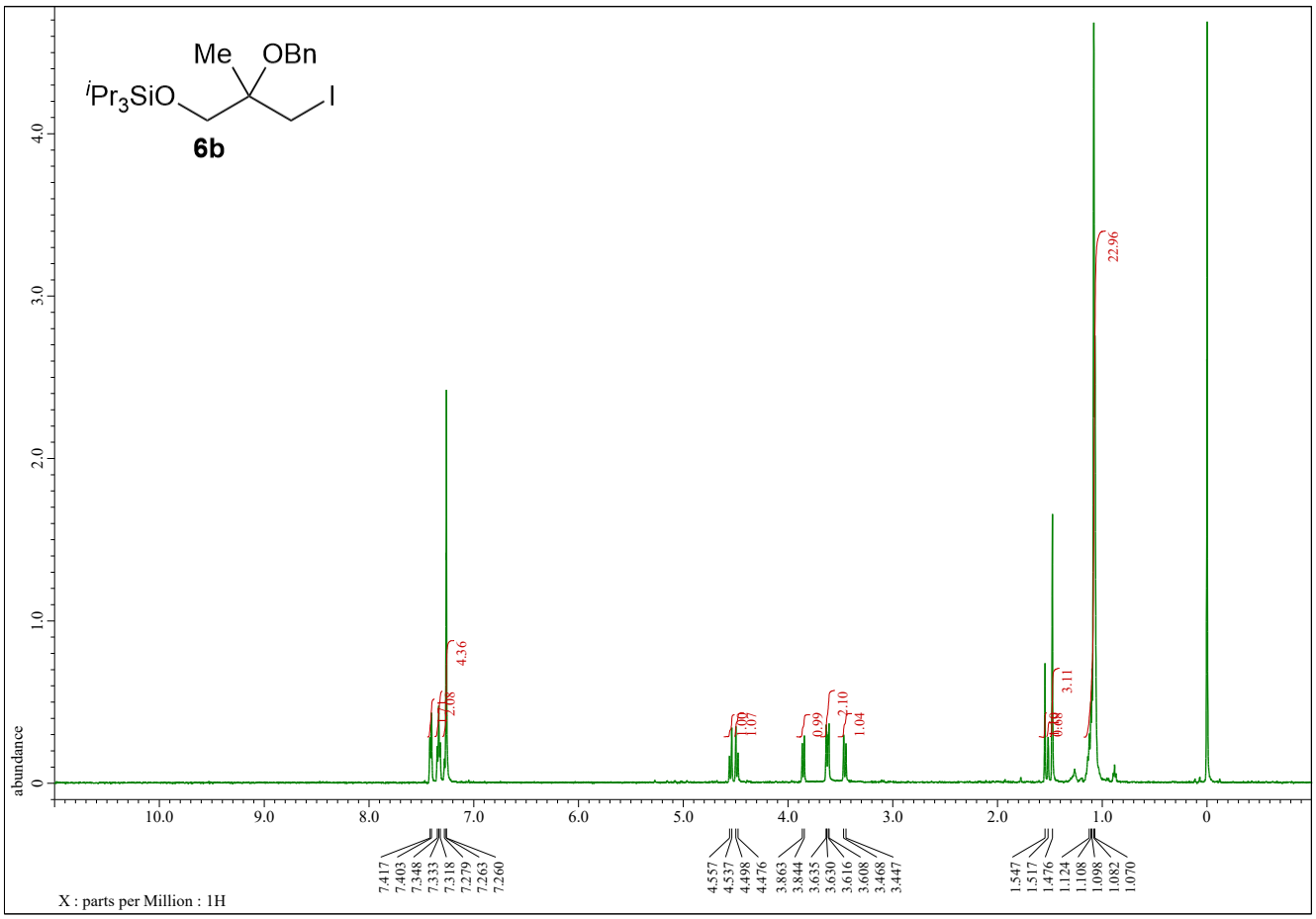


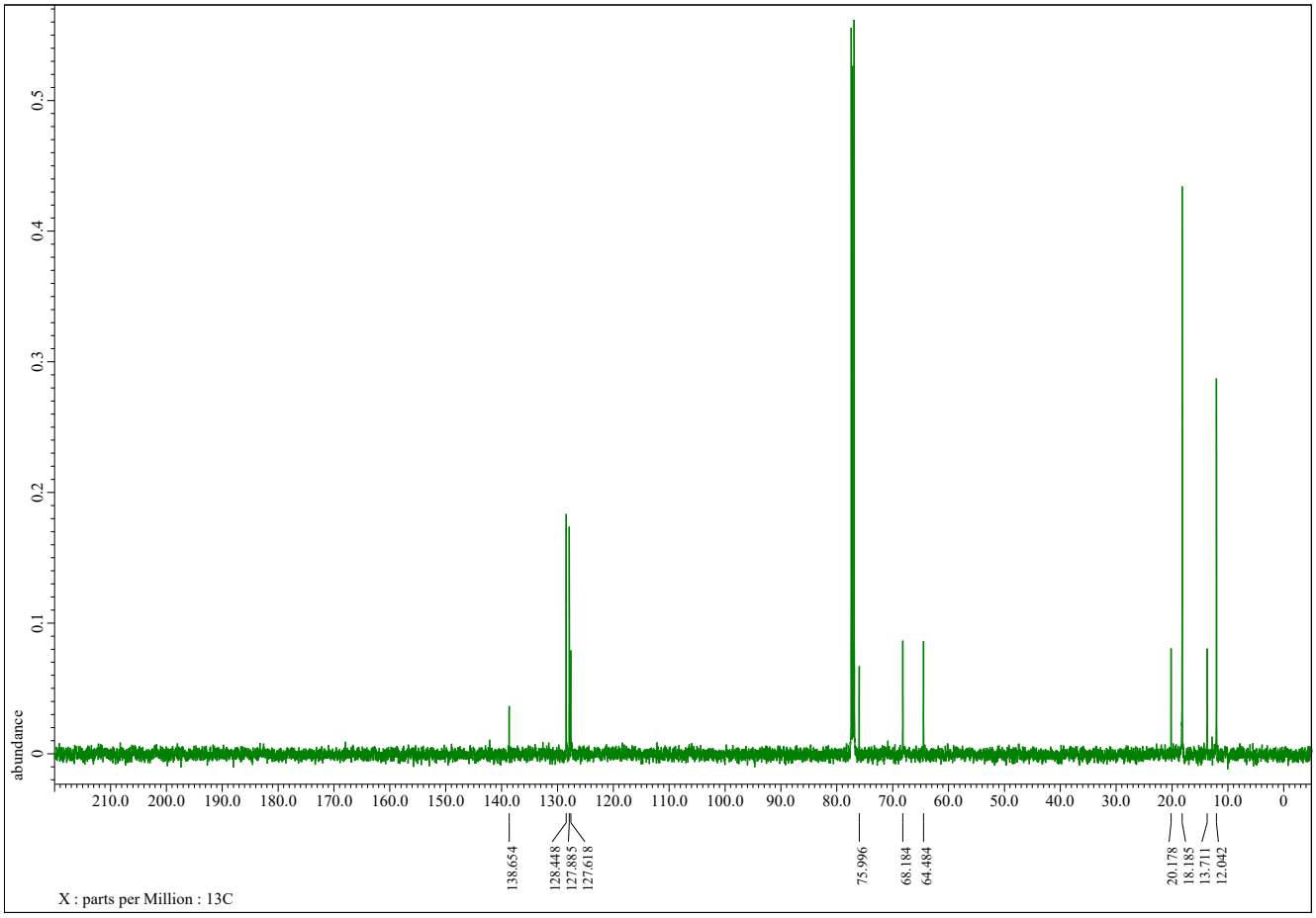
$^{1}H/^{13}C$ NMR spectra of iodoether **6a** (500/126 MHz, $CDCl_3$)



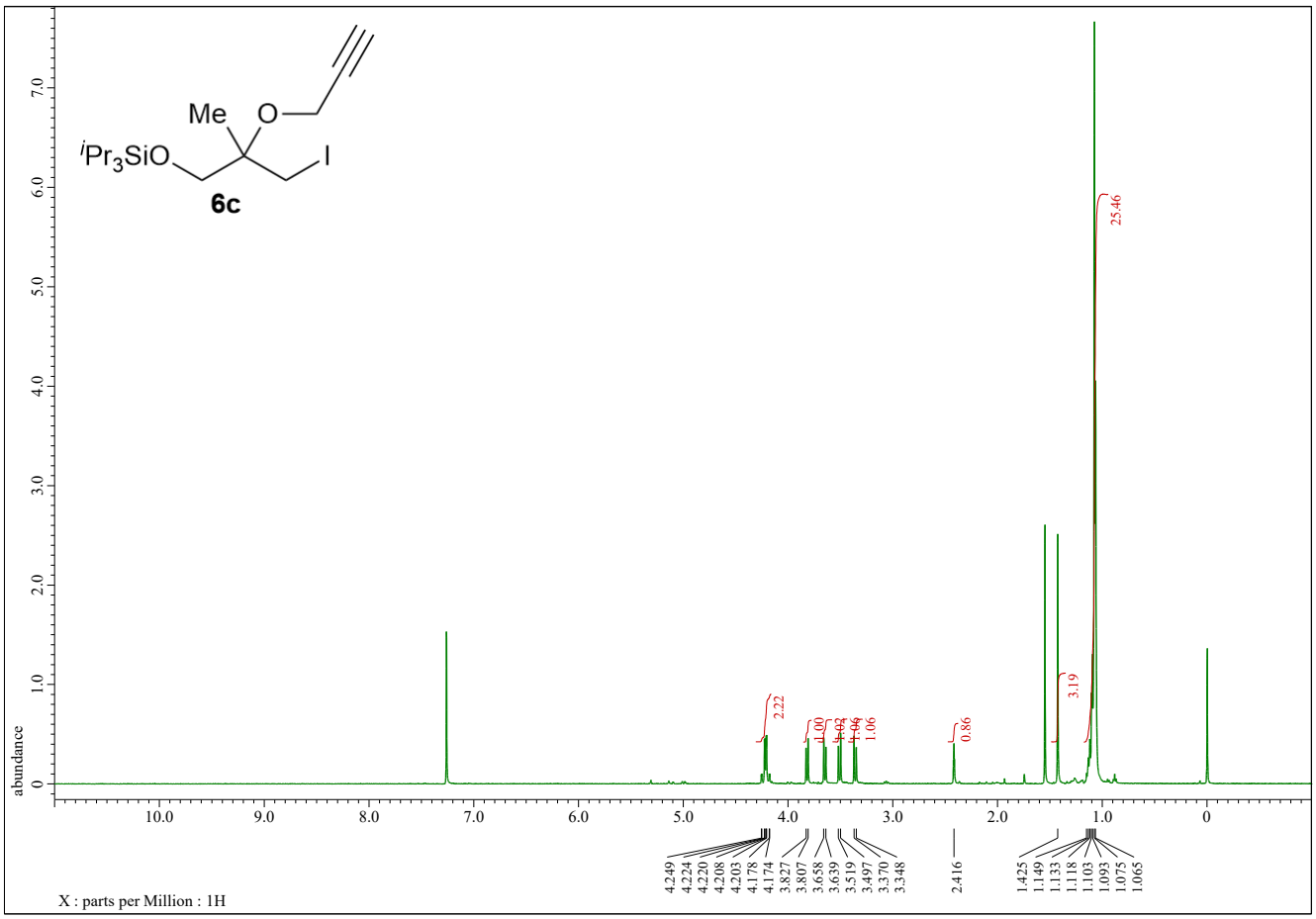


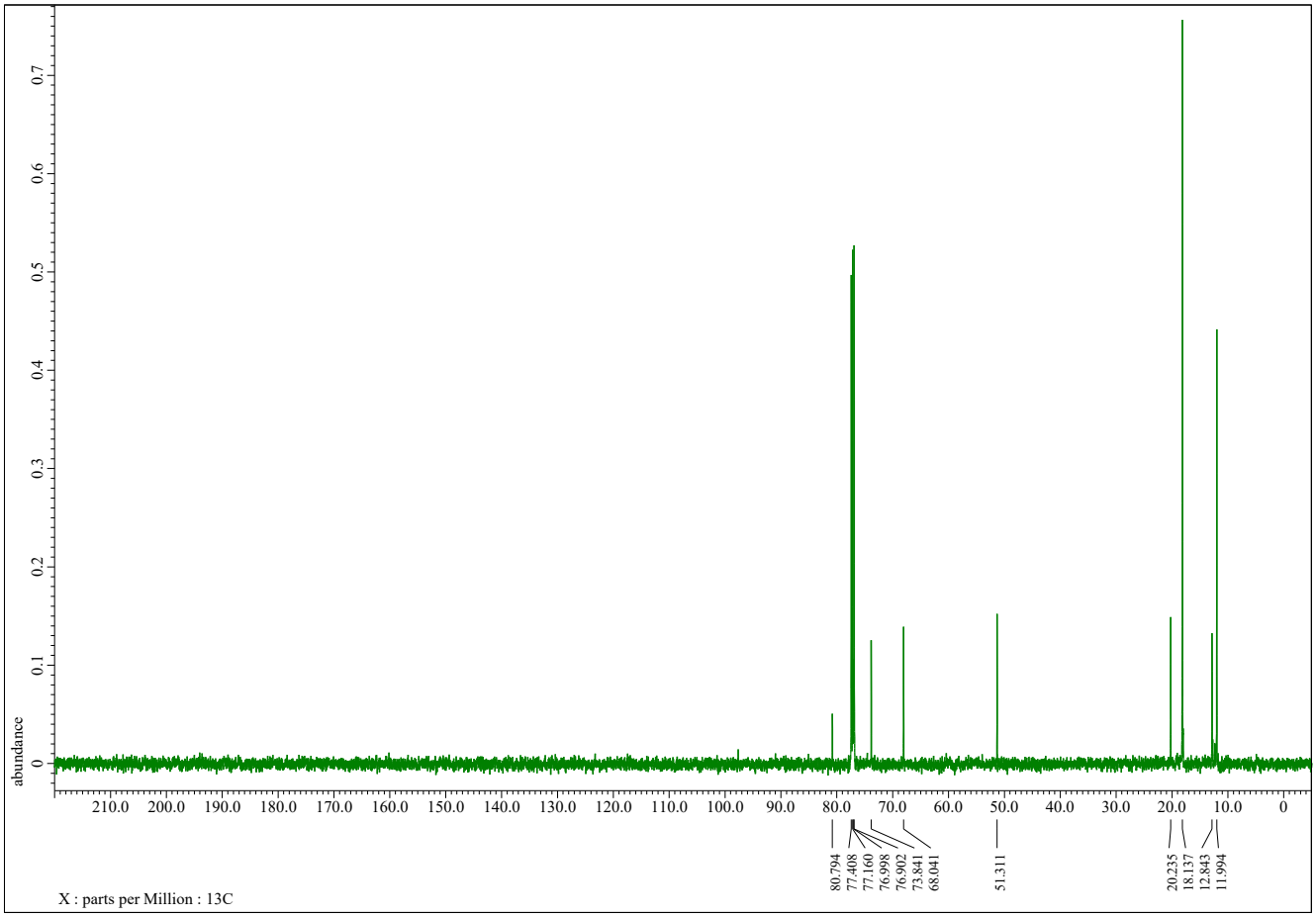
$^{1}H/^{13}C$ NMR spectra of iodoether **6b** (500/126 MHz, $CDCl_3$)



