
Iterative Synthesis of Alkenes by Insertion of Lithiated Epoxides into Boronic Esters

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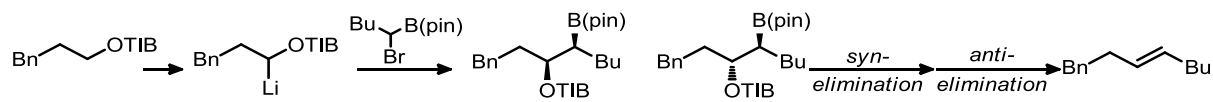
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Author contribution: S. Fritsch conducted experiments towards exploiting the different steric demand of alkyl substituents for the synthesis of **3f** and **3g**. All other experiments were conducted by K. Bojaryn. C. Hirschhäuser conceived the project and wrote the manuscript.

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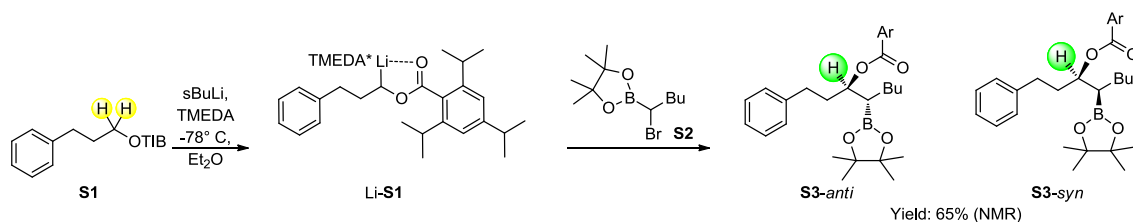
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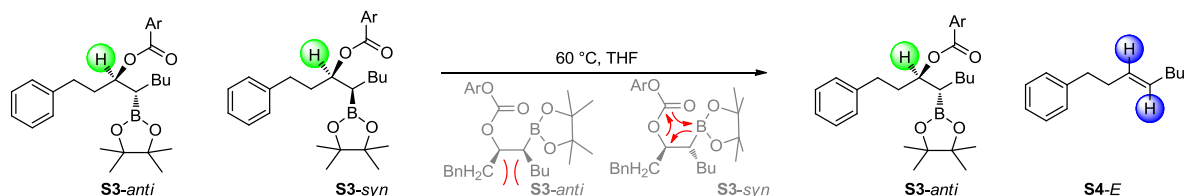
Preceding Experiments

Alkene Formation from a lithiated Benzoate and an α -Halo Boronic Ester

In an attempt to react α -halo boronic esters with chiral carbanions generated by direct lithiation, we found that lithiated *N,N*-diisopropylcarbamates reacted poorly with α -haloboronic esters like **S2**. Although numerous different conditions were tested these reactions delivered poor yields (<20%) and were plagued by competing alkene formation. Lithiated benzoates (Li-**S1**) on the other hand performed much better in this type of reaction.



Benzoate **S1** (1.42 equiv.) was lithiated at $-78\text{ }^{\circ}\text{C}$ with *s*BuLi (1.39 equiv.) and TMEDA (1.39 equiv.) in dry Et_2O (3 h). A solution of **S2** (1.00 equiv.) in Et_2O was added at the same temperature and after 1 h a solution of ZnCl_2 (3.9 equiv.) was added. The reaction mixture was stirred for 19 h during which the cooling bath was allowed to warm up to rt. After an aqueous workup (NH_4Cl) a mixture of substitution products of type **S3** was isolated. The ^1H NMR (**A**, see next page) of the crude product in CDCl_3 revealed a broad multiplet 5.32–5.39 ppm (highlighted in **green**), which was attributed to **S3-anti** and **S3-syn**, as well as a triplet at 4.34 ppm (highlighted in **yellow**), characteristic for **S1**.¹ Based on later addition of an internal standard, yields of 18% for **S1** and 65% for **S3-anti** and **S3-syn** were calculated. A ratio of diastereomers **S3-anti** and **S3-syn** could not be determined from the data.

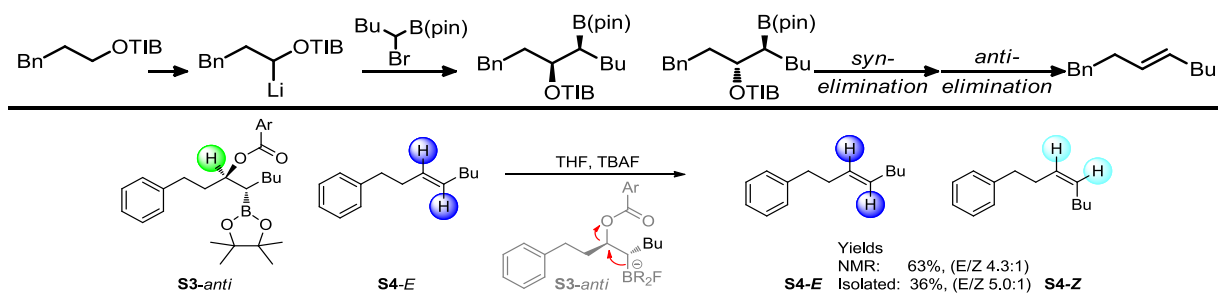


As alkene formation was a major side reaction for *N,N*-diisopropylcarbamates we attempted to deliberately induce thermal *syn*-elimination for benzoates of type **S3** by heating. Therefore, the complete sample was dried *in vacuo* to remove CDCl_3 before redissolving it in THF. After heating at $60\text{ }^{\circ}\text{C}$ for 2 h, the solvent was removed *in vacuo* and another ^1H NMR (**B**) was recorded in CDCl_3 . It revealed a doublet of triplets at 5.44 ppm ($J=4.8, 2.5\text{ Hz}$, highlighted in **dark blue**),² which is characteristic for the *E*-olefin **S4-E**. However, the corresponding signal for the *Z*-olefin **S4-Z**, a complex multiplet at 5.34–5.45 ppm (300 MHz CDCl_3 , highlighted in **light blue**),³ could not be assigned unambiguously as the broad multiplet assigned to **S3** has a similar shift. In total the integral of signals in this area had increased by 150%, relative to the triplet at 4.34 ppm which had been assigned to **S1**. This is consistent with reaction of **S3-syn** to **S4-E**, while **S3-anti** remained. Since heating most likely induced a *syn*-elimination of **S3**, it is reasonably understandable that **S3-anti** reacts significantly slower than **S3-syn**. In **S3-anti** the alkyl substituents have to adopt a *syn*-periplanar orientation in order to accommodate the eclipsed conformation necessary. Based on these assumptions we attempted to convert left over **S3-anti** to **S4-E** as well using a base induced *anti*-elimination. Therefore, the complete sample was evaporated again to remove CDCl_3 .

¹ R. Larouche-Gauthier, T. G. Elford, V. K. Aggarwal, *J. Am. Chem. Soc.* **2011**, 133, 16794–16797.

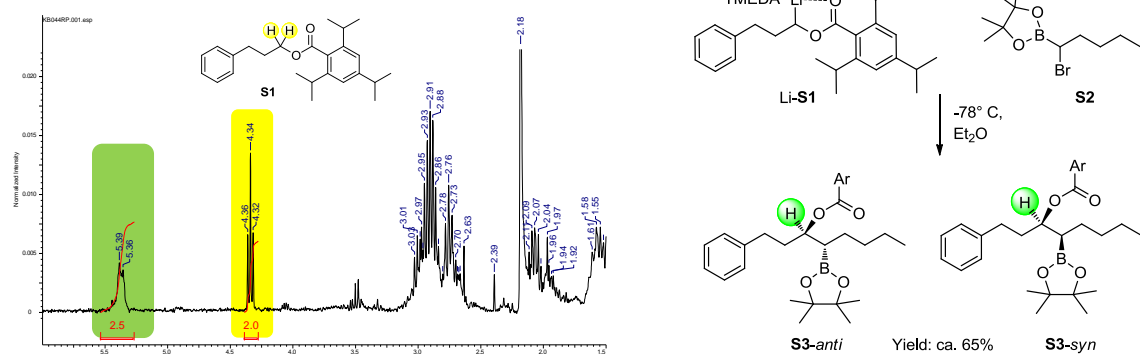
² X. Guo, J. Wang, C.-J. Li, *Org. Lett.* **2010**, 12, 3176–3178. Here the relevant signal was reported as a multiplet from 5.38–5.46 ppm.

³ H. Dang, N. Cox, G. Lalic, *Angew. Chem. Int. Edit.* **2014**, 53, 752–756.

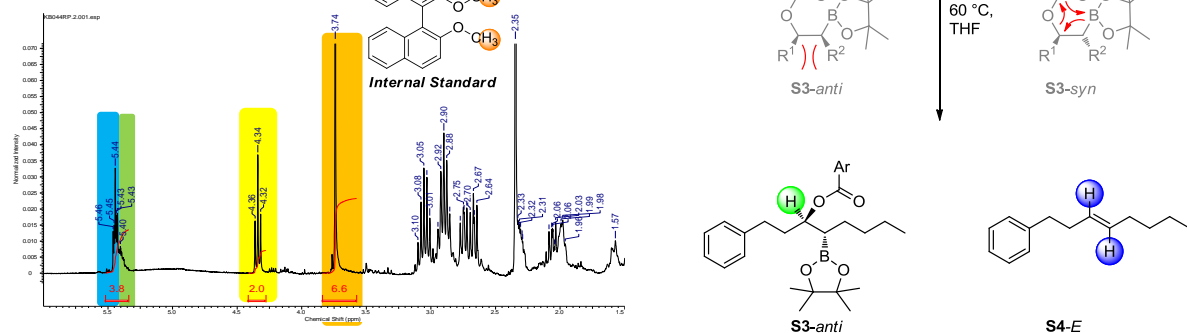


The material was dissolved in THF and TBAF (6.25 equiv.) was added. After stirring at rt for 17 h and aqueous workup (CyHex+Et₂O/NH₄Cl) another ¹H NMR (**C**) of the crude material revealed formation of a 4.3:1 mixture of **S4-E/S4-Z** in 63% yield, judging by the internal standard. Purification by column chromatography delivered a 5:1 mixture of **S4-E/S4-Z** (36% isolated yield).⁴ The reduction in yield and increase in *de* upon isolation, could be due to rigorous drying *in vacuo* (Boiling points predicted by SciFinder: **S4-E** 280 °C, **S4-Z**, 260 °C). We briefly attempted to apply this reaction to the synthesis of trisubstituted alkenes but turned to the epoxide based strategy described in the main article after Blakemore's publication on the topic.⁵

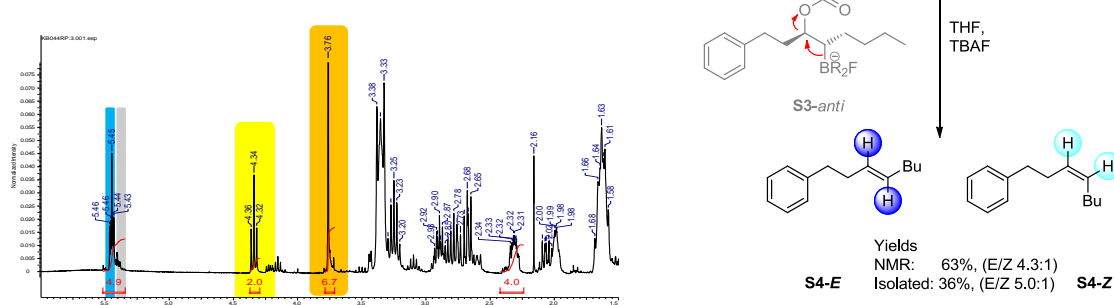
A



B

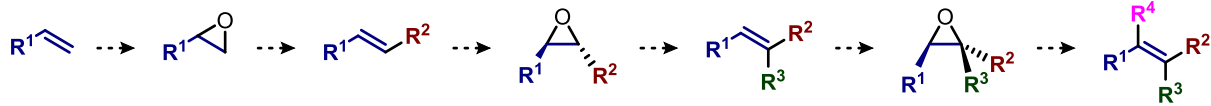


C

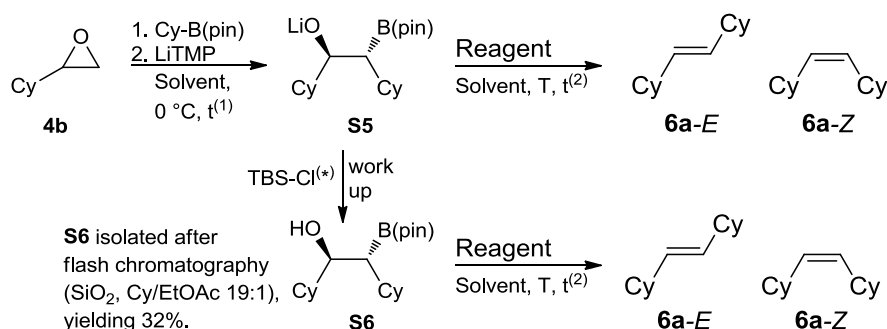


⁴ ¹H NMR **S4-E** (300 MHz, CHLOROFORM-d): δ = 0.79 - 0.95 (m, 3 H), 1.20 - 1.36 (m, 4 H), 1.90 - 2.05 (m, 2 H), 2.20 - 2.39 (m, 2 H), 2.58 - 2.83 (m, 2 H), 5.44 (dt, *J* = 4.8, 2.5 Hz, 2 H), 7.12 - 7.23 (m, 3 H), 7.23 - 7.35 (m, 2 H) ppm. **c.f ref 2.**
¹H NMR **S4-Z** (300 MHz, CDCl₃): δ = 7.39 - 7.24 (m, 2H), 7.24 - 7.11 (m, 3H), 5.56 - 5.21 (m, 2H), 2.66 (t, *J* = 7.7 Hz, 2H), 2.46 - 2.23 (m, 2H), 2.10 - 1.87 (m, 2H), 1.41 - 1.15 (m, 4H), 0.88 (t, *J* = 6.7 Hz, 3H) ppm. Overlaying signals reproduced from ref. 3.

⁵ Wu, X. Sun, K. Potter, Y. Cao, L. N. Zakharov, P. R. Blakemore, *Angew. Chem. Int. Edit.* **2016**, 55, 12285-12289.



Early Attempts at the Synthesis of Alkenes from Epoxide Insertion Products



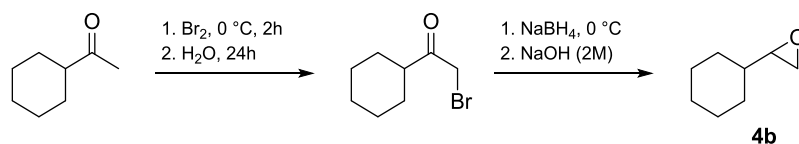
Comment: (*) TBS-Cl was used with the intention to isolate the corresponding silylether. This was not achieved, but the free alcohol **S6** was obtained instead.

Entry	Elimination-precursor	Solvent	t ⁽¹⁾	Reagent(s)	T	t ⁽²⁾	Yield Alkene	E/Z-ratio
1	S5 ^(D)	THF	o.n. ^(B)	MsCl	0 °C	2 h	47%	16.2:1
2	S5 ^(D)	THF	o.n. ^(B)	AcCl	0 °C	2 h	26% ^(A)	3:1
3	S5 ^(D)	THF	o.n. ^(B)	1. <i>n</i> BuLi 2. MsCl	-78 °C	o.n. ^(B)	51% ^(A)	only <i>E</i> -isomere
4	S5 ^(D)	THF	1 h	1. ZnCl ₂ 2. <i>n</i> BuLi 3. MsCl	1. 0 °C 2. -78 °C 3. -78 °C	1. 1 h 2. 10 min 3. 1 h ^(C)	73%	5.2:1
5	S6 ^(E)	THF	/	1 M HCl ^(F)	rt	7 d	95% ^(A)	only <i>E</i> -isomere
6	S6 ^(E)	MeCN	/	1 M HCl ^(F)	rt	7 d	41% ^(A)	only <i>E</i> -isomere
7	S6 ^(E)	THF	/	1. TBAF 2. 1 M HCl ^(F)	0 °C	7 d	34%	0.8:1
8	S6 ^(E)	MeCN	/	1. TBAF 2. 1 M HCl ^(F)	0 °C	7 d	33%	1.4:1

(A) Yield obtained by ¹H NMR using dimethylbinol as an internal standard. (B) The reaction mixture was allowed to warm up to rt overnight. (C) The reaction mixture was allowed to warm up to rt within 1 h. (D) **S5** was prepared from **4b** and reacted directly to alkene **6a** without any isolation. (E) **S6** was isolated before the reaction. (F) Aqueous solution.



2-Cyclohexyloxirane (**4b**)



To a solution of cyclohexyl methyl ketone (10 mL, 72.6 mmol) in MeOH (60 mL) at 0 °C bromine (3.8 mL, 72.6 mmol) was added *via* a dropping funnel over the course of 1 h. The reaction mixture was stirred for 2 h at 0 °C before water (60 mL) was added and stirring was continued at rt overnight. The reaction mixture was diluted with Et₂O (100 mL) and the phases were separated. The aqueous phase was re-extracted with Et₂O (100 mL) and the combined organic layers were neutralized with aq. K₂CO₃ (10%, ca. 300 mL). The organic phase was separated, dried over MgSO₄ and concentrated *in vacuo* yielding 2-bromo-1-cyclohexylethanone (13.03 g, 63.9 mmol, 88%) as colorless oil. The crude product was dissolved in MeOH (136 mL) and cooled to 0 °C before NaBH₄ (3.63 g, 95.9 mmol) was added in small portions. The reaction mixture was stirred for 30 min at 0 °C and concentrated *in vacuo*. The residue was partitioned between water (270 mL) and Et₂O (3x70 mL). The combined organic layers were washed with sat. aq. NH₄Cl and brine, dried over MgSO₄ and concentrated *in vacuo*. The residue was dissolved in THF (200 mL) and aq. NaOH (2 M, 136 mL) was added. The reaction mixture was stirred at rt for 2 h, after which water (340 mL) was added and the suspension was extracted with Et₂O (4x50 mL). The combined organic layers were washed with brine (100 mL) and dried over MgSO₄. The solvent was removed on a rotary evaporator^[*] and 2-cyclohexyloxirane **4b** (4.40 g, 34.9 mmol, 55%) was obtained as a colorless oil after distillation^[**] (7 mbar, 49 °C).

¹H NMR (300 MHz, CDCl₃) δ = 2.56 (dd, J = 2.3, 4.2 Hz, 2 H), 2.42 - 2.29 (m, 1 H), 1.75 (m, 1 H), 1.67 - 1.49 (m, 4 H), 1.27 - 0.90 (m, 6 H).

¹³C NMR (75 MHz, CDCl₃) δ = 56.6, 46.0, 40.4, 29.7, 28.8, 26.3, 25.7, 25.5.

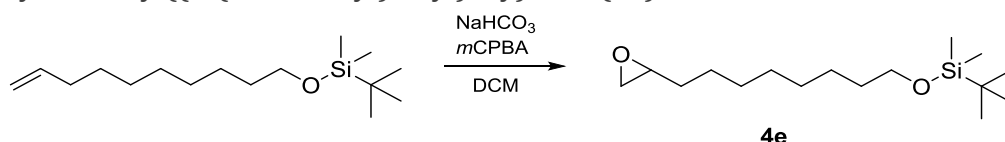
¹H- and ¹³C NMR data were consistent with those previously reported.⁸

CAUTION: Although no toxicological data is available for the product, similar compounds (e.g. 2-ethyloxirane) are suspected carcinogens. Furthermore, the intermediate 2-bromo-1-cyclohexylethanone is a lacrimator. Handle both compounds in fume cupboard only.

[*] We advise to use a rotary evaporator, which is positioned in a fume hood. Some of the volatile product can evaporate with the solvent.

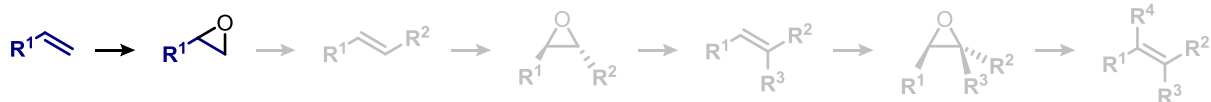
[**] For the distillation a diaphragm pump positioned in fume hood was used to avoid exposure to the product.

tert.-Butyldimethyl((8-(oxiran-2-yl)octyl)oxy)silan (**4e**)



To a solution of *tert*.-butyl(dec-9-en-1-yloxy)dimethylsilane⁹ (1.004 g, 3.70 mmol) in DCM (30 mL) were added NaHCO₃ (1.56 g, 18.5 mmol) and *m*CPBA (957 mg, 5.54 mmol) at rt and the reaction mixture was stirred overnight. An aq. solution of Na₂S₂O₃ (5%, 30 mL) was added at 0 °C over the course of five minutes, after which stirring was continued at rt for 15 min. The phases were separated,

⁸ Huang, K.; Wang, H.; Stepanenko, V.; De Jesús, M.; Torruellas, C.; Correa, W.; Ortiz-Marciales, M. *J. Org. Chem.* **2011**, 76, 1883–1886.



and the aqueous layer was extracted with DCM (2x30 mL). The combined organic layers were washed with a 1:1 mixture of brine and saturated aq. NaHCO_3 , dried over MgSO_4 and concentrated *in vacuo*. Chromatography (SiO_2 , CyHex) yielded epoxide **4e** (677 mg, 2.36 mmol, 64%) as a colorless oil.

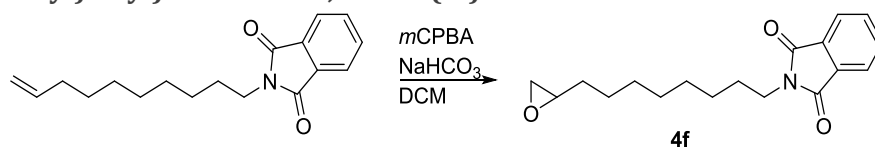
R_f = 0.22 (CyHex/EtOAc, 9:1).

$^1\text{H NMR}$ (300 MHz, CHLOROFORM-d) δ = 3.59 (t, J =6.6 Hz, 2 H), 2.86 - 2.94 (m, 1 H), 2.74 (dd, J =5.2, 3.9 Hz, 1 H), 2.46 (dd, J =5.0, 2.8 Hz, 1 H), 1.21 - 1.58 (m, 14 H), 0.89 (s, 9 H), 0.03 (s, 6 H) ppm.

$^{13}\text{C NMR}$ (CHLOROFORM-d , 75 MHz): δ = 63.3, 52.4, 47.1, 32.9, 32.5, 30.9, 29.5, 29.3, 26.0, 25.8, 18.4, -5.3 ppm.

^1H - and ^{13}C NMR data were consistent with those previously reported.⁹

2-(8-(Oxiran-2-yl)octyl)isoindolin-1,3-dione (**4f**)



To a solution of 1-phthalimidodec-9-en¹⁰ (816 mg, 2.86 mmol) in DCM (40 mL) were added NaHCO_3 (752 mg, 9 mmol) and *m*CPBA (795 mg, 4.6 mmol) at rt and the reaction mixture was stirred overnight. An aq. solution of $\text{Na}_2\text{S}_2\text{O}_3$ (5%, 30 mL) was added at 0 °C over the course of five minutes, after which stirring was continued at rt for 15 min. The phases were separated, and the aqueous layer was extracted with DCM (2x30 mL). The combined organic layers were washed with a 1:1 mixture of brine and saturated aq. NaHCO_3 (30 mL), dried over MgSO_4 and concentrated *in vacuo*. Chromatography (SiO_2 , CyHex/EtOAc 9:1) yielded epoxide **4f** (644 mg, 2.03 mmol, 71%) as a colorless oil, containing 16% CyHex.

R_f = 0.10 (CyHex/EtOAc, 9:1),

$^1\text{H NMR}$ (300 MHz, CHLOROFORM-d) δ = 7.80 - 7.87 (m, 2 H), 7.67 - 7.74 (m, 2 H), 3.67 (t, J =6.9 Hz, 2 H), 2.88 (ddt, J =5.5, 4.0, 2.6 Hz, 1 H), 2.73 (dd, J =5.0, 3.8 Hz, 1 H), 2.45 (dd, J =5.2, 2.7 Hz, 1 H), 1.67 (t, J =7.04 Hz, 2 H), 1.27 - 1.59 (m, 12 H) ppm.

$^{13}\text{C NMR}$ (75 MHz, CHLOROFORM-d) δ = 143.6, 139.8, 130.8, 128.3, 126.5, 126.5, 32.0, 29.9, 29.8, 29.6, 29.4, 28.9, 22.8, 22.0, 14.6, 14.2 ppm.

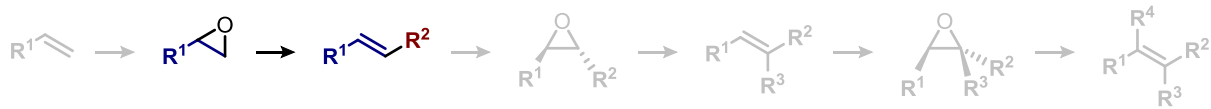
IR: $\tilde{\nu}$ = 2927 (m, br), 2848 (m), 2159 (w, br), 1770, (m), 1694 (s), 1611 (w), 1464 (m), 1431 (m), 1398 (m), 1188 (w), 1055 (m), 875 (m), 718 (s) cm^{-1} .

MS m/z (ESI^+): 324.2 ($\text{M}+\text{Na}^+$, 100%), 242.2 ($\text{M}+\text{Na}^++\text{H}_2\text{O}$, 24%), 356.2 ($\text{M}+\text{Na}^++\text{MeOH}$, 18%).

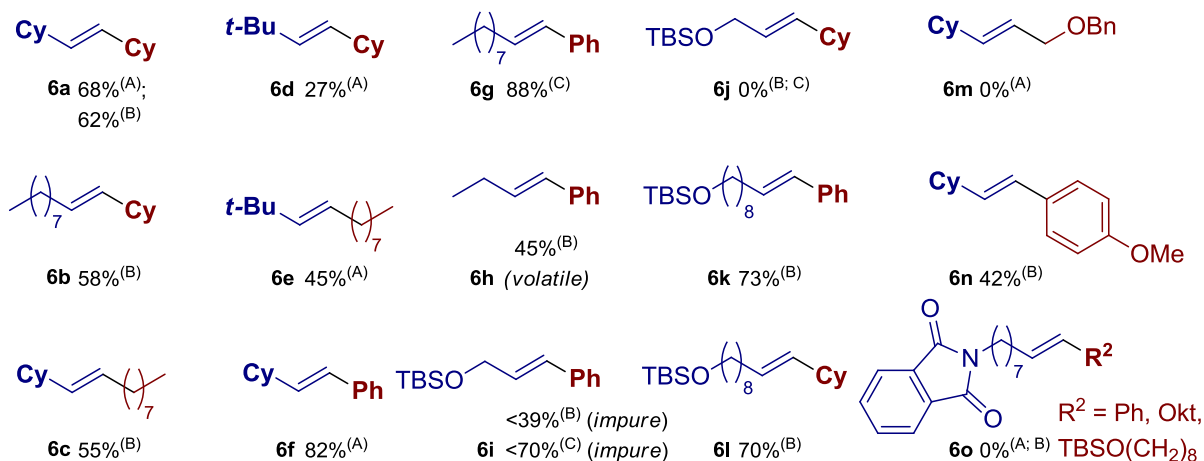
HR-MS m/z (ESI^+): found: $[\text{M}+\text{H}^+]$ 302.1759, $\text{C}_{12}\text{H}_{23}\text{NO}_3\text{Na}$ calculated 302.1751 and $[\text{M}+\text{Na}^+]$ 324.1579, $\text{C}_{12}\text{H}_{23}\text{NO}_3\text{Na}$ calculated: 324.1570.

⁹ L. Balas, J. Bertrand-Michel, F. Viars, J. Faugere, C. Lefort, S. Caspar-Bauguil, D. Langin, T. Durand, *Org. & Biomol. Chem.* **2016**, *14*, 9012–9020.

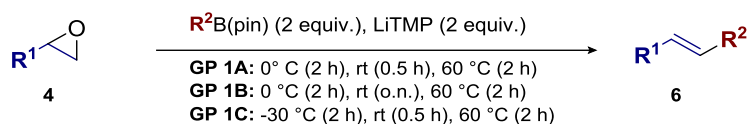
¹⁰ C. Hirschhäuser, J. Velcicky, D. Schlawe, E. Hessler, A. Majdalani, J.-M. Neudörfl, A. Prokop*, T. Wieder, H.-G. Schmalz*, *Chem. Eur. J.* **2013**, *19*, 13017–13029.



Synthesis of Disubstituted Alkenes



General Procedure GP1: Synthesis of Disubstituted Alkenes

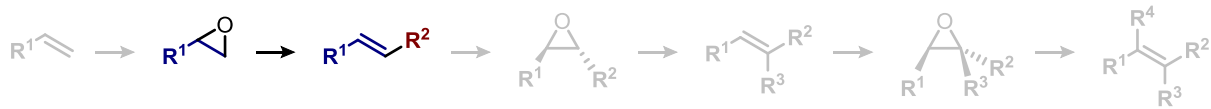


A solution of LiTMP was freshly prepared in a dried Schlenk tube by addition of *n*BuLi in hexanes (2 equiv.) to 2,2,6,6-tetramethylpiperidin (TMP, 2.2 equiv.) in dry THF (1.7 – 2.1 mL/mmol of epoxide **4**) at 0 °C and stirring for 30 min at rt. This LiTMP solution was added dropwise to an equal volume solution of epoxide **4** (1 equiv.) and boronic ester (2.0 equiv.) in dry THF (3.5 – 4.7 mL/mmol of epoxide **4**) at 0 °C (**GP1A** and **1B**) or -30 °C (**GP1C**). Stirring was continued for 2 h at the same temperature. The reaction mixture was allowed to warm up to room temperature for 30 min (**GP1A** and **1C**) or overnight (**GP1B**) before the reaction mixture was heated to 60 °C for 2 h.^[*] The reaction mixture was cooled to room temperature, transferred into a separation funnel with the help of Et₂O and washed (3x) with NaOH (1 M).^[**] The combined aqueous layers were re-extracted with Et₂O (2x). The combined organic layers were dried with Na₂SO₄ and concentrated *in vacuo*. The residue was purified by column chromatography.

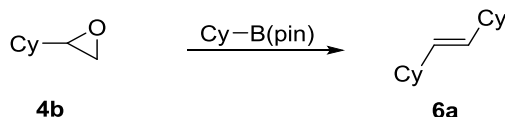
Comments: ^[*] The difference between **GP1A** and **GP1B**, i.e. whether the reaction is warmed up to room temperature for 30 min or overnight respectively, is a matter of convenience. For comparison **6a** (R¹=R²=Cy) was prepared according to **GP1A** and **GP1B** with 68% and 62% yield, respectively. ^[**] When necessary, brine was added to aid phase separation.

Sample Procedure: A solution of LiTMP was prepared by addition of *n*BuLi in hexanes (2.8 mL, 4.49 mmol, 1.55 mol/L) to 2,2,6,6-tetramethylpiperidin (0.83 mL, 5.39 mmol) in dry THF (6 mL) at 0 °C. After stirring for 0.5 h at room temperature, this mixture was added dropwise to a solution of epoxide **4a** (280 mg, 2.25 mmol) and octylboronic acid pinacol ester (1.08 g, 4.49 mmol) stirred at 0 °C in dry THF (8 mL). Stirring at 0 °C was continued for 2 h. The reaction mixture was allowed to warm up to room temperature overnight, after which the reaction mixture was heated to 60 °C for 2 h. The reaction mixture was cooled to room temperature, transferred into a separation funnel with Et₂O and washed with aq. NaOH (1 M, 2x50 mL) and brine (50 mL). The combined aqueous layers were re-extracted with Et₂O (2x50 mL). The combined organic layers were dried with Na₂SO₄ and concentrated *in vacuo*. Column chromatography (SiO₂, CyHex/EtOAc, 19:1) afforded alkene **6c** (272 mg, 1.23 mmol, 55%) as a colorless oil. R_f = 0.72 (CyHex/EtOAc, 19:1). ¹H NMR (300 MHz, CHLOROFORM-*d*) δ = 5.27 - 5.42 (m, 2 H), 1.85 - 2.02 (m, 3 H), 1.59 - 1.74 (m, 5 H), 0.80 - 1.40 (m, 20 H) ppm. ¹³C NMR (75 MHz, CHLOROFORM-*d*): δ = 136.4, 127.8, 40.7, 33.3, 32.7, 31.9, 29.7, 29.5, 29.3, 29.1, 26.3, 26.2, 22.7, 14.1 ppm. ¹H- and ¹³C NMR data were consistent with those previously reported.¹¹

¹¹ G. Cahiez, O. Gager, J. Buendia, C. Patinote, *Chem. Eur. J.* **2012**, *18*, 5860–5863.



(E)-1,2-Dicyclohexylethene (6a)



Following GP1A a solution of LiTMP (0.88 mmol), was reacted with epoxide **4b** (0.40 mmol) and cyclohexyl pinacol boronic ester (0.80 mmol) to yield **6a** (52 mg, 0.27 mmol, 68%) as a colorless oil after chromatography (SiO₂, CyHex).

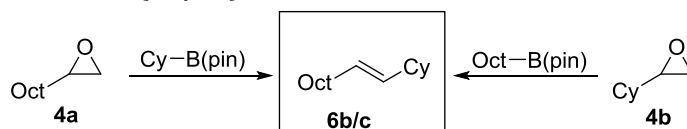
$R_f = 0.61$ (CyHex).

¹H NMR (300 MHz, CHLOROFORM-*d*) $\delta = 5.30$ (dd, $J=3.60, 1.72$ Hz, 2 H), 0.93 - 1.92 (m, 22 H) ppm.

¹³C NMR (75 MHz, CHLOROFORM-*d*) $\delta = 133.8, 40.7, 33.4, 26.3, 26.2$ ppm.

¹H- and ¹³C NMR data were consistent with those previously reported.¹²

(E)-Dec-1-en-1-ylcyclohexan (6b/6c)



Following GP1B a solution of LiTMP (0.88 mmol), was reacted with epoxide **4a** (0.40 mmol) and cyclohexyl pinacol boronic ester (0.80 mmol) to yield **6b** (51 mg, 0.27 mmol, 58%) as a colorless oil after chromatography (SiO₂, CyHex/EtOAc, 19:1).

Following GP1B a solution of LiTMP (4.95 mmol), was reacted with epoxide **4b** (2.25 mmol) and octyl pinacol boronic ester (4.50 mmol) to yield **6c** (272 mg, 1.22 mmol, 55%) as a colorless oil after chromatography (SiO₂, CyHex/EtOAc, 19:1). Also see sample procedure on page 7.

$R_f = 0.72$ (CyHex/EtOAc, 19:1).

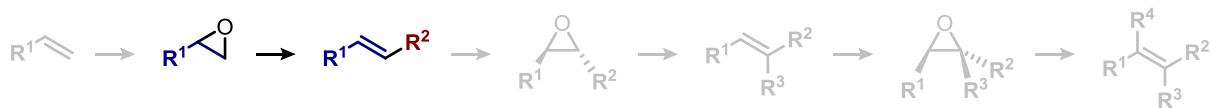
¹H NMR (300 MHz, CHLOROFORM-*d*) $\delta = 5.27 - 5.42$ (m, 2 H), 1.85 - 2.02 (m, 3 H), 1.59 - 1.74 (m, 5 H), 0.80 - 1.40 (m, 20 H) ppm.

¹³C NMR (75 MHz, CHLOROFORM-*d*): $\delta = 136.4, 127.8, 40.7, 33.3, 32.7, 31.9, 29.7, 29.5, 29.3, 29.1, 26.3, 26.2, 22.7, 14.1$ ppm.

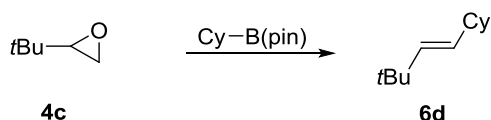
¹H- and ¹³C NMR data were consistent with those previously reported.¹³

¹² G. Opitz, T. Ehliis, K. Rieth, *Chem. Ber.* **1990**, 123, 1989–1998.

¹³ G. Cahiez, O. Gager, J. Buendia, C. Patinote, *Chem. Eur. J.* **2012**, 18, 5860–5863.



(E)-3,3-Dimethyl-1-buten-1-ylcyclohexan (**6d**)



Following GP1B a solution of LiTMP (5.24 mmol), was reacted with epoxide **4c** (2.38 mmol) and cyclohexyl pinacol boronic ester (4.76 mmol) to yield **6d** (173 mg, 0.64 mmol, 27%) as a colorless oil after chromatography (SiO₂, CyHex/EtOAc, 19:1). Yield corrected for 40 wt% of impurity based on subsequent transformations.

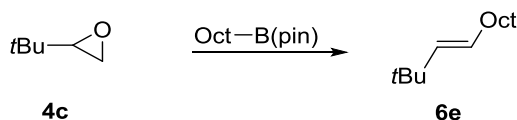
R_f = 0.71 (Cyhex/EtOAc, 9:1).

¹H-NMR (300 MHz, CDCl₃): δ = 0.97 (s, 9 H), 1.05-1.80 (m, 11 H), 5.25 (dd, J = 15.6, 6.6 Hz, 1 H), 5.36 (d, J = 15.6, 1 H) ppm.

¹³C-NMR (75 MHz, CDCl₃): δ = 138.9, 130.8, 40.7, 33.4, 32.5, 26.9, 26.3, 26.3 ppm.

¹H- and ¹³C NMR data were consistent with those previously reported.¹⁴

(E)-2,2-Dimethyl-3-dodecen (**6e**)



Following GP1B a solution of LiTMP (0.88 mmol), was reacted with epoxide **4c** (0.40 mmol) and octyl pinacol boronic ester (0.80 mmol) to yield **6e** (35 mg, 0.18 mmol, 45%) as a colorless oil after chromatography (SiO₂, CyHex/EtOAc, 19:1).

R_f = 0.67 (Cyhex/EtOAc, 9:1).

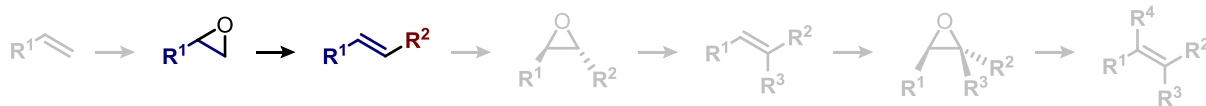
¹H-NMR (300 MHz, CDCl₃): δ = 5.25-5.46 (m, 2 H), 1.93-1.99 (m, 2 H), 1.26 (m, 12 H), 0.98 (s, 9 H), 0.88 (t, J = 6.87 Hz, 3 H), ppm.

¹³C-NMR (75 MHz, CDCl₃): δ = 141.4, 124.8, 32.7, 31.9, 29.8, 29.7, 29.5, 29.4, 29.3, 29.1, 22.7, 14.1 ppm.

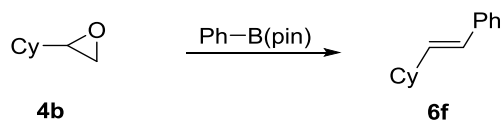
¹H- and ¹³C NMR data were consistent with those previously reported.¹⁵

¹⁴ T. M. Yuan, T. Y. Luh, *J. Org. Chem.* **1992**, 57, 4550–4552.