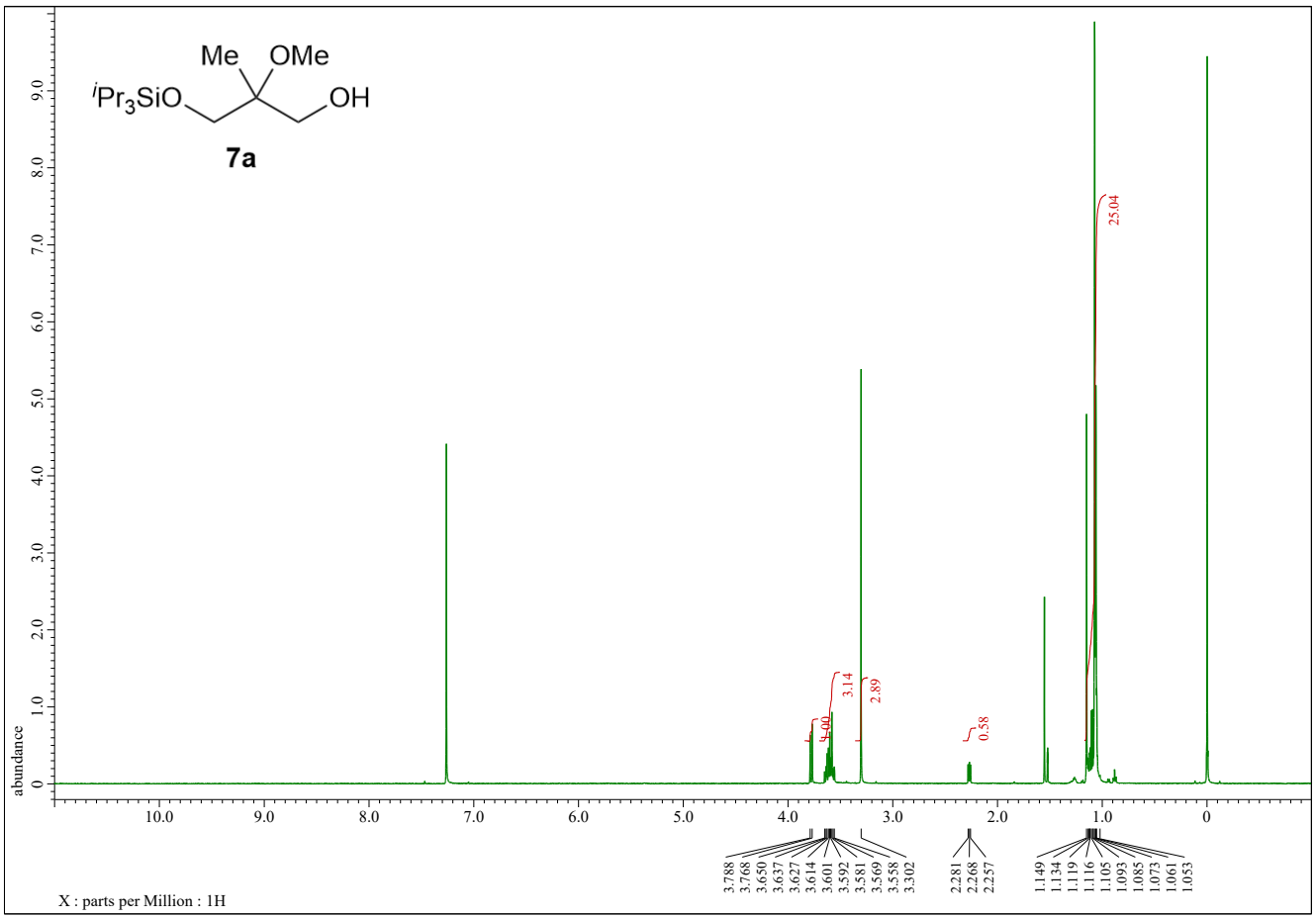


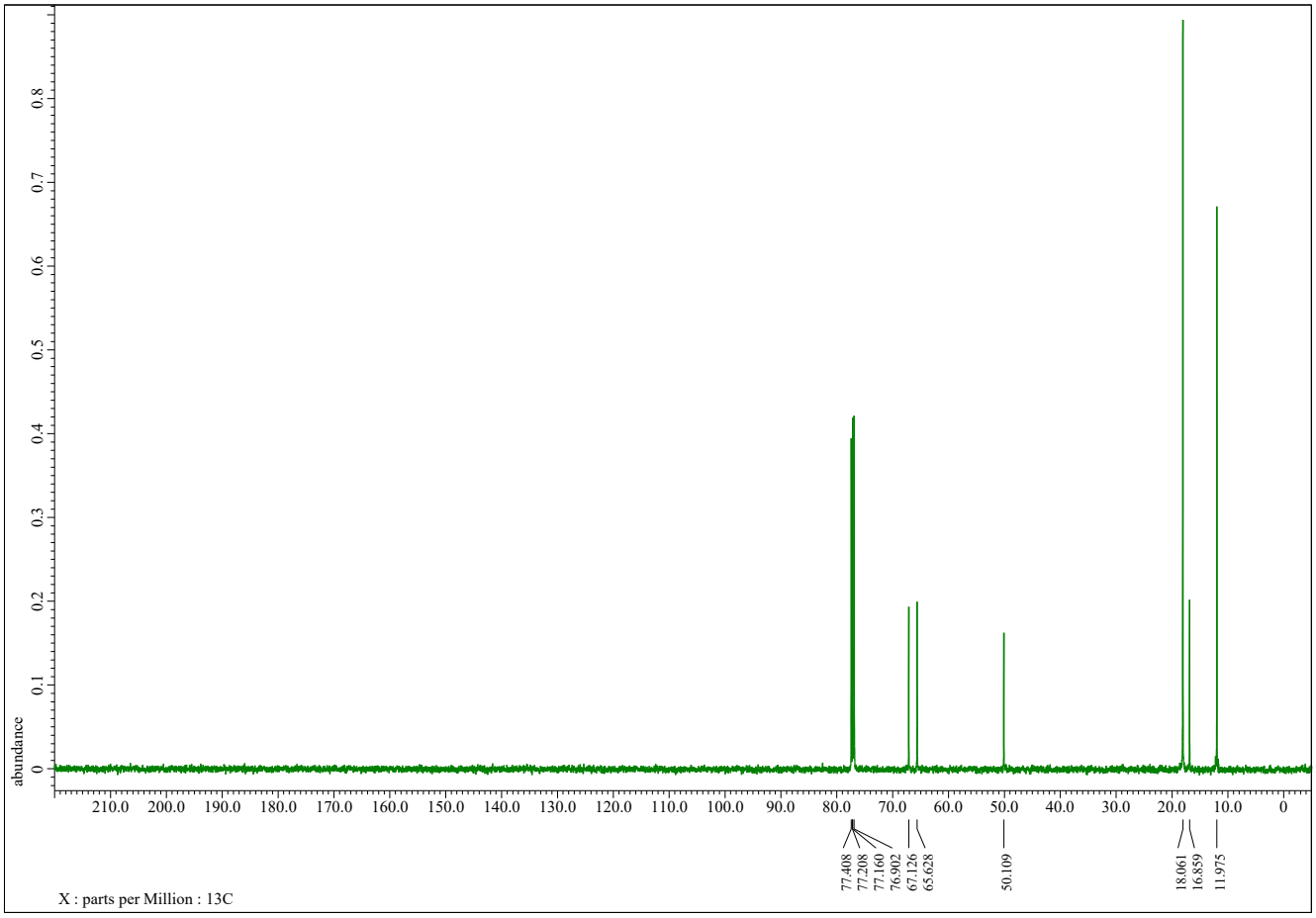
$^{1}H/^{13}C$ NMR spectra of iodoether **6c** (500/126 MHz, $CDCl_3$)



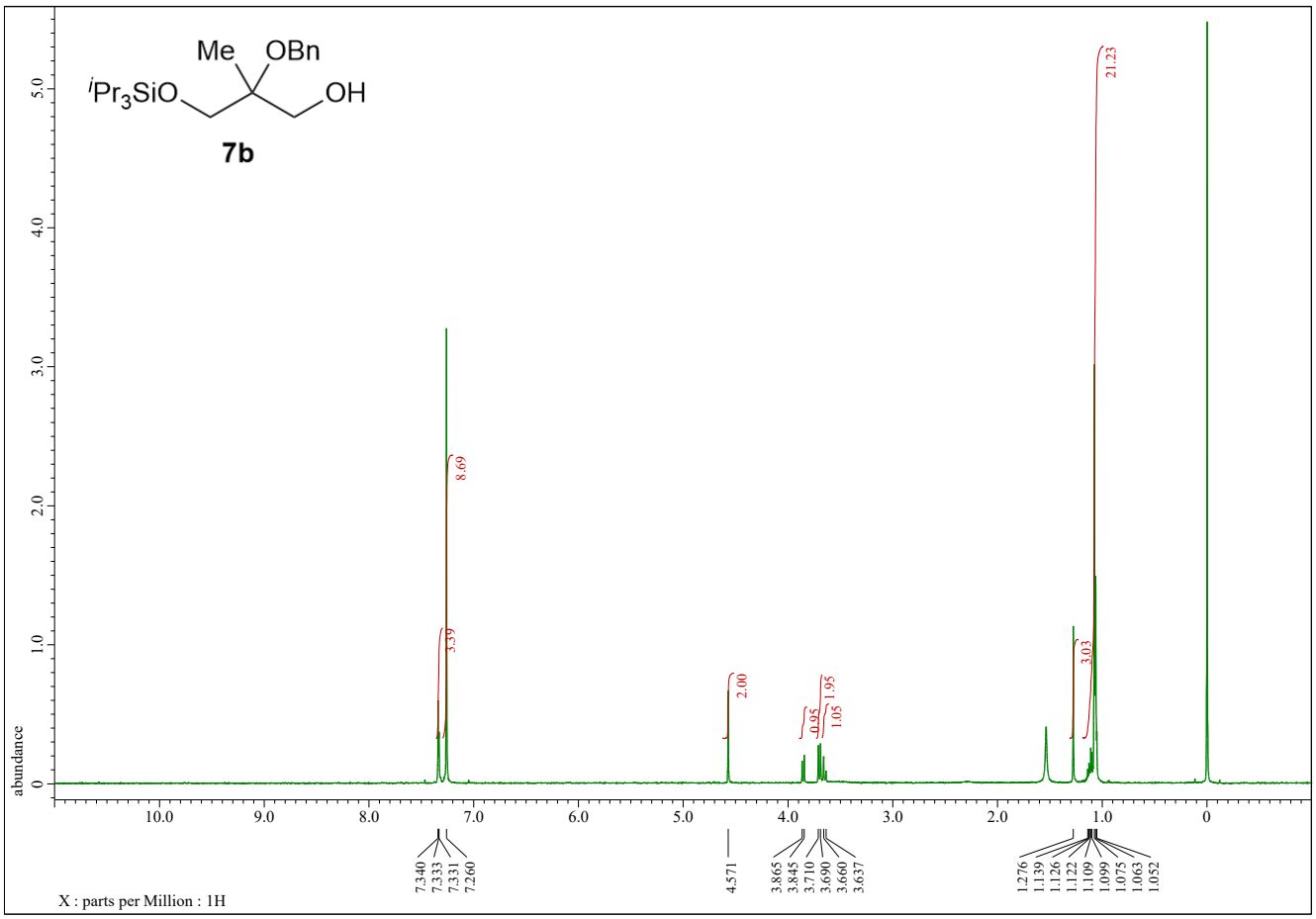


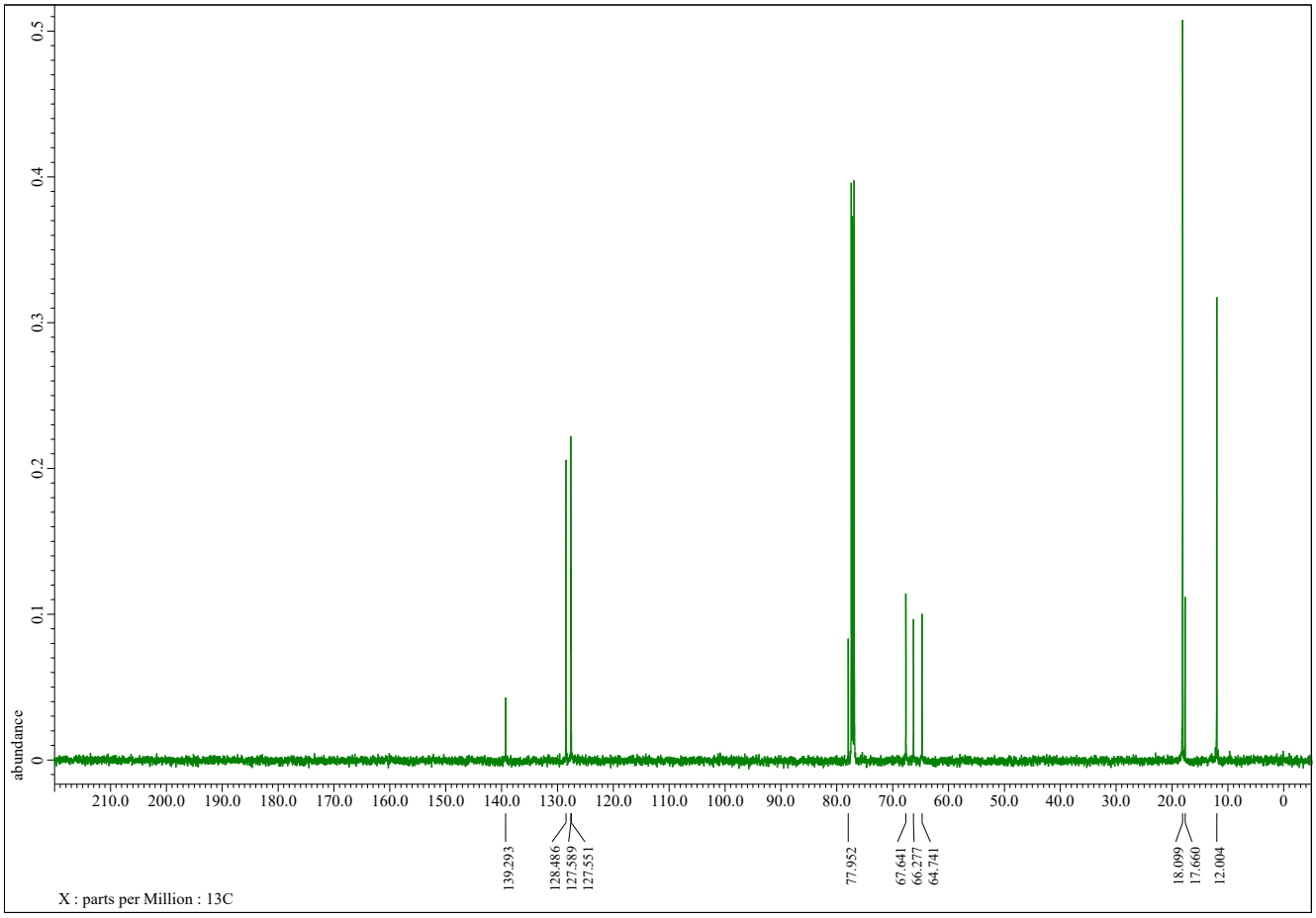
$^{1}H/^{13}C$ NMR spectra of alcohol **7a** (500/126 MHz, $CDCl_3$)



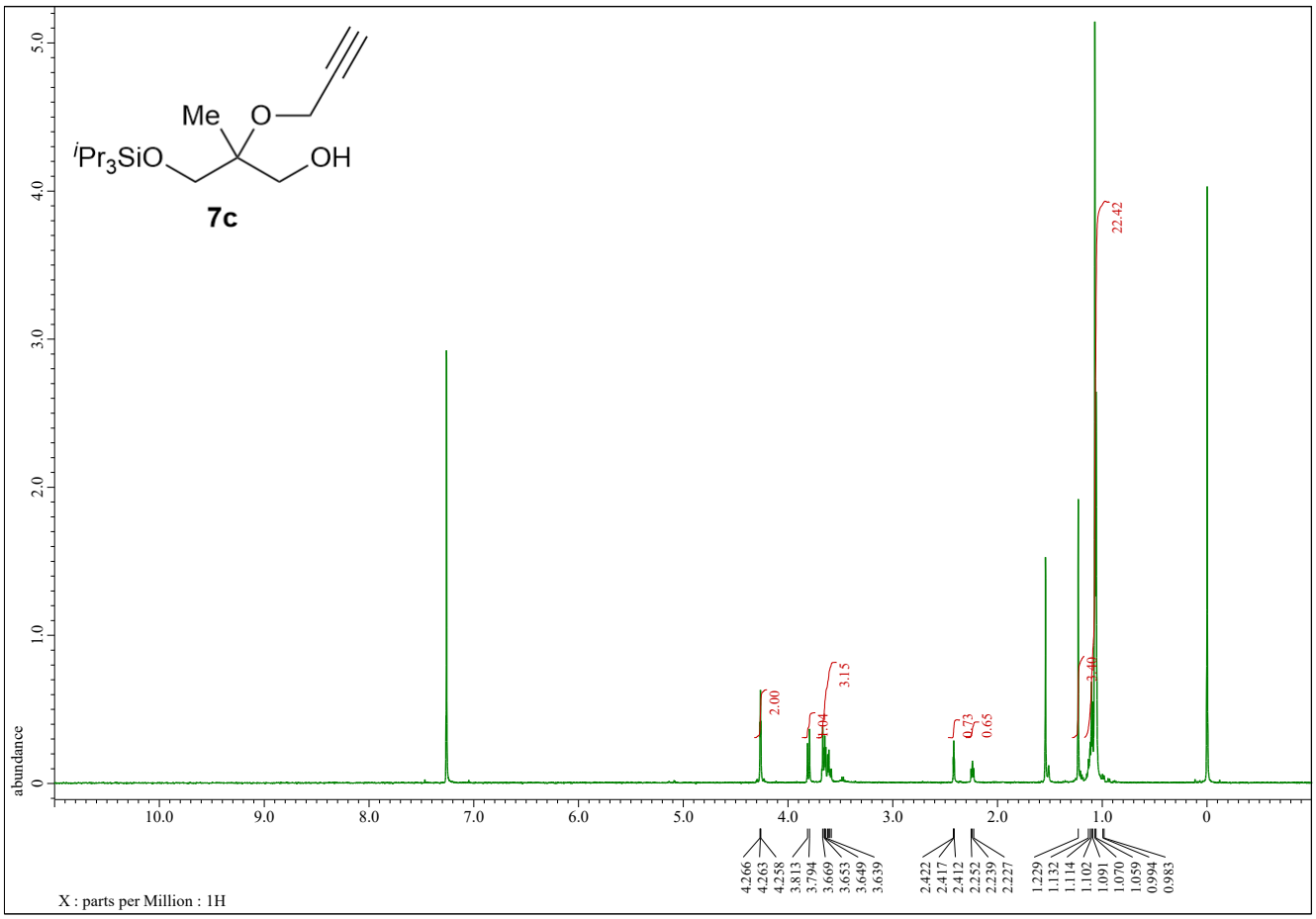


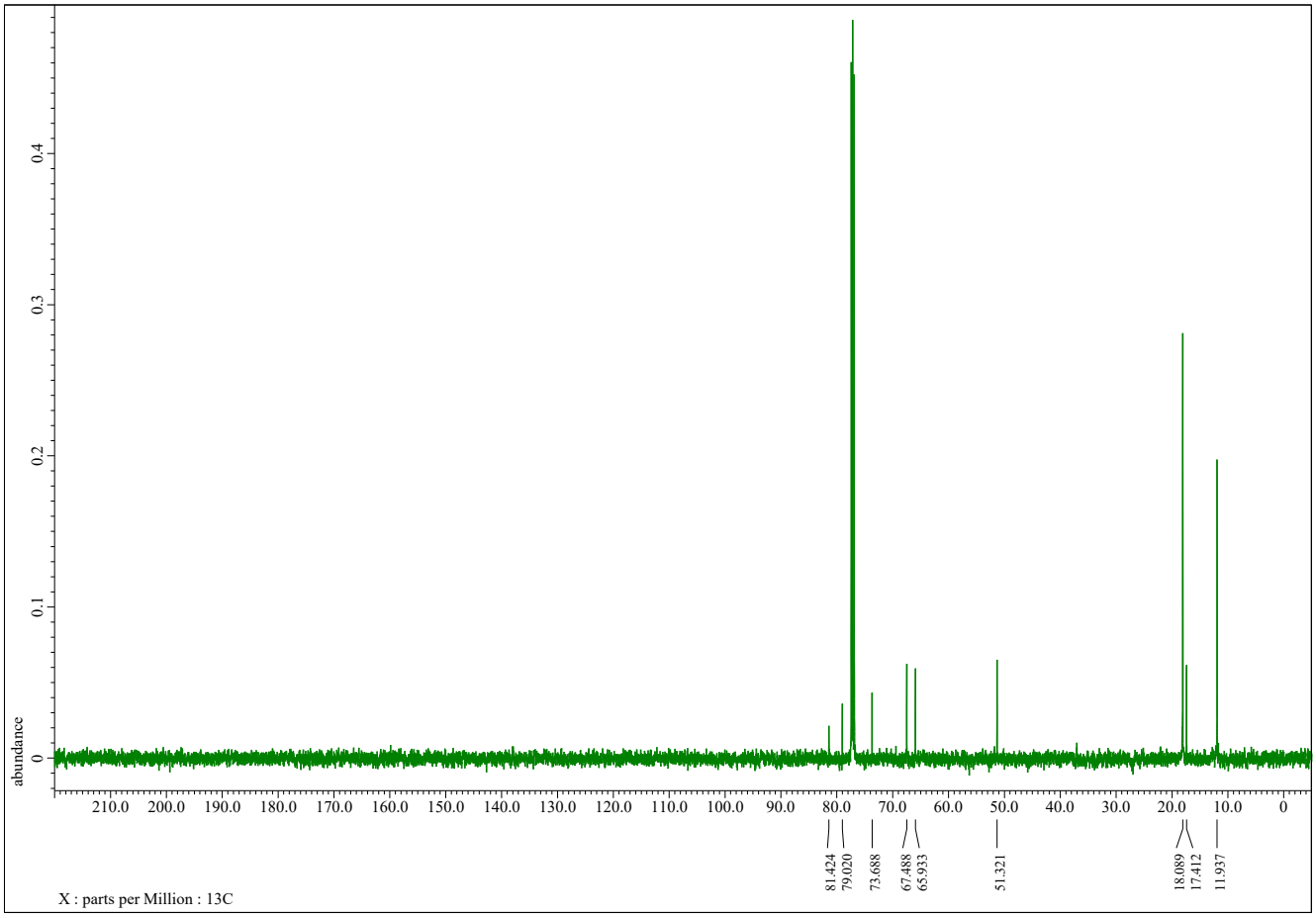
$^{1}H/^{13}C$ NMR spectra of alcohol **7b** (500/126 MHz, $CDCl_3$)