¹⁵ First report of compound: G.H. Posner, K.A. Babiak, *J. Organomet. Chem.* **1979**, 177, 299-307. NMR Data was compared to the octen-congener: G. Cahiez, H. Avedissian, *Synthesis* **1998**, 1998, 1199–1205.



(E)-(2-Cyclohexylvinyl)benzen (6f)



Following GP1A a solution of LiTMP (0.88 mmol), was reacted with epoxide **4b** (0.46 mmol) and phenyl pinacol boronic ester (0.80 mmol) to yield **6f** (70 mg, 0.38 mmol, 82%) as a colorless oil after chromatography (SiO₂, CyHex).

$R_f = 0.38$ (CyHex).

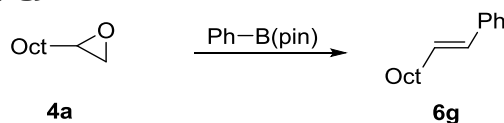
¹H-NMR (300 MHz, CHLOROFORM-*d*) $\delta = 7.23 - 7.44$ (m, 4 H), 7.09 - 7.22 (m, 1 H), 6.35 (d, $J=15.6$ Hz, 1 H), 6.18 (dd, $J=15.9, 6.9$ Hz, 1 H), 2.02 - 2.26 (m, 1 H), 1.61 - 1.88 (m, 4 H), 1.09 - 1.45 ppm (m, 4 H) ppm.

¹³C NMR (75 MHz, CHLOROFORM-*d*) $\delta = 138.22, 137.02, 128.60, 127.37, 126.87, 126.09, 41.31, 33.12, 26.34, 26.20$ ppm.

¹H- and ¹³C NMR data were consistent with those previously reported.¹⁶

Comment: Prolonged heating at 60 °C lead to a reduction in yield in this case, probably due to decomposition of the styrene derivative.

(E)-Dec-1-en-1-ylbenzen (6g)



Following GP1C a solution of LiTMP (0.70 mmol), was reacted with epoxide **4a** (0.35 mmol) and phenyl pinacol boronic ester (0.64 mmol) to yield **6g** (67 mg, 0.31 mmol, 88%) as a colorless oil after chromatography (SiO₂, CyHex/EtOAc, 19:1).

$R_f = 0.62$ (CyHex/EtOAc, 19:1).

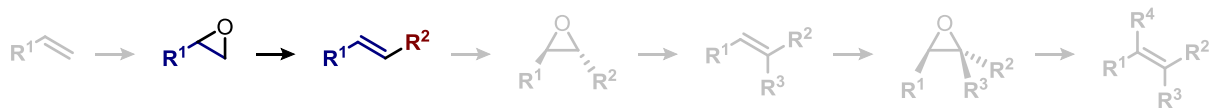
¹H NMR (300 MHz, CHLOROFORM-*d*) $\delta = 7.27 - 7.38$ (m, 4H), 7.14 - 7.22 (m, 1 H), 6.38 (d, $J=16.3$ Hz, 1 H), 6.16 - 6.29 (m, 1 H), 2.15 - 2.26 (m, 2 H), 1.41 - 1.53 (m, 2 H), 1.17 - 1.40 (m, 10 H), 0.80 - 0.95 (m, 3 H) ppm.

¹³C NMR (75 MHz, CHLOROFORM-*d*) $\delta = 138.1, 131.4, 129.8, 128.6, 126.9, 126.1, 33.2, 32.1, 29.7, 29.6, 29.5, 29.4, 22.8, 14.3$ ppm.

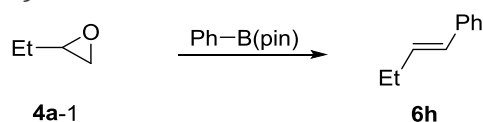
¹H- and ¹³C NMR data were consistent with those previously reported.¹⁷

¹⁶ M. J. Rawling, J. H. Rowley, M. Campbell, A. R. Kennedy, J. A. Parkinson, N. C. O. Tomkinson, *Chem. Sci.* **2014**, 5, 1777–1785.

¹⁷ P. Andrews, C. M. Latham, M. Magre, D. Willcox, S. Woodward, *Chem. Comm.* **2013**, 49, 1488.



(E)-But-1-en-1-ylbenzen (6h)



Following GP1B a solution of LiTMP (10.78 mmol), was reacted with epoxide **4a-1** (4.90 mmol) and phenyl pinacol boronic ester (9.80 mmol) to yield **6h** (393 mg, 2.97 mmol, 54%) as a colorless oil after chromatography (SiO₂, CyHex).

R_f = 0.50 (CyHex/EtOAc, 19:1).

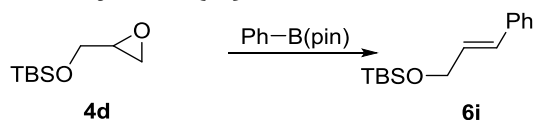
¹H NMR (300 MHz, CHLOROFORM-*d*) δ = 7.21 - 7.35 (m, 4 H), 7.12 - 7.20 (m, 1 H), 6.36 (d, J =16.0 Hz, 1 H), 6.18 - 6.29 (m, 1 H), 2.14 - 2.27 (m, 2 H), 1.07 (t, J =7.3 Hz, 3 H) ppm.

¹³C NMR (75 MHz, CHLOROFORM-*d*) δ = 138.12, 132.80, 128.96, 128.62, 126.89, 126.06, 26.21, 13.81 ppm.

¹H NMR data was consistent with a previous report.¹⁸

Comment: The reaction was conducted several times on different scales and isolated yields varied considerably as **the product is volatile**.

tert.-Butyl(cinnamyloxy)dimethylsilan (6i)



Following GP1C a solution of LiTMP (0.66 mmol), was reacted with epoxide **4d** (0.30 mmol) and phenyl pinacol boronic ester (0.53 mmol) to yield **6i** (53 mg, <0.21 mmol, <70%) as a colorless oil after chromatography (SiO₂, CyHex/EtOAc, 19:1). The product contained a R-OTBS type impurity, which could not be removed by repeated chromatography. NMR signals were obtained from mixture (see appendix for spectra).

R_f = 0.40 (CyHex/EtOAc, 19:1).

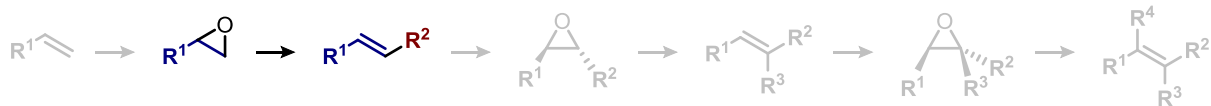
¹H-NMR (300 MHz, CHLOROFORM-*d*): δ = 7.21 - 7.41 (m, 5 H), 6.59 (d, J =16.0 Hz, 1 H), 6.29 (dt, J =15.0, 5.0 Hz, 1 H), 4.36 (dd, J =5.0, 1.6 Hz, 2 H), 0.95 (s, 9 H), 0.12 (s, 6 H) ppm.

¹³C NMR (75 MHz, CHLOROFORM-*d*) δ = 137.1, 129.5, 129.2, 128.5, 127.3, 126.4, 63.9, 26.0, 18.4, -5.1 ppm.

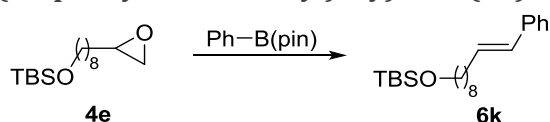
¹H- and ¹³C NMR data were consistent with those previously reported¹⁹

¹⁸ J. Li, J. Peng, Y. Bai, L. Chen, G. Lai, *Phosphorus Sulfur* **2011**, 186, 1621–1625.

¹⁹ J. J. Loman, V. A. Pistritto, C. B. Kelly, N. E. Leadbeater, *Synlett* **2016**, 27, 2372–2377.



(E)-tert.-Butyldimethyl((10-phenyldec-9-en-1-yl)oxy)silan (6k)



Following GP1B a solution of LiTMP (0.88 mmol), was reacted with epoxide **4e** (0.41 mmol) and phenyl pinacol boronic ester (0.80 mmol) to yield **6k** (104 mg, 0.31 mmol, 75%) as a colorless oil after chromatography (SiO₂, CyHex).

R_f = 0.58 (CyHex/EtOAc, 19:1).

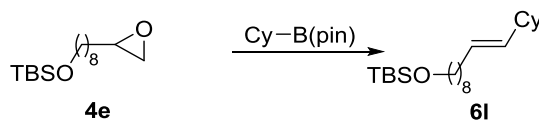
¹H NMR (300 MHz, CHLOROFORM-*d*) δ = 7.24 - 7.37 (m, 4 H), 7.14 - 7.22 (m, 1 H), 6.38 (d, J =15.6 Hz, 1 H), 6.17 - 6.28 (m, 1 H), 3.56 - 3.64 (t, 2 H), 2.15 - 2.27 (m, 2 H), 1.41 - 1.59 (m, 2 H), 1.23 - 1.41 (m, 10 H), 0.87 - 0.98 (m, 9 H), 0.03 - 0.12 (m, 6 H) ppm.

¹³C-NMR (75 MHz, CHLOROFORM-*d*) δ = 138.0, 131.2, 129.7, 128.4, 126.7, 125.9, 63.3, 33.0, 32.9, 29.5, 29.4, 29.4, 29.2, 26.0, 25.8, 18.4, -5.3 ppm.

IR: $\tilde{\nu}$ = 2925 (m), 2854 (m), 2160 (w), 2027 (w, br.), 1973 (w, br.), 1458 (m), 1254 (m), 1095 (s), 962 (m), 833 (s), 773 (s), 741 (m), 690 (m) cm⁻¹.

HR-MS m/z (ESI⁺): found: $[M+H]^+$ 347.2767, C₂₂H₃₈OSiH calculated 347.2765 and $[M+Na]^+$ 369.2587, C₂₂H₃₈OSiNa calculated 369.2584.

(E)-tert.-Butyl((10-cyclohexyldec-9-en-1-yl)oxy)dimethylsilan (6l)



Following GP1B a solution of LiTMP (0.88 mmol), was reacted with epoxide **4e** (0.40 mmol) and cyclohexyl pinacol boronic ester (0.80 mmol) to yield **6l** (109 mg, 0.31 mmol, 77%) as a colorless oil after chromatography (SiO₂, CyHex).

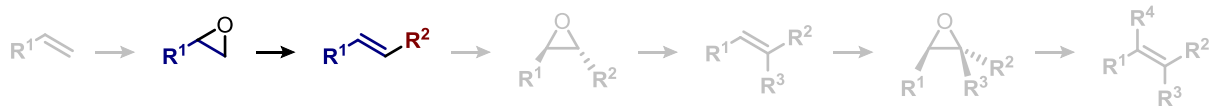
R_f = 0.64 (CyHex/EtOAc, 19:1).

¹H NMR (300 MHz, CHLOROFORM-*d*) δ = 5.31 - 5.37 (m, 2 H), 3.60 (t, J =6.57 Hz, 2 H), 1.44 - 2.01 (m, 11 H), 0.96 - 1.39 (m, 16 H), 0.90 (s, 9 H), 0.06 (s, 6 H) ppm.

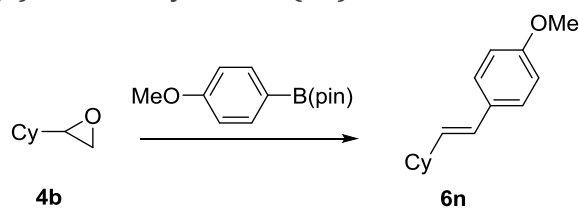
¹³C-NMR (75 MHz, CHLOROFORM-*d*) δ = 136.5, 127.8, 63.4, 40.8, 33.4, 33.0, 32.7, 29.8, 29.6, 29.5, 29.1, 27.0, 26.3, 26.2, 26.1, 25.9, 18.4, -5.0 ppm.

IR: $\tilde{\nu}$ = 2924 (s), 2852 (m), 1449 (w), 2160 (w), 2027 (w, br.), 1977 (w, br.), 1506 (w), 1458 (w), 1253 (m), 1097 (s), 966 (w), 833 (s), 773 (s) cm⁻¹.

HR-MS m/z (ESI⁺): found: $[M+H]^+$ 353.3239, C₂₂H₄₄OSiH calculated: 353.3234 and $[M+Na]^+$ 375.3056, C₂₂H₃₈OSiNa calculated: 375.3054.



(*E*)-1-(2-Cyclohexylvinyl)-4-methoxybenzen (**6n**)



Following GP1B a solution of LiTMP (1.76 mmol), was reacted with epoxide **4b** (0.86 mmol) and *ortho*-methoxyphenyl pinacol boronic ester (1.60 mmol) to yield **6n** (75 mg, 0.36 mmol, 40%) as a yellow oil after chromatography (SiO₂, CyHex/EtOAc, 19:1). *The material obtained after chromatography contained 71% of 6n, 15.5% of boronic ester and 13.5% epoxide 4b starting material. The yield was corrected accordingly.*

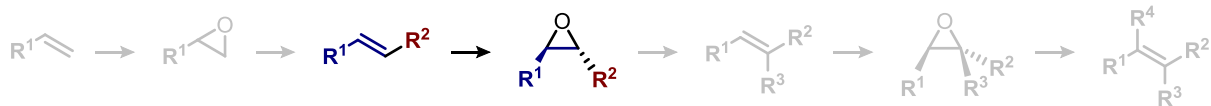
R_f = 0.42 (CyHex/EtOAc, 19:1).

¹H NMR (300 MHz, CHLOROFORM-*d*) δ = 7.25 - 7.32 (m, 2 H), 6.81 - 6.87 (m, 2 H), 6.29 (d, *J*=15.9 Hz, 1 H), 6.04 (dd, *J*=15.9, 6.9 Hz, 1 H), 3.80 (s, 3 H), 2.03 - 2.19 (m, 1 H), 1.62 - 1.93 (m, 5 H), 1.08 - 1.43 (m, 5 H) ppm.

¹³C NMR (75 MHz, CHLOROFORM-*d*) δ = 158.6, 134.8, 130.9, 127.0, 126.5, 113.9, 55.3, 41.1, 33.1, 26.2, 26.1 ppm.

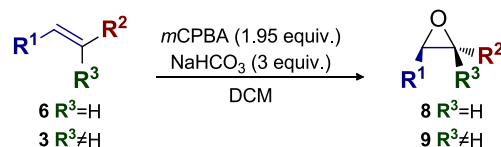
¹H- and ¹³C NMR data were consistent with those previously reported.²⁰

²⁰ C. Wang, Y. Lei, M. Guo, Q. Shang, H. Liu, Z. Xu, R. Wang, *Org. Lett.* **2017**, *19*, 6412–6415.



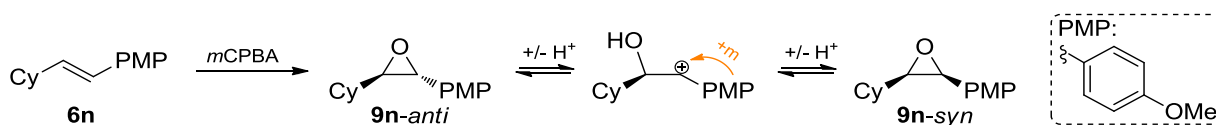
Synthesis/Sources of Disubstituted Epoxides

General Procedure GP2: Epoxidation of Di- and Trisubstituted Alkenes

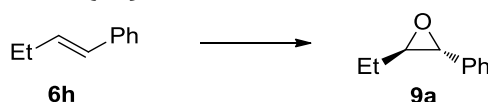


NaHCO_3 (3 equiv.) and $m\text{CPBA}$ (1.95 equiv.) were added to a solution of alkene in DCM (ca. 13 ml/mmol of alkene) and the mixture was stirred overnight at room temperature. Afterwards the reaction mixture was cooled to 0 °C before an equal volume of aq. $\text{Na}_2\text{S}_2\text{O}_3$ (5%) was added. Stirring was continued for 5 min. at 0 °C and 15 min. at room temperature. The mixture was washed with equal volumes of brine, saturated aq. NaHCO_3 . The combined aqueous phases were re-extracted with DCM (3x) and the combined organic extracts were dried over MgSO_4 . The solvent was removed *in vacuo* and the crude product was purified by column chromatography.

Comment: Although this is a known problem,²¹ it should be mentioned that such epoxides, which can open up and form stabilized cations, are particularly vulnerable to acid mediated epimerization. This tendency is reduced by the addition of base (here NaHCO_3 , which intercepts meta-chlorobenzoic acid) and no epimerization was observed for the compounds reported below. However, attempts to epoxidize e.g. **6n** with this (and a comparable biphasic)²² system consistently led to epimerization.



(2*R*,3*R*)-2-Ethyl-3-phenyloxiran (**9a**)



According to **GP2** alkene **6h** (210 mg, 1.59 mmol) was transformed into epoxide **9a** (180 mg, 1.21 mmol, 76%), isolated as a colorless oil after column chromatography (SiO_2 , CyHex/EtOAc 19:1).

R_f = 0.42 (CyHex/EtOAc, 19:1).

¹H-NMR (300 MHz, CHLOROFORM-*d*) δ = 7.24 - 7.38 (m, 5 H), 3.63 (d, J =2.2 Hz, 1 H), 2.95 (td, J =5.5, 2.2 Hz, 1 H), 1.67 - 1.79 (m, 2 H), 1.07 (t, J =7.5 Hz, 3 H) ppm.

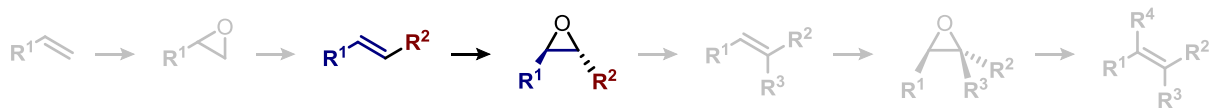
¹³C NMR (75 MHz, CHLOROFORM-*d*) δ = 137.9, 128.4, 127.9, 125.5, 64.1, 58.3, 25.4, 9.8 ppm.

¹H- and ¹³C NMR data were consistent with those previously reported.²³

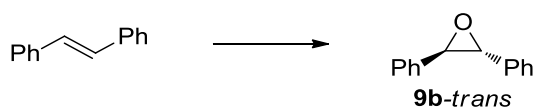
²¹ R. S. Mohan, K. Gavardin, S. Kyere, D. L. Whalen, *J. Org. Chem.* **2000**, 65, 1407–1413.

²² G. Moyna, H. J. Williams, A. I. Scott, *Synthetic Commun.* **1996**, 26, 2235–2239.

²³ H. Mang, J. Gross, M. Lara, C. Goessler, H. E. Schoemaker, G. M. Guebitz, W. Kroutil, *Angew. Chem. Int. Edit.* **2006**, 45, 5201–5203.



***trans*-2,3-Diphenyloxirane (**9b-trans**)**



According to **GP2** stilbene (3.00 g, 16.6 mmol) was transformed into epoxide **9b-trans** (2.96 g, 7.23 mmol, 91%), isolated as a colorless oil after column chromatography (SiO₂, CyHex/EtOAc 30:1).

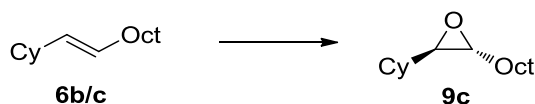
R_f = 0.34 (CyHex/EtOAc, 19:1).

¹H-NMR (300 MHz, CHLOROFORM-*d*) δ = 7.28 - 7.49 (m, 10 H), 3.89 (s, 2 H) ppm.

¹³C NMR (75 MHz, CHLOROFORM-*d*) δ = 137.1, 128.6, 128.3, 125.5, 62.8 ppm.

¹H- and ¹³C NMR data were consistent with those previously reported.²⁴

2-Cyclohexyl-3-octyloxiran (9c**)**



According to **GP2**^(*) alkene **6b/c** (140 mg, 0.63 mmol) was transformed into epoxide **9c** (112 mg, 0.47 mmol, 75%), isolated as a colorless oil after column chromatography (SiO₂, CyHex/EtOAc 7:3).

R_f = 0.74 (Cyhex/EtOAc, 7:3).

¹H-NMR (300 MHz, CHLOROFORM-*d*): δ = 2.68-2.73 (m, 1 H), 2.42-2.47 (dd, J = 8.8, 2.2 Hz, 1 H), 1.80-1.90 (m, 1 H), 1.00-1.69 (m, 24 H), 0.88 (t, J = 6.9 Hz, 3 H) ppm.

¹³C-NMR (75 MHz, CDCl₃): δ = 63.3, 57.7, 40.2, 32.2, 31.8, 29.8, 29.5, 29.4, 29.2, 29.1, 26.3, 26.1, 25.7, 25.6, 22.6, 14.1 ppm.

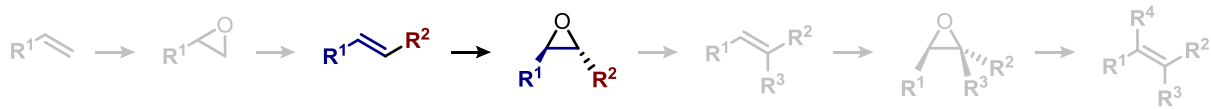
IR: $\tilde{\nu}$ = 2925 (s), 2853 (m), 2360 (m), 2339 (m), 1652 (w), 1559 (w), 1539 (w), 1456 (w), 668 (s), 625 (w), 619 (w) cm⁻¹.

MS m/z (ESI^{+/−}): Compound was not detected by ESI. Identity was confirmed by comparison to data reported for 2-cyclohexyl-3-hexyloxiran.²⁵

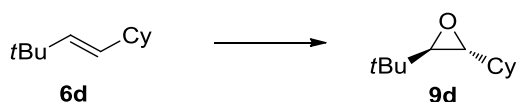
^(*)**Comment:** In divergence from GP2, the product was isolated after stirring for only 3 h.

²⁴ G. Anilkumar, S. Bhor, M. K. Tse, M. Klawonn, B. Bitterlich, M. Beller, *Tetrahedron-Asymmetry* **2005**, 16, 3536–3561.

²⁵ T. Satoh, Y. Kaneko, K. Yamakawa, *Bull. Chem. Soc. Jpn.* **1986**, 59, 2463–2470.



2-Cyclohexyl-3-(2-methyl-2-propanyl) oxiran (**9d**)



According to **GP2**^(*) alkene **6d** (104 mg, 1.04 mmol) was transformed into epoxide **9d** (84 mg, 0.46 mmol, 44%), isolated as a colorless oil after column chromatography (SiO₂, CyHex/EtOAc 7:3).

R_f = 0.70 (Cyhex/EtOAc, 7:3).

¹H-NMR (300 MHz, CDCl₃): δ = 2.56 (dd, J =6.6, 2.5 Hz, 1 H), 2.47 - 2.53 (m, 1 H), 1.82 - 1.95 (m, 1 H), 1.56 - 1.80 (m, 4 H), 1.01 - 1.31 (m, 6 H), 0.91 (s, 9 H) ppm.

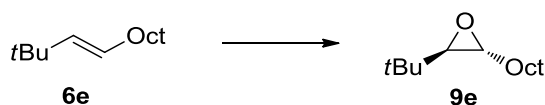
¹³C-NMR (75 MHz, CDCl₃): δ = 66.0, 59.9, 40.4, 30.5, 29.9, 29.1, 26.3, 25.8, 25.7, 25.5 ppm.

IR: $\tilde{\nu}$ = 2360 (s), 2341 (s), 1653 (w), 668 (s) cm⁻¹.

MS m/z (ESI^{+/−}): Compound was not detected by ESI. Identity was confirmed by comparison to other compounds of this series.

^(*)**Comment:** In divergence from GP2, the product was isolated after stirring for only 3 h.

2-Octyl-3-(2-methyl-2-propanyl) oxiran (**9e**)



According to **GP2**^(*) alkene **6e** (15 mg, 0.077 mmol) was transformed into epoxide **9e** (12 mg, 0.031 mmol, 40%), isolated as a colorless oil after column chromatography (SiO₂, CyHex/EtOAc 7:3). *Yield corrected for grease impurity.*

R_f = 0.80 (Cyhex/EtOAc, 7:3).

¹H-NMR (300 MHz, CDCl₃): δ = 2.74-2.82 (m, 1 H), 2.46 (d, J = 2.49 Hz, 1 H), 1.35-1.65 (m, 14 H), 0.88-0.91 (m, 12 H) ppm.

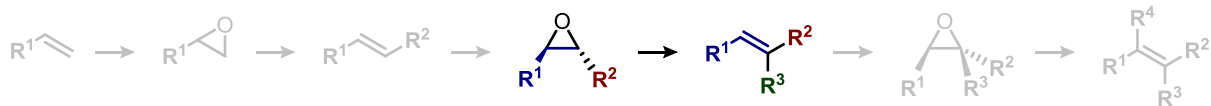
¹³C-NMR (75 MHz, CDCl₃): δ = 67.0, 55.5, 32.3, 31.8, 30.7, 29.7, 29.4, 29.2, 26.2, 25.9, 22.6, 14.1 ppm.

IR: $\tilde{\nu}$ = 3744 (w), 2923 (s), 2854 (m), 2360 (m), 1700 (w), 1652 (w), 668 (s) cm⁻¹.

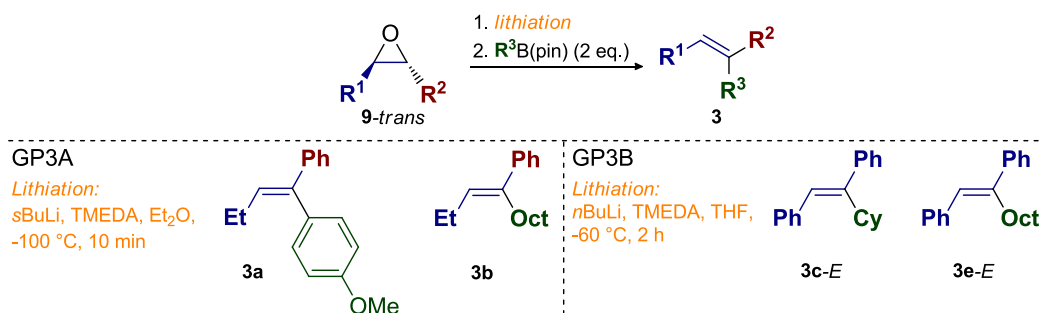
MS m/z (ESI^{+/−}): Compound was not detected by ESI. Identity was confirmed by comparison to data reported for 2-Propyl-3-(2-methyl-2-propanyl) oxiran²⁶

^(*)**Comment:** In divergence from GP2, the product was isolated after stirring for only 3 h.

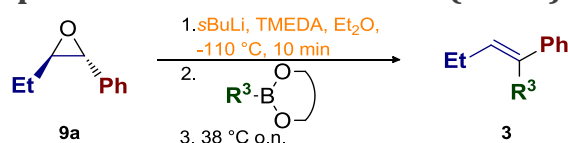
²⁶ A. K. Yudin, J. P. Chiang, H. Adolfsson, C. Copéret, *J. Org. Chem.* **2001**, 66, 4713–4718.



Synthesis of Trisubstituted Alkenes from *trans*-Epoxides

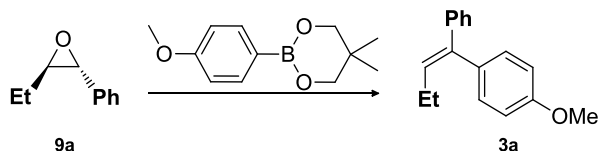


General Procedure Optimized for reaction of 9a (GP3A)



At -110 °C sBuLi in hexanes (1.2 equiv.) was added dropwise to a solution of epoxide **9a** and TMEDA (3 equiv.) in dry Et₂O (1.5 mL/mmol of **9a**). After stirring for 10 min at the same temperature, a solution of appropriate boronic ester in Et₂O (2.2 equiv., 0.34 M) was added and stirring was continued for 2 h at -110 °C. The reaction mixture was allowed to warm up to room temperature for 0.5 h and heated to 38 °C overnight. The solvent was removed *in vacuo* and the residue was purified by column chromatography (Al₂O₃, CyHex).

(*Z*)-1-Methoxy-4-(1-phenylbut-1-en-1-yl)benzen (**3a**)



According to **GP3A** epoxide **9a** (154 mg, 1.04 mmol) was reacted with *p*-methoxyphenyl neopentyl boronic ester to yield **3a** (156 mg, 0.65 mmol, 63%).

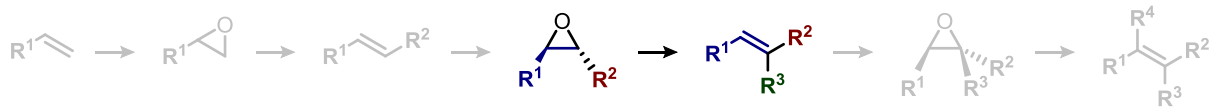
R_f = 0.60 (CyHex/EtOAc, 19:1).

¹H-NMR (300 MHz, CHLOROFORM-*d*) δ = 7.29 - 7.50 (m, 5 H), 7.17 - 7.29 (m, 2 H), 6.95 - 7.10 (m, 2 H), 6.15 (t, J =7.3 Hz, 1 H), 3.97 (s, 3 H), 2.27 (quin, J =7.5 Hz, 2 H), 1.17 ppm (t, J =7.5 Hz, 3 H) ppm.

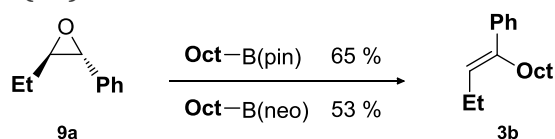
¹³C NMR (75 MHz, CHLOROFORM-*d*) δ = 158.5, 143.2, 140.5, 132.6, 131.5, 131.0, 128.0, 127.3, 126.7, 113.5, 55.2, 23.2, 14.5 ppm.

¹H- and ¹³C NMR data were consistent with those previously reported.²⁷

²⁷ K. Mondal, S. C. Pan, *Eur. J. Org. Chem.* **2015**, 2015, 2129–2132.



(*E*)-4-Phenyl-3-dodecene (**3b**)



According to **GP3A** epoxide **9a** (52 mg, 0.35 mmol) was reacted with octyl pinacol boronic ester to yield **3b** (56 mg, 0.23 mmol, 65%). When the reaction was conducted with octyl neopentyl boronic ester **3b** was obtained in 53% yield.

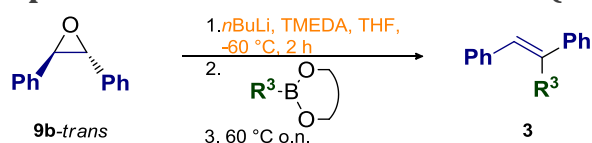
$R_f = 0.71$ (CyHex/EtOAc, 19:1).

$^1\text{H-NMR}$ (300 MHz, CHLOROFORM-*d*) $\delta = 7.14 - 7.44$ (m, 5 H), 5.66 (t, $J=7.2$ Hz, 1 H), 2.42 - 2.60 (m, 2 H), 2.24 (quin, $J=7.4$ Hz, 2 H), 1.18 - 1.46 (m, 12 H), 1.09 (t, $J=7.5$ Hz, 3 H), 0.73 - 0.96 (m, 3 H) ppm.

$^{13}\text{C-NMR}$ (75 MHz, CHLOROFORM-*d*) $\delta = 143.5, 139.7, 130.6, 128.1, 126.3, 126.3, 31.9, 29.7, 29.6, 29.4, 29.3, 28.8, 22.6, 21.9, 14.4, 14.1$ ppm.

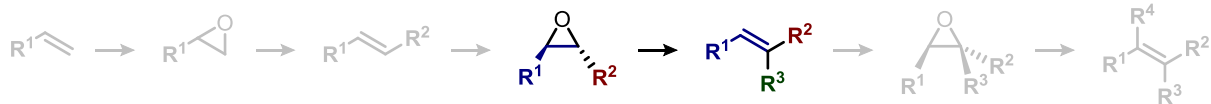
^1H - and ^{13}C NMR data were consistent with those previously reported for (*E*)-4-Phenyl-3-octene.²⁸ Identity was further confirmed after subsequent epoxidation (*v.i.*).

General Procedure Optimized for reaction of **9b-trans** (GP3B)

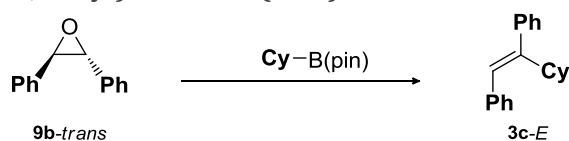


At $-60\text{ }^\circ\text{C}$ *n*BuLi in hexanes (1.5 equiv.) was added dropwise to a solution of epoxide **9b-trans** and TMEDA (3 equiv.) in dry THF (6.5 – 7.8 mL/mmol of **9b-trans**). After stirring for 2 h at the same temperature, a solution of appropriate boronic ester in THF (2 equiv., 0.61 – 1.0 M) was added and stirring was continued for 2 h at $-60\text{ }^\circ\text{C}$. The reaction mixture was allowed to warm up to room temperature for 0.5 h and heated to $60\text{ }^\circ\text{C}$ overnight. The reaction mixture was transferred with a small amount of Et_2O into a separation funnel and extracted with aqueous NaOH (1 M, 3x). The aqueous layers were re-extracted with Et_2O (2x) and the combined organic layers were dried over Na_2SO_4 , concentrated *in vacuo* and purified by chromatography.

²⁸ J. Gerard, L. Hevesi, *Tetrahedron* **2001**, 57, 9109-9121.



(*E*)-(1-Cyclohexylethen-1,2-diyl)dibenzen (**3c-E**)



According to **GP3B** epoxide **9b-trans** (104 mg, 0.53 mmol) was reacted with cyclohexyl pinacol boronic ester to yield **3c-E** (60 mg, 0.23 mmol, 44%, *de* 95%), as a colorless oil after chromatography (SiO₂, CyHex).

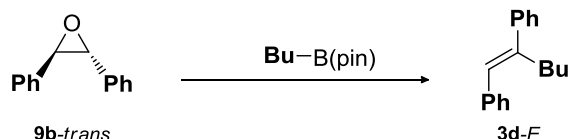
R_f = 0.58 (CyHex/EtOAc, 19:1).

¹H-NMR (300 MHz, CHLOROFORM-*d*) δ = 7.07 - 7.48 (m, 10 H), 6.31 (s, 1 H), 2.79 - 3.05 (m, 1 H), 0.92 - 1.85 ppm (m, 10 H) ppm.

¹³C NMR (75 MHz, CHLOROFORM-*d*) δ = 149.4, 143.3, 137.9, 128.9, 128.8, 128.4, 128.2, 127.5, 126.5, 126.4, 40.4, 32.1, 26.3, 25.9 ppm.

¹H- and ¹³C NMR data for the *Z*-isomer were previously reported and examination of the spectra published by Zhang et al. revealed contamination with the *E*-isomer (**3c-E**). The *de* for our reaction was determined through integration of the olefinic signals at 6.31 (s, 1H, *E*-isomer) ppm and 6.38 (s, 1H, *Z*-isomer) ppm.²⁹ The reaction was also conducted using **GP1A** and **GP3A** delivering **3c** in 29% and 9% yield, respectively.

(*E*)-Hex-1-en-1,2-diyl)dibenzen (**3d-E**)



According to **GP3B** epoxide **9b-trans** (300 mg, 1.53 mmol) was reacted with butyl pinacol boronic ester to yield **3d-E** (111 mg, 0.47 mmol, 31%, *de* 94%) as a colorless oil after chromatography (SiO₂, CyHex).

R_f = 0.52 (CyHex/EtOAc, 19:1).

¹H-NMR (300 MHz, CHLOROFORM-*d*) δ = 7.20 - 7.51 (m, 10 H), 6.70 (s, 1 H), 2.64 - 2.76 (m, 2 H), 1.27 - 1.46 (m, 4 H), 0.81 - 0.88 (m, 3 H) ppm.

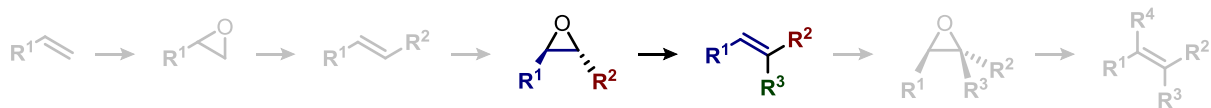
¹³C NMR (75 MHz, CHLOROFORM-*d*) δ = 143.4, 143.2, 138.4, 128.8, 128.6, 128.3, 128.2, 128.1, 127.1, 126.6, 126.5, 125.5, 30.9, 30.0, 22.8, 13.9 ppm.

¹H- and ¹³C NMR data were consistent with those previously reported.³⁰ The *de* was determined through integration of olefinic signals at 6.70 (s, 1H, *E*-isomer) ppm and 6.44 (s, 1H, *Z*-isomer) ppm.³¹

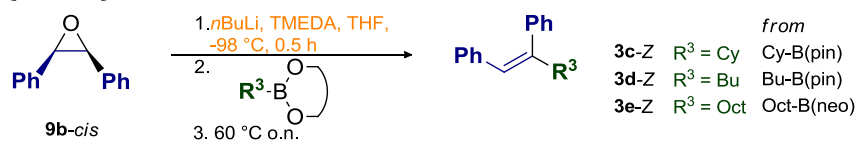
²⁹ Q.-Q. Wang, Z.-X. Wang, X.-Y. Zhang, X.-S. Fan, *Asian J. Org. Chem.* **2017**, 6, 1445–1450.

³⁰ F. Xue, J. Zhao, T. S. A. Hor, *Chem. Commun.* **2013**, 49, 10121.

³¹ E/Z Relationship according to: D. M. Hodgson, M. J. Fleming, S. J. Stanway, *J. Org. Chem.* **2007**, 72, 4763–4773.

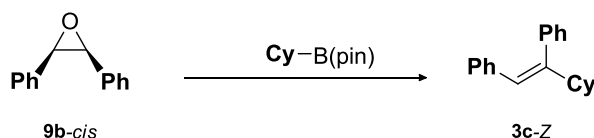


Synthesis of Trisubstituted Alkenes from *cis*-Stilbene Oxide – General Procedure (GP3C)



At -98°C $n\text{BuLi}$ in hexanes (1.5 equiv.) was added dropwise to a solution of epoxide **9b-cis** and TMEDA (1.5 equiv.) in dry THF (8 mL/mmol of **9b-cis**). After stirring for 0.5 h at the same temperature, a solution of appropriate boronic ester in THF (2.0 equiv., 0.50 M) was added and stirring was continued for 10 min at -98°C . The reaction mixture was allowed to warm up to room temperature for 0.5 h and heated to 60°C overnight. The reaction mixture was transferred with a small amount of Et_2O into a separation funnel and extracted with aqueous NaOH (1 M, 3x). The aqueous layers were re-extracted with Et_2O (2x) and the combined organic layers were dried over Na_2SO_4 , concentrated *in vacuo* and purified by chromatography over Al_2O_3 .

(*Z*)-(1-Cyclohexylethen-1,2-diyl)dibenzen (**3c-Z**)



According to **GP3C** epoxide **9b-cis** (49 mg, 0.25 mmol) was reacted with cyclohexyl pinacol boronic ester to yield **3c-Z** (58 mg, 0.22 mmol, 88%), as a colorless oil after chromatography (Al_2O_3 , CyHex/EtOAc, 20:1).