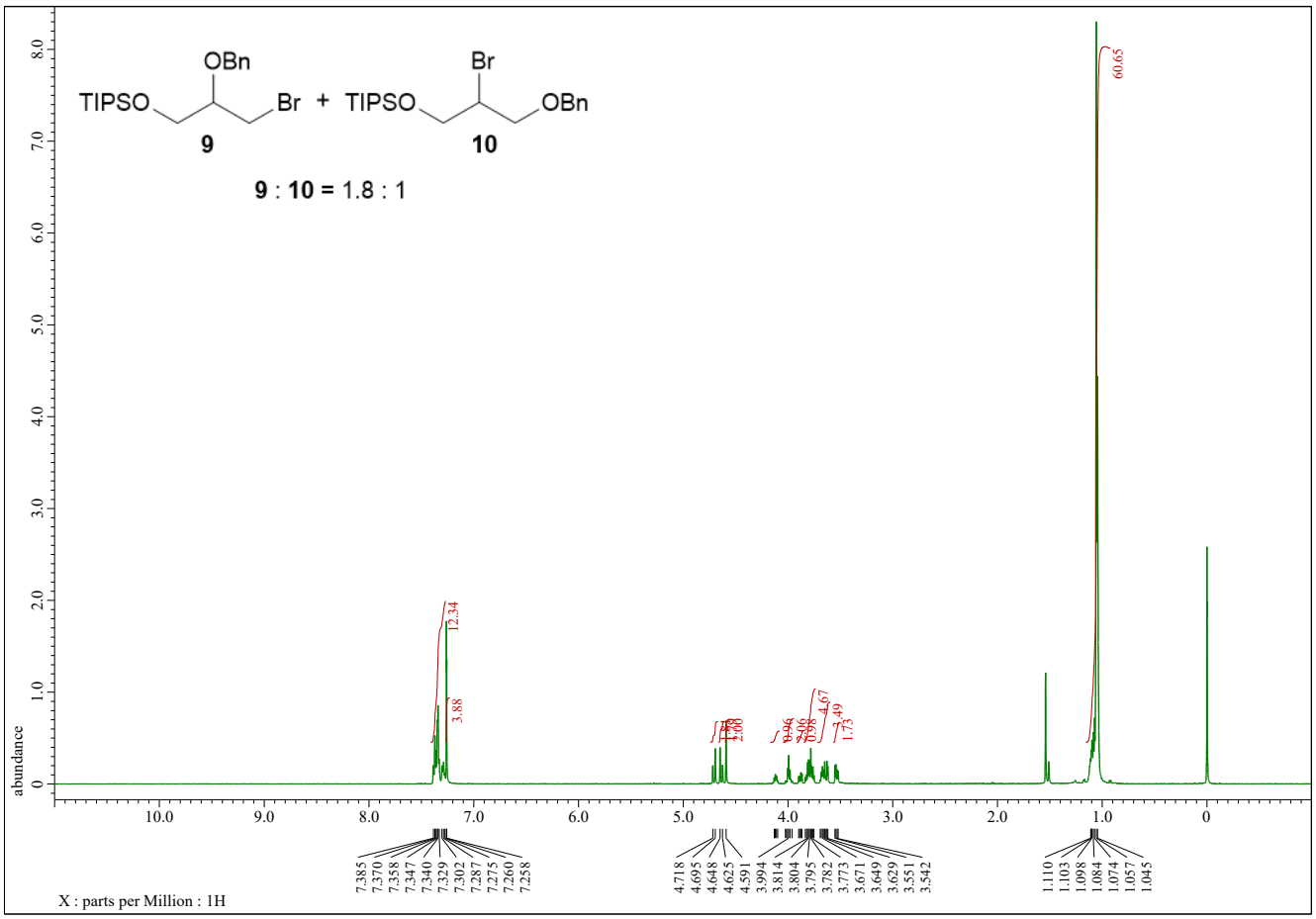


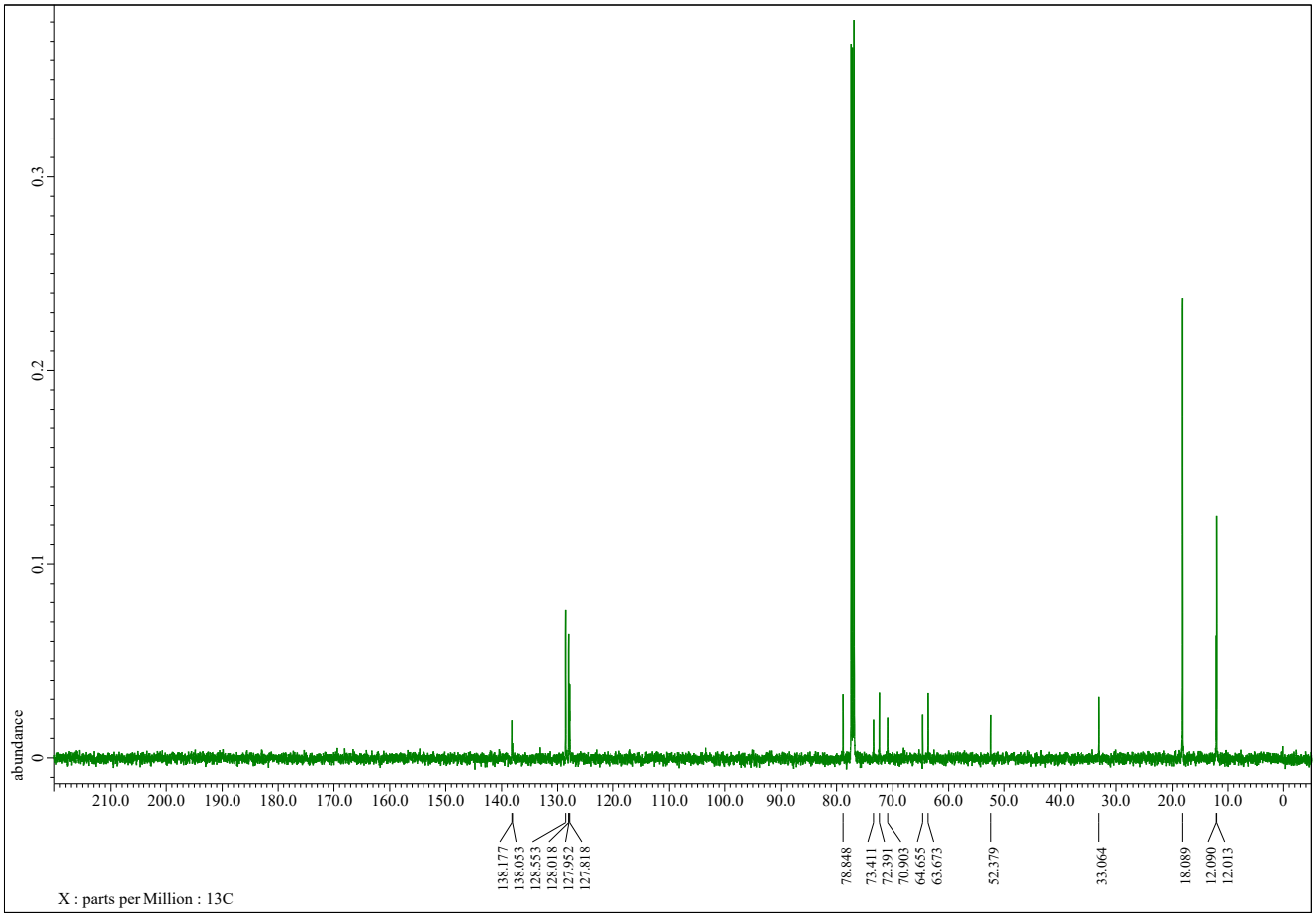
$^{1}H/^{13}C$ NMR spectra alcohol **7c** (500/126 MHz, $CDCl_3$)



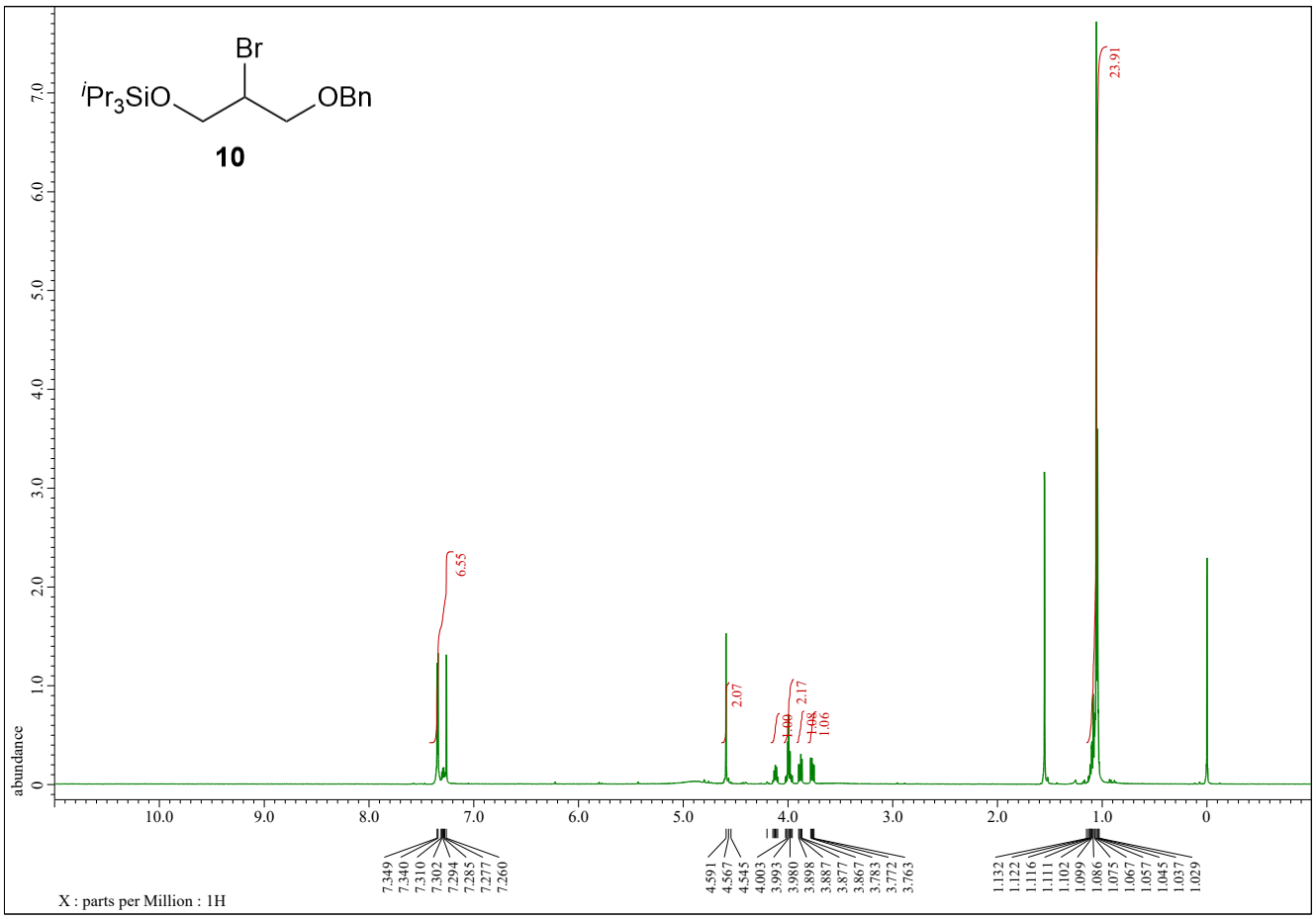


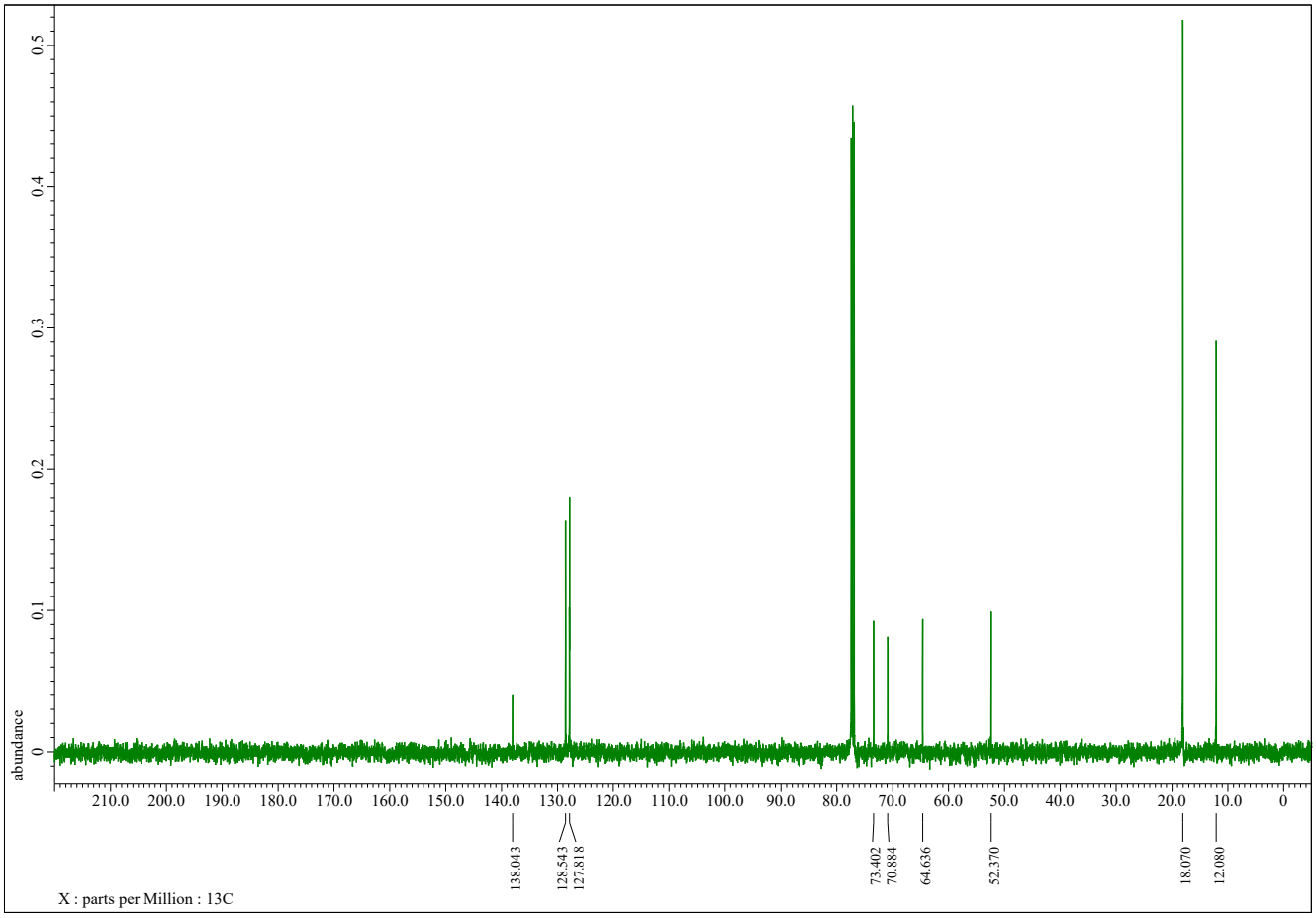
$^{1}H/^{13}C$ NMR spectra of a 1.8 mixture of **9** and **10** (500/126 MHz, $CDCl_3$)



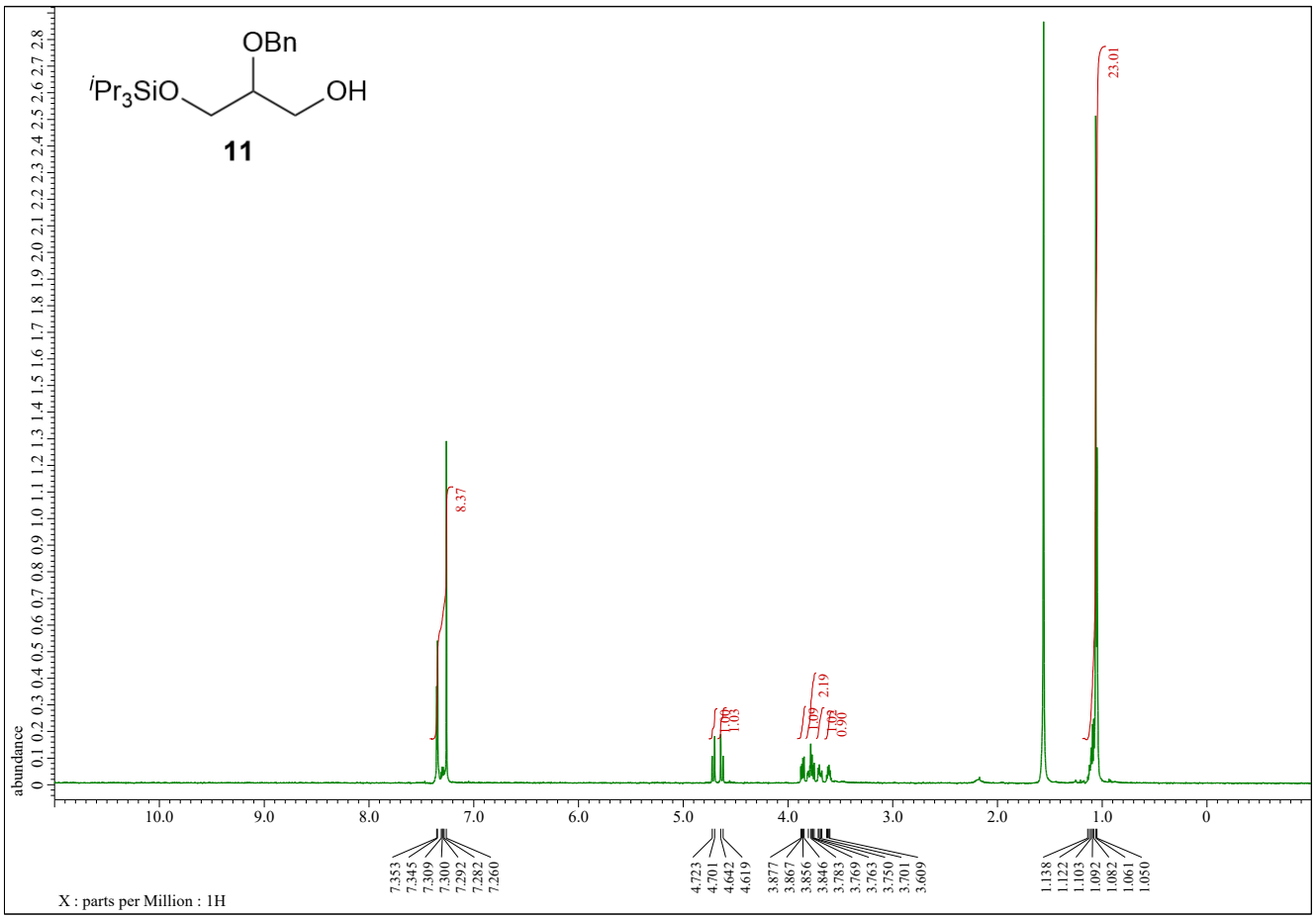


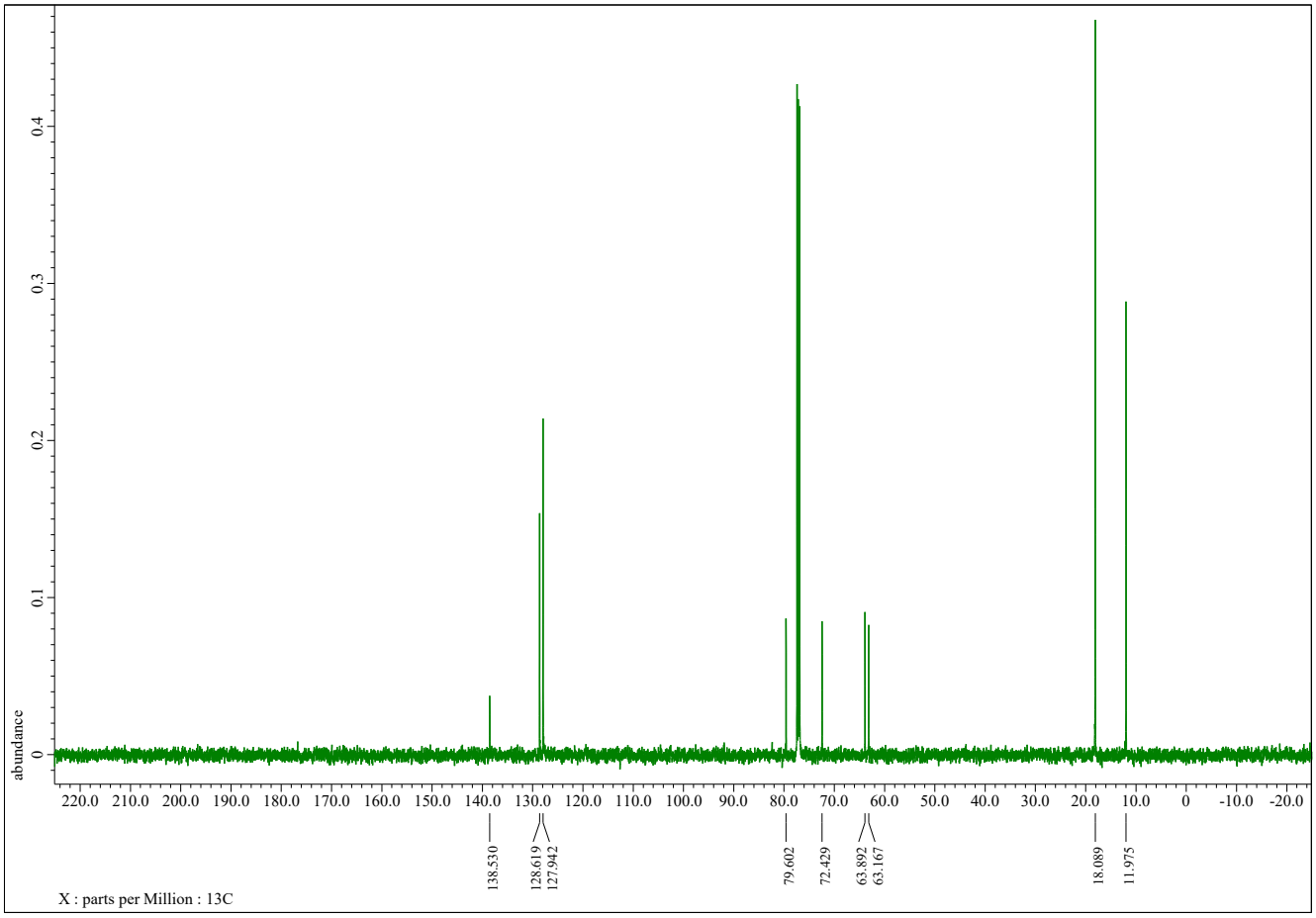
$^{1}H/^{13}C$ NMR spectra of secondary bromide **10** (500/126 MHz, $CDCl_3$)



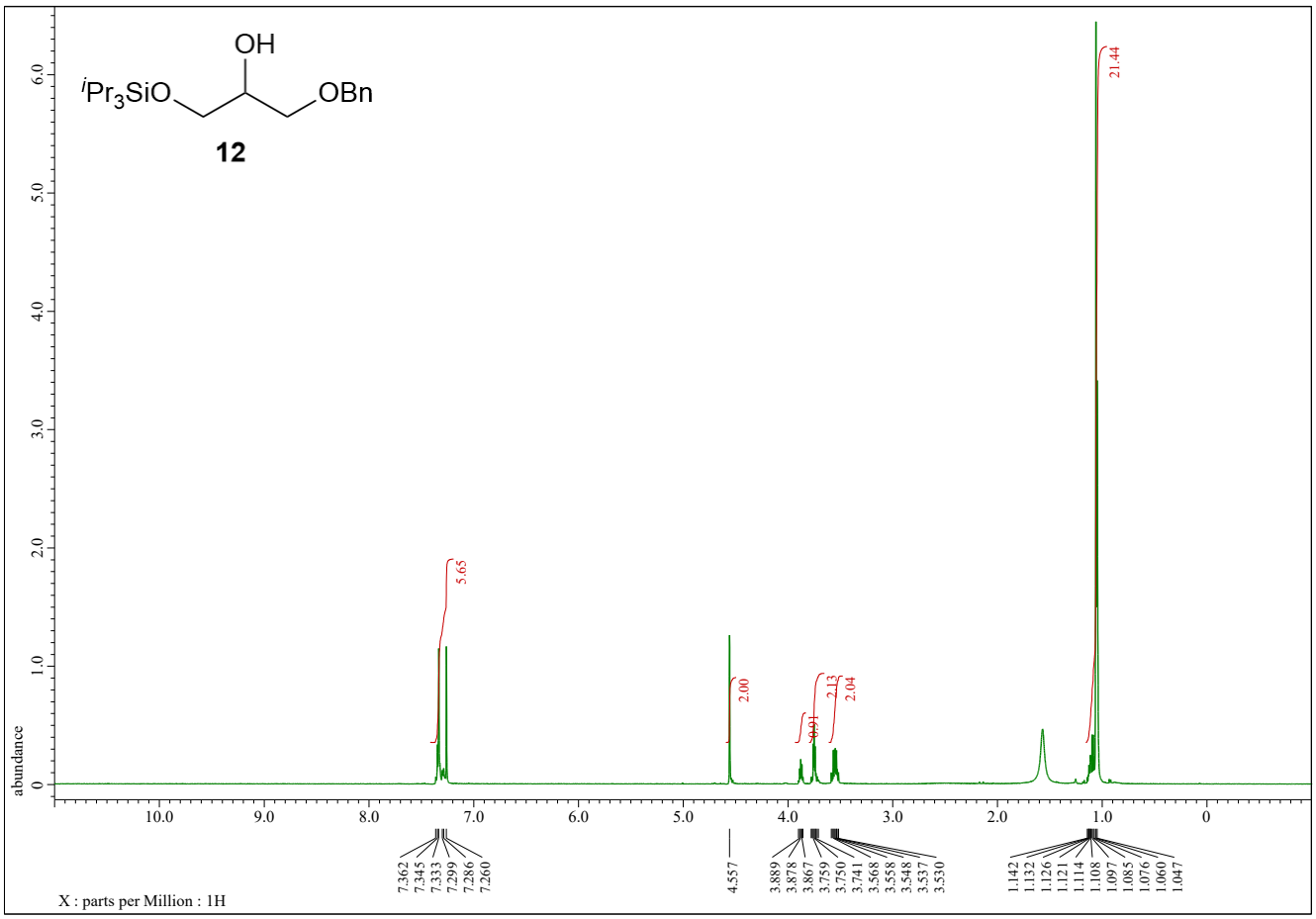


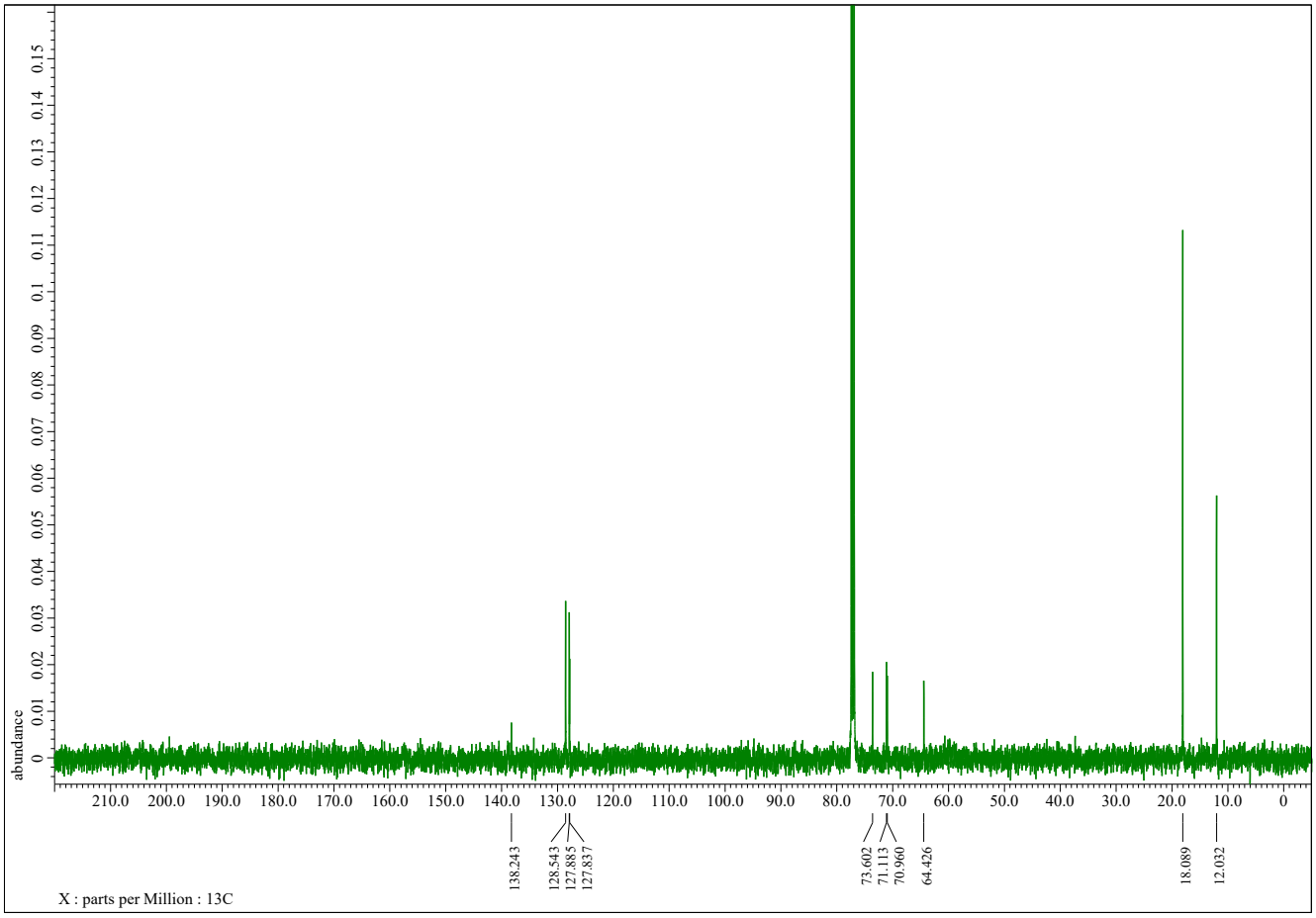
$^{1}H/^{13}C$ NMR spectra of primary alcohol **11** (500/126 MHz, $CDCl_3$)