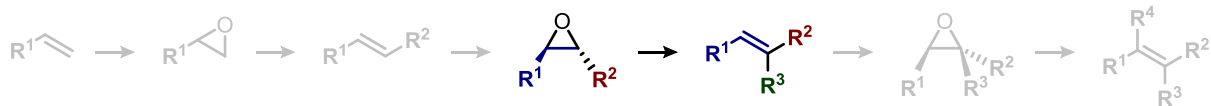
$R_f = 0.76$ (Al_2O_3 , CyHex/EtOAc, 20:1).

$^1\text{H-NMR}$ (300 MHz, $\text{CHLOROFORM-}d$) $\delta = 7.20 - 7.36$ (m, 3 H), $6.92 - 7.18$ (m, 5 H), $6.71 - 6.91$ (m, 2 H), 6.39 (s, 1 H), $2.19 - 2.44$ (m, 1 H), $1.54 - 1.96$ (m, 5 H), $1.03 - 1.40$ (m, 5 H) ppm.

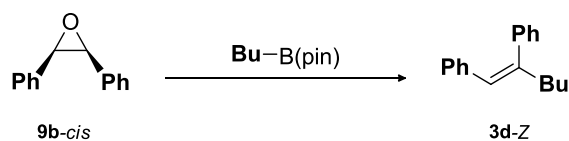
$^{13}\text{C NMR}$ (75 MHz, $\text{CHLOROFORM-}d$) $\delta = 148.9, 141.6, 137.7, 129.0, 128.9, 128.3, 127.7, 126.6, 125.9, 124.5, 47.7, 32.3, 26.8, 26.3$ ppm.

$^1\text{H-}$ and $^{13}\text{C NMR}$ data were consistent with those previously reported.³²

³² Q.-Q. Wang, Z.-X. Wang, X.-Y. Zhang, X.-S. Fan, *Asian J. Org. Chem.* **2017**, 6, 1445–1450.



(Z)-Hex-1-en-1,2-diylidibenzen (3d-Z)



According to **GP3C** epoxide **9b-cis** (49 mg, 0.25 mmol) was reacted with butyl pinacol boronic ester to yield **3d-Z** (56 mg, 0.24 mmol, 95%) as a colorless oil after chromatography (Al_2O_3 , CyHex).

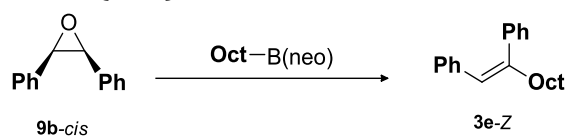
$R_f = 0.74$ (Al_2O_3 , CyHex/EtOAc, 20:1).

$^1\text{H-NMR}$ (300 MHz, CHLOROFORM-d) $\delta = 7.19 - 7.39$ (m, 3 H), 7.10 - 7.18 (m, 2 H), 6.97 - 7.11 (m, 3 H), 6.81 - 6.96 (m, 2 H), 6.42 (s, 1 H), 2.48 (td, $J=7.3, 1.3$ Hz, 2 H), 1.16 - 1.46 (m, 4 H), 0.89 (t, $J=7.2$ Hz, 2 H) ppm.

$^{13}\text{C NMR}$ (75 MHz, CHLOROFORM-d) $\delta = 143.6, 141.5, 137.6, 129.0, 128.5, 128.4, 127.8, 126.8, 126.1, 126.0, 40.4, 30.1, 22.3, 13.9$ ppm.

$^1\text{H-}$ and $^{13}\text{C NMR}$ data were consistent with those previously reported.³³

(Z)-Dec-1-en-1,2-diylidibenzen (3e-Z)



According to **GP3C** epoxide **9b-cis** (50 mg, 0.25 mmol) was reacted with octyl neopentyl boronic ester to yield **3e-Z** (57 mg, 0.19 mmol, 78%) as a colorless oil after chromatography (Al_2O_3 , CyHex/EtOAc, 20:1).

$R_f = 0.80$ (Al_2O_3 , CyHex/EtOAc, 20:1).

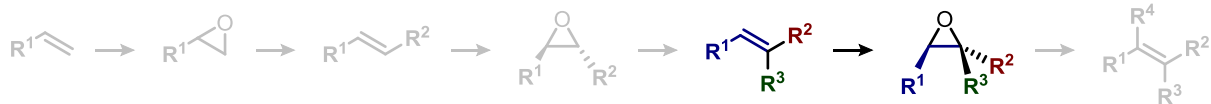
$^1\text{H-NMR}$ (300 MHz, CHLOROFORM-d) $\delta = 7.22 - 7.36$ (m, 3 H), 7.00 - 7.22 (m, 5 H), 6.86 - 6.98 (m, 2 H), 6.44 (s, 1 H), 2.27 - 2.66 (m, 2 H), 1.06 - 1.49 (m, 12 H), 0.73 - 0.98 (m, 3 H) ppm.

$^{13}\text{C NMR}$ (75 MHz, CHLOROFORM-d) $\delta = 143.6, 141.5, 137.6, 129.0, 128.5, 128.4, 127.8, 126.8, 126.1, 126.0, 40.7, 31.9, 29.4, 29.3, 29.2, 27.9, 22.6, 14.1$ ppm.

$^1\text{H-}$ and $^{13}\text{C NMR}$ data were consistent with those previously reported.³⁴

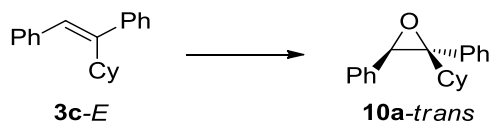
³³ B. C. Chary, S. Kim, D. Shin, P. H. Lee, *Chem. Comm.* **2011**, 47, 7851.

³⁴ G. Liu, L. Kong, J. Shen, G. Zhu, *Org. Biomol. Chem.* **2014**, 12, 2310–2321.



Synthesis of Trisubstituted Epoxides

(2*R*,3*R*)-2-Cyclohexyl-2,3-diphenyloxiran (**10a-trans**)



According to **GP2** alkene **3c-E** (200 mg, 0.76 mmol) was transformed into epoxide **10a-trans** (200 mg, 0.60 mmol, 83%), isolated as a white solid after column chromatography (SiO₂, CyHex/EtOAc 19:1).

R_f = 0.41 (CyHex/EtOAc, 19:1).

¹H-NMR (600 MHz, CHLOROFORM-*d*) δ = 7.30 - 7.60 (m, 10 H), 4.11 (s, 1 H), 1.87 - 2.01 (m, 1 H), 1.63 - 1.73 (m, 1 H), 1.37 - 1.52 (m, 3 H), 1.31 (tt, J =12.1, 3.3 Hz, 1 H), 1.13 (qt, J =13.0, 3.4 Hz, 1 H), 0.97 (qd, J =12.5, 3.5 Hz, 1 H), 0.83 - 0.93 (m, 2 H), 0.73 - 0.82 (m, 1 H) ppm

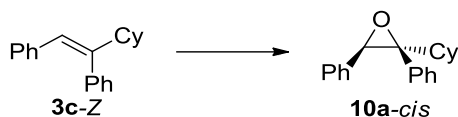
¹³C-NMR (75 MHz, CHLOROFORM-*d*) δ = 139.2, 135.5, 130.5, 128.2, 128.0, 127.6, 127.5, 127.4, 126.6, 70.7, 64.7, 39.8, 28.9, 28.2, 26.0, 25.8 ppm.

IR: $\tilde{\nu}$ = 3086 (w), 3064 (w), 3032 (w), 2929 (m), 2855 (m), 2360 (w), 2161 (w, br.), 2024 (w, br.), 1967 (w, br.), 1446 (m), 882 (m), 767 (m), 754 (s), 693 (s) cm⁻¹.

MS m/z (ESI⁺): 301.2 (M+Na⁺, 100%).

HR-MS m/z (ESI⁺): found: [M+H⁺] 279.1744, C₂₀H₂₂OH calculated: 279.1743.

(2*R*,3*R*)-2-Cyclohexyl-2,3-diphenyloxiran (**10a-cis**)



According to **GP2** alkene **3c-Z** (58 mg, 0.22 mmol) was transformed into epoxide **10a-cis** (58 mg, 0.21 mmol, 94%), isolated as a white solid after column chromatography (Al₂O₃, CyHex).

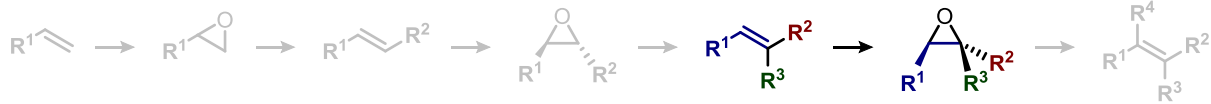
R_f = 0.67 (Al₂O₃, CyHex/EtOAc, 20:1).

¹H-NMR (300 MHz, CHLOROFORM-*d*) δ = 7.02 - 7.20 (m, 32 H), 6.87 - 7.19 (m, 10 H), 4.16 (s, 1 H), 1.57 - 2.15 (m, 6 H), 0.97 - 1.36 (m, 5 H) ppm.

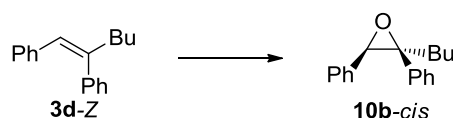
¹³C-NMR (75 MHz, CHLOROFORM-*d*) δ = 136.0, 135.6, 128.9, 127.5, 127.2, 127.1, 126.9, 126.4, 72.3, 63.5, 46.4, 29.3, 28.4, 26.3, 26.1, 26.0 ppm.

IR: $\tilde{\nu}$ = 3086 (w), 3060 (w), 3028 (w), 2927 (w), 2852 (w), 2360 (s), 2339 (s), 1446 (w), 754 (w), 717 (w), 698 (m), 667 (w) cm⁻¹.

MS (ESI, 70 eV): found: [M+H⁺] 279.1740, calculated: [M+H⁺] 279.1743.



(2*R*,3*R*)-2-butyl-2,3-diphenyloxirane (**10b-cis**)



According to **GP2** alkene **3d-Z** (46 mg, 0.19 mmol) was transformed into epoxide **10b-cis** (53 mg, 0.16 mmol, 84%, *yield corrected for 12% CyHex*), isolated as a colorless oil after column chromatography (Al_2O_3 , CyHex).

$R_f = 0.60$ (Al_2O_3 , CyHex/EtOAc, 20:1).

$^1\text{H-NMR}$ (300 MHz, $\text{CHLOROFORM-}d$) $\delta = 7.04 - 7.22$ (m, 8 H), 6.91 - 7.06 (m, 2 H), 4.15 (s, 1 H), 2.01 - 2.24 (m, 1 H), 1.75 - 1.95 (m, 1 H), 1.13 - 1.59 (m, 4 H), 0.89 (t, $J=6.9$ Hz, 3 H) ppm.

$^{13}\text{C-NMR}$ (75 MHz, $\text{CHLOROFORM-}d$) $\delta = 137.1, 135.7, 127.7, 127.6, 127.5, 127.2, 127.0, 126.5, 69.3, 64.6, 38.7, 27.0, 22.8, 14.0$ ppm.

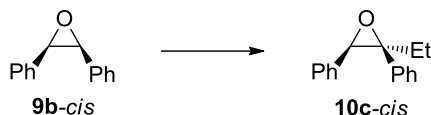
IR: $\tilde{\nu} = 3032$ (w), 2954 (w), 2937 (w), 2870 (w), 2856 (w), 2160 (w), 2027 (w, br.), 1977 (w, br.), 1496 (w), 1456 (w), 1201 (w), 1076 (w), 912 (w), 885 (w), 860 (w), 754 (m), 698 (s) cm^{-1} .

MS m/z (ESI^+): 253.0 ($\text{M}+\text{H}^+$, 100%).

HR-MS m/z (ESI^+): found: $[\text{M}+\text{H}^+]$ 253.160, $\text{C}_{18}\text{H}_{20}\text{OH}$ calculated 253.159.

Comment: Using butyl iodide instead of ethyl iodide, the conditions reported below for the synthesis of **10c-cis** were also used for preparation of **10b-cis** in 96% yield.

(2*R*,3*R*)-2-Ethyl-2,3-diphenyloxirane (**10c-cis**)



To a solution of **9b-cis** (202 mg, 1.03 mmol) in THF (8 mL) at -98°C was added $s\text{BuLi}$ in Hexanes (0.9 mL, 1.35 M, 1.22 mmol) in a drop wise manner. After stirring for 0.5 h ethyl iodide (0.1 mL, 1.22 mmol) was added. The reaction mixture was allowed to reach rt and stirred overnight after which saturated aq. NH_4Cl (4 mL) was added and the mixture was transferred into a separation funnel containing brine (10 mL). After extraction with EtOAc (3x10 mL) the combined organic phases were dried over Na_2SO_4 and concentrated *in vacuo*. The residue was purified by chromatography (Al_2O_3 , CyHex/EtOAc 30:1), yielding **10c-cis** (216 mg, 0.96 mmol, 94%) as a colorless oil.^[*]

$R_f = 0.70$ (Al_2O_3 , CyHex/EtOAc, 10:1).

$^1\text{H-NMR}$ (300 MHz, CDCl_3): $\delta = 7.03 - 7.41$ (m, 10 H), 4.27 (s, 1 H), 2.28 (dq, $J=14.1, 7.5$ Hz, 1 H),^[**] 2.01 (dq, $J=14.3, 7.2$ Hz, 1 H), 1.10 (t, $J=7.5$ Hz, 3 H) ppm.

$^{13}\text{C-NMR}$ (75 MHz, CDCl_3): $\delta = 136.8, 135.7, 127.8, 127.6, 127.2, 127.0, 126.5, 69.9, 64.4, 31.8, 9.1$ ppm.



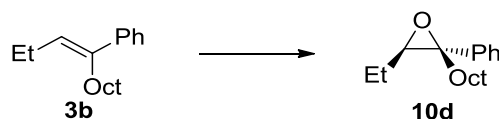
¹H- and ¹³C NMR data were consistent with those previously reported.³⁵

Comments:

[*] These conditions were also used to prepare the other diastereomer (**10c-trans**) from *trans*-stilbene oxide (**9b-trans**). This delivered a 7:1 mixture of **10c-trans** and the *ortho*-lithiation product in 57% yield.

[**] Resolution of this signal in a 300 MHz NMR required application of a Lorenz-Gaussian window function upon Fourier-Transformation.

(2*R*,3*R*)-3-Ethyl-2-octyl-2-phenyloxirane (**10d**)



According to **GP2** alkene **3b** (56 mg, 0.23 mmol) was transformed into epoxide **10d** (42 mg, 0.16 mmol, 67%), isolated as a colorless oil after column chromatography (SiO₂, CyHex/EtOAc 19:1).

R_f = 0.57 (CyHex/EtOAc, 9:1).

¹H-NMR (300 MHz, CHLOROFORM-*d*) δ = 7.12 - 7.42 (m, 5 H), 2.78 (t, *J*=6.4 Hz, 1 H), 1.98 - 2.22 (m, 1 H), 1.59 - 1.83 (m, 3 H), 1.15 - 1.48 (m, 12 H), 1.10 (t, *J*=7.5 Hz, 3 H), 0.87 (t, *J*=6.6 Hz, 3 H) ppm.

¹³C-NMR (75 MHz, CHLOROFORM-*d*) δ = 141.8, 128.2, 127.0, 125.9, 67.7, 64.7, 31.8, 31.1, 29.8, 29.4, 29.2, 25.1, 22.6, 22.0, 14.1, 10.6 ppm.

IR: $\tilde{\nu}$ = 3064 (w), 3035 (w), 2955 (m), 2924 (m), 2855 (m), 2360 (s), 2341 (s), 2158 (w, br.), 2026 (w, br.), 1653 (m), 1559 (m), 1507 (m), 1457 (m), 905 (w), 744 (m), 698 (s), 668 (s) cm⁻¹.

MS *m/z* (ESI⁺): 283.2 (M+Na⁺, 100%).

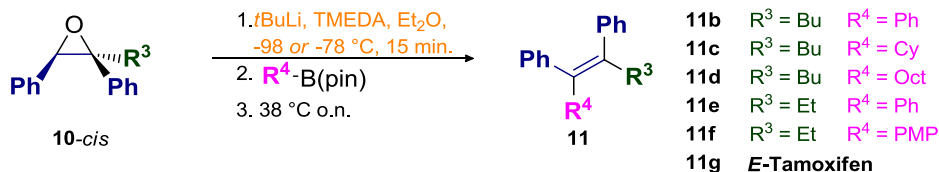
HR-MS *m/z* (ESI⁺): found: [M+Na⁺] 283.2038, C₁₈H₂₈ONa calculated: 283.2032.

Comment: This compound was prepared to confirm structure **3b**.

³⁵ S. Oudeyer, E. Léonel, J. P. Paugam, J.-Y. Nédélec, *Synthesis* **2004**, 389–400.

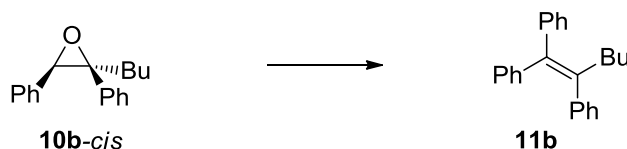


Synthesis of Tetrasubstituted Alkenes – General Procedure (GP4)



At -78 °C $t\text{BuLi}$ in pentane (1.1-1.3 equiv.) was added dropwise to a solution of epoxide **10-cis** and TMEDA (6 equiv.) in dry Et_2O (9-10 mL/mmol of **10-cis**). After stirring for 15 min. at the same temperature, a solution of appropriate boronic ester in Et_2O (2.0 equiv., 0.40-0.44 M) was added. The reaction mixture was allowed to warm up to room temperature for 0.5 h and heated to 38 °C overnight. The reaction mixture was transferred with a small amount of Et_2O into a separation funnel and extracted with aqueous NaOH (1 M, 3x). The aqueous layers were re-extracted with Et_2O (2x) and the combined organic layers were dried over Na_2SO_4 , concentrated *in vacuo* and purified by chromatography.

Hex-1-ene-1,1,2-triyltribenzene (**11b**)



According to **GP4** epoxide **10b-cis** (50 mg, 0.20 mmol) was transformed into alkene **11b** (20 mg, 0.06 mmol, 32%) at -78 °C, isolated as a white solid after column chromatography (Al_2O_3 , CyHex).

$R_f = 0.55$ (SiO_2 , CyHex/ EtOAc , 20:1).

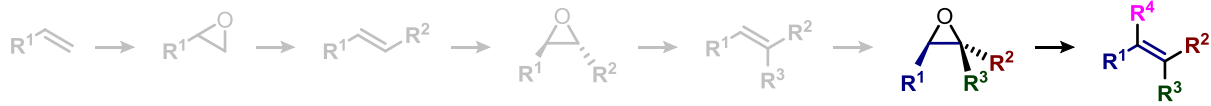
$^1\text{H-NMR}$ (300 MHz, $\text{CHLOROFORM-}d$) $\delta = 7.33 - 7.38$ (m, 2 H), $7.24 - 7.31$ (m, 3 H), $7.10 - 7.18$ (m, 5 H), $6.97 - 7.05$ (m, 3 H), $6.86 - 6.95$ (m, 2 H), 2.45 (t, $J=7.5$ Hz, 2 H), $1.17 - 1.37$ (m, 4 H), 0.79 (t, $J=7.2$ Hz, 3 H) ppm.

$^{13}\text{C-NMR}$ (75 MHz, $\text{CHLOROFORM-}d$) $\delta = 143.5, 143.1, 142.5, 141.1, 139.0, 130.7, 129.6, 129.5, 128.1, 127.8, 127.3, 126.5, 126.1, 125.7, 35.6, 31.1, 22.8, 13.9$ ppm.

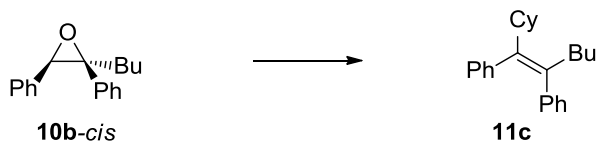
$^1\text{H-}$ and ^{13}C NMR data were consistent with those previously reported.³⁶

Comment: When deprotonation was attempted at -98 °C the product was isolated in 22% yield.

³⁶ C. Zhou, R. C. Larock, *J. Org. Chem.* **2005**, *70*, 3765–3777.



(Z)-(1-Cyclohexylhex-1-ene-1,2-diyl)dibenzene (**11c**)



According to **GP4** epoxide **10b-cis** (50 mg, 0.20 mmol) was transformed into alkene **11c** (36 mg, 0.11 mmol, 56%) at -78 °C, isolated as a colorless oil after column chromatography (Al_2O_3 , CyHex).

$R_f = 0.62$ (CyHex/EtOAc, 20:1).

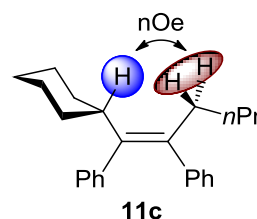
$^1\text{H-NMR}$ (300 MHz, CHLOROFORM-d) $\delta = 6.81 - 7.08$ (m, 10 H), 2.81 (tt, $J=11.9, 3.1$ Hz, 1 H), 2.45 - 2.63 (m, 2 H), 1.56 - 1.84 (m, 5 H), 1.25 - 1.46 (m, 5 H), 0.95 - 1.22 (m, 4 H), 0.91 (t, $J=6.9$ Hz, 3 H) ppm.

$^{13}\text{C-NMR}$ (75 MHz, CHLOROFORM-d) $\delta = 143.9, 143.4, 141.2, 138.1, 130.7, 129.4, 127.1, 126.7, 125.2, 125.1, 41.3, 33.4, 32.2, 31.0, 26.8, 25.9, 22.7, 14.0$ ppm.

IR: $\tilde{\nu} = 3078$ (w), 3053 (w), 3020 (w), 2925 (m), 2852 (w), 2360 (w), 2339 (w), 1489 (w), 1442 (w), 771 (w), 698 (s) cm^{-1} .

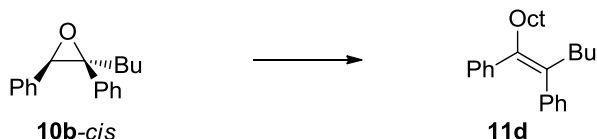
HR-MS m/z (ESI^+): found: $[\text{M}+\text{Na}^+]$ 341.2240, $\text{C}_{24}\text{H}_{30}\text{Na}$ calculated: 341.2240.

Stereochemical assignment: A clear nOe signal between the allylic cyclohexyl CH (2.81, tt, $J=11.3, 3.3$ Hz), and the allylic butyl CH_2 (2.55, m) confirmed formation of the Z-olefin **11c**.



Comment: When deprotonation was attempted at -98 °C the product was isolated in 28% yield.

(Z)-Tetradec-5-ene-5,6-diyl dibenzene (**11d**)



According to **GP4** epoxide **10b-cis** (50 mg, 0.20 mmol) was transformed into alkene **11d** (45 mg, 0.13 mmol, 64%) at -78 °C, isolated as a colorless oil after column chromatography (Al_2O_3 , CyHex).

$R_f = 0.58$ (CyHex/EtOAc, 20:1).

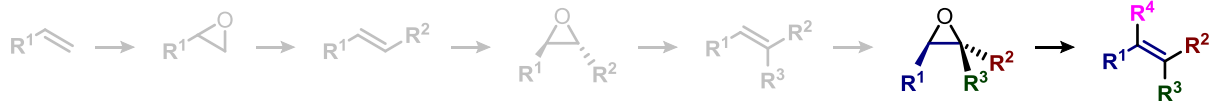
$^1\text{H-NMR}$ (300 MHz, CHLOROFORM-d) $\delta = 6.86 - 7.12$ (m, 10 H), 2.47 - 2.60 (m, 4 H), 1.16 - 1.40 (m, 16 H), 0.89 (t, $J=6.6$ Hz, 6 H) ppm.

$^{13}\text{C-NMR}$ (75 MHz, CHLOROFORM-d) $\delta = 143.6, 138.3, 138.3, 129.8, 127.3, 125.3, 34.3, 34.1, 31.9, 30.7, 29.6, 29.5, 29.3, 28.4, 22.7, 22.6, 14.1, 14.0$ ppm.

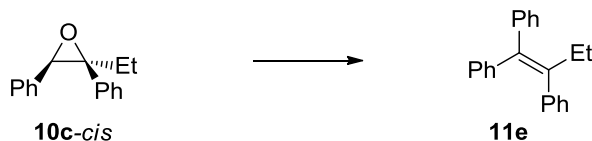
IR: $\tilde{\nu} = 3078$ (w), 3057 (w), 3020 (w), 2924 (m), 2856 (w), 1441 (w), 769 (m), 896 (s) cm^{-1} .

HR-MS m/z (ESI^+): found: $[\text{M}+\text{Na}^+]$ 371.2710, $\text{C}_{18}\text{H}_{28}\text{ONa}$ calculated: 371.2709.

Comment: When deprotonation was attempted at -98 °C the product was isolated in 36% yield. As the allylic signals overlapped, no confirmation of the configuration by nOe was possible in this case.



But-1-ene-1,1,2-triyltribenzene (11e)



According to **GP4** epoxide **10c-cis** (50 mg, 0.22 mmol) was transformed into alkene **11e** (26 mg, 0.09 mmol, 41%) at -78 °C, isolated as a white solid after column chromatography (Al_2O_3 , CyHex).

$R_f = 0.70$ (Al_2O_3 , CyHex/EtOAc, 20:1).

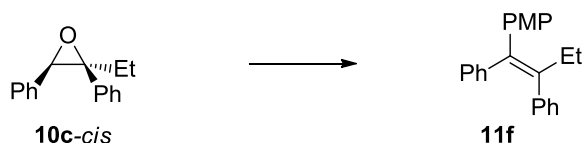
$^1\text{H-NMR}$ (300 MHz, CHLOROFORM-d) $\delta = 7.23 - 7.39$ (m, 5 H), 7.07 - 7.20 (m, 5 H), 6.94 - 7.05 (m, 3 H), 6.85 - 6.94 (m, 2 H), 2.49 (q, $J=7.5$ Hz, 2 H), 0.95 (t, $J=7.5$ Hz, 3 H) ppm.

$^{13}\text{C-NMR}$ (75 MHz, CHLOROFORM-d) $\delta = 143.5, 143.0, 142.2, 142.2, 138.8, 130.7, 129.7, 129.4, 128.1, 127.8, 127.3, 126.6, 126.1, 125.7, 29.0, 13.5$ ppm.

$^1\text{H-}$ and ^{13}C NMR data were consistent with those previously reported.³⁷

Comment: When deprotonation was attempted at -98 °C the product was isolated in 35% yield.

(E)-(1-(4-Methoxyphenyl)but-1-ene-1,2-diyl)dibenzene (11f)



According to **GP4** epoxide **10c-cis** (51 mg, 0.23 mmol) was transformed into alkene **11e** (69 mg, 0.20 mmol, 87%) at -78 °C, isolated as a white solid after column chromatography (Al_2O_3 , CyHex).

$R_f = 0.57$ (Al_2O_3 , CyHex/EtOAc, 20:1).

$^1\text{H-NMR}$ (300 MHz, CHLOROFORM-d) $\delta = 6.97 - 7.21$ (m, 10 H), 6.83 - 6.95 (m, 4 H), 3.84 (s, 3 H), 2.53 (q, $J=7.5$ Hz, 2 H), 0.96 (t, $J=7.5$ Hz, 3 H) ppm.

$^{13}\text{C-NMR}$ (75 MHz, CHLOROFORM-d) $\delta = 158.3, 143.4, 142.4, 141.9, 138.4, 136.0, 130.8, 130.6, 129.7, 127.7, 127.3, 126.0, 125.6, 55.2, 29.0, 13.6$ ppm.

$^1\text{H-}$ and ^{13}C NMR data were consistent with those previously reported.³⁸

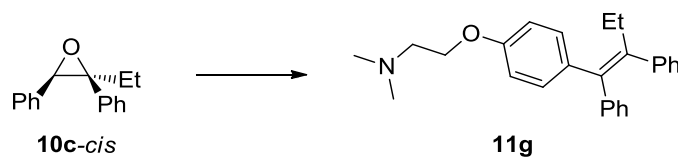
Comment: When deprotonation was attempted at -98 °C the product was isolated in 61% yield. (*) Sample initially contaminated with 10% starting material. Yield corrected accordingly.

³⁷ Z. He, S. Kirchberg, R. Fröhlich, A. Studer, *Angew. Chem., Int. Ed.* **2012**, 51, 3699–3702.

³⁸ B. X. Li, D. N. Le, K. A. Mack, A. McClory, N.-K. Lim, T. Cravillon, S. Savage, C. Han, D. B. Collum, H. Zhang, et al., *J. Am. Chem. Soc.* **2017**, 139, 10777–10783.



(E)-2-(4-(1,2-diphenylbut-1-en-1-yl)phenoxy)-N,N-dimethylethanamine (11g)



According to **GP4** epoxide **10c-cis** (47 mg, 0.21 mmol) was transformed into alkene **11g** (49 mg, 0.13 mmol, 63%) at -78 °C, isolated as a white solid after column chromatography (Al_2O_3 , DCM/MeOH 99:1).

$R_f = 0.25$ (Al_2O_3 , DCM/MeOH, 9:1).

$^1\text{H-NMR}$ (300 MHz, CHLOROFORM-d) δ = 6.96 - 7.21 (m, 10 H), 6.85 - 6.94 (m, 4 H), 4.12 (t, $J=5.8$ Hz, 2 H), 2.79 (t, $J=5.6$ Hz, 2 H), 2.52 (q, $J=7.3$ Hz, 2 H), 2.39 (s, 6 H), 0.95 (t, $J=7.4$ Hz, 3 H) ppm.

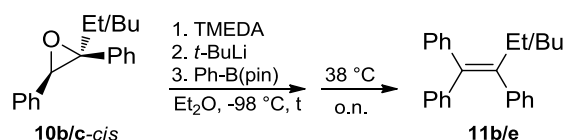
$^{13}\text{C-NMR}$ (75 MHz, CHLOROFORM-d) δ = 157.7, 143.5, 142.6, 142.1, 138.6, 136.3, 130.9, 130.7, 129.9, 127.9, 127.4, 126.2, 125.8, 114.3, 65.9, 58.4, 46.0, 29.2, 13.7 ppm.

^1H - and ^{13}C NMR data were consistent with those previously reported.³⁹

Comment: The boronic ester employed was not completely soluble in Et_2O and added as a suspension in 1 mL dry Et_2O . Therefore the flask and syringe were rinsed with additional Et_2O (1 mL).

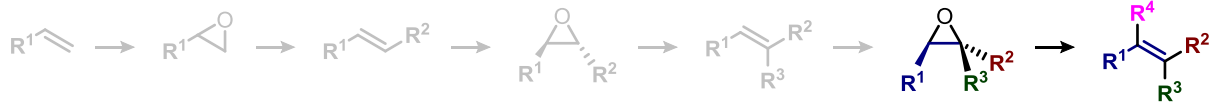
Optimization Experiments

The following experiments were carried out in order to optimize **GP 4** using a mixture of **10b/c-cis**. These experiments indicate that lithiation times of 15-30 min at -98 °C are optimal. While shorter lithiation times led to incomplete conversion, longer lithiation times could very well lead to decomposition of the formed carbenoids.

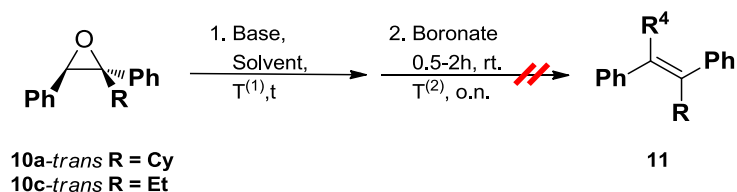


Entry	t	Yield Alkene
1	5 min	48%
2	15 min	60%
3	30 min	62%
4	60 min	50%

³⁹ K. Itami, T. Kamei, J. Yoshida, *J. Am. Chem. Soc.* **2003**, 125, 14670–14671.



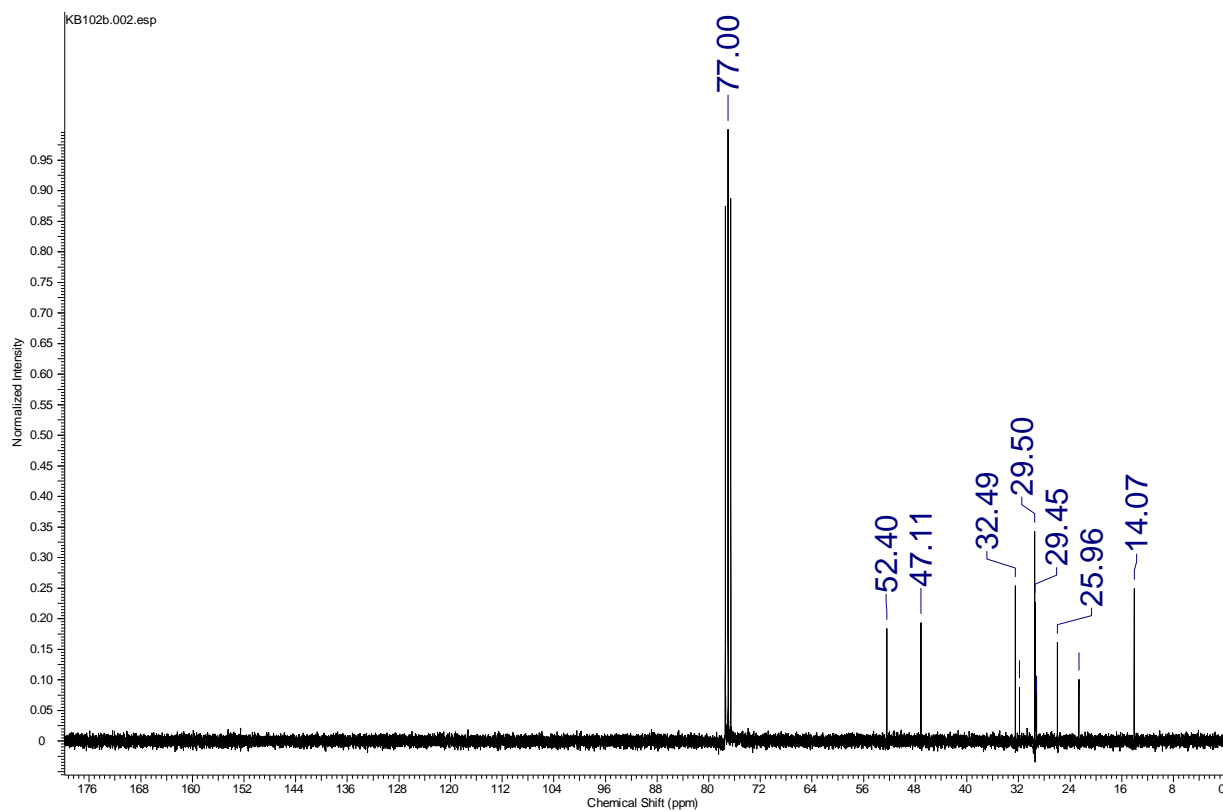
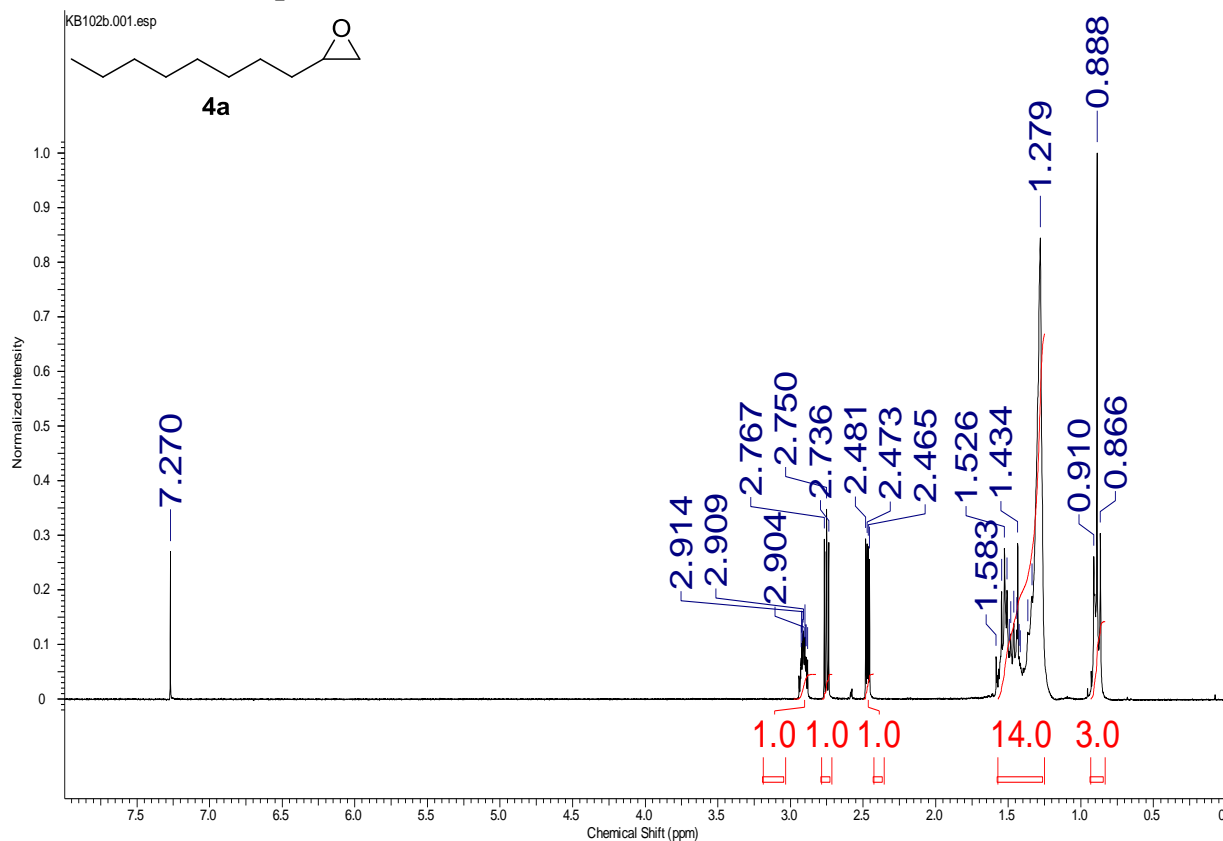
Failed Attempts at Quarternary Alkene Synthesis from 10-*trans*

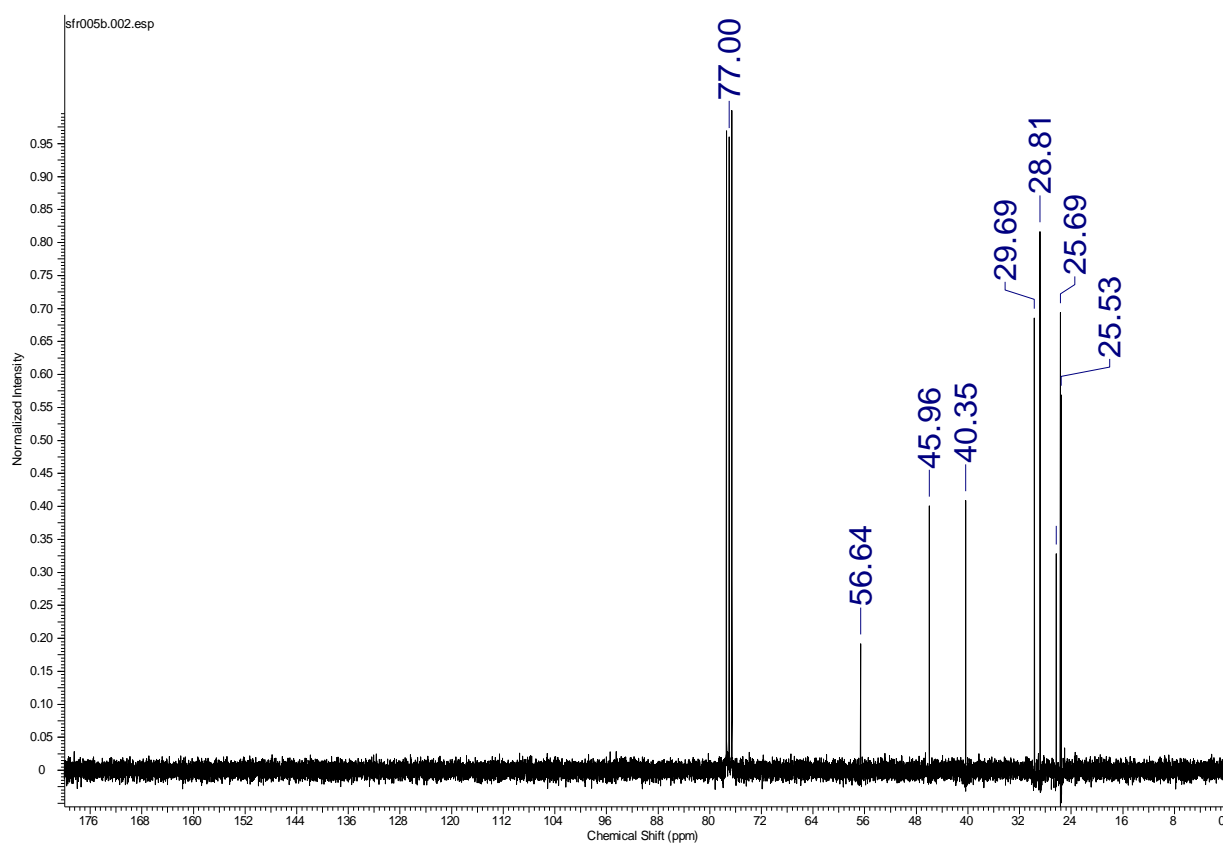
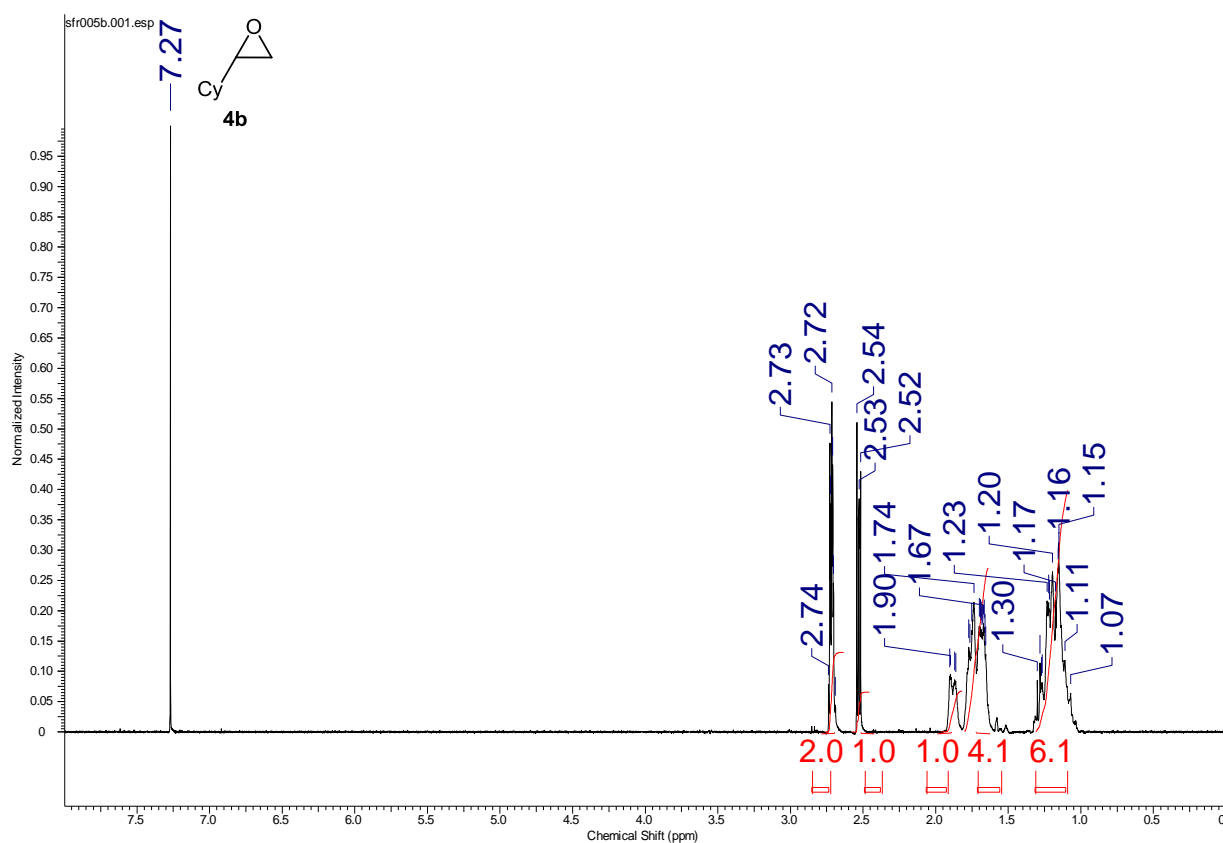


Entry	Base	Solvent	T ⁽¹⁾	t ⁽¹⁾	Boronate	R	T ⁽²⁾	Result
1	LiTMP	THF	0 °C	30 min.	PMP-B(neo) (<i>in situ</i>)	Cyclohexyl	60 °C	no conversion of 10a- <i>trans</i>
2	sBuLi (TMEDA 3 equiv.)	Et ₂ O	-110 °C	10 min.	PMP-B(pin)	Cyclohexyl	38 °C	no conversion of 10a- <i>trans</i>
3	tBuLi (TMEDA 3 equiv.)	Et ₂ O	-110 °C	10 min.	PMP-B(neo)	Cyclohexyl	38 °C	no conversion of 10a- <i>trans</i>
4	nBuLi (TMEDA 3 equiv.)	THF	-60 °C	2 h	PMP-B(neo)	Cyclohexyl	60 °C	no conversion of 10a- <i>trans</i>
5	sBuLi (TMEDA 3 equiv.)	PhMe	-50 °C	30 min.	PMP-B(neo)	Cyclohexyl	100 °C	no conversion of 10a- <i>trans</i>
6	sBuLi (TMEDA 3 equiv.)	PhMe	-50 °C	2 h	PMP-B(neo)	Cyclohexyl	100 °C	no conversion of 10a- <i>trans</i>
7	tBuLi (TMEDA 6 equiv.)	Et ₂ O	-98 °C	5 min	Ph-B(neo)	Ethyl	38 °C	no conversion of 10c- <i>trans</i>
8	tBuLi (TMEDA 6 equiv.)	Et ₂ O	-78 °C	2 h	Ph-B(neo)	Ethyl	38 °C	no conversion of 10c- <i>trans</i>
9	tBuLi (TMEDA 6 equiv.)	Et ₂ O	-50 °C	2 h	Ph-B(neo)	Ethyl	38 °C	no conversion of 10c- <i>trans</i>
10	KOt-Bu n-BuLi ^(a)	THF	-78 °C to -48 °C	2 h	Ph-B(neo)	Cyclohexyl	60 °C	 13 (>95%)*
11	KOt-Bu n-BuLi ^(b)	THF	-78 °C to -48 °C	2 h	Ph-B(neo)	Cyclohexyl	60 °C	 13 (>95%)*

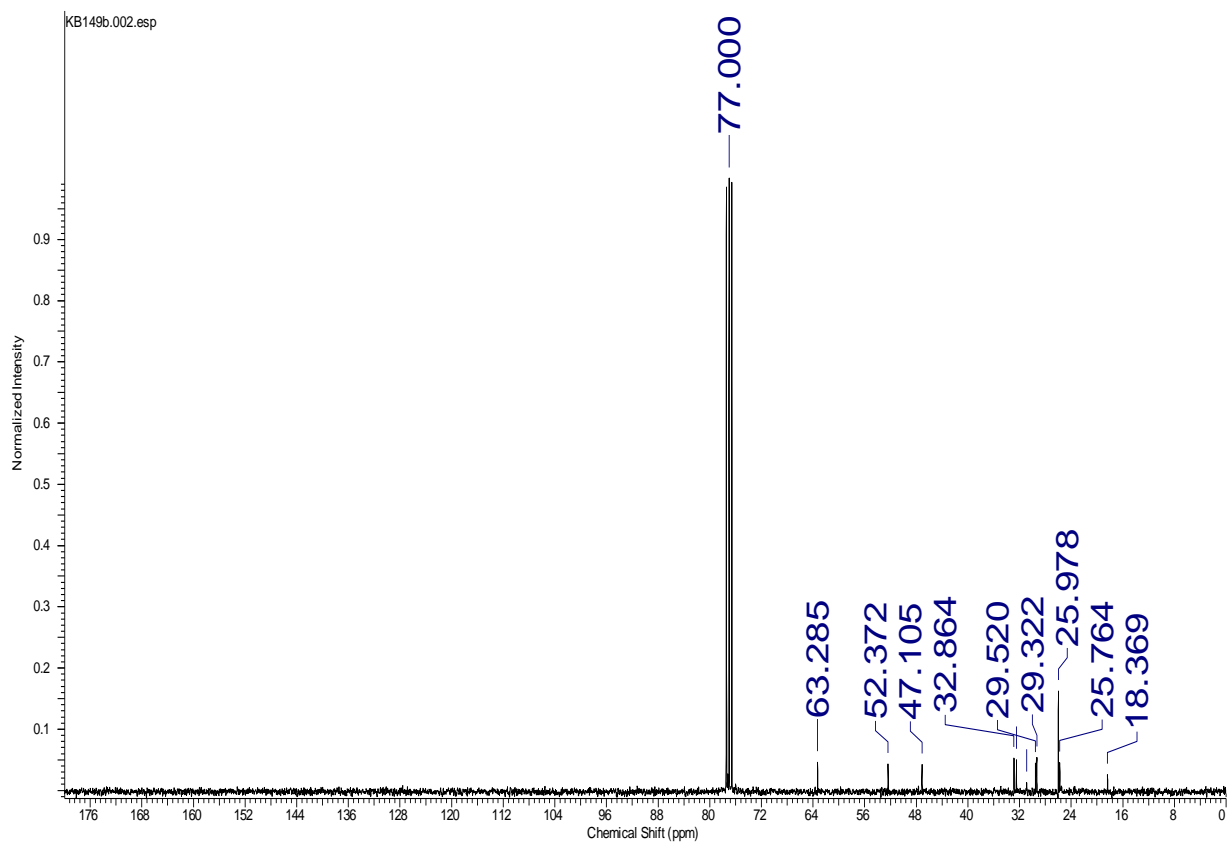
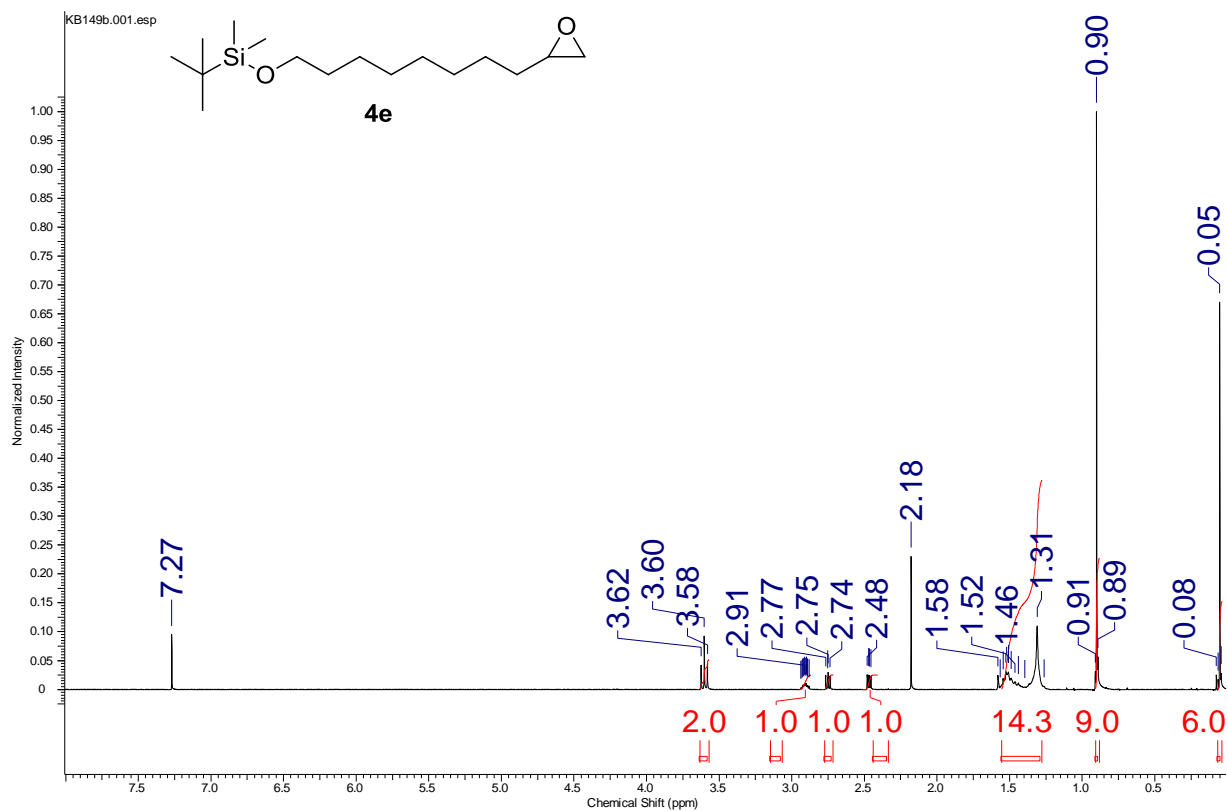
(*) Yield of **13** was obtained by ¹H NMR using methyl benzoate as an internal standard.

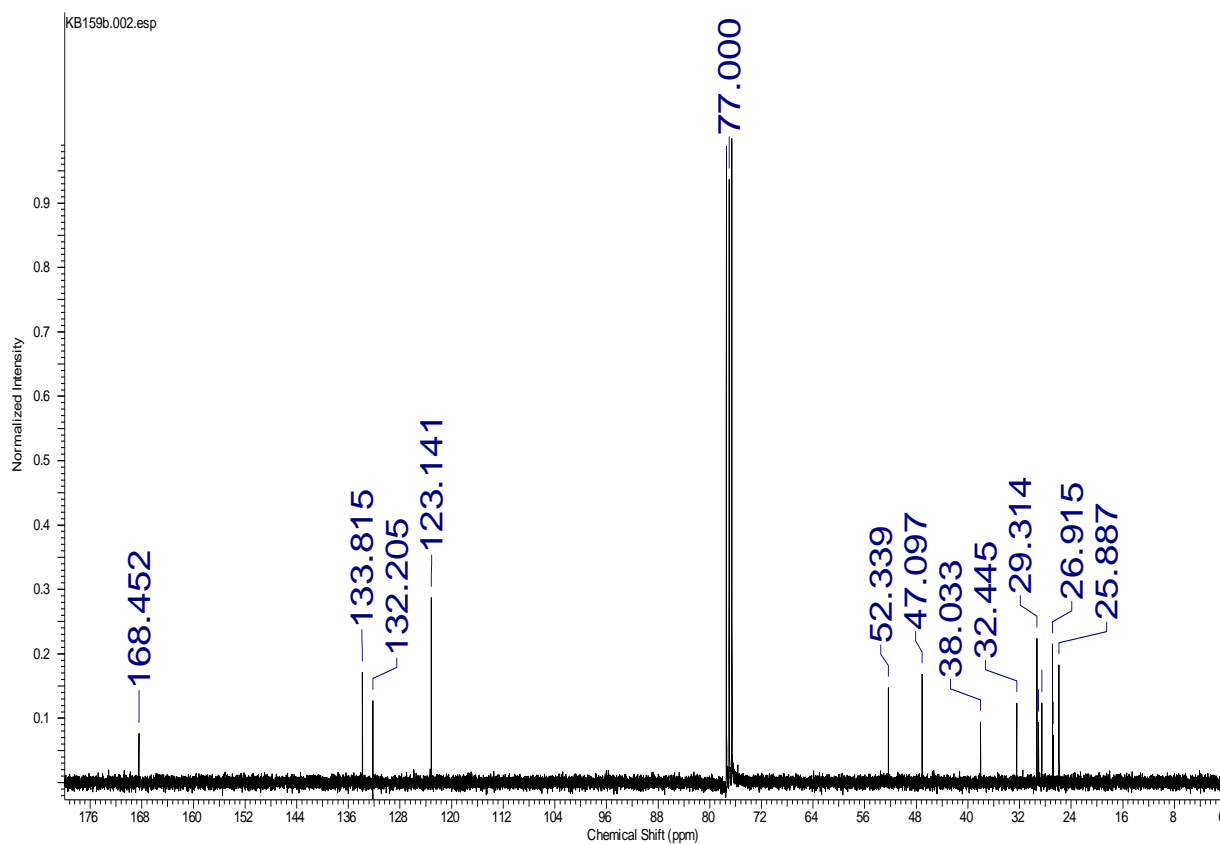
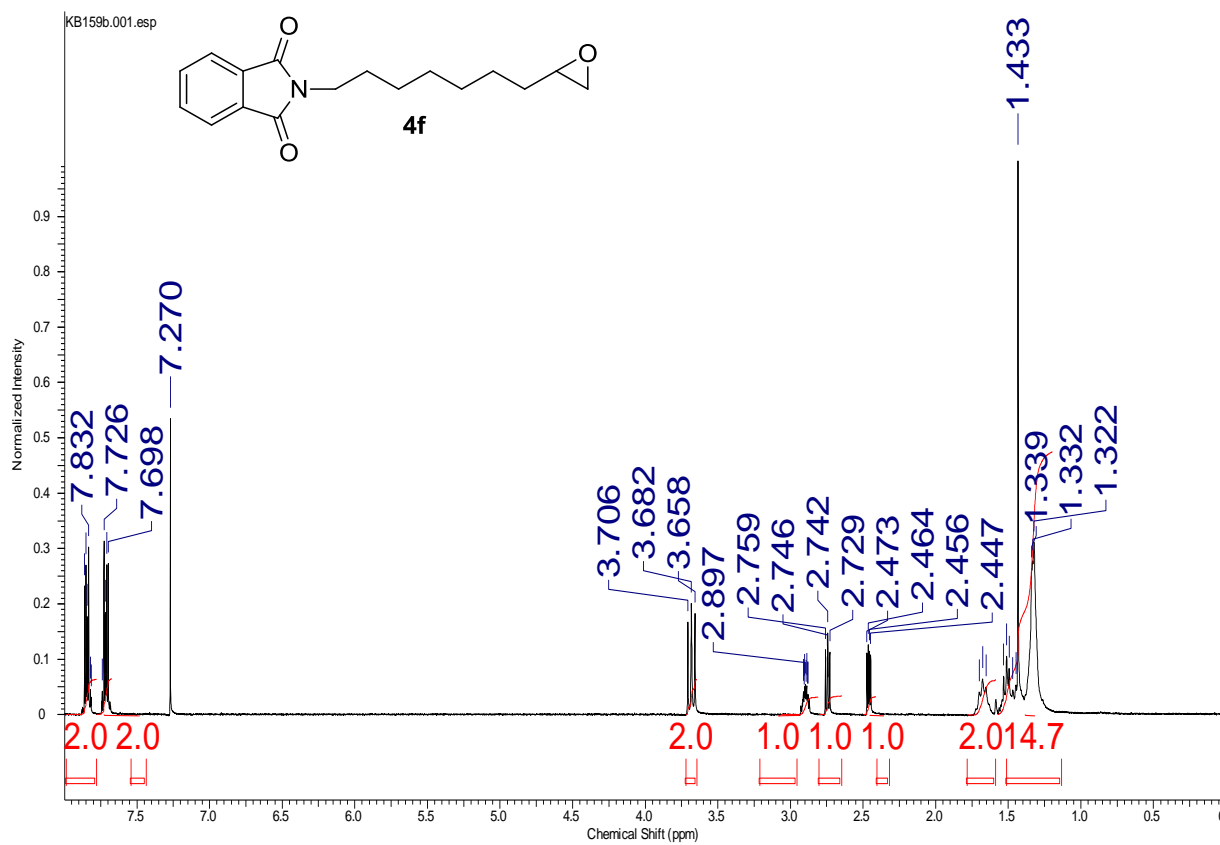
Selected NMR-Spectra

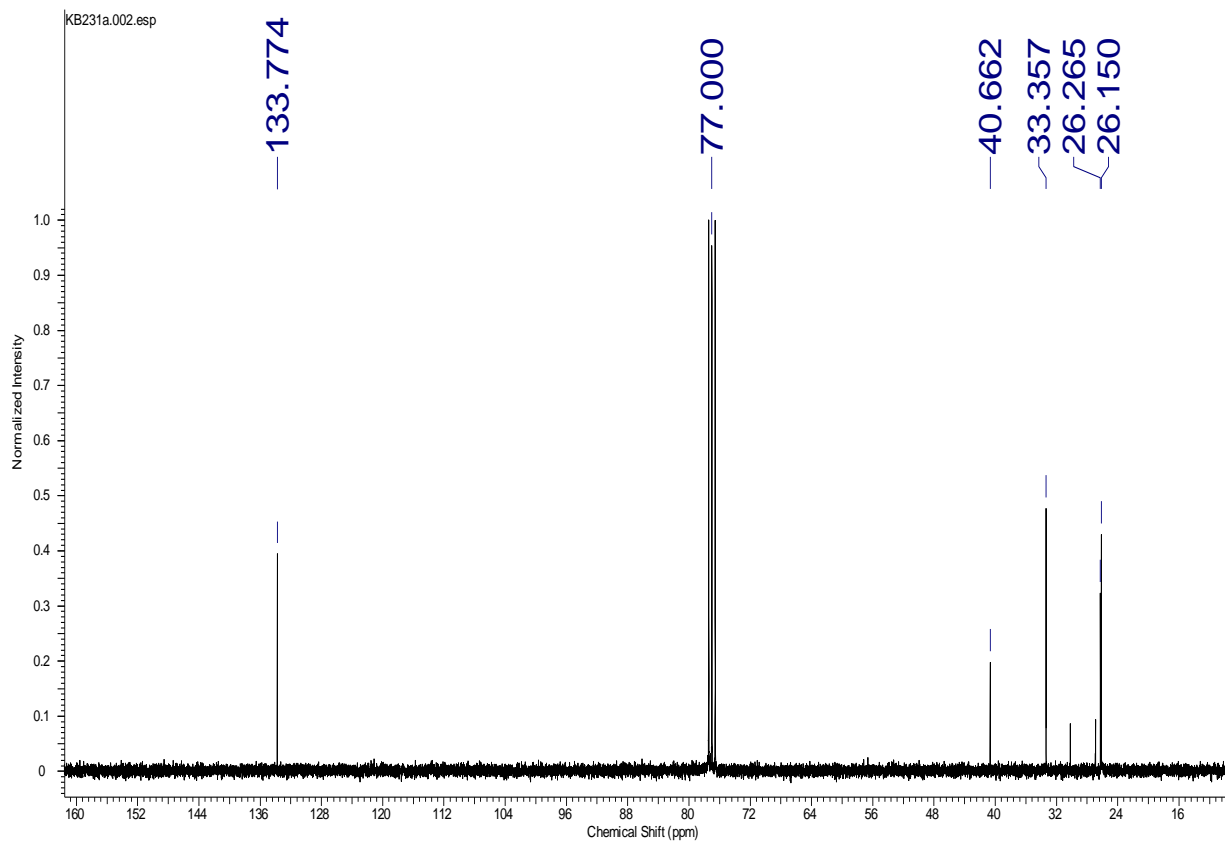
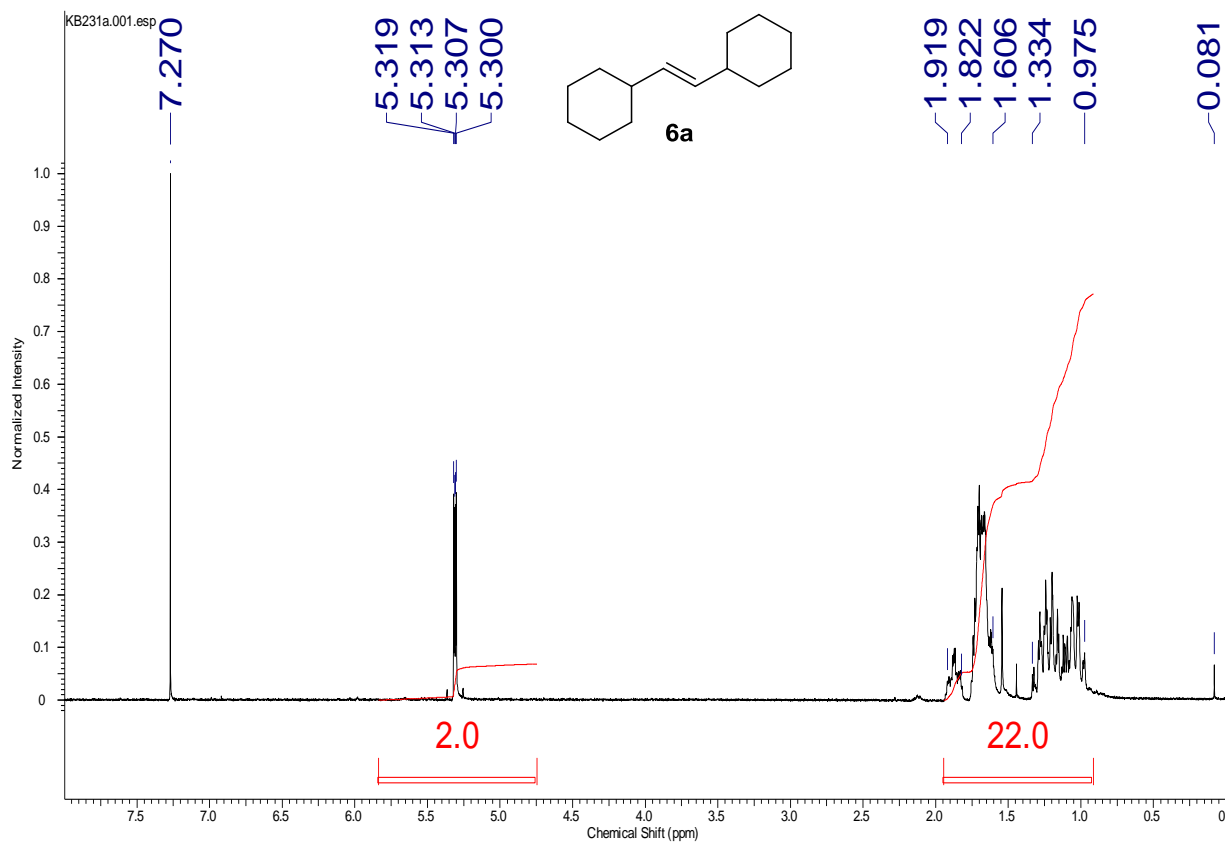




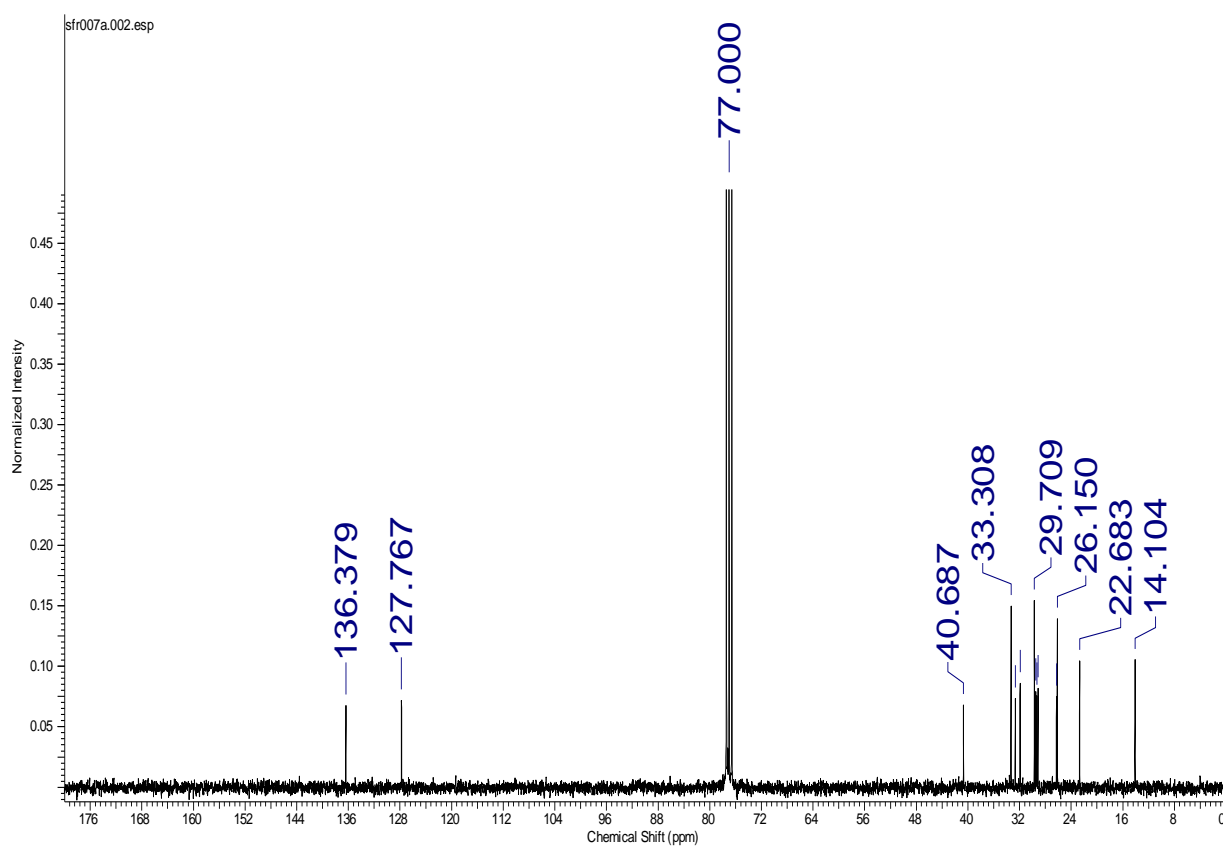
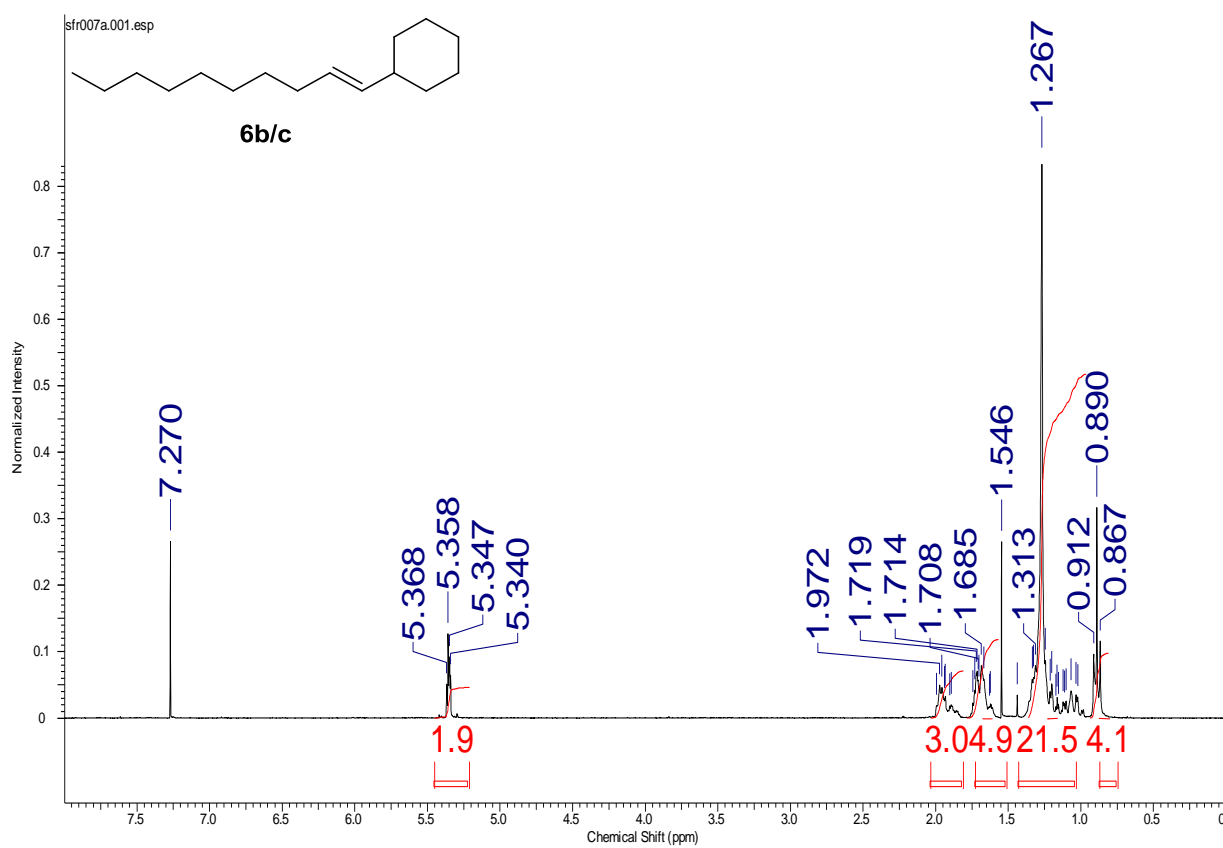
Selected NMR-Spectra

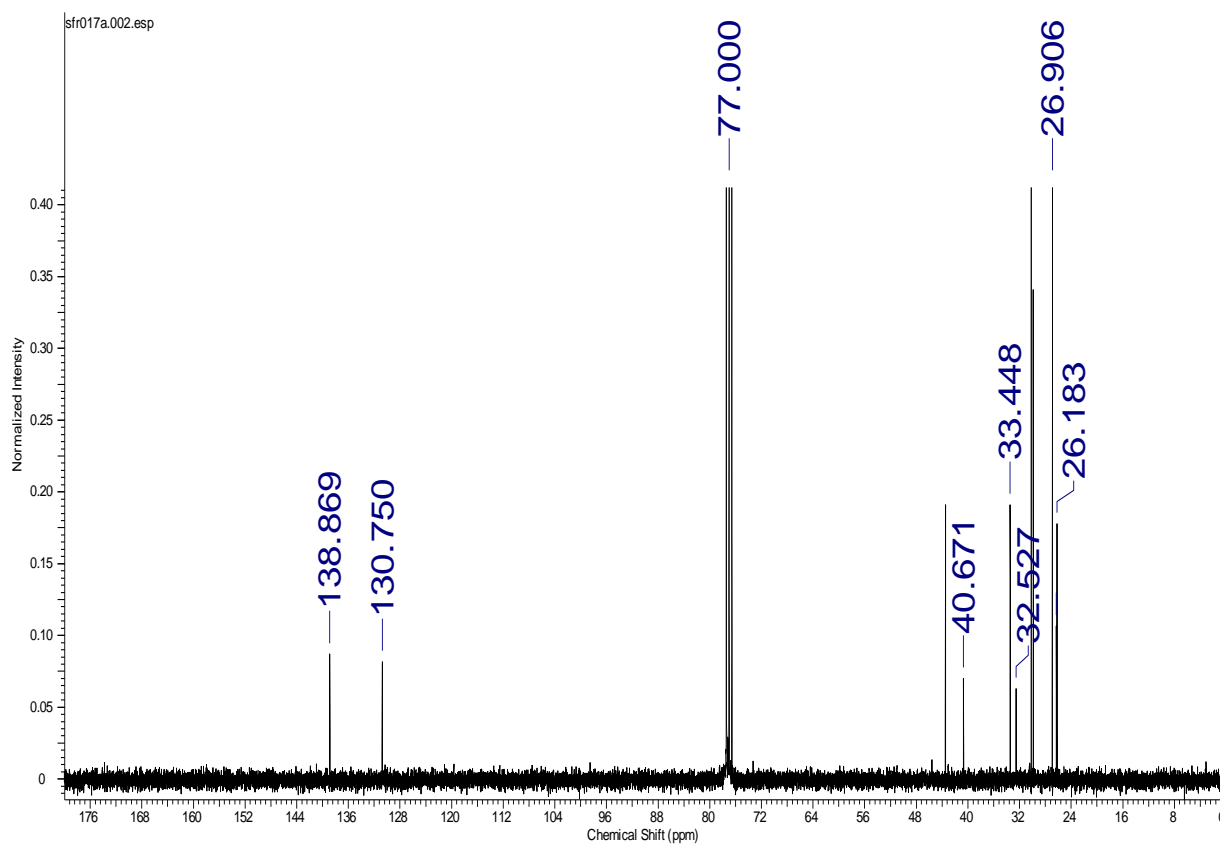
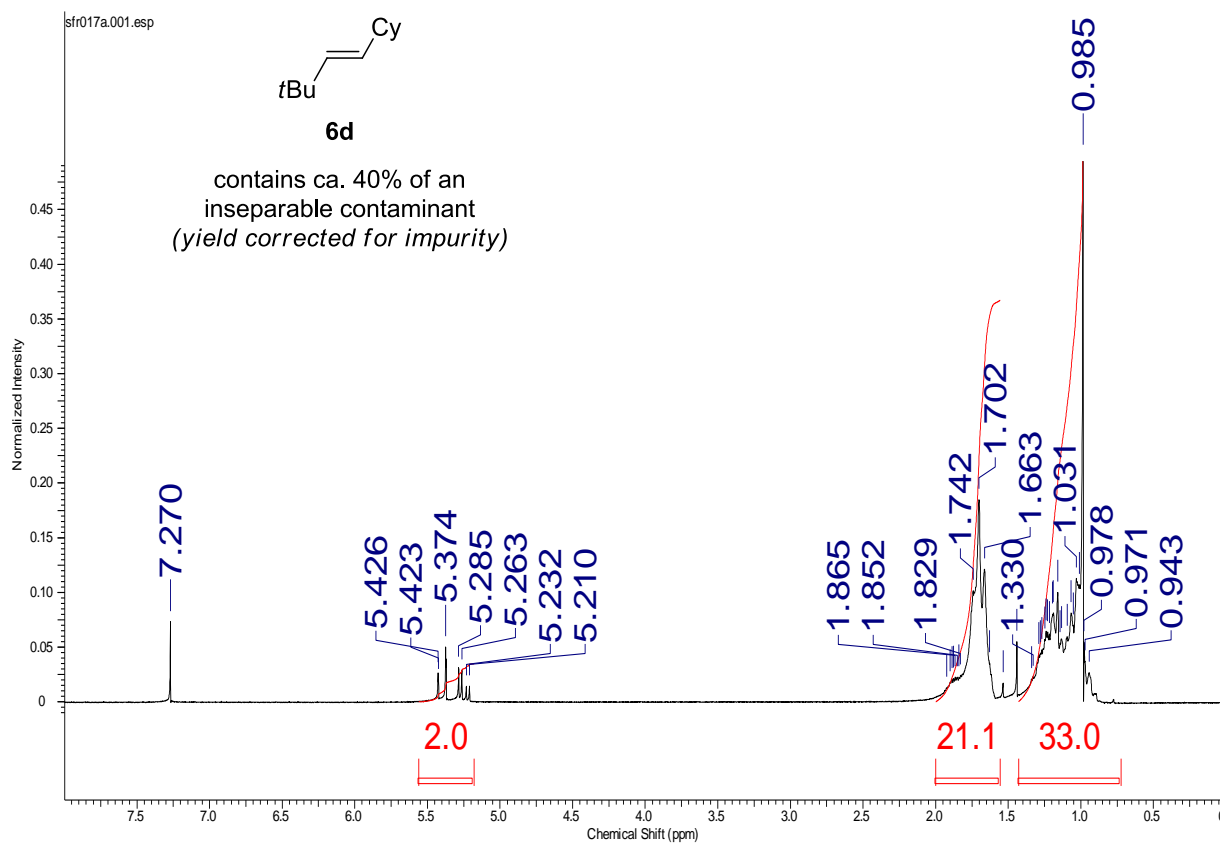