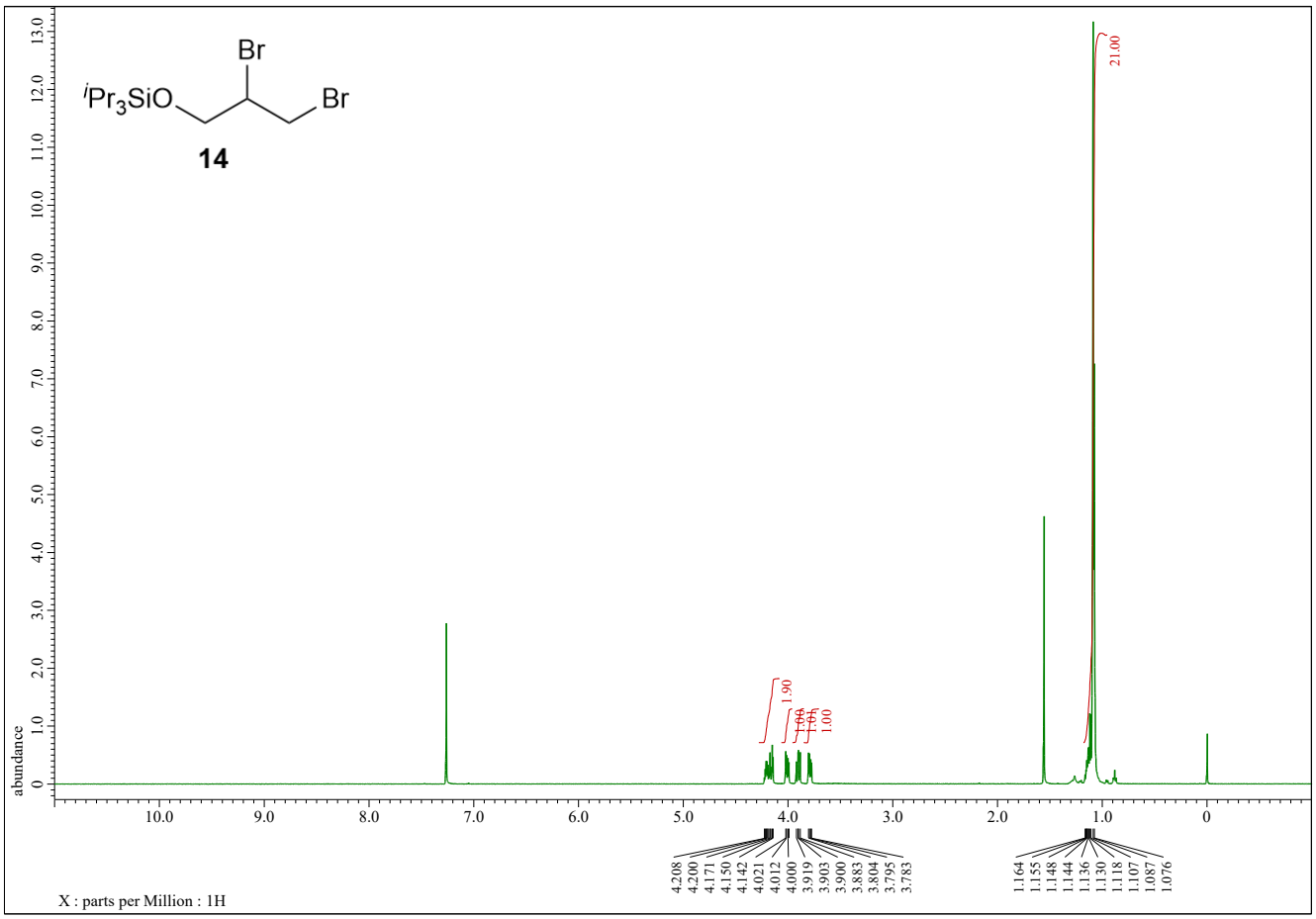


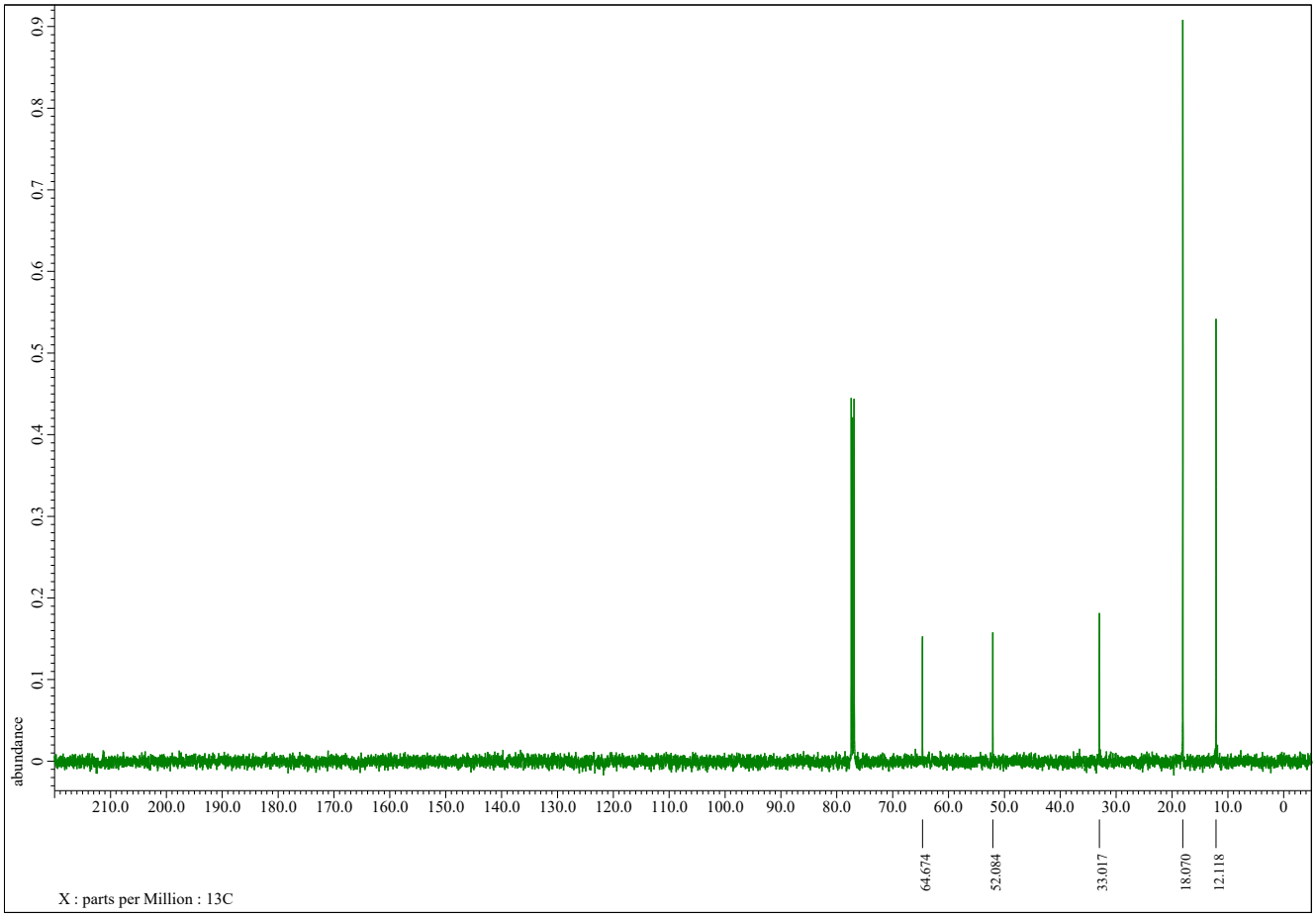
$^{1}H/^{13}C$ NMR spectra of secondary alcohol **12** (500/126 MHz, $CDCl_3$)



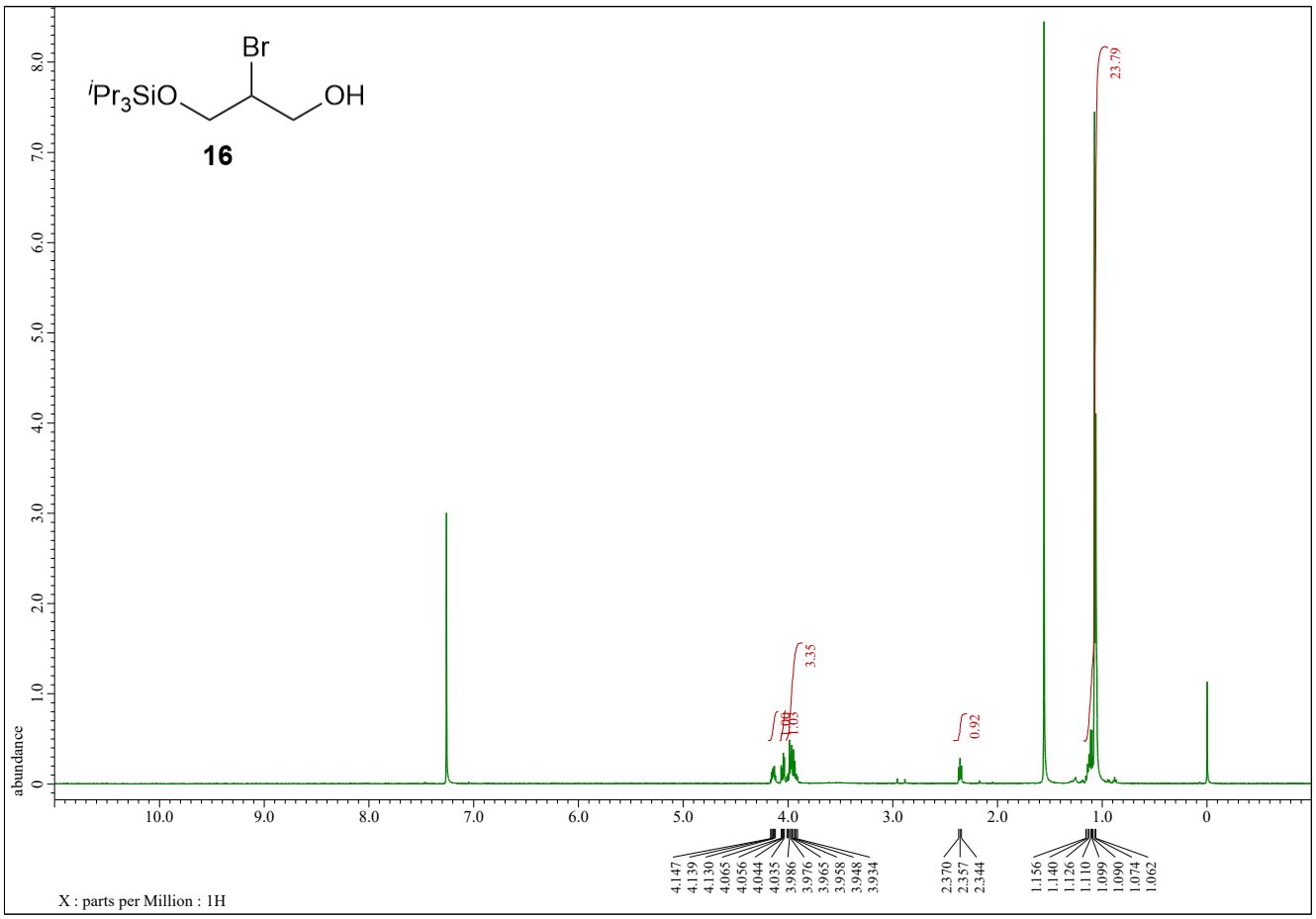


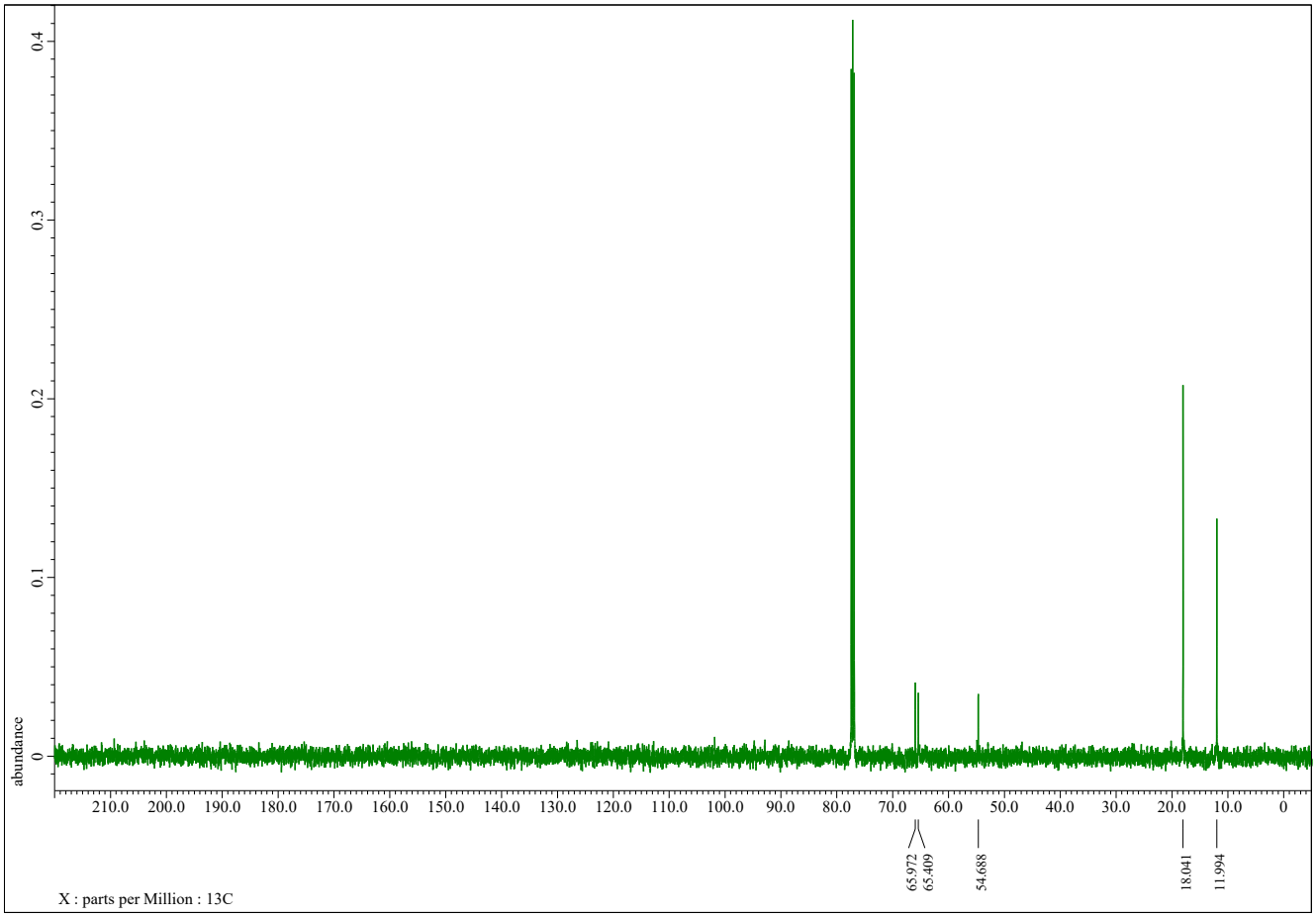
$^{1}H/^{13}C$ NMR spectra of dibromide **14** (500/126 MHz, $CDCl_3$)