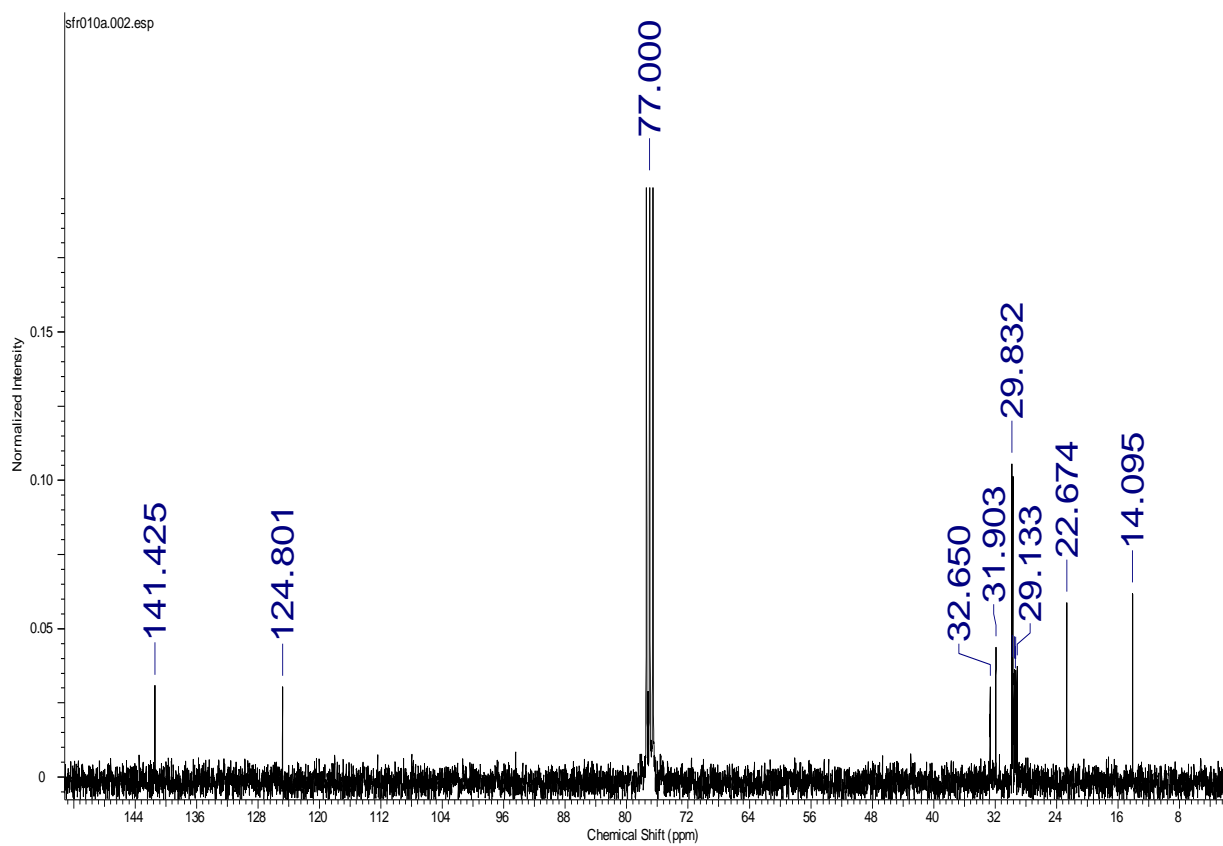
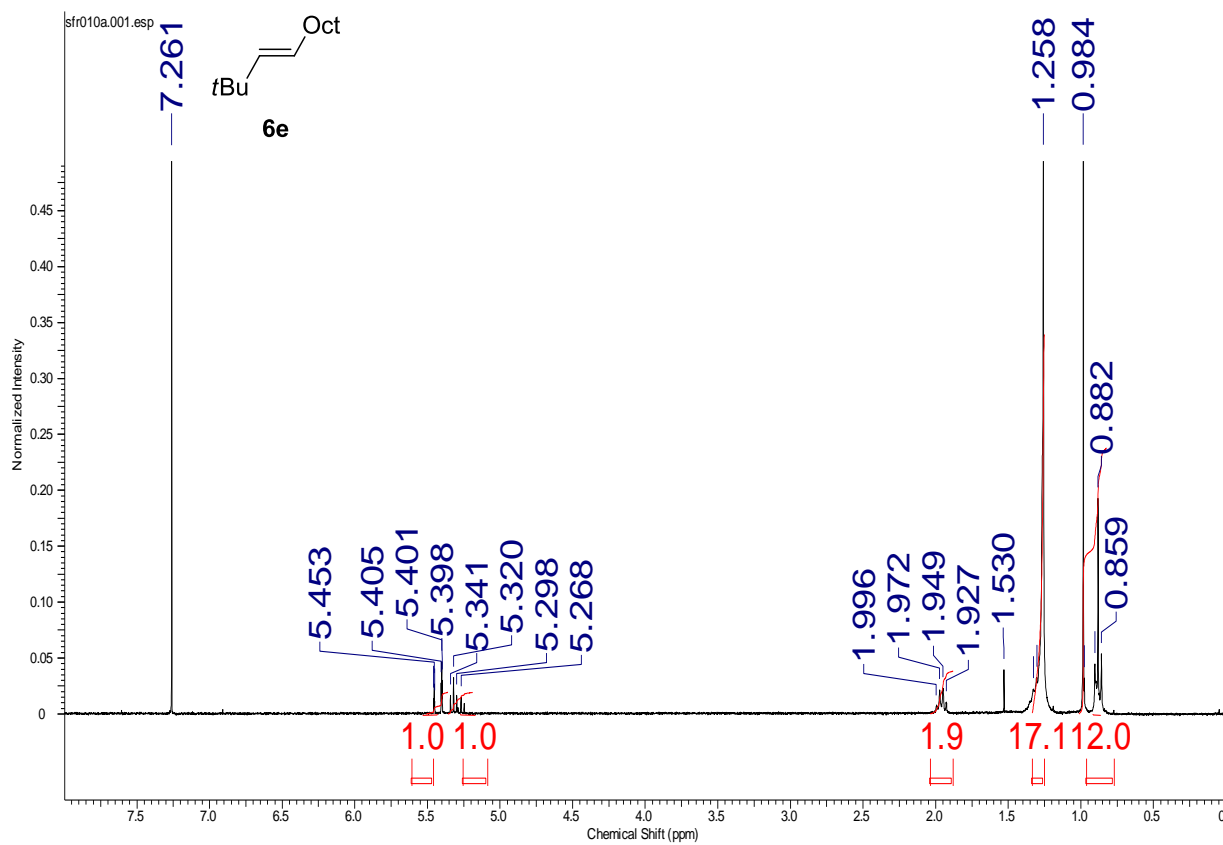


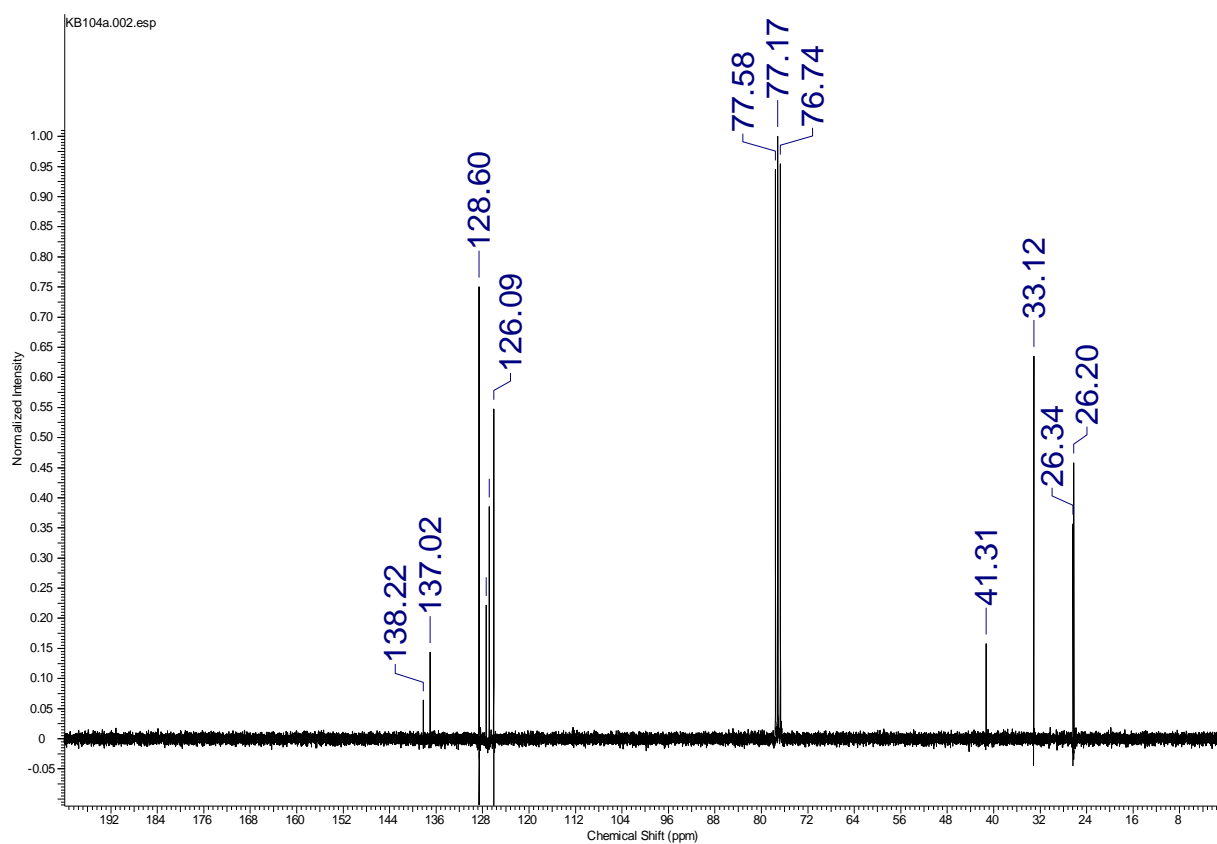
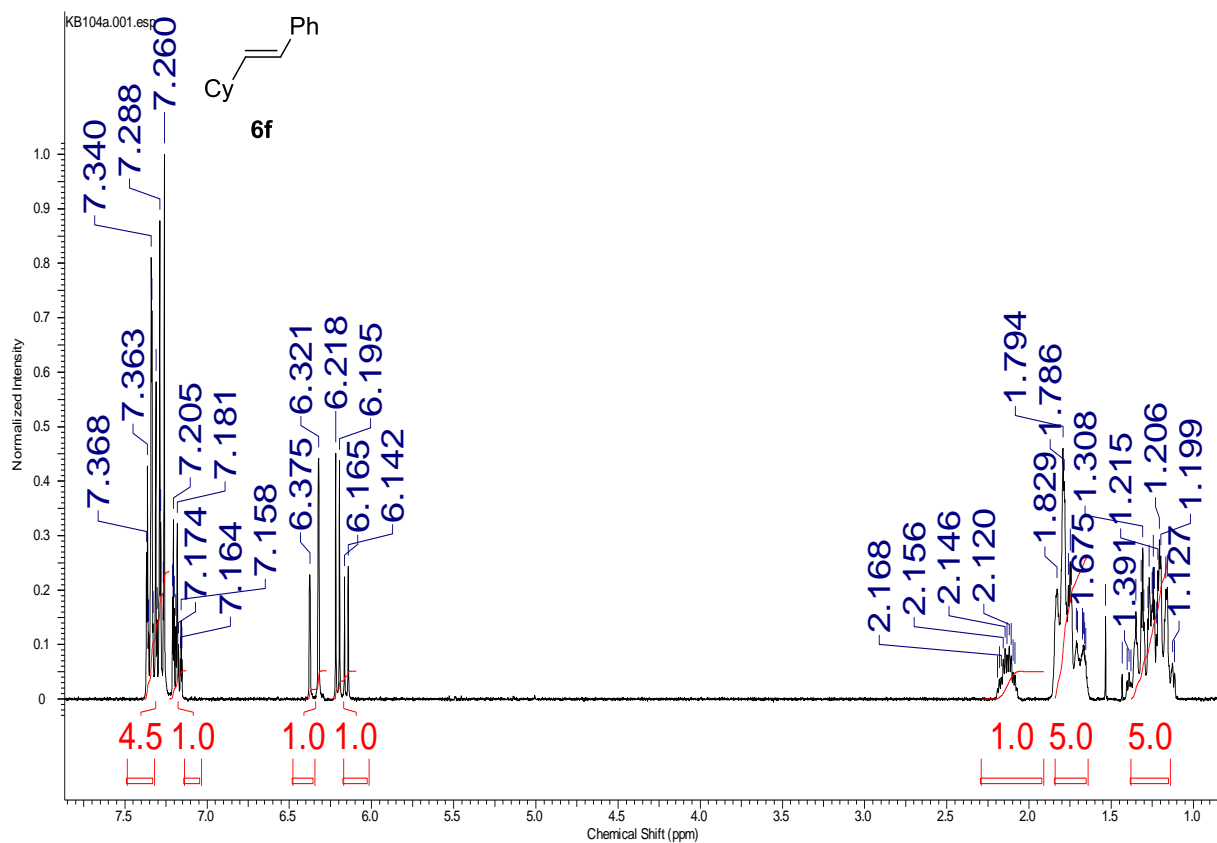


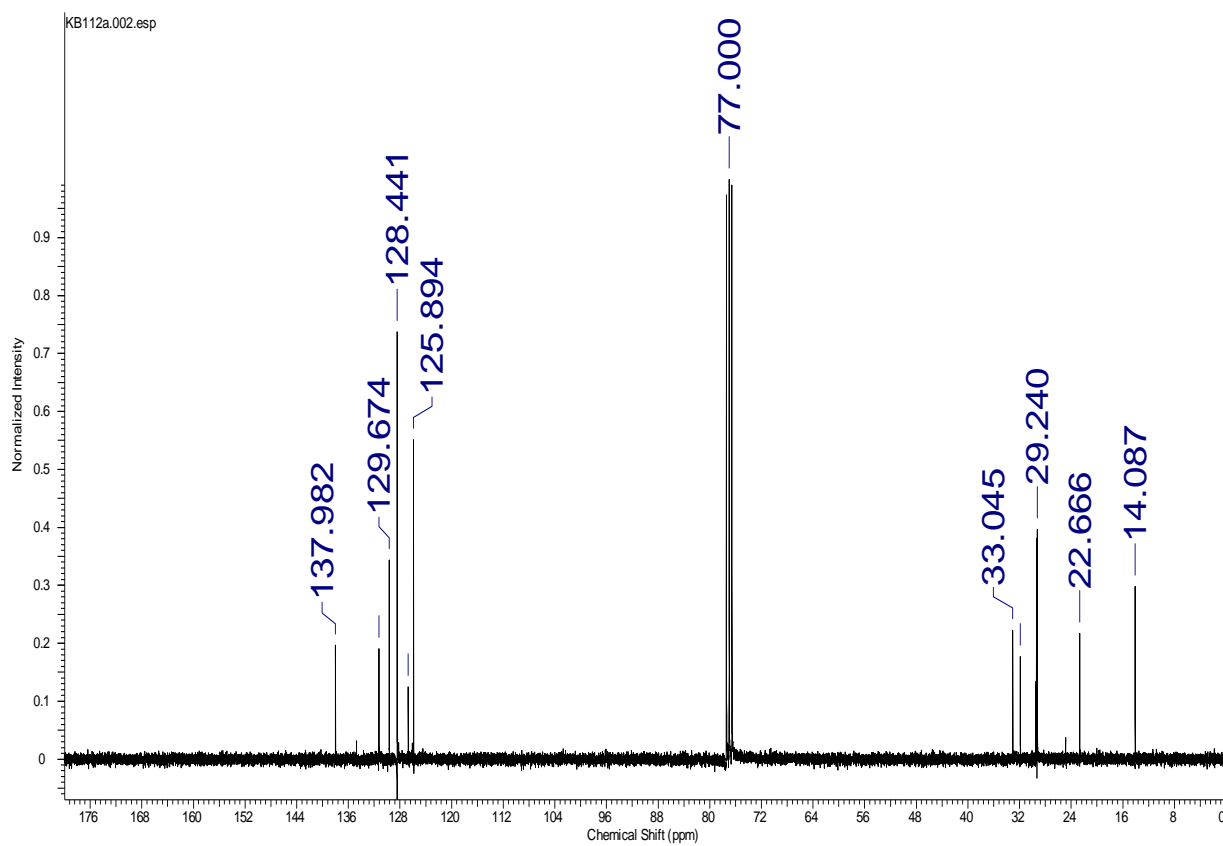
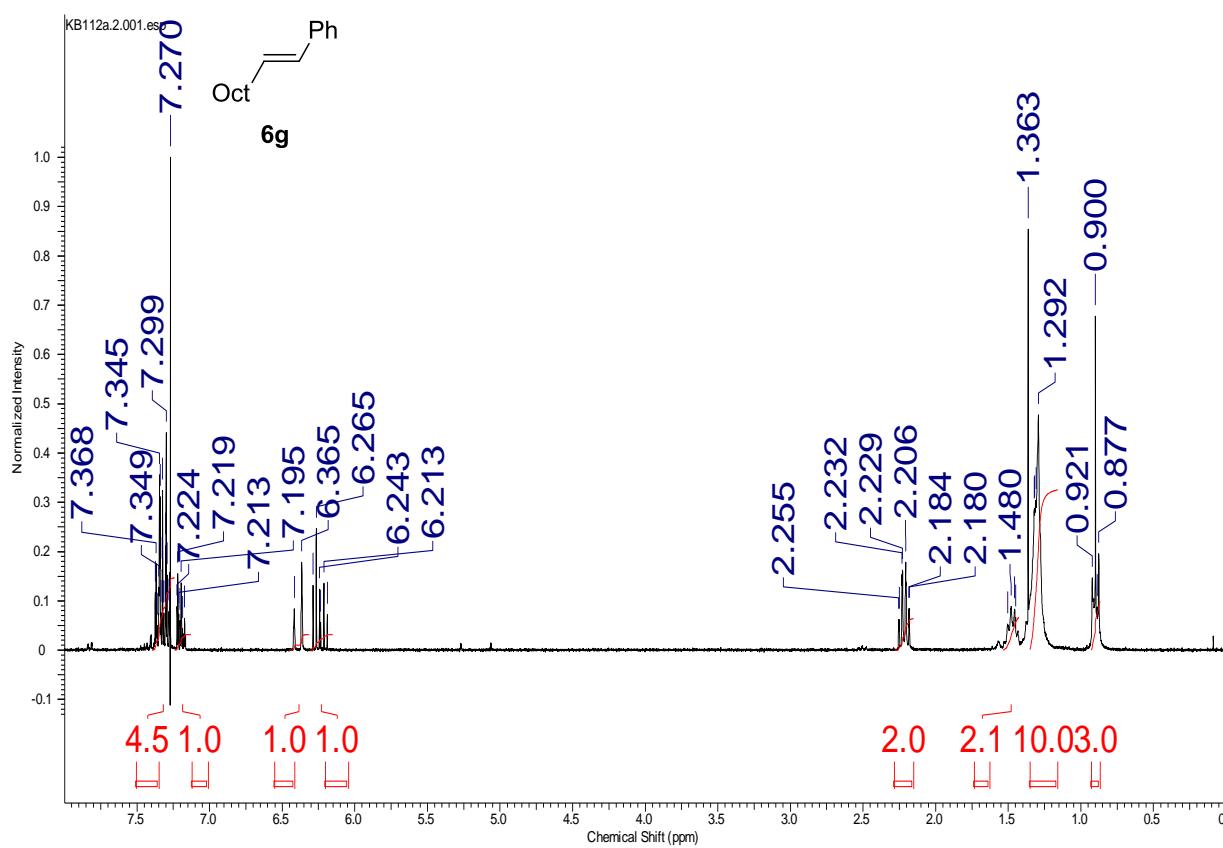
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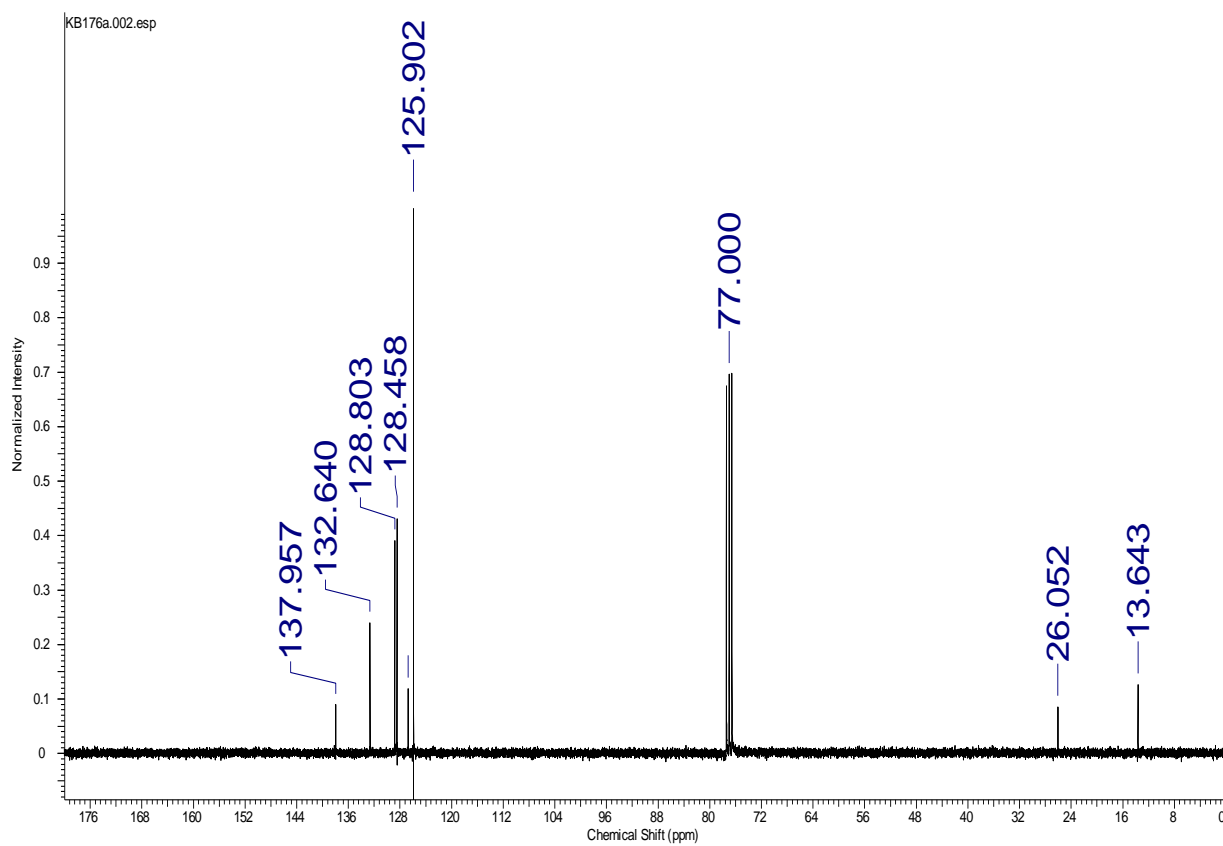
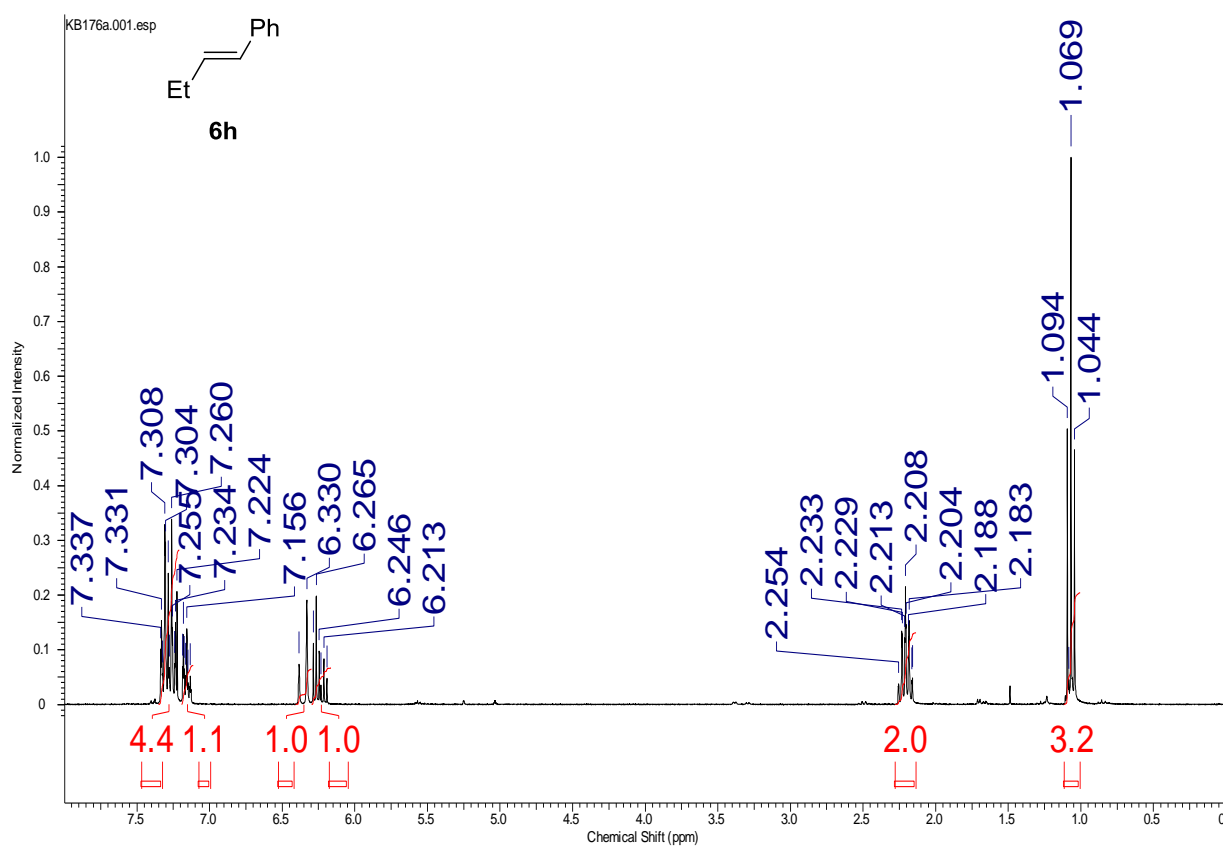


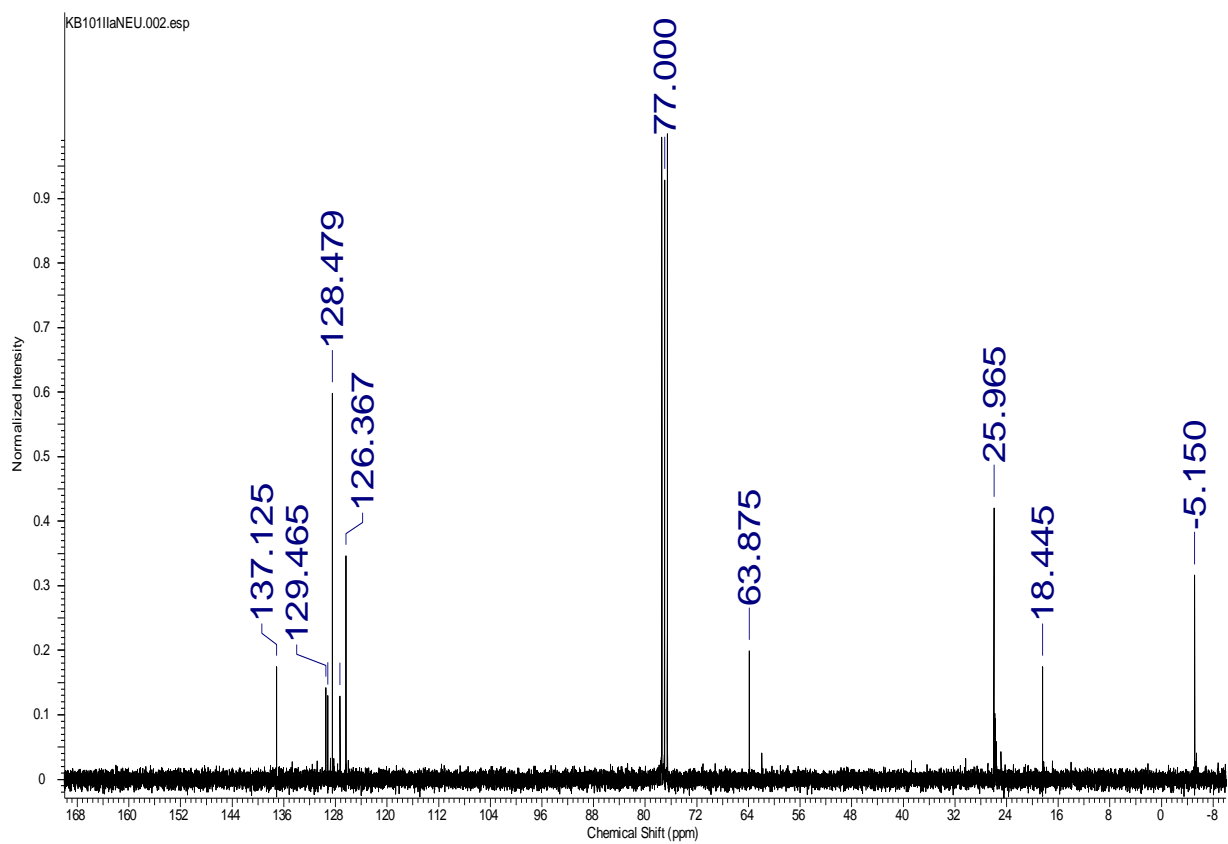
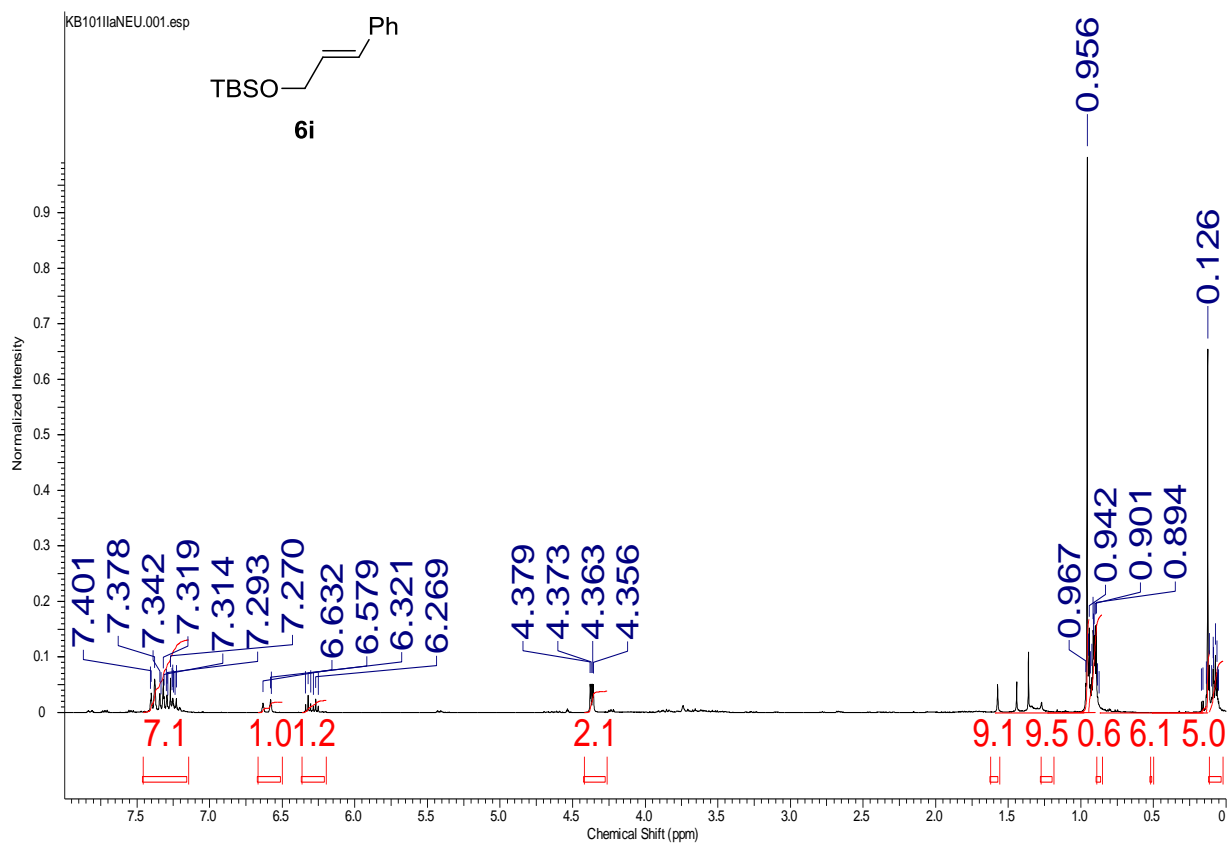




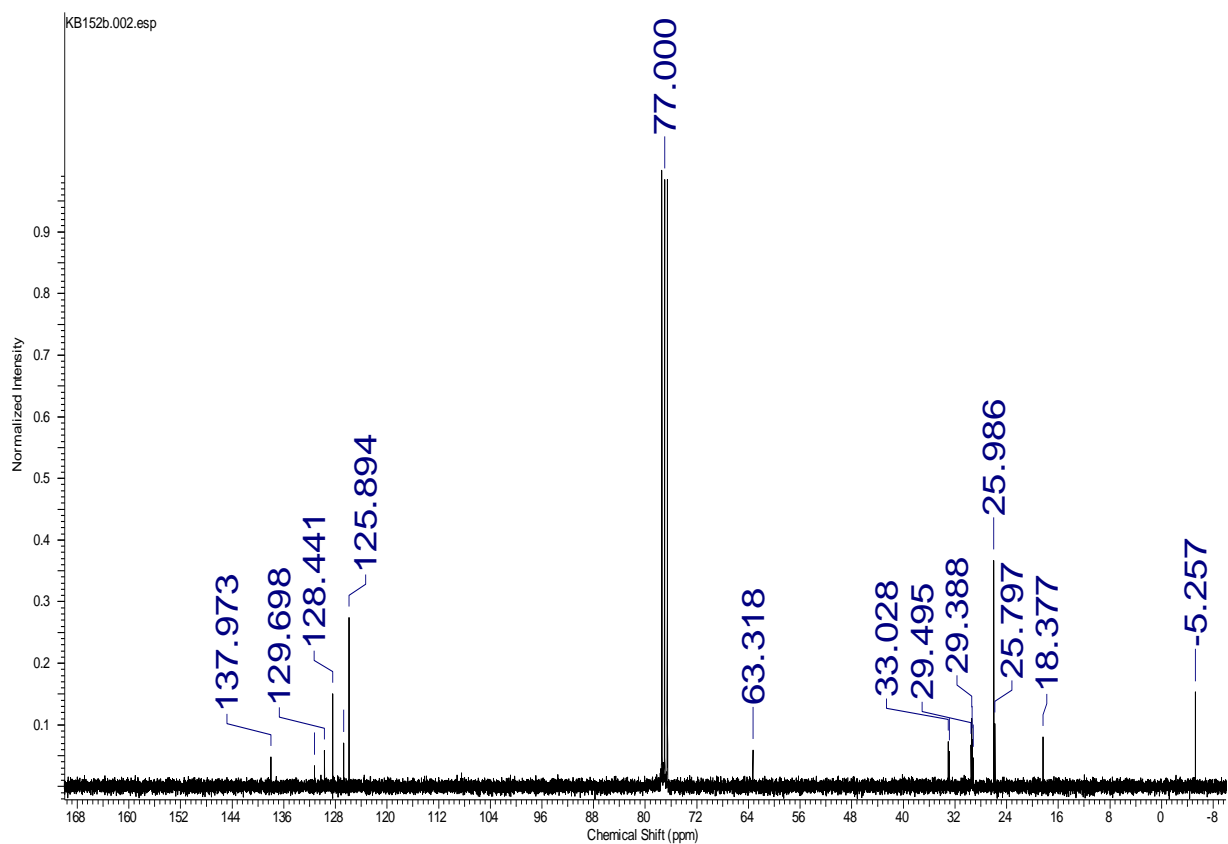
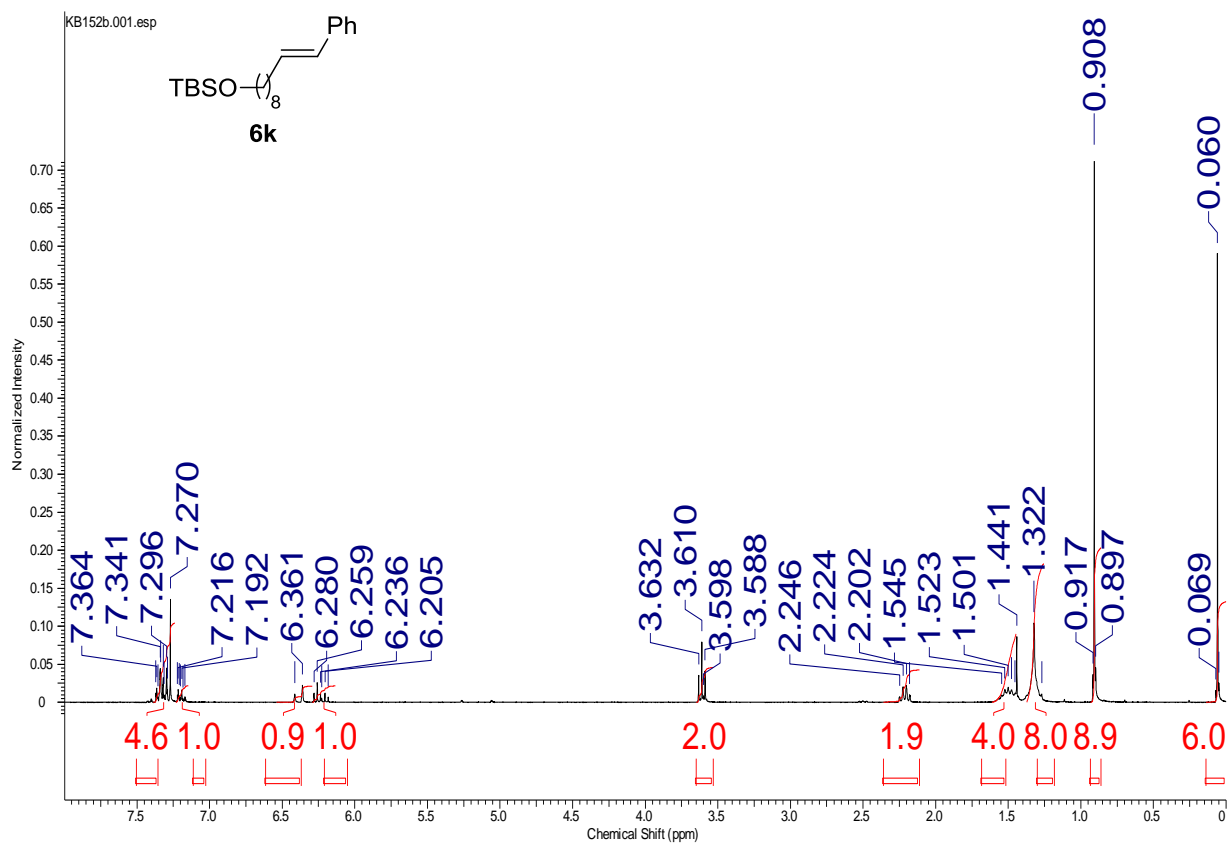




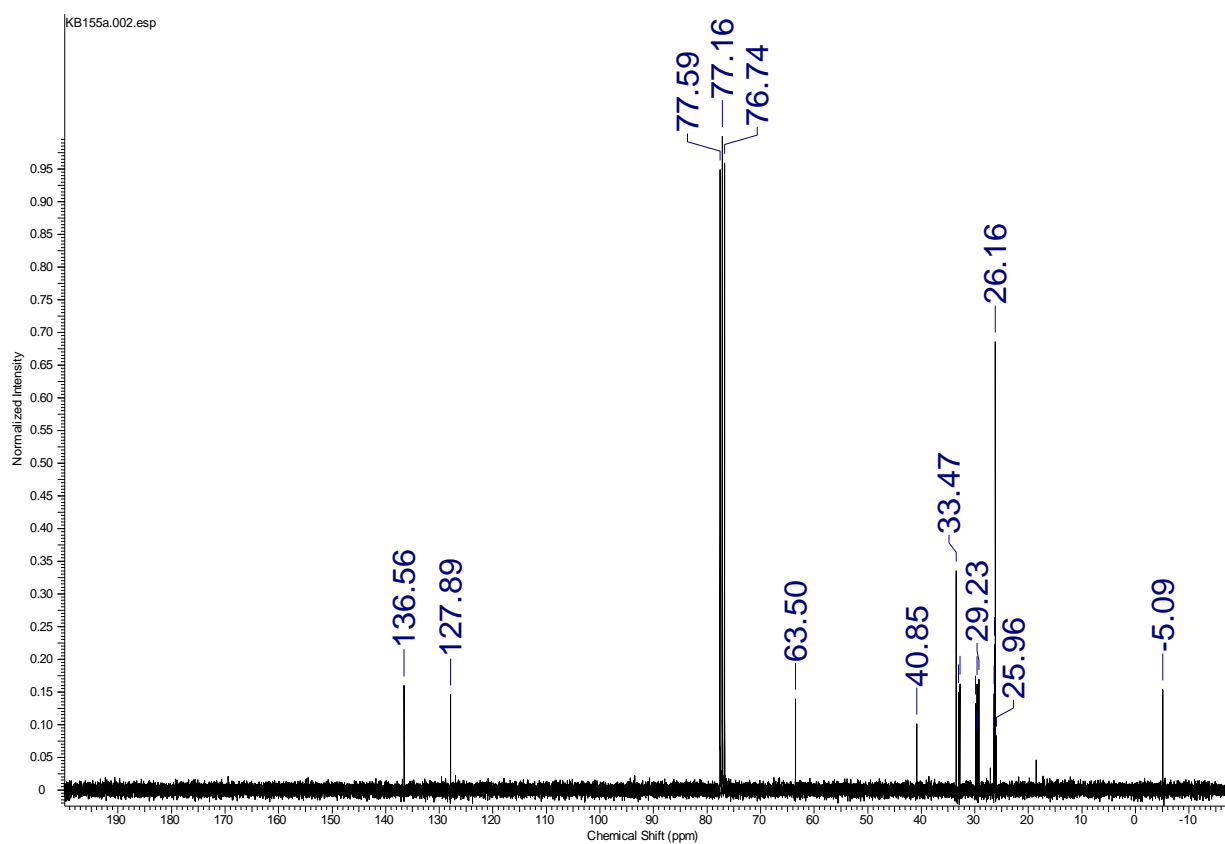
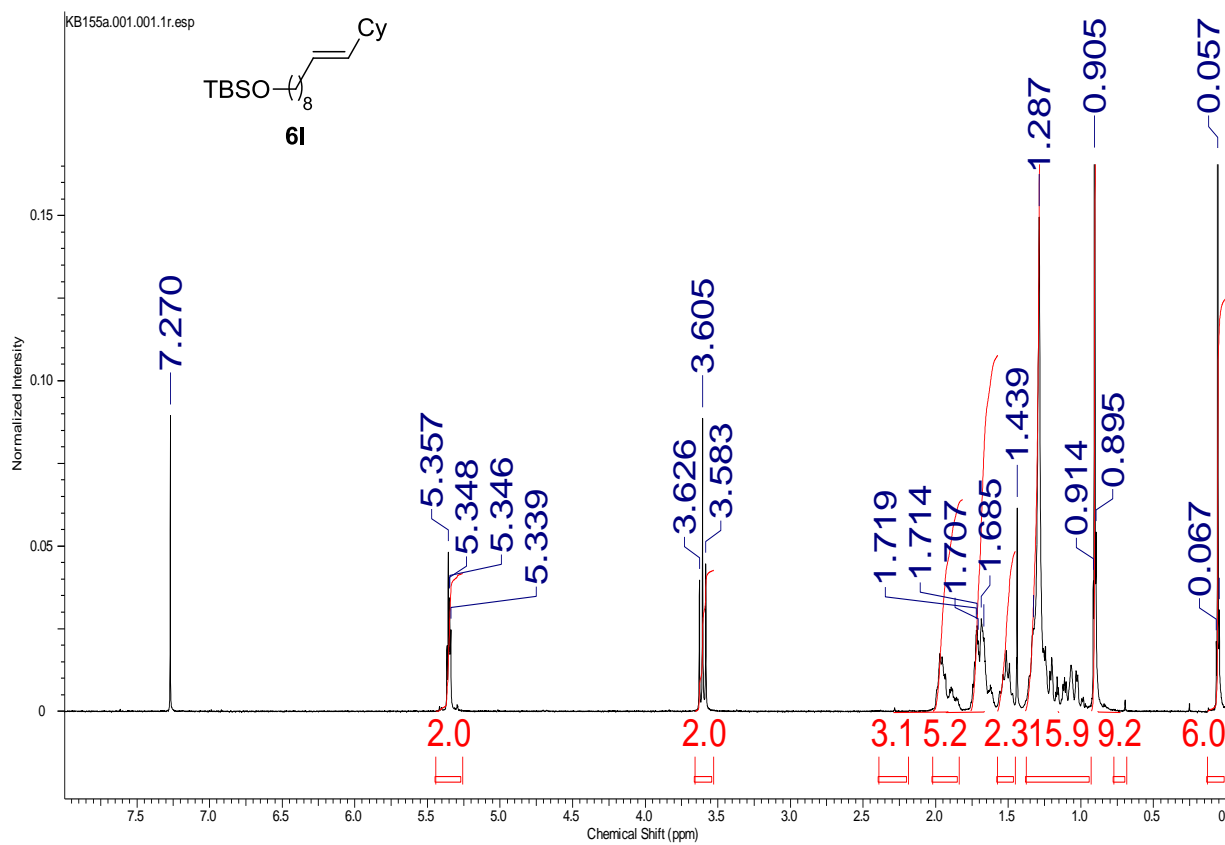


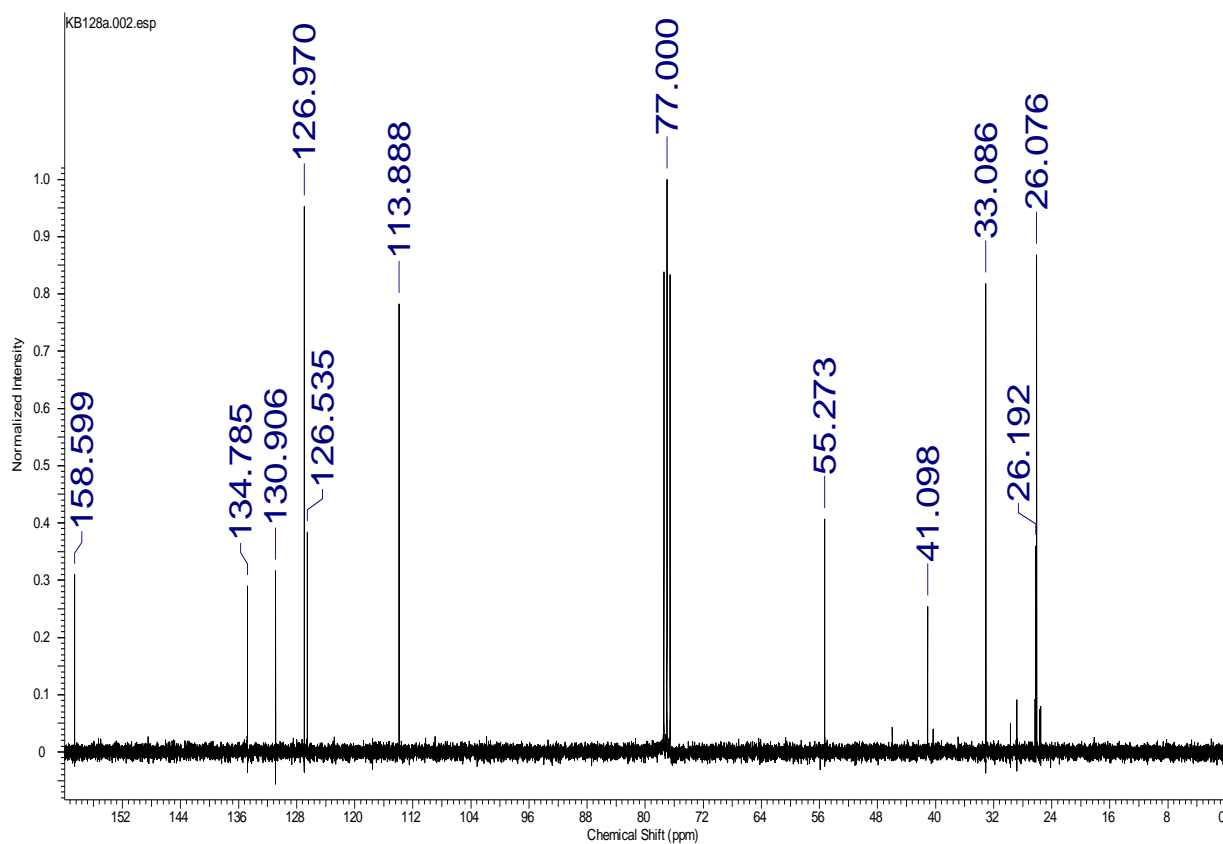
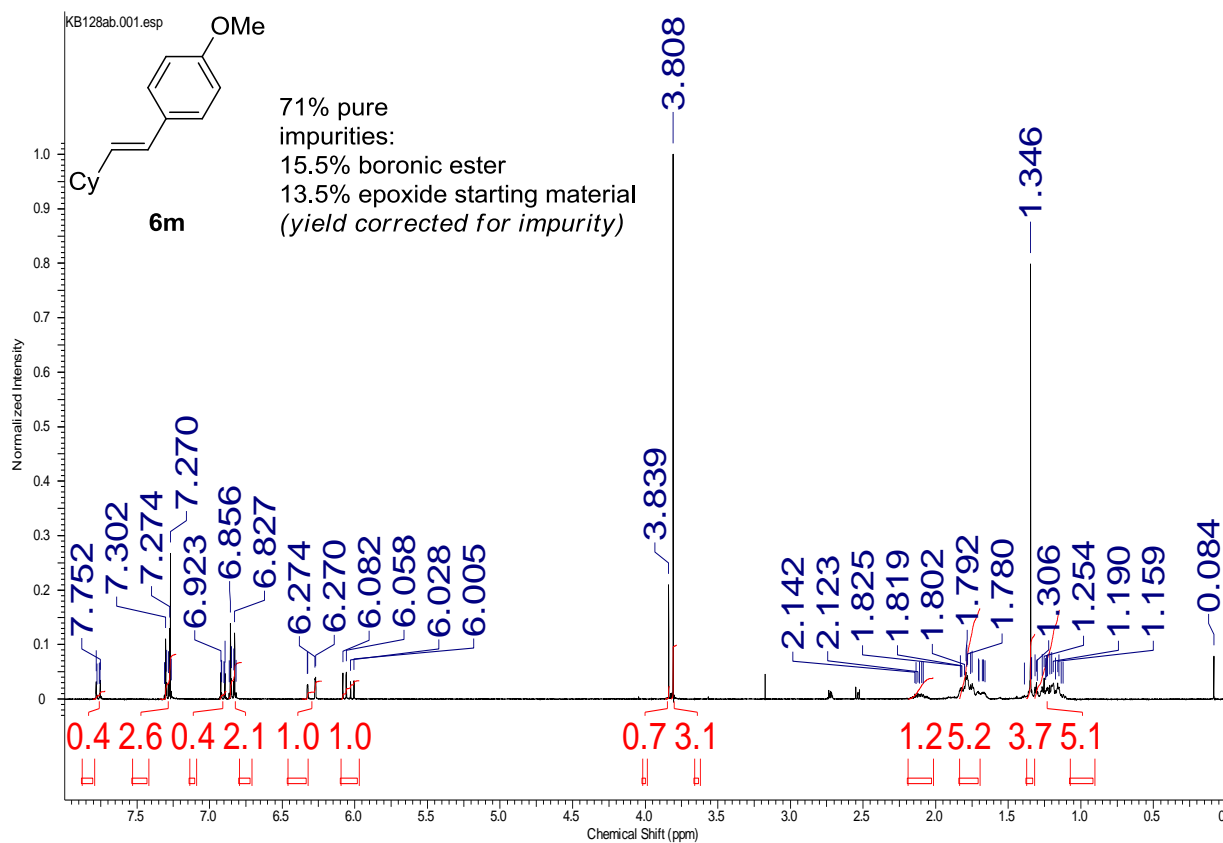


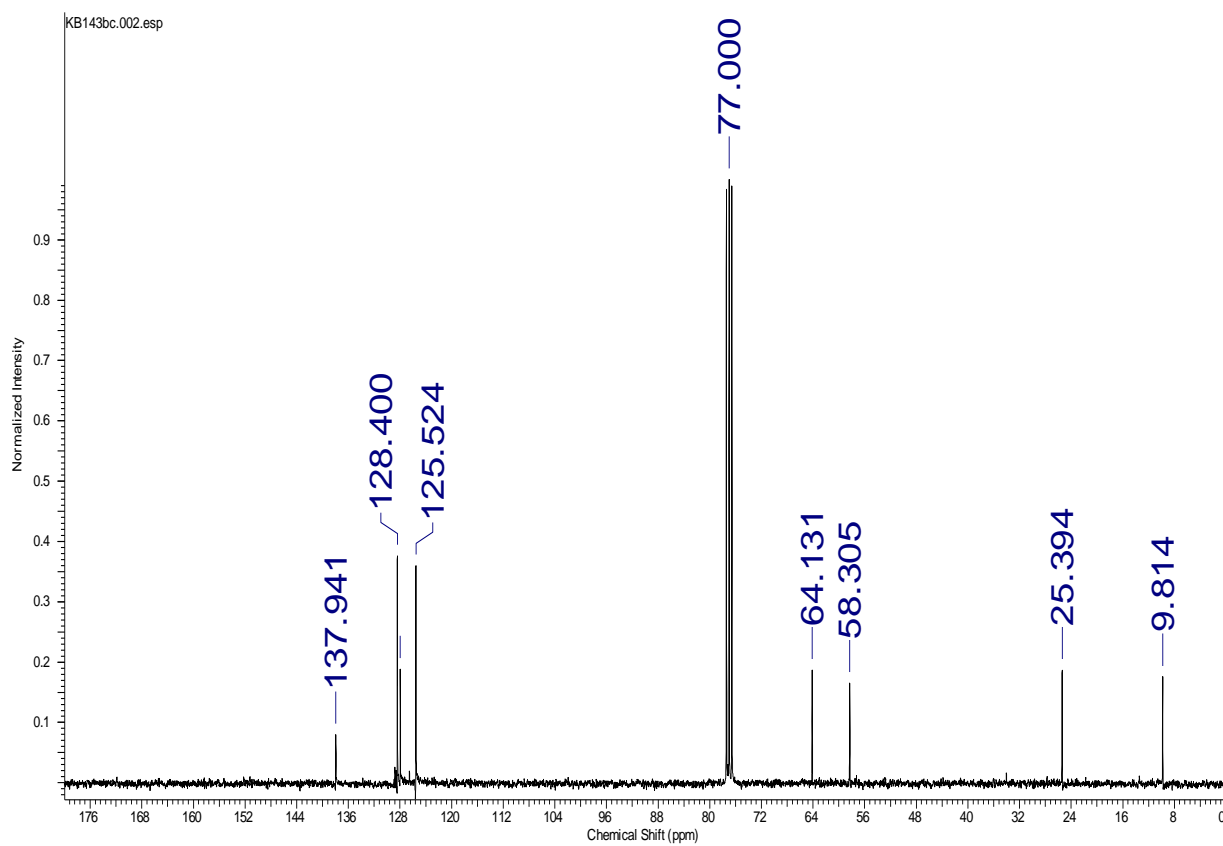
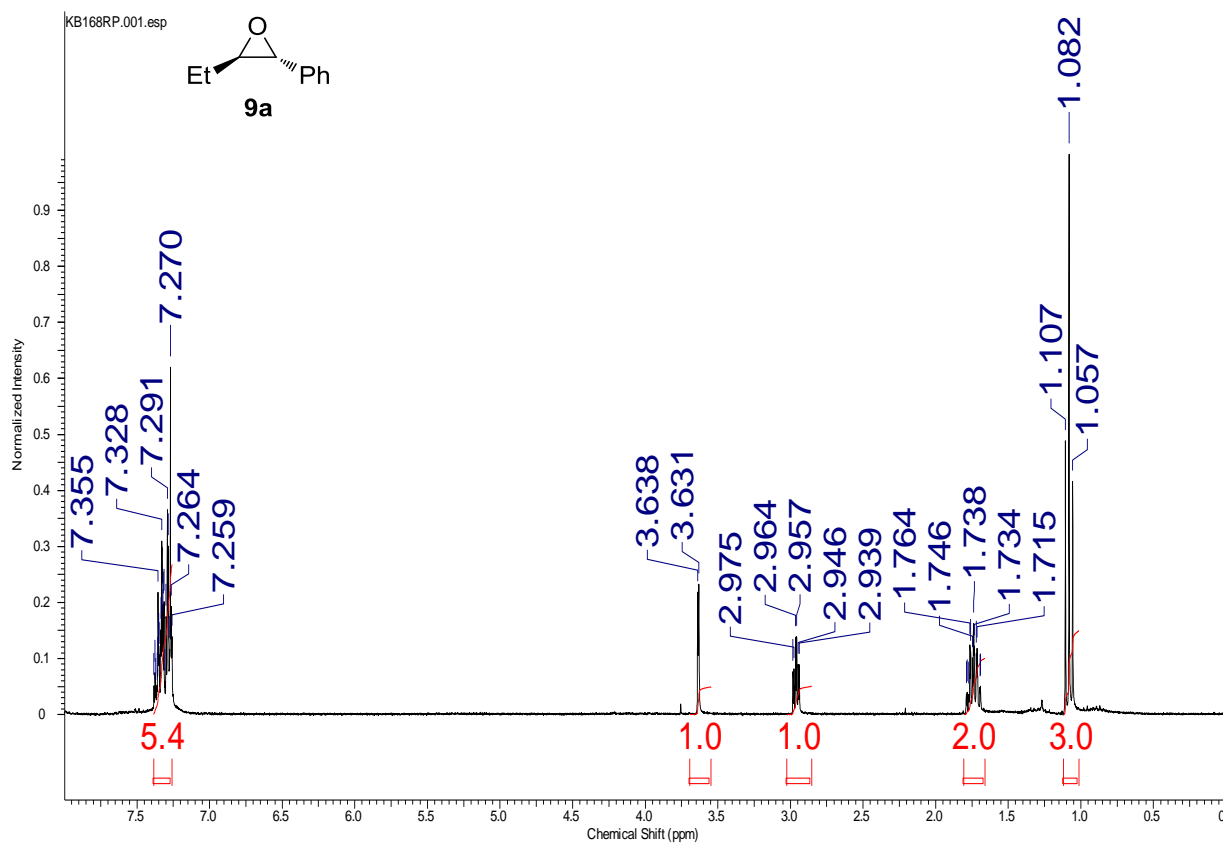
Selected NMR-Spectra

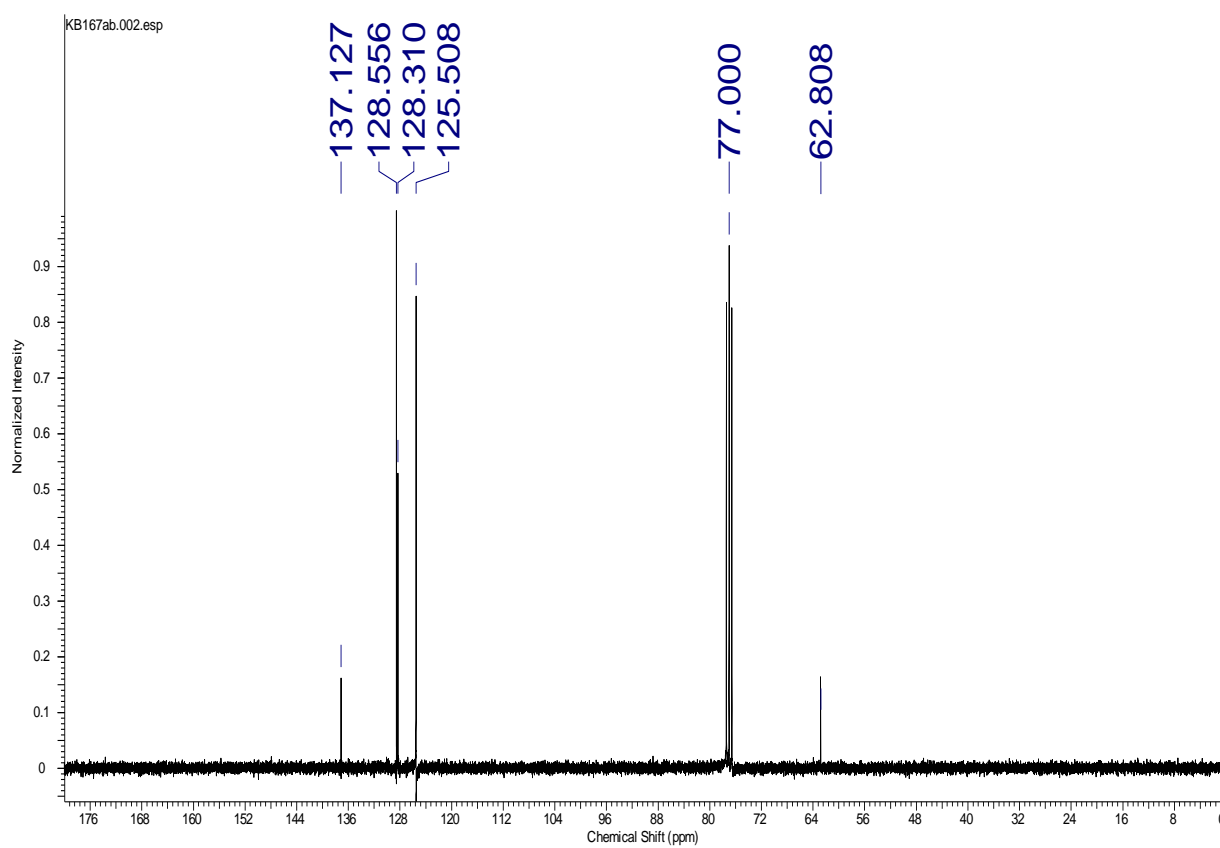
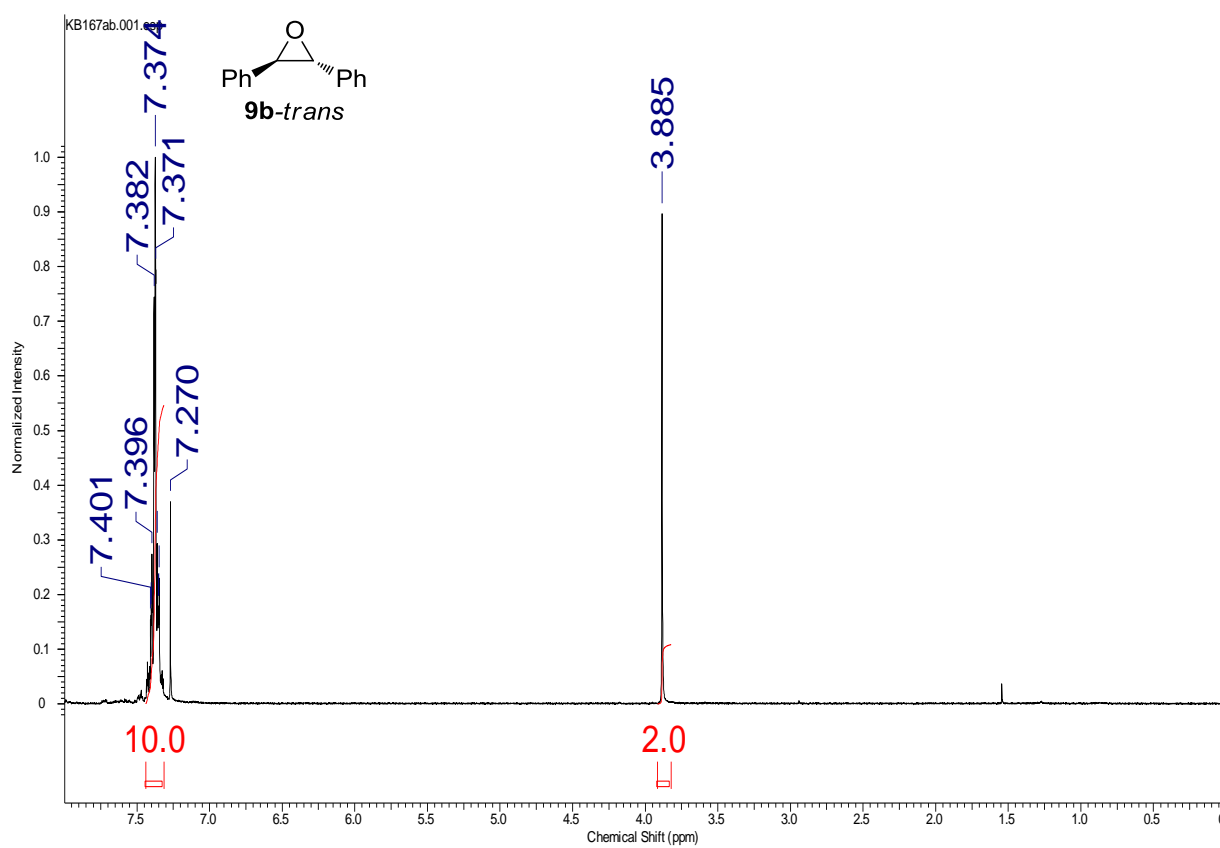


Selected NMR-Spectra

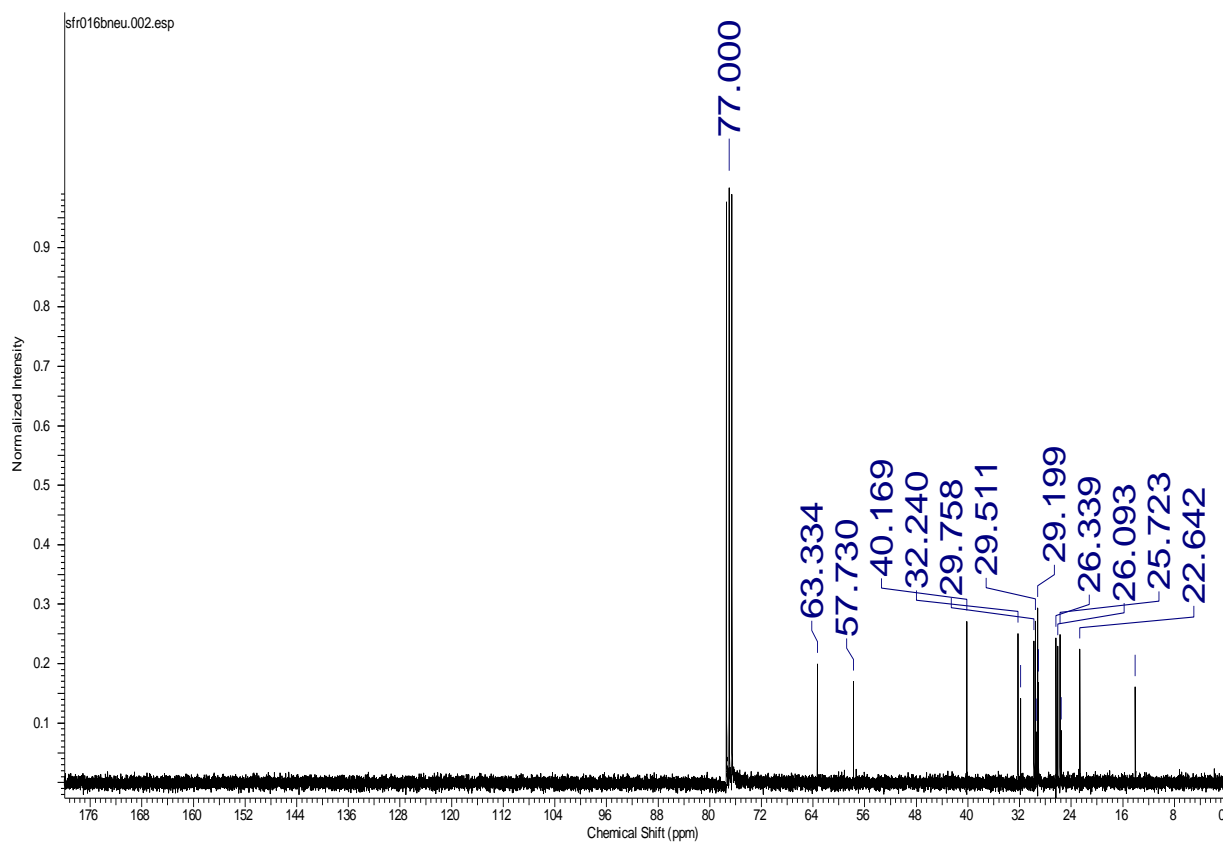
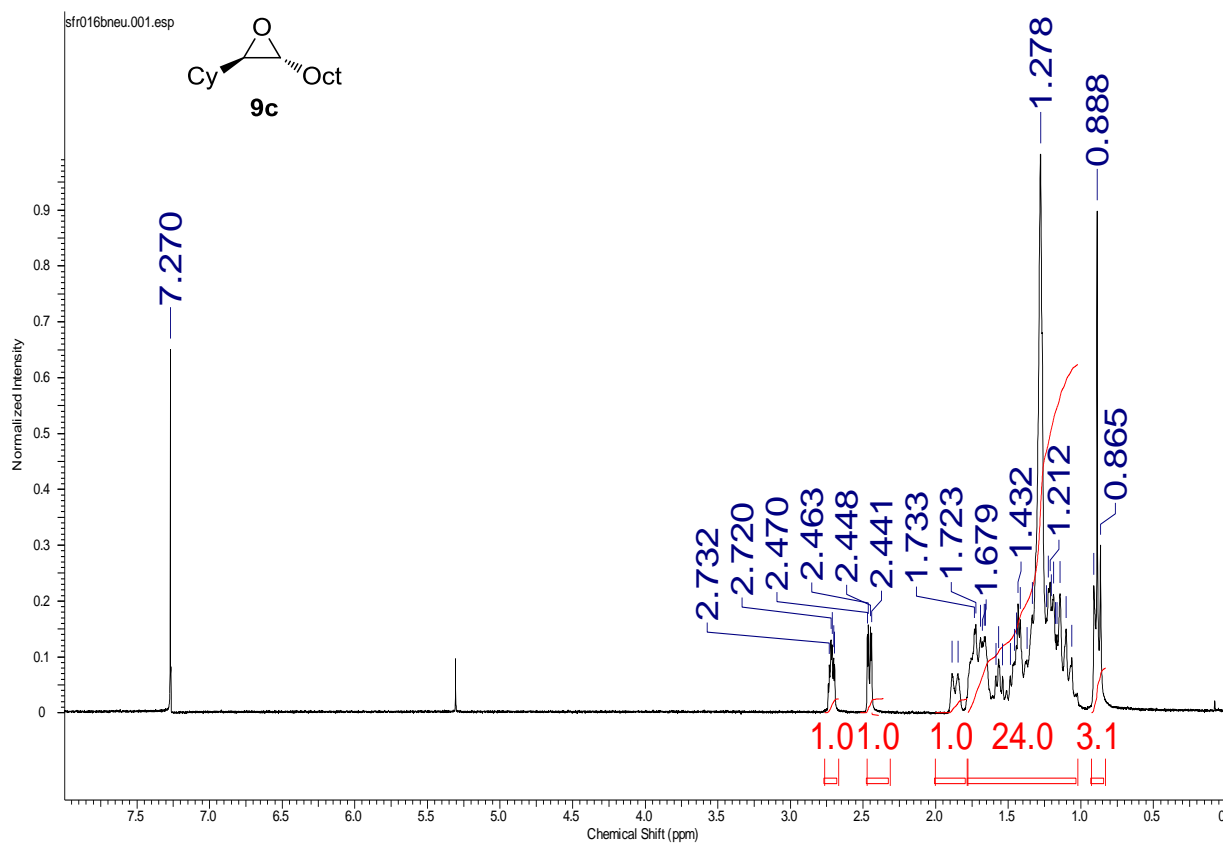




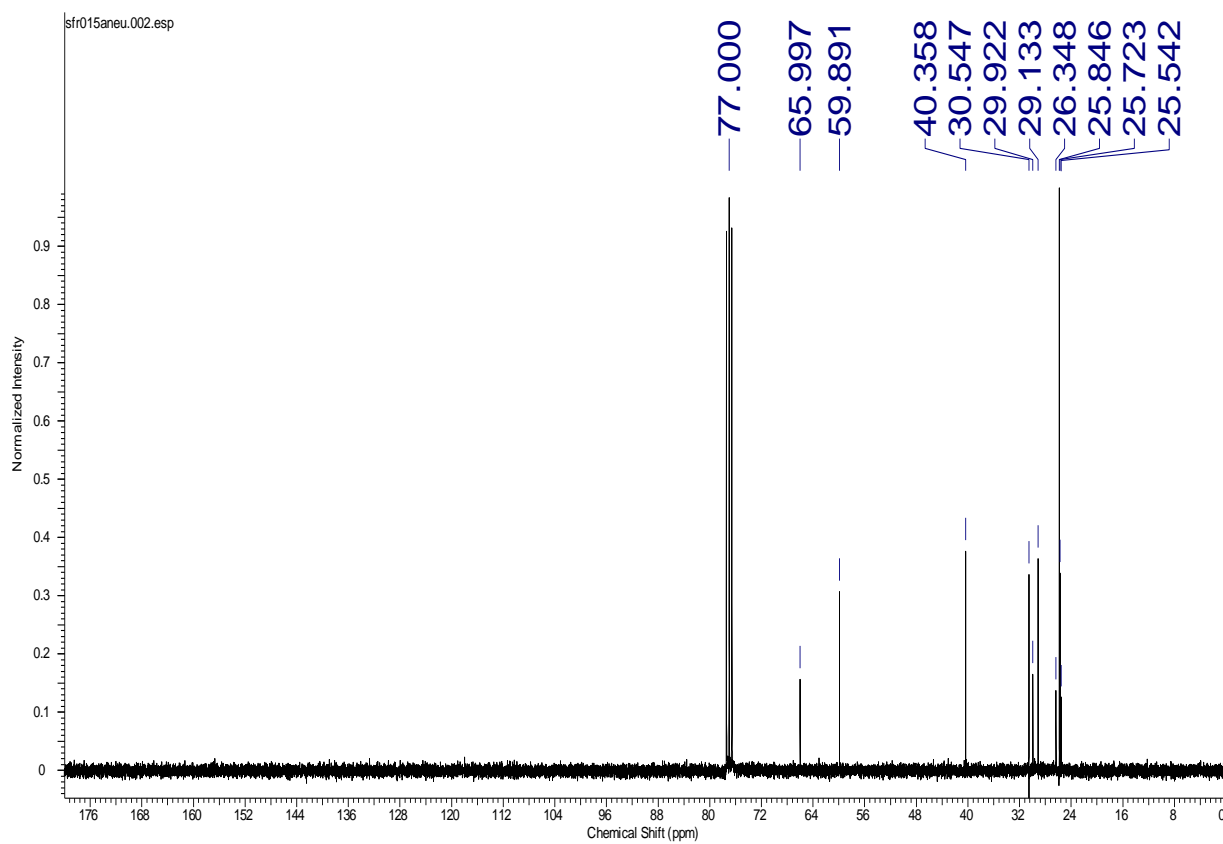
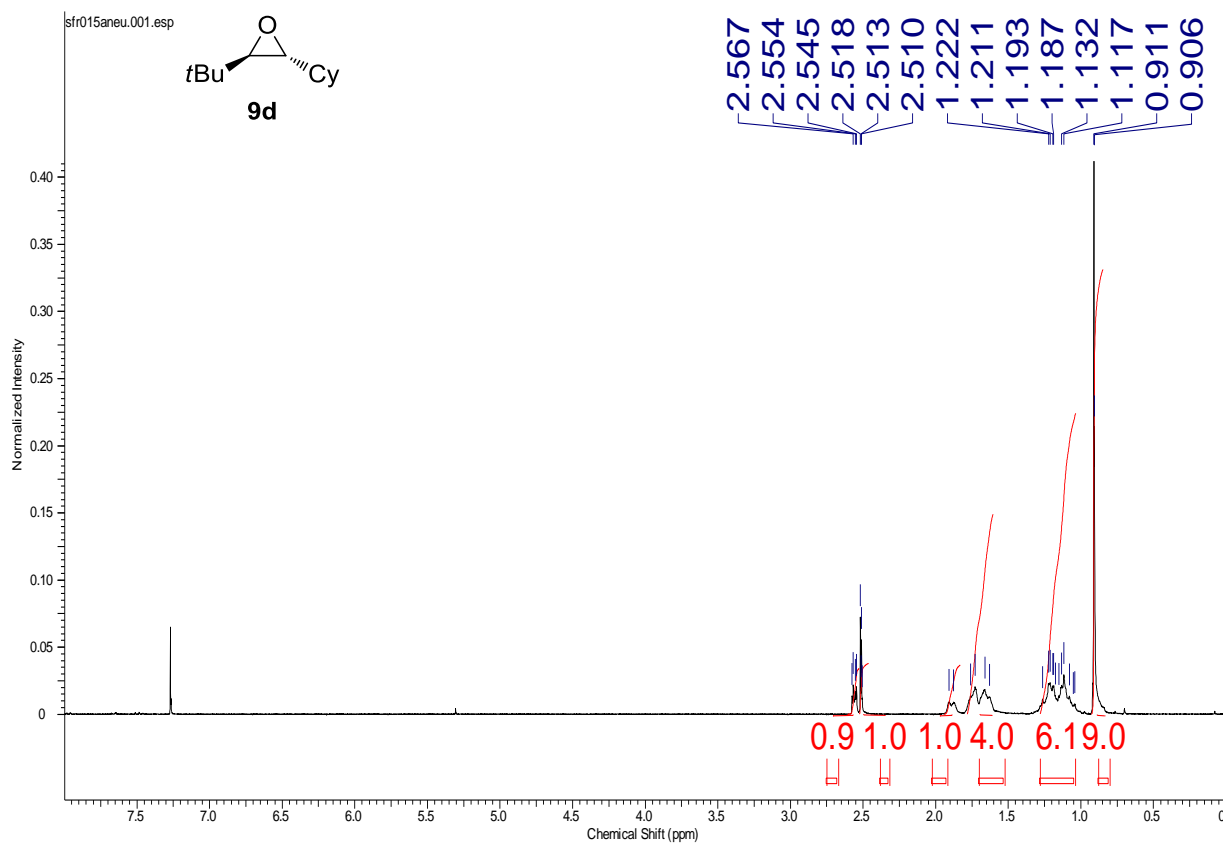