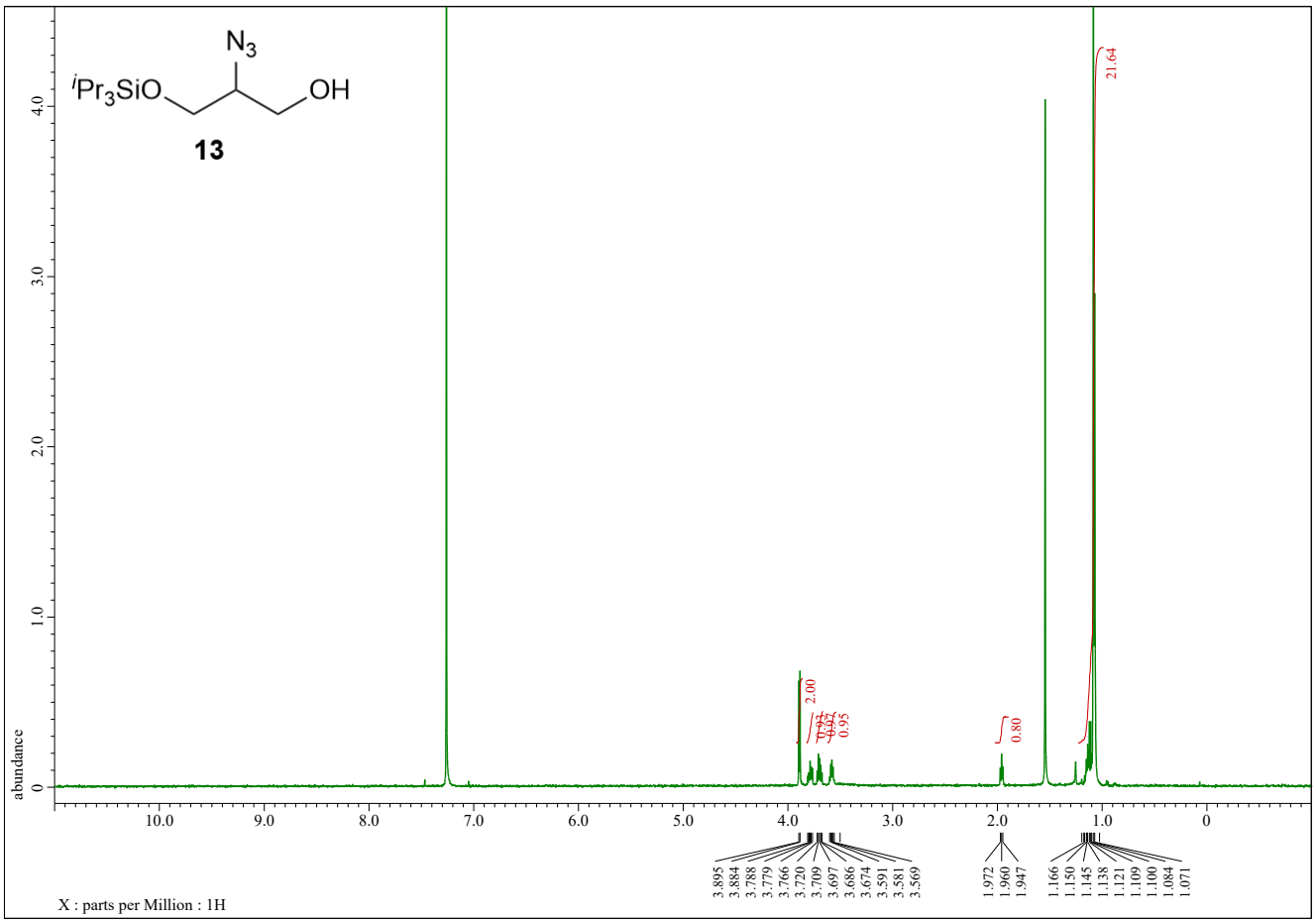


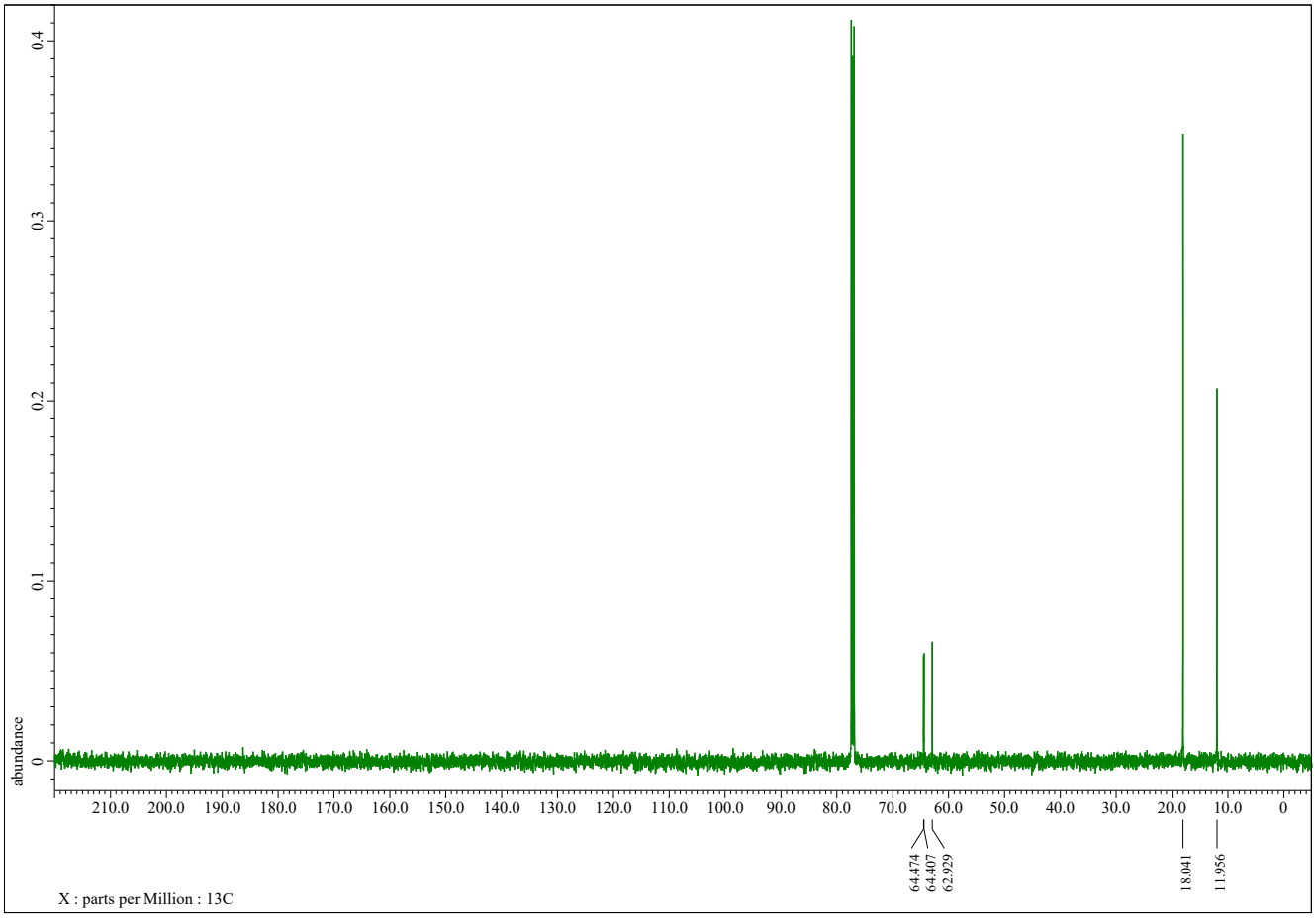
$^{1}H/^{13}C$ NMR spectra of bromohydrin **16** (500/126 MHz, $CDCl_3$)



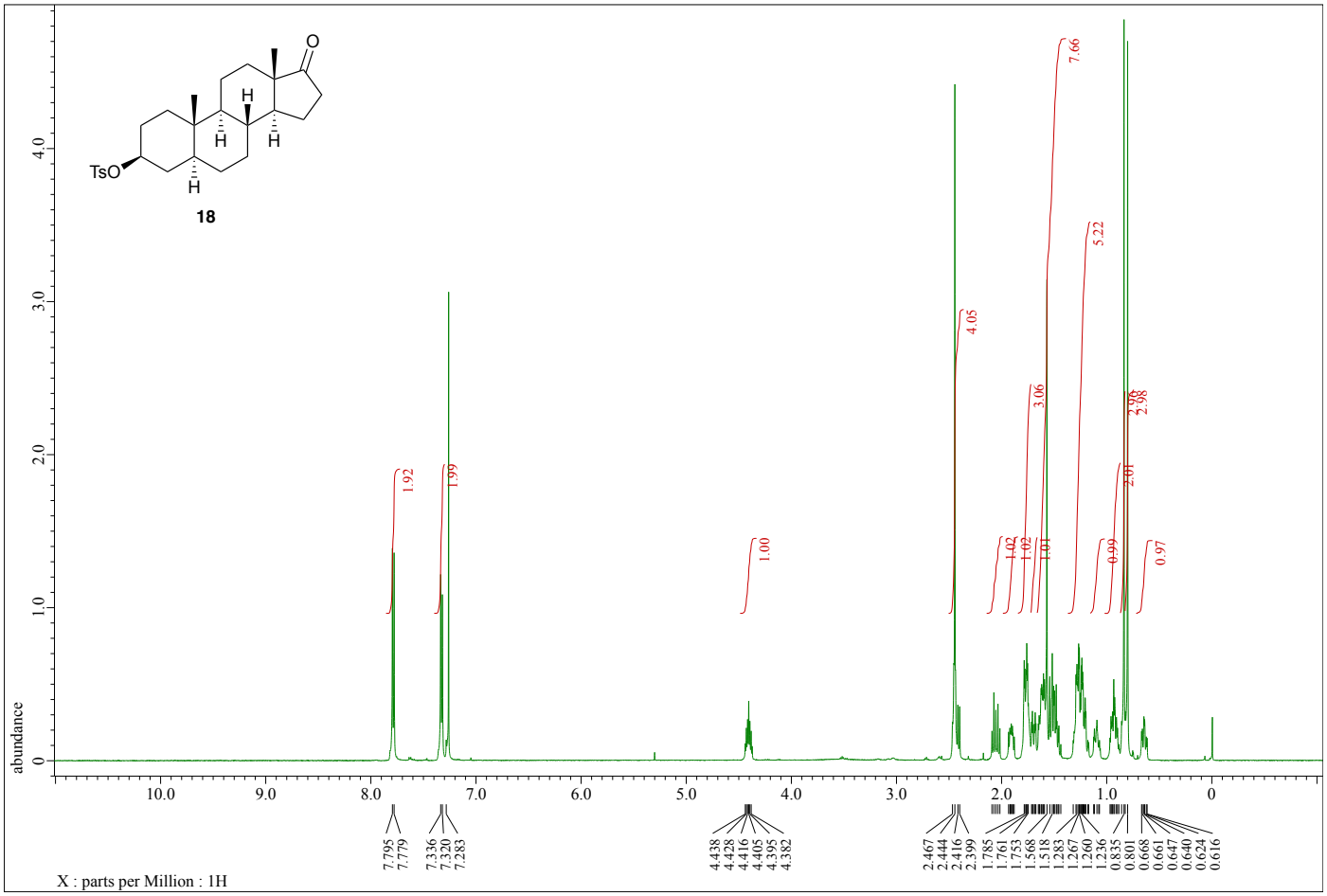


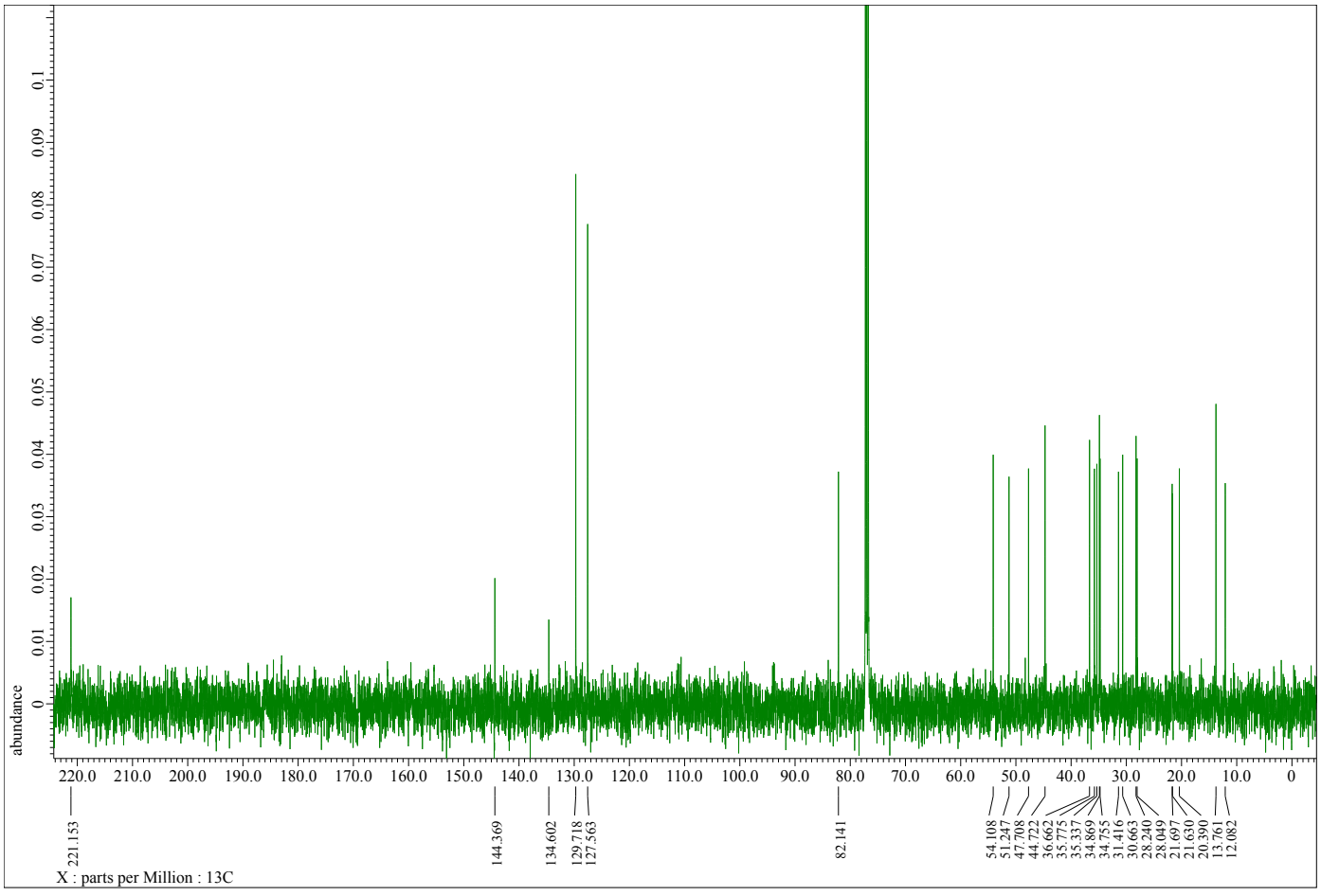
$^{1}H/^{13}C$ NMR spectra of azidoalcohol **13** (500/126 MHz, $CDCl_3$)