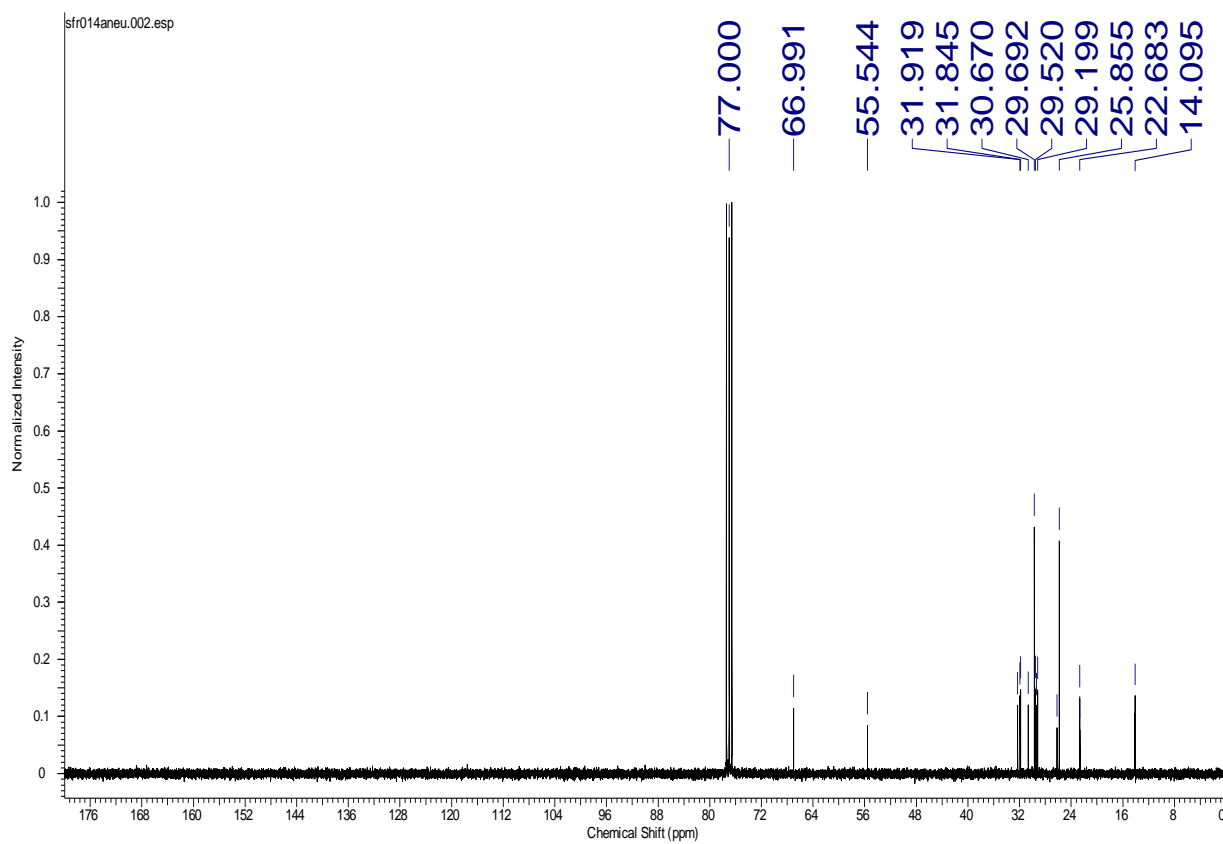
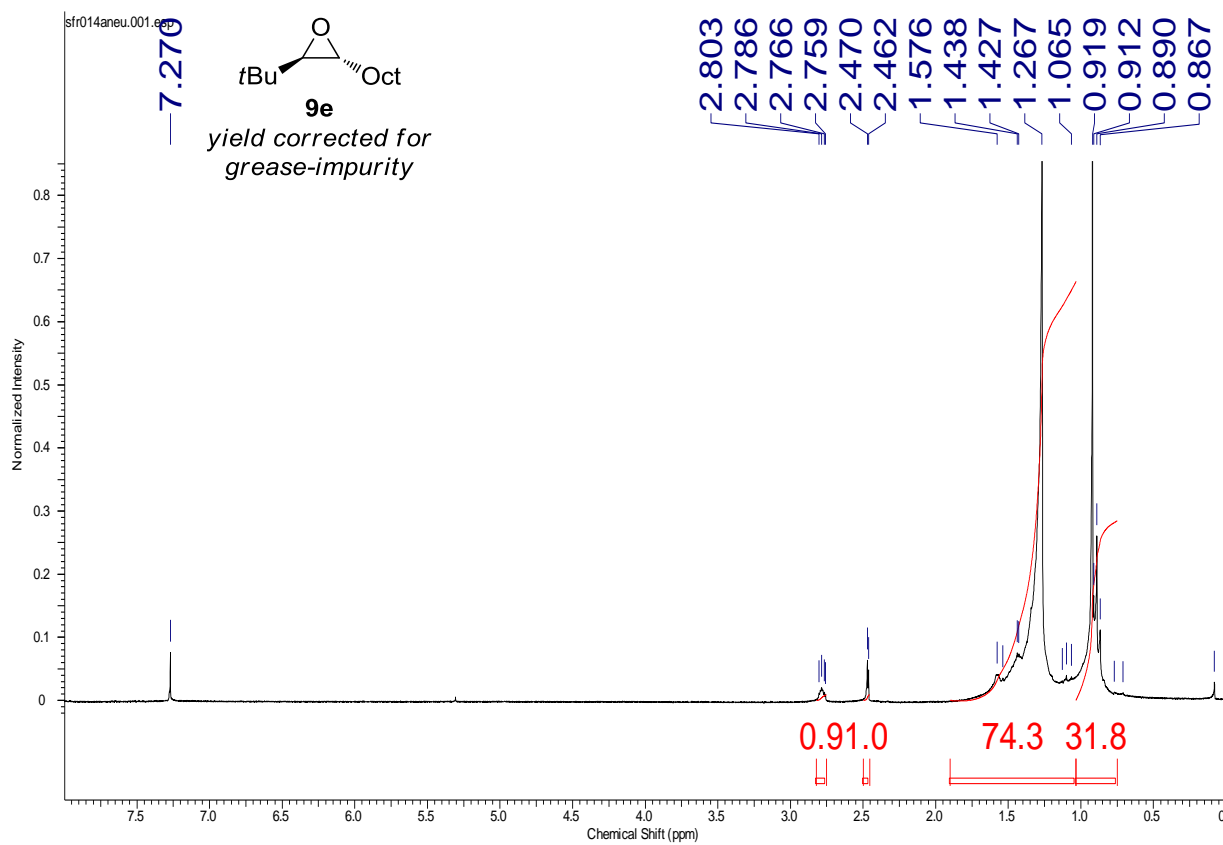


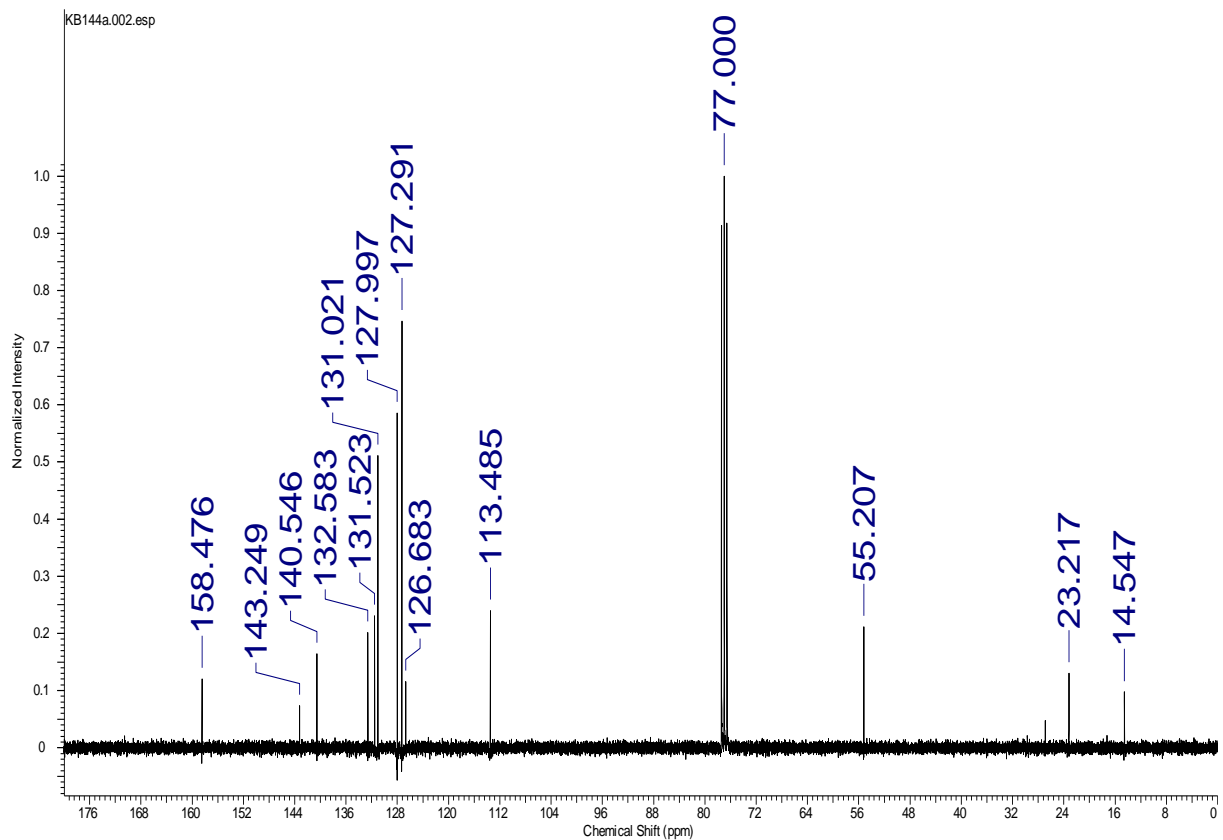
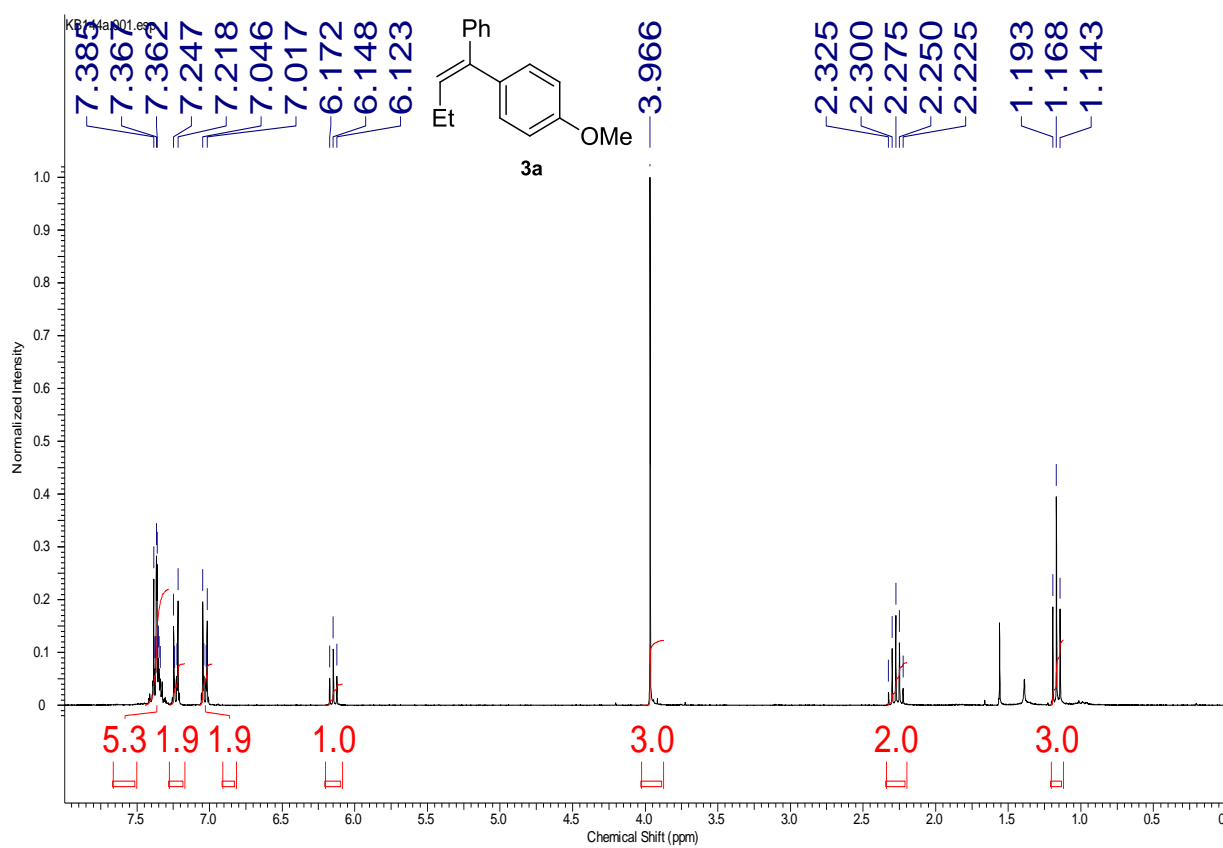
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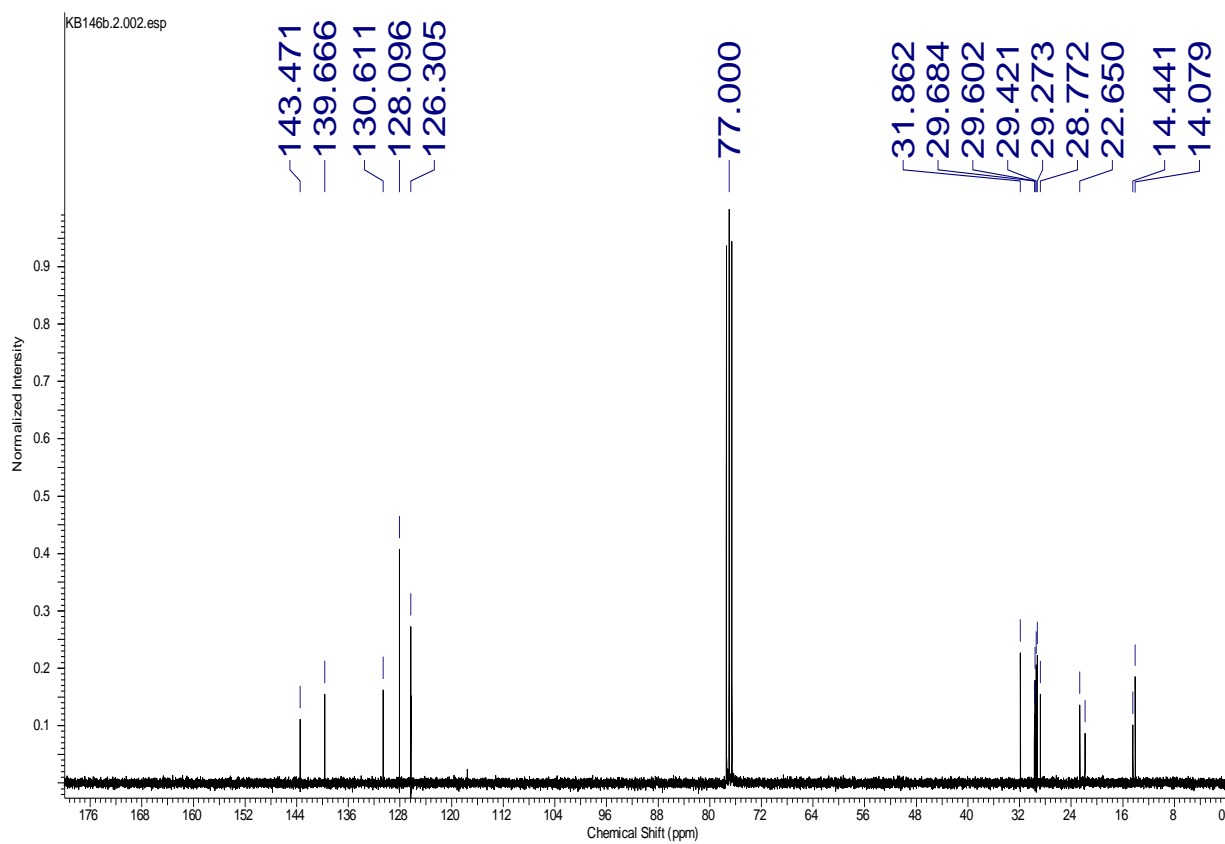
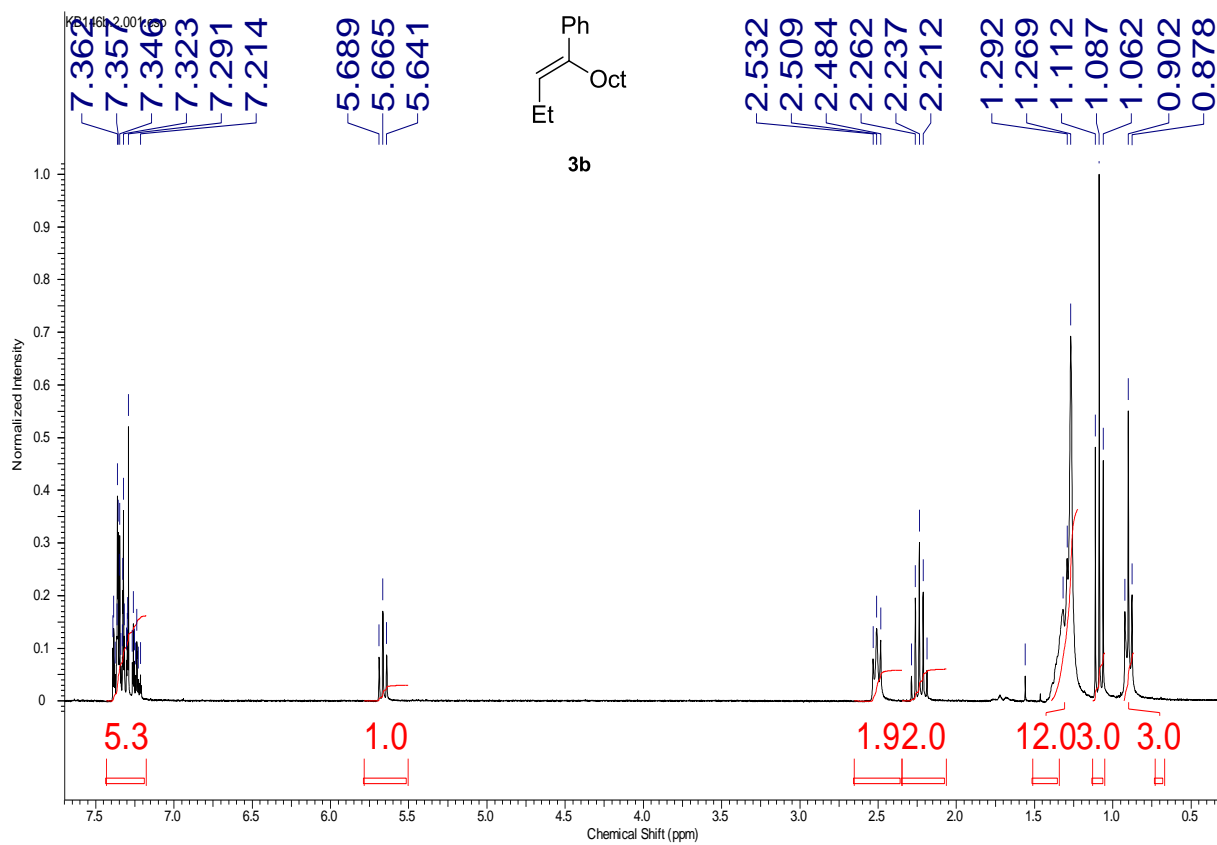


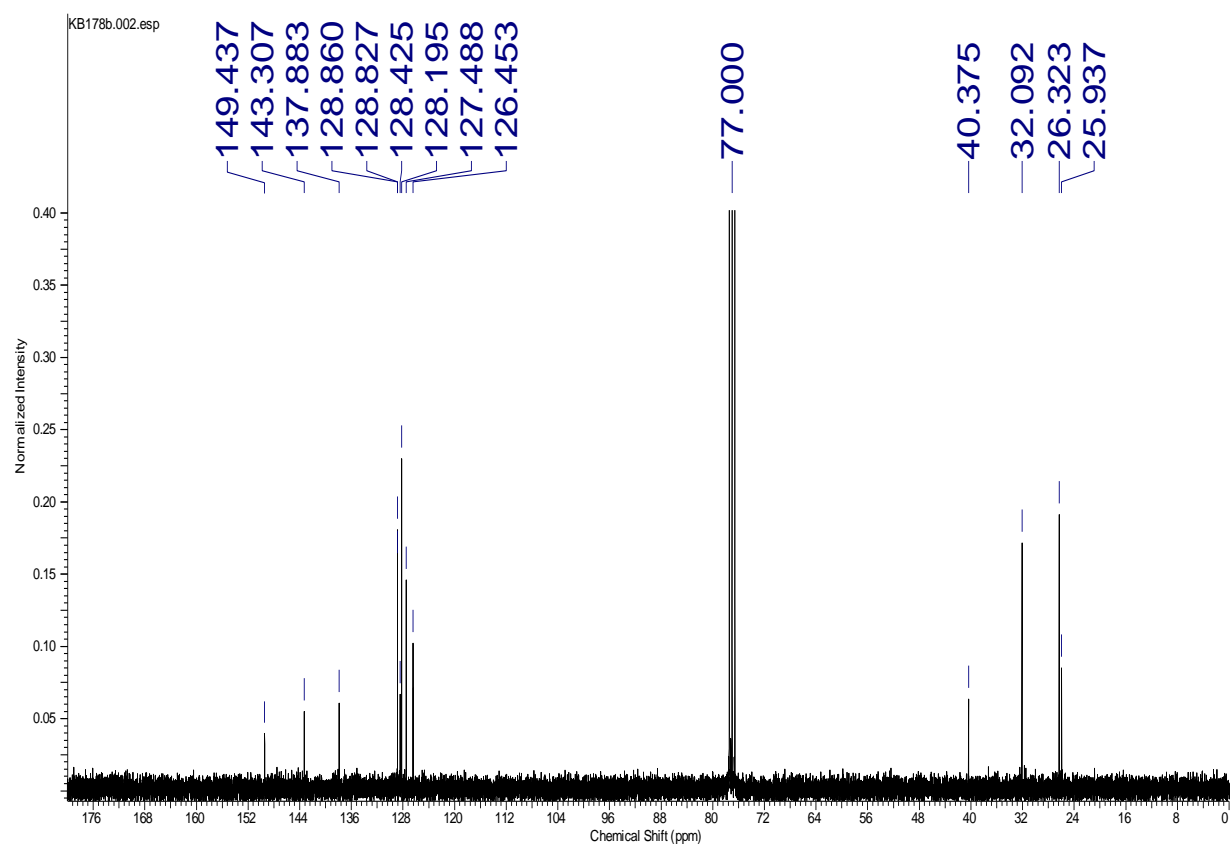
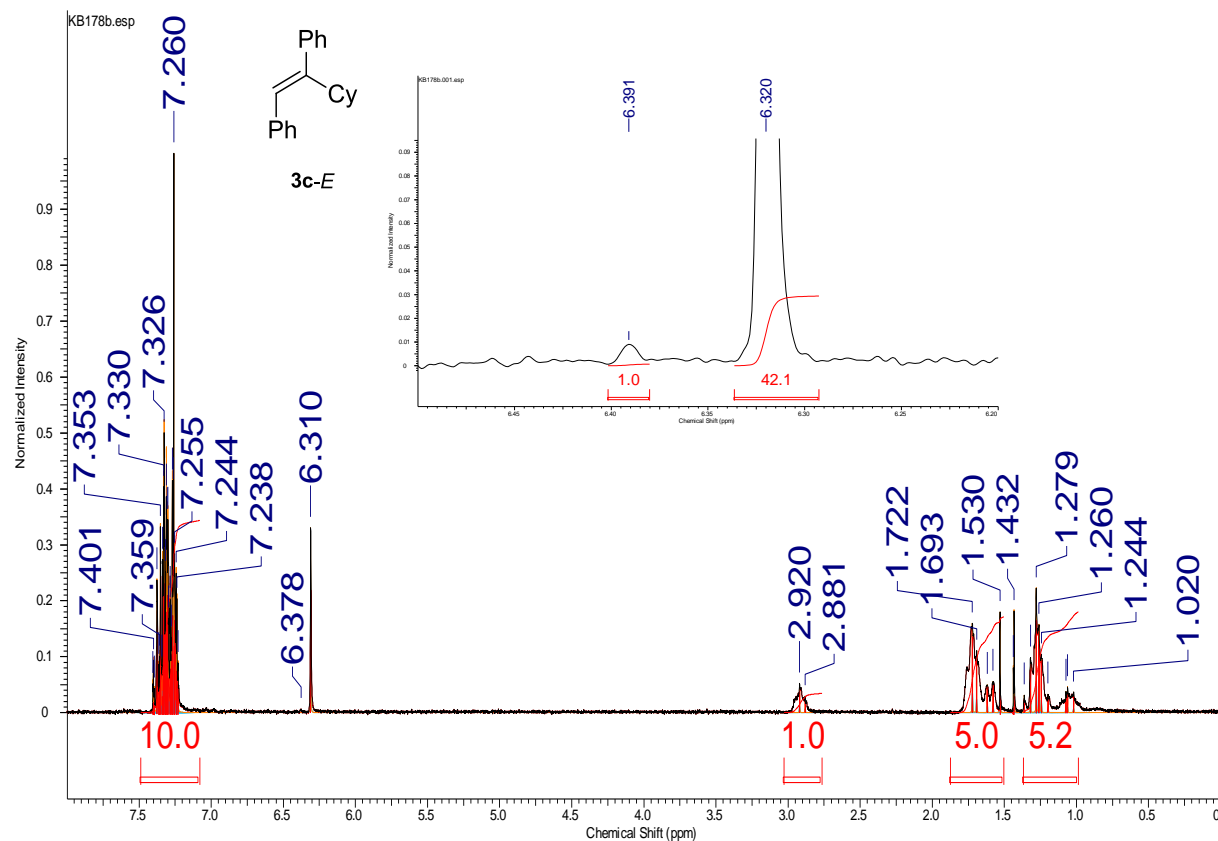
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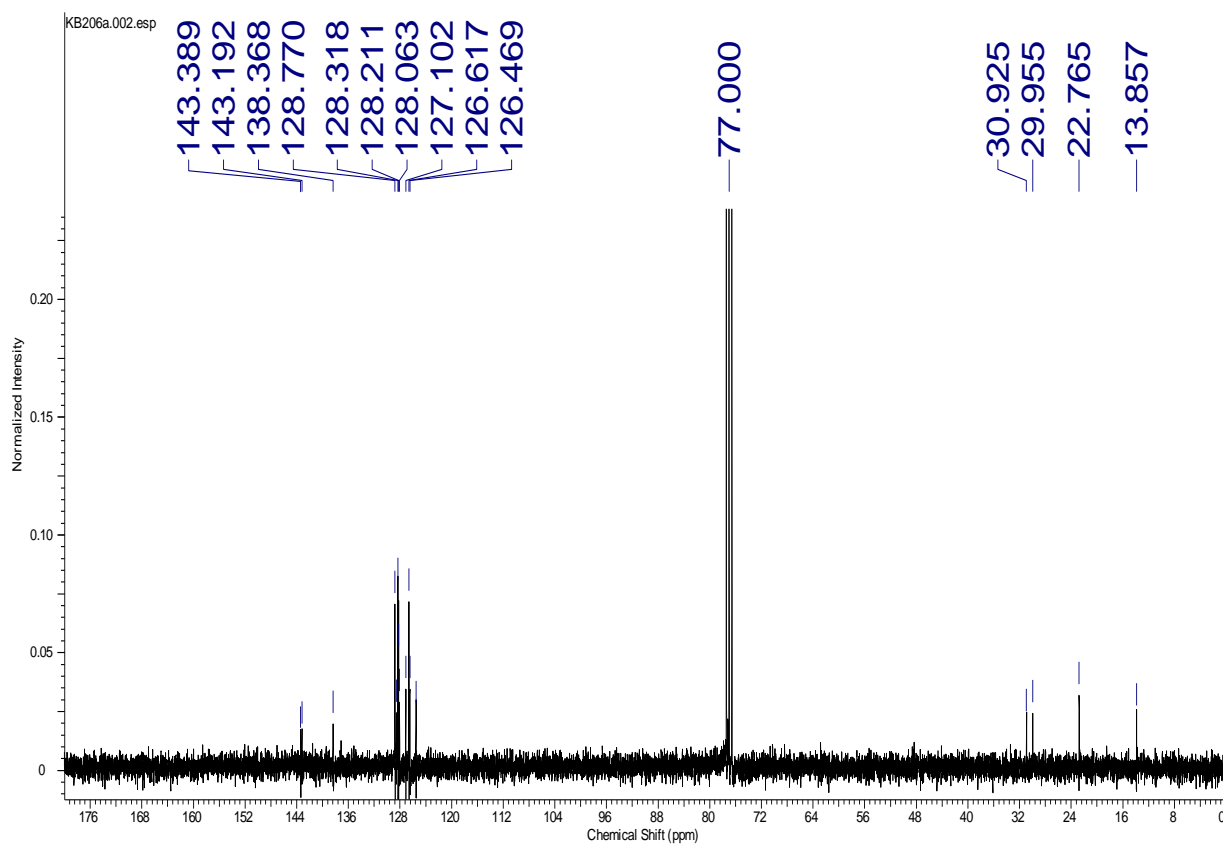
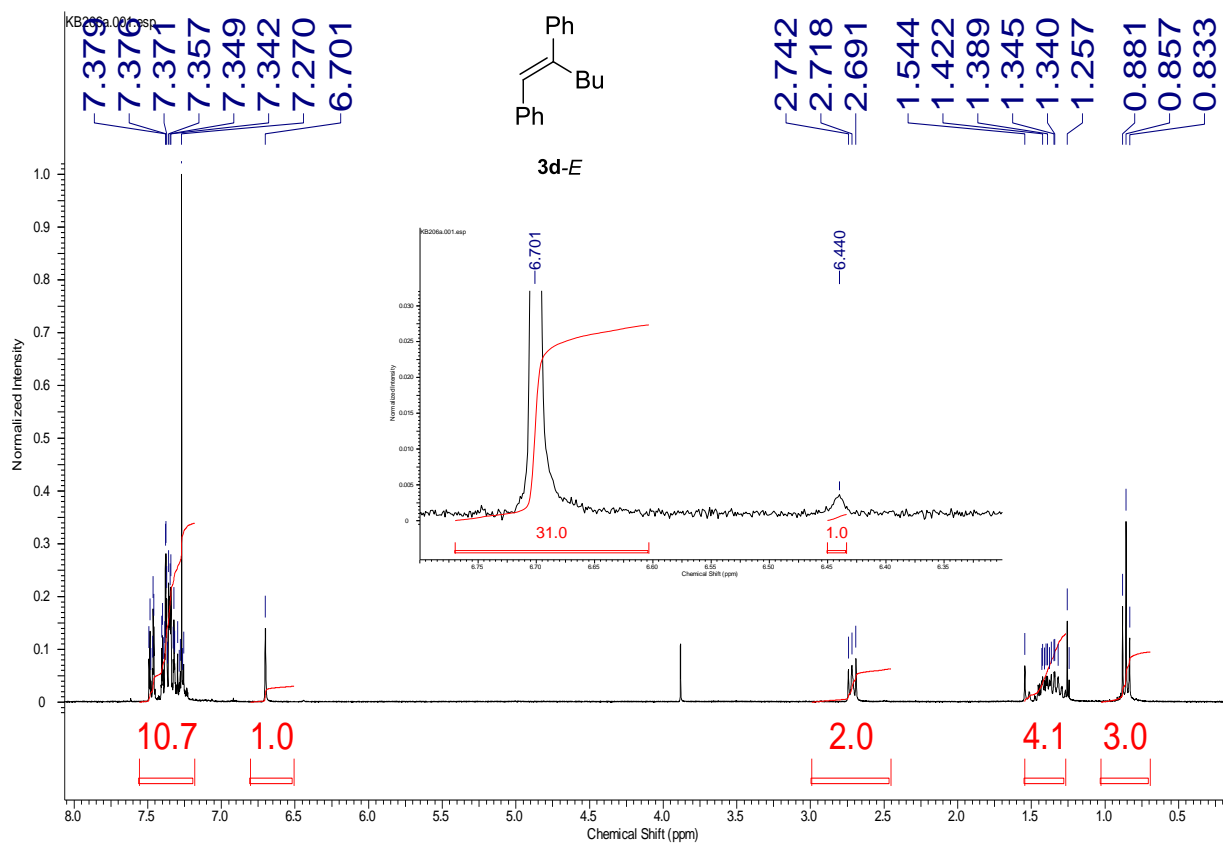


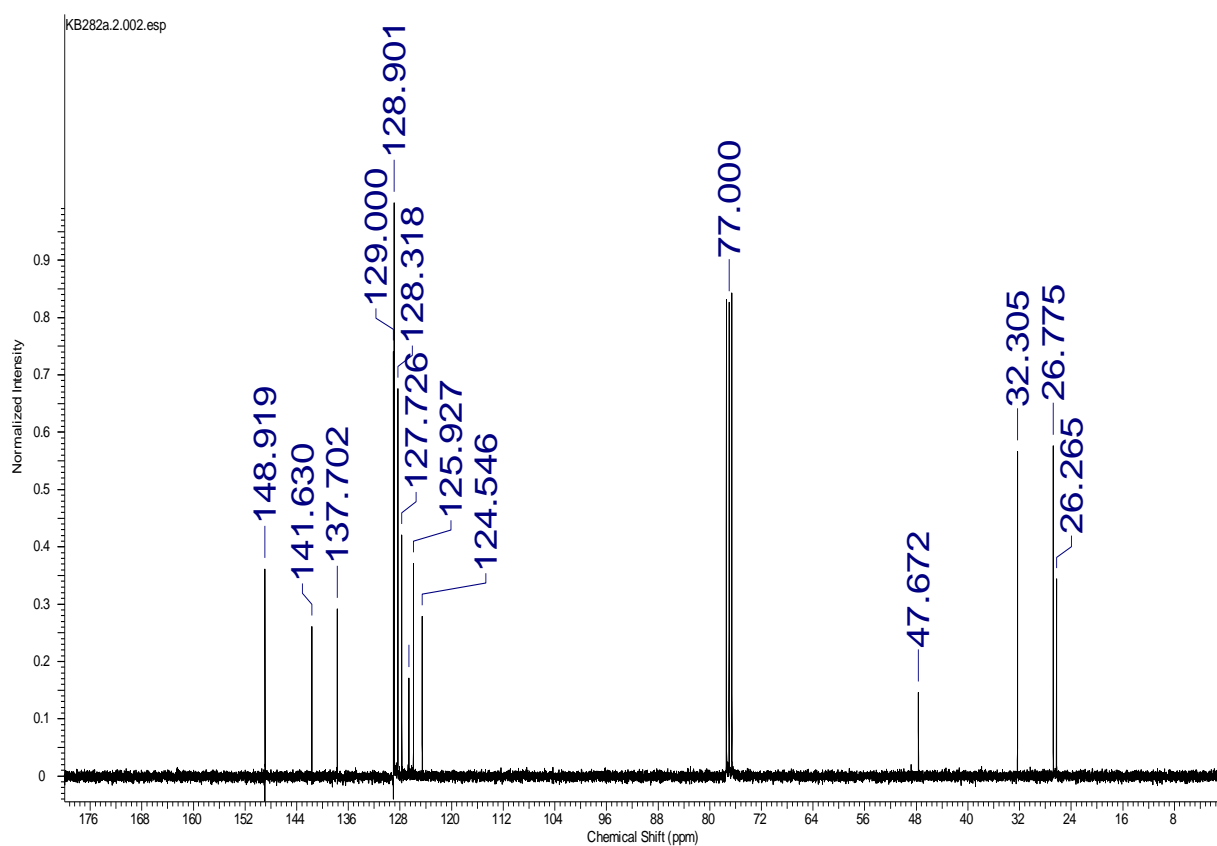
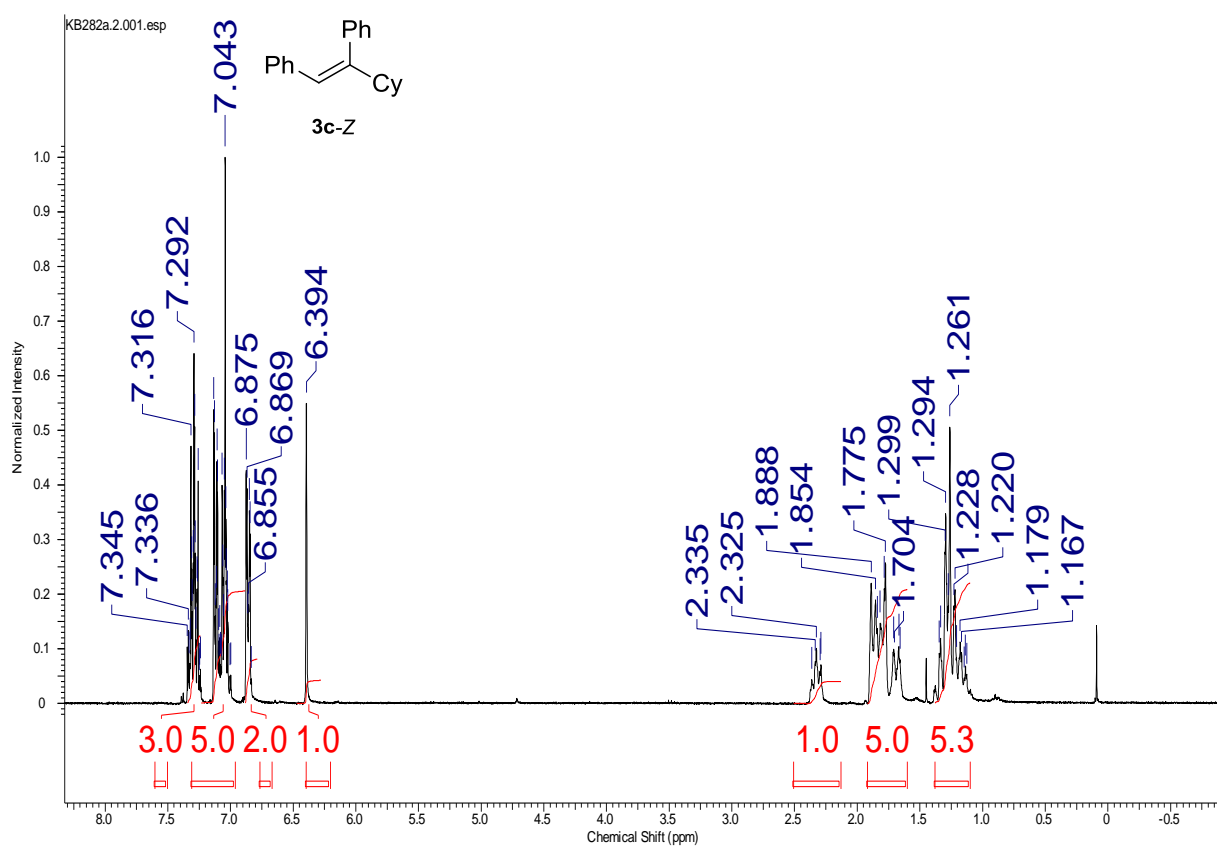


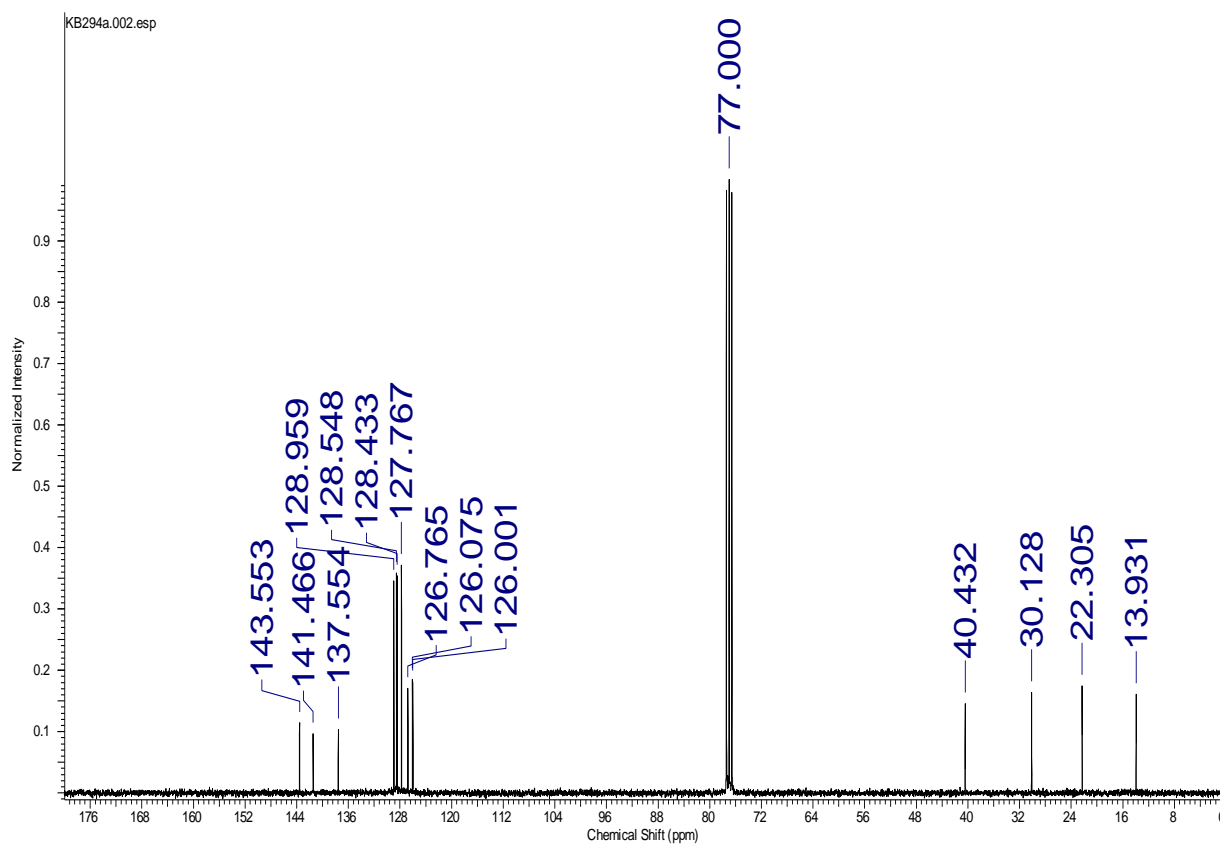
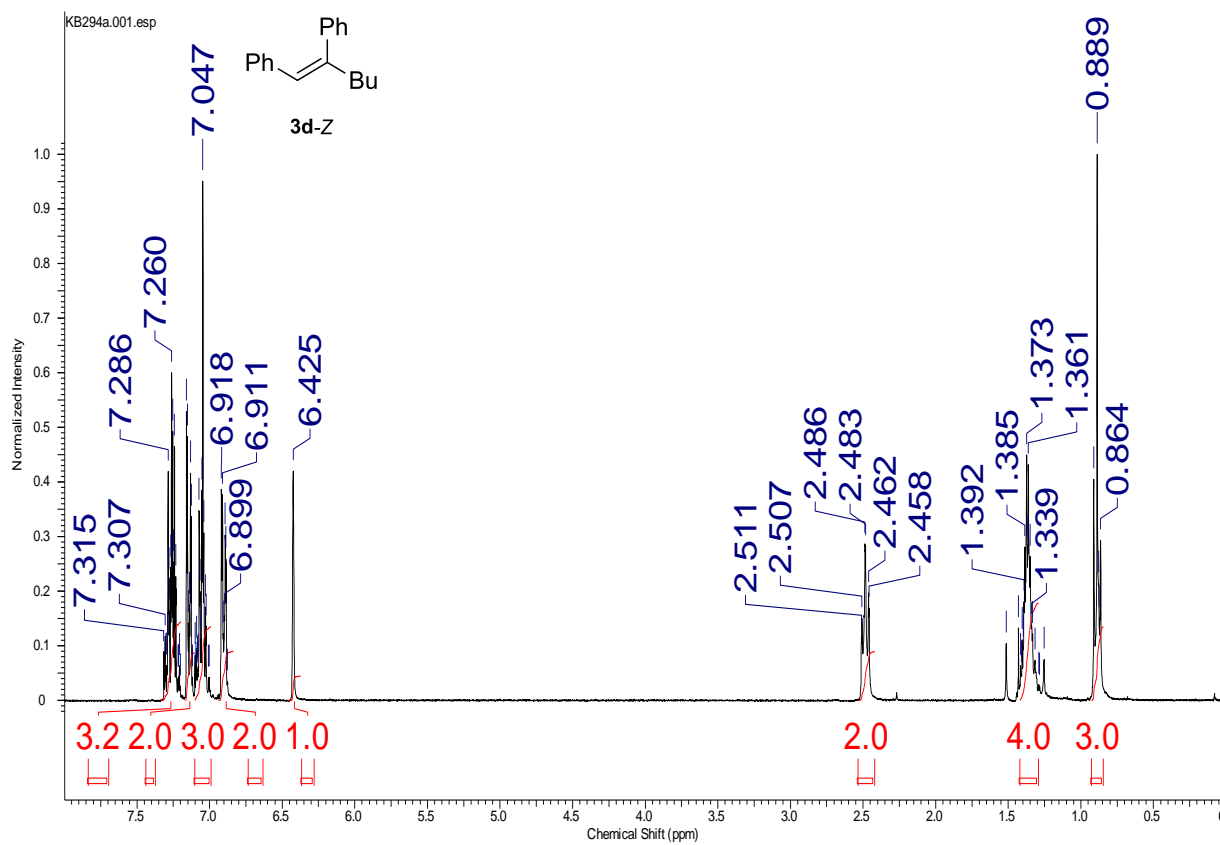


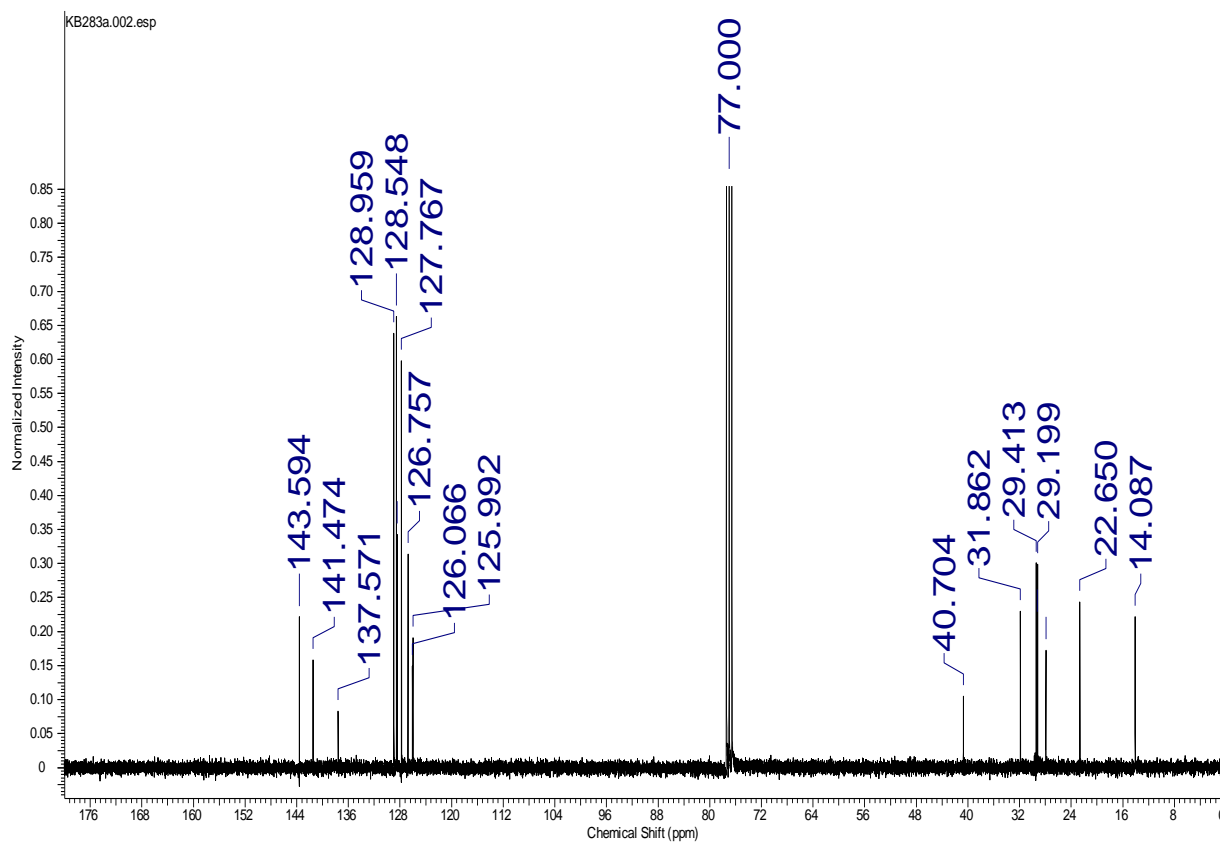
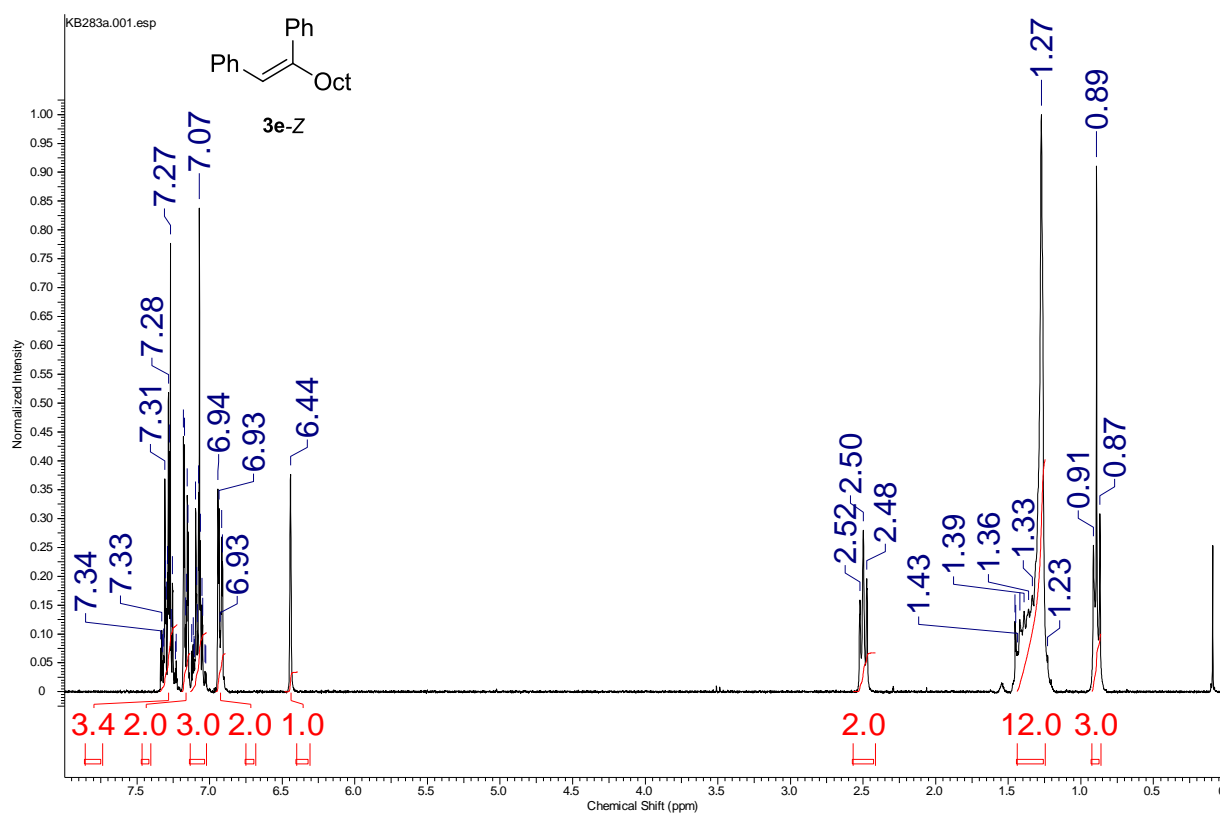


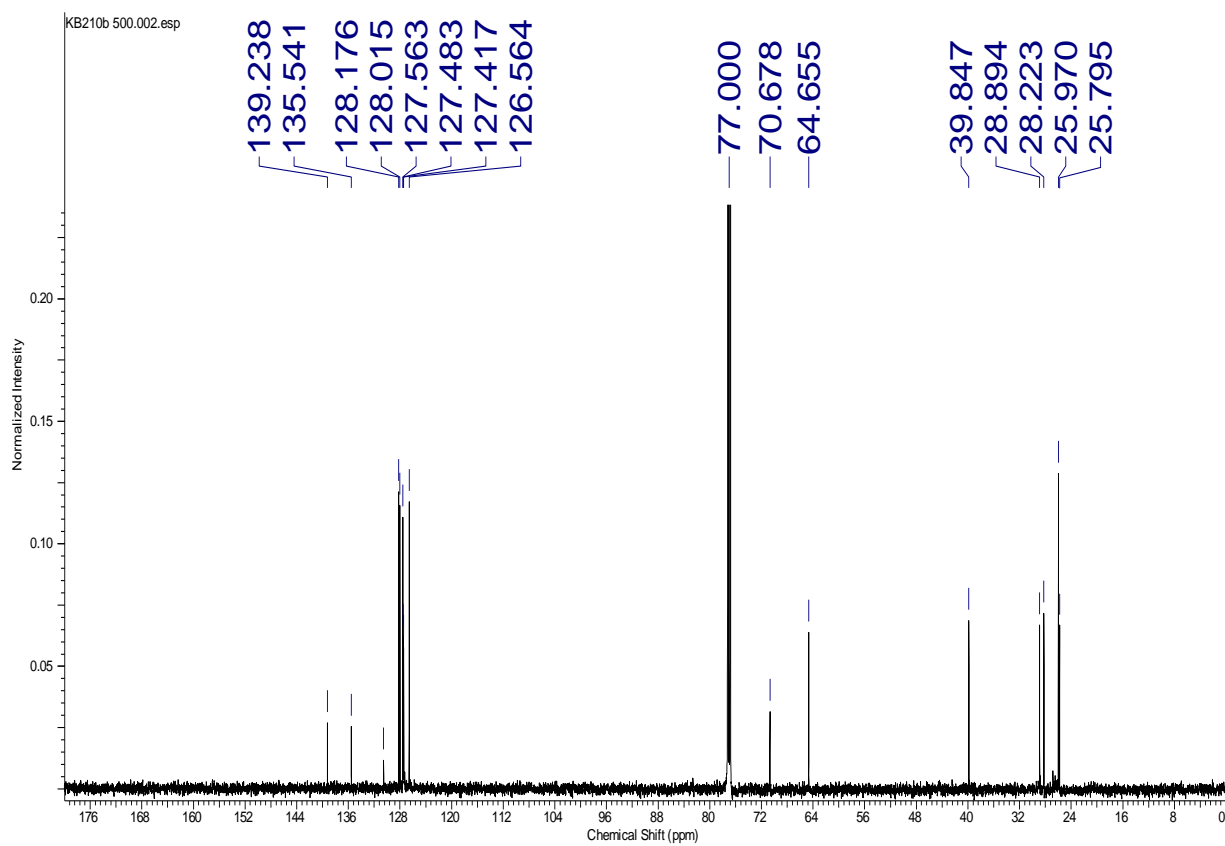
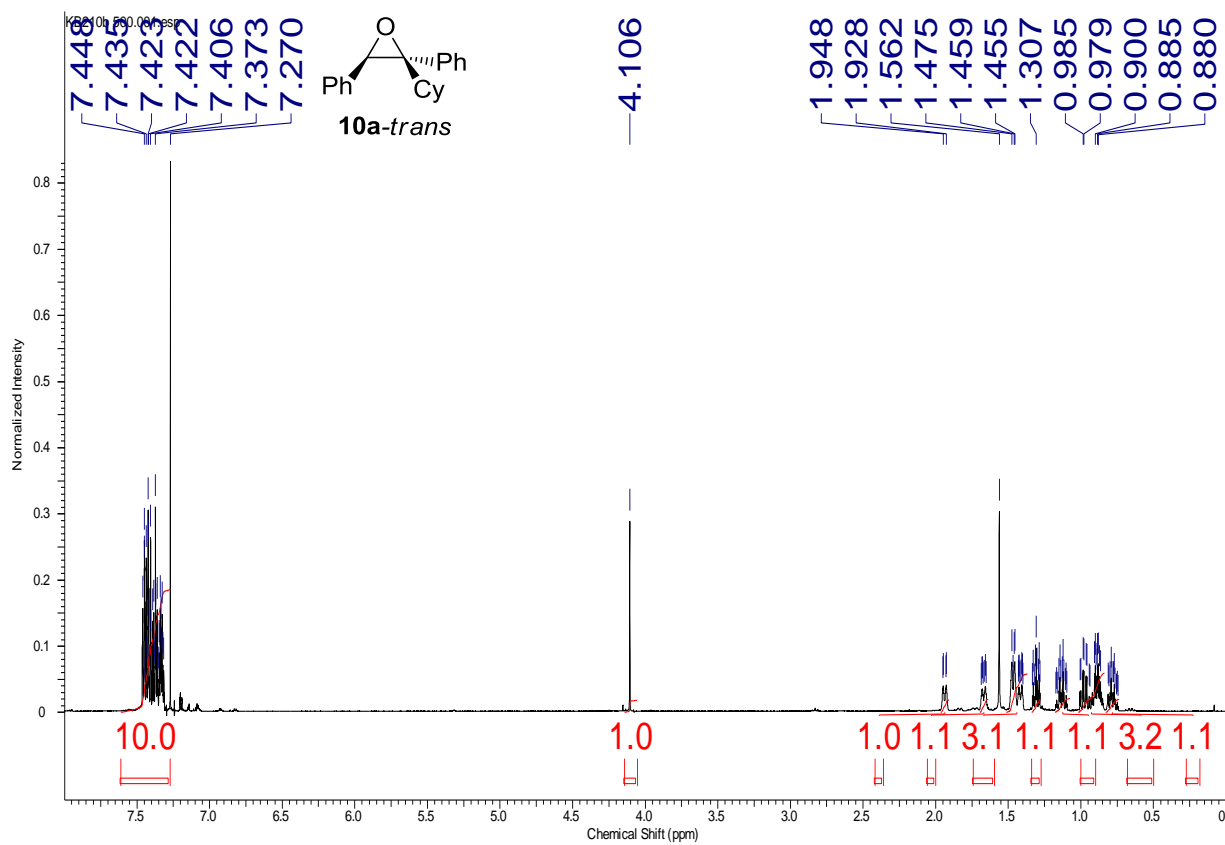


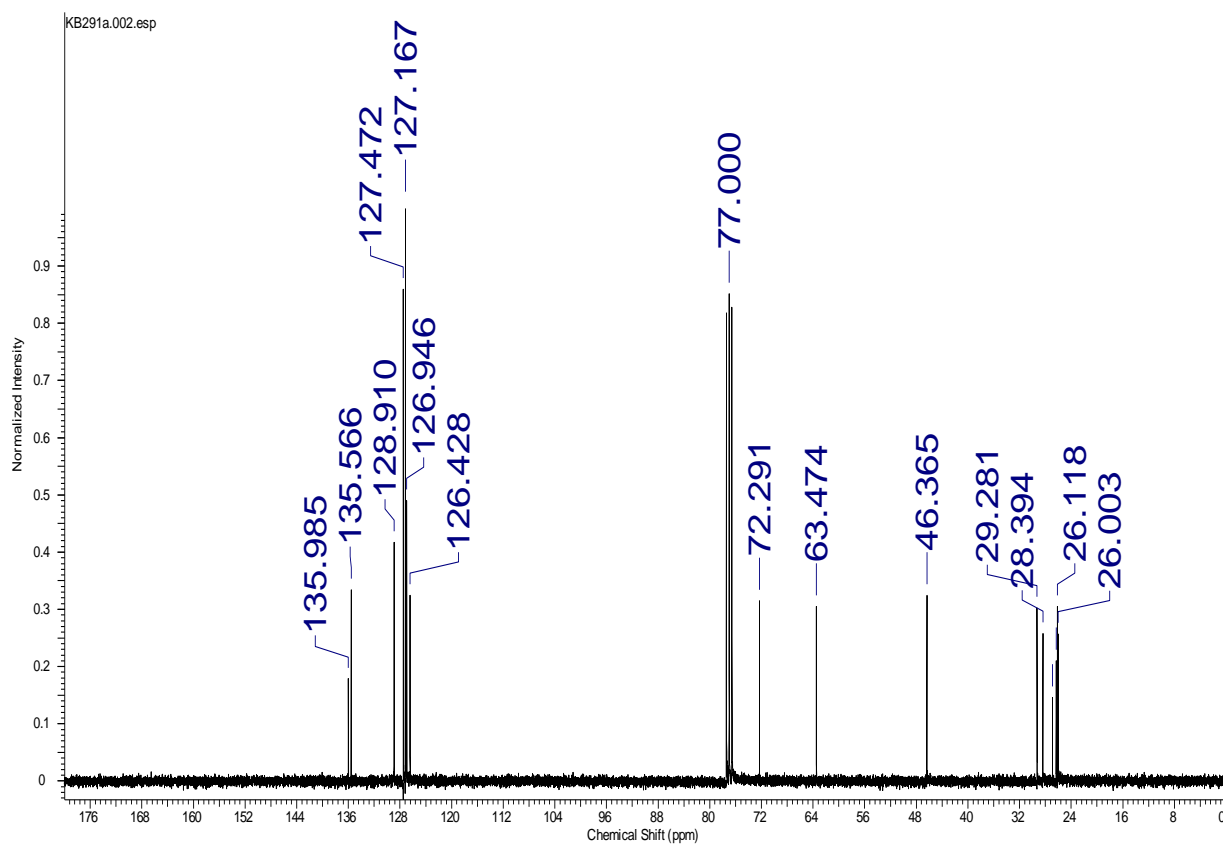
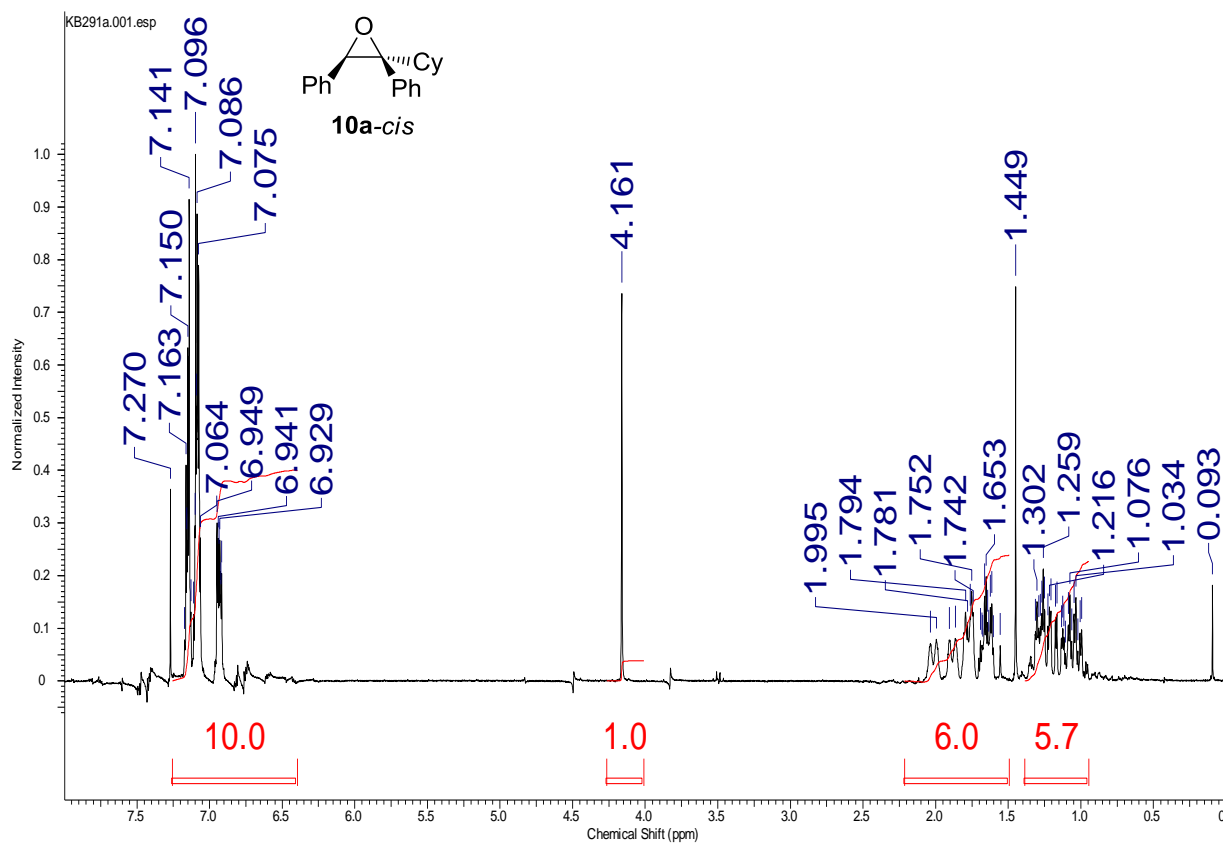


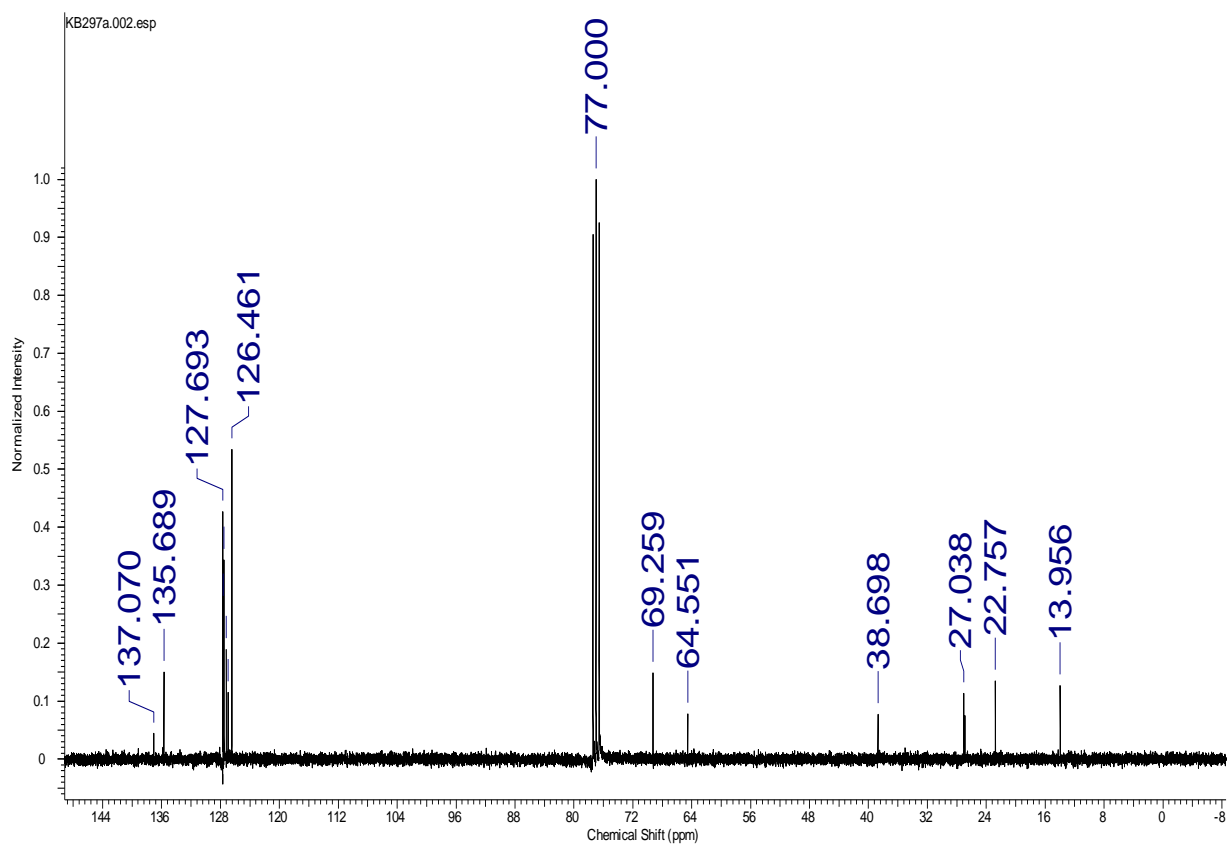
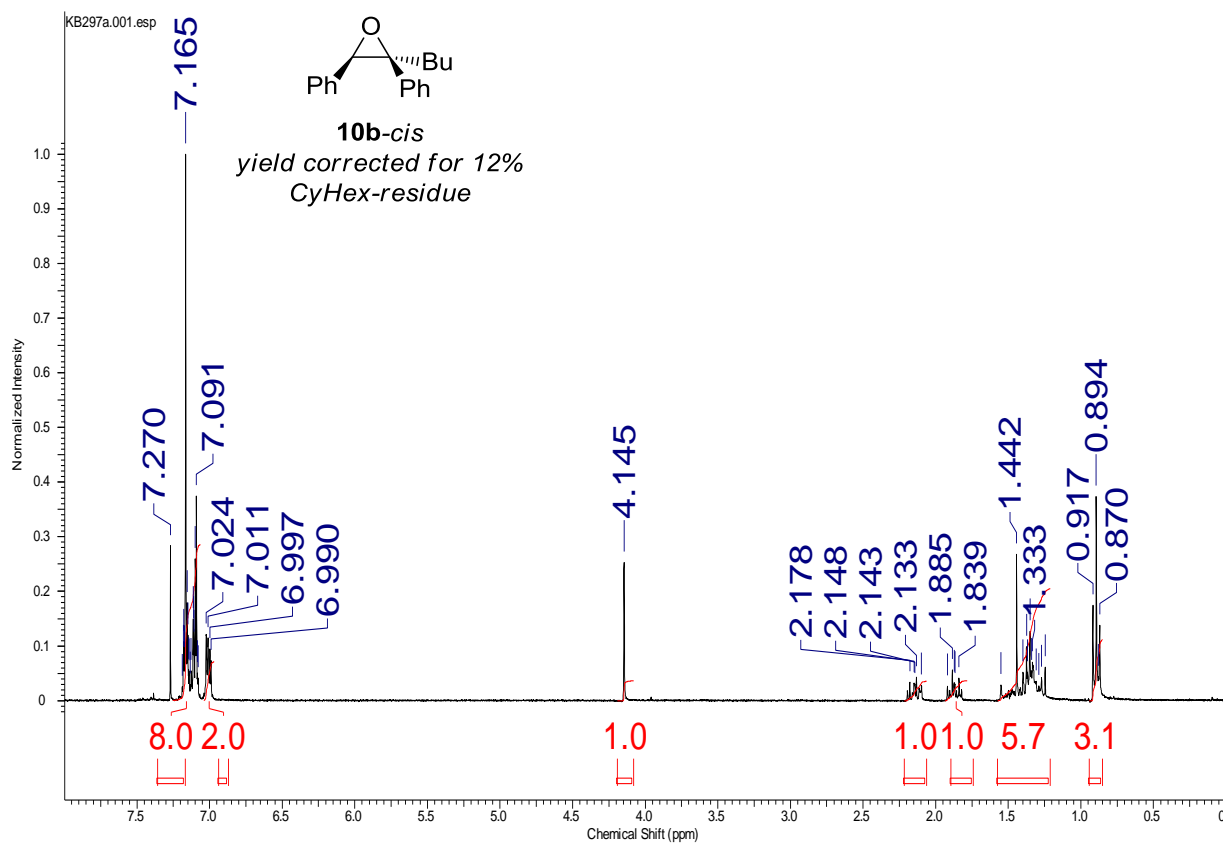


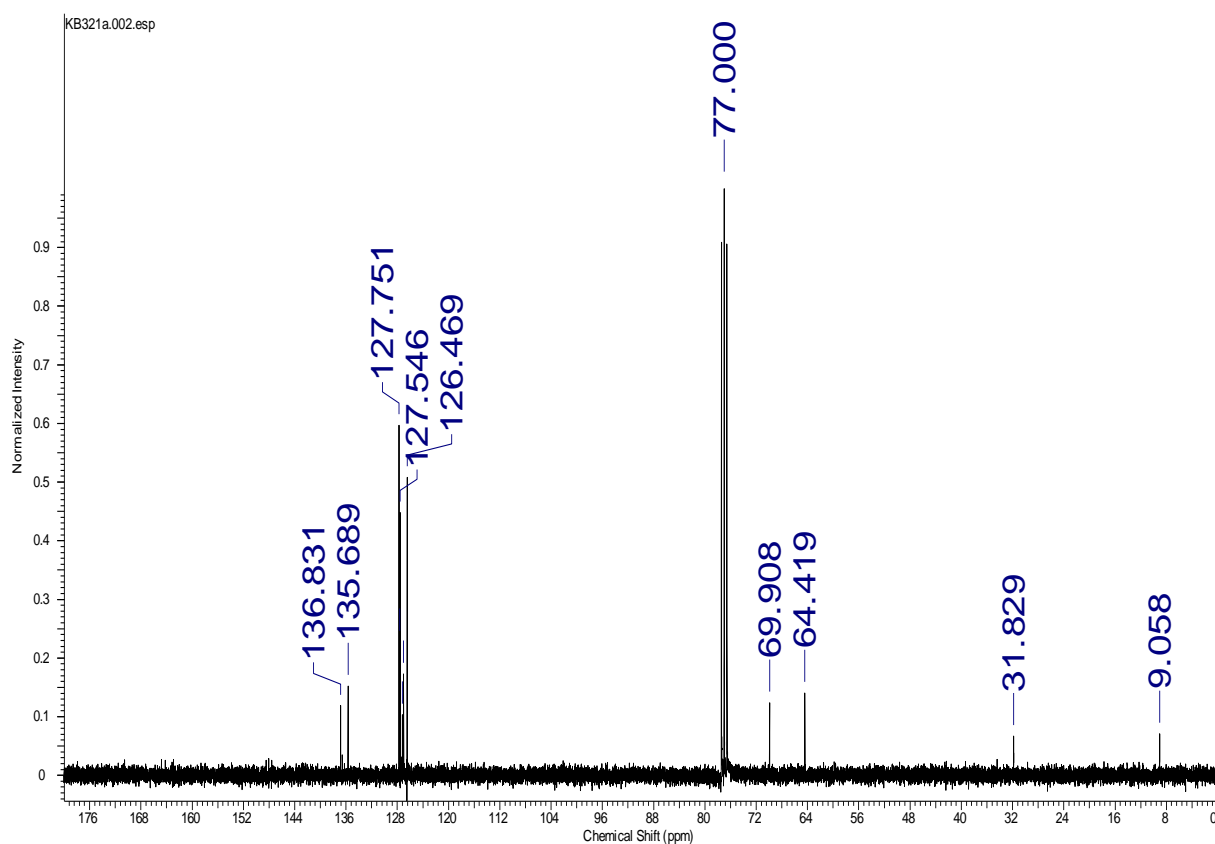