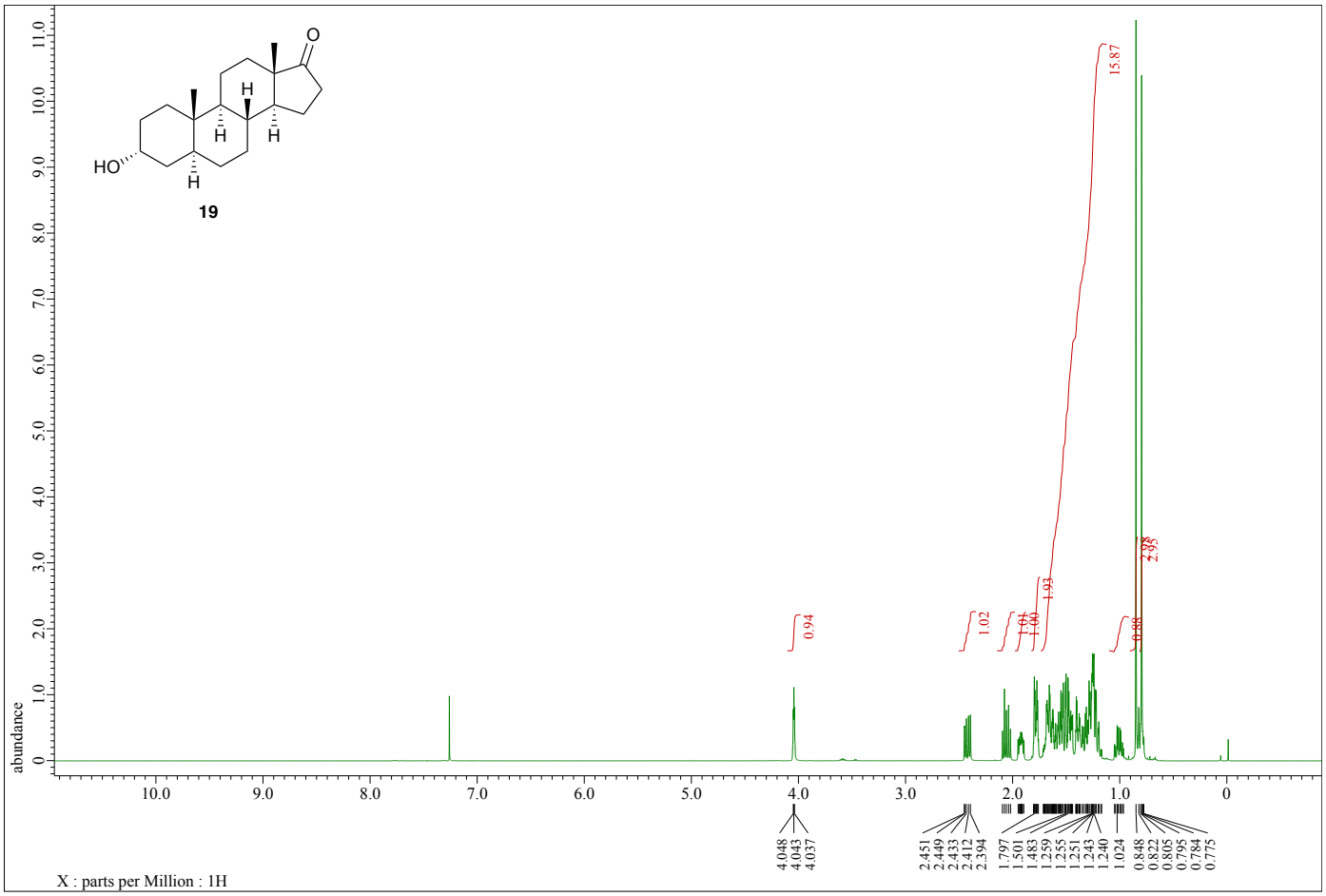


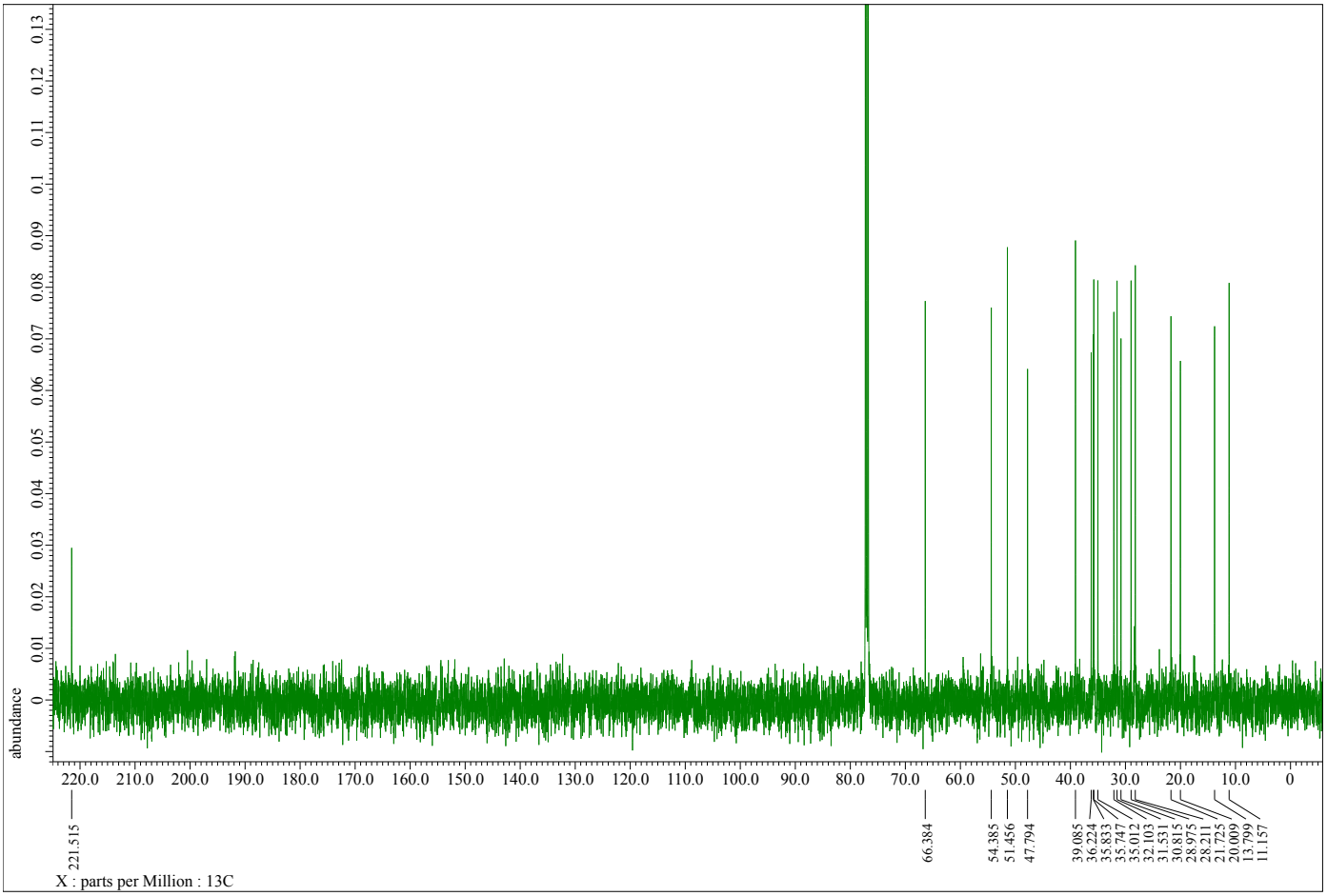
$^{1}H/^{13}C$ NMR spectra of tosylate **18** (500/126 MHz, $CDCl_3$)



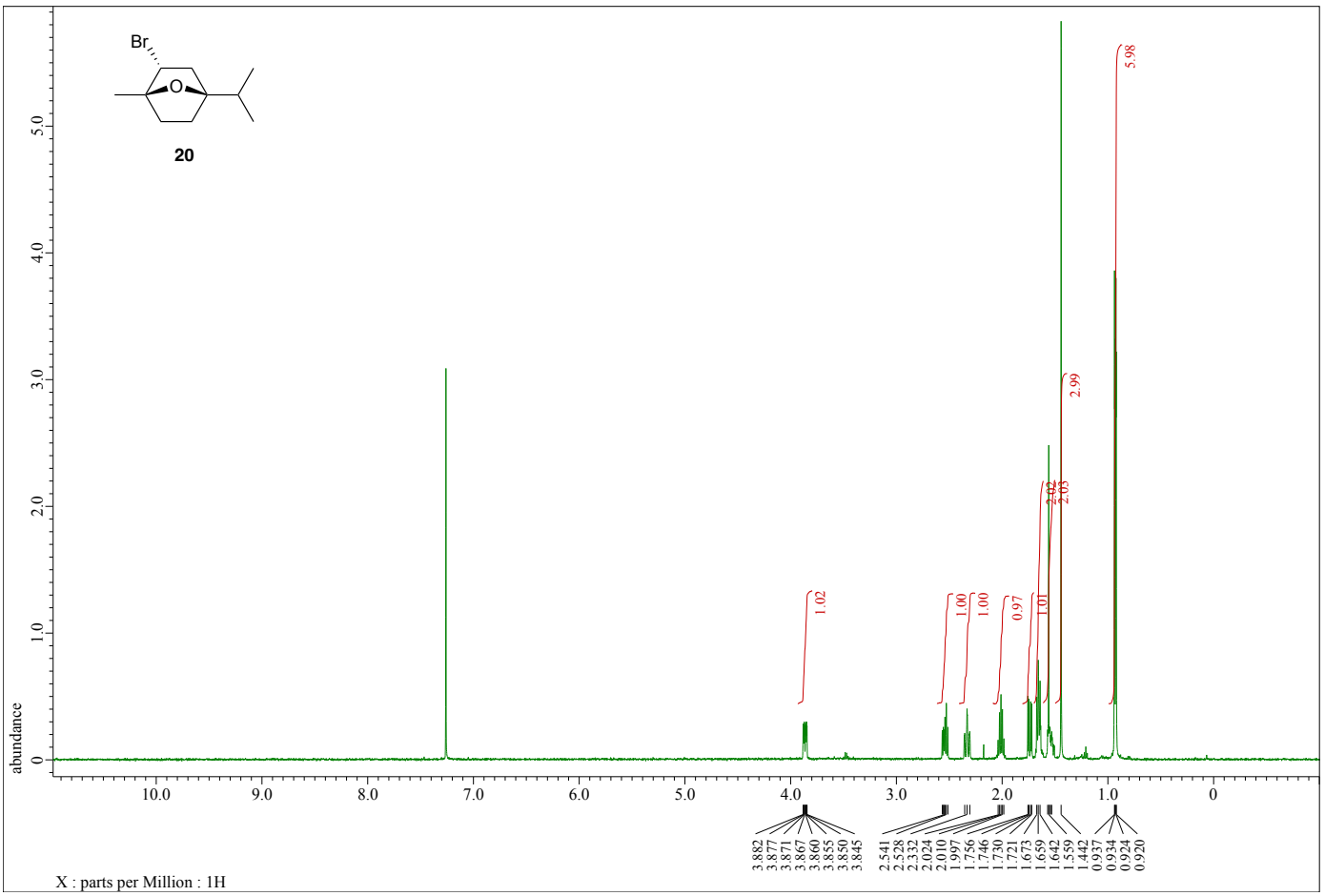


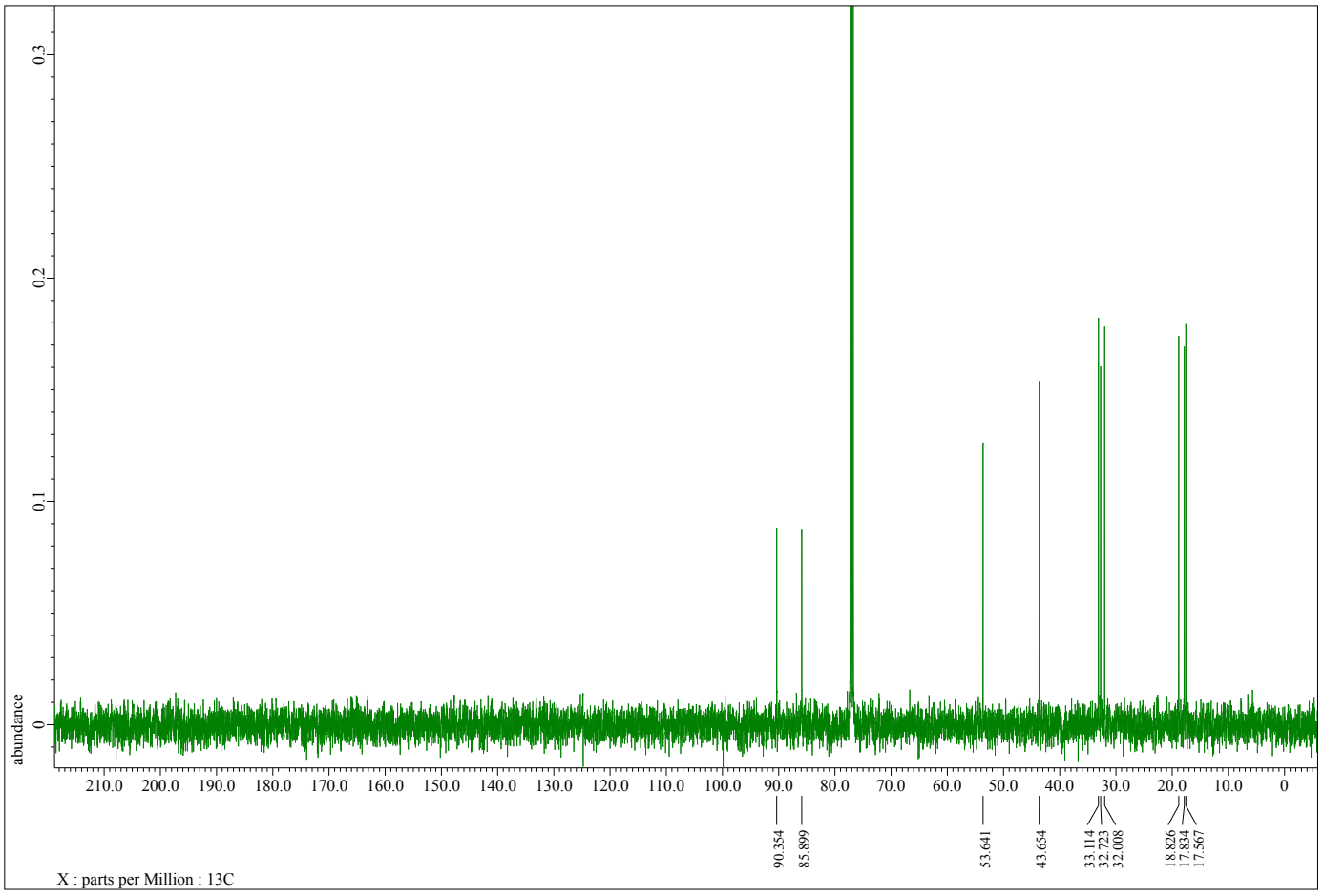
$^{1}H/^{13}C$ NMR spectra of androsterone **19** (500/126 MHz, $CDCl_3$)





$^{1}H/^{13}C$ NMR spectra of bromide **20** (500/126 MHz, $CDCl_3$)





^{1}H NMR spectrum of alcohol **21** (500 MHz, $CDCl_3$) and ^{13}C NMR spectrum of **21** (126 MHz, benzene-d_6)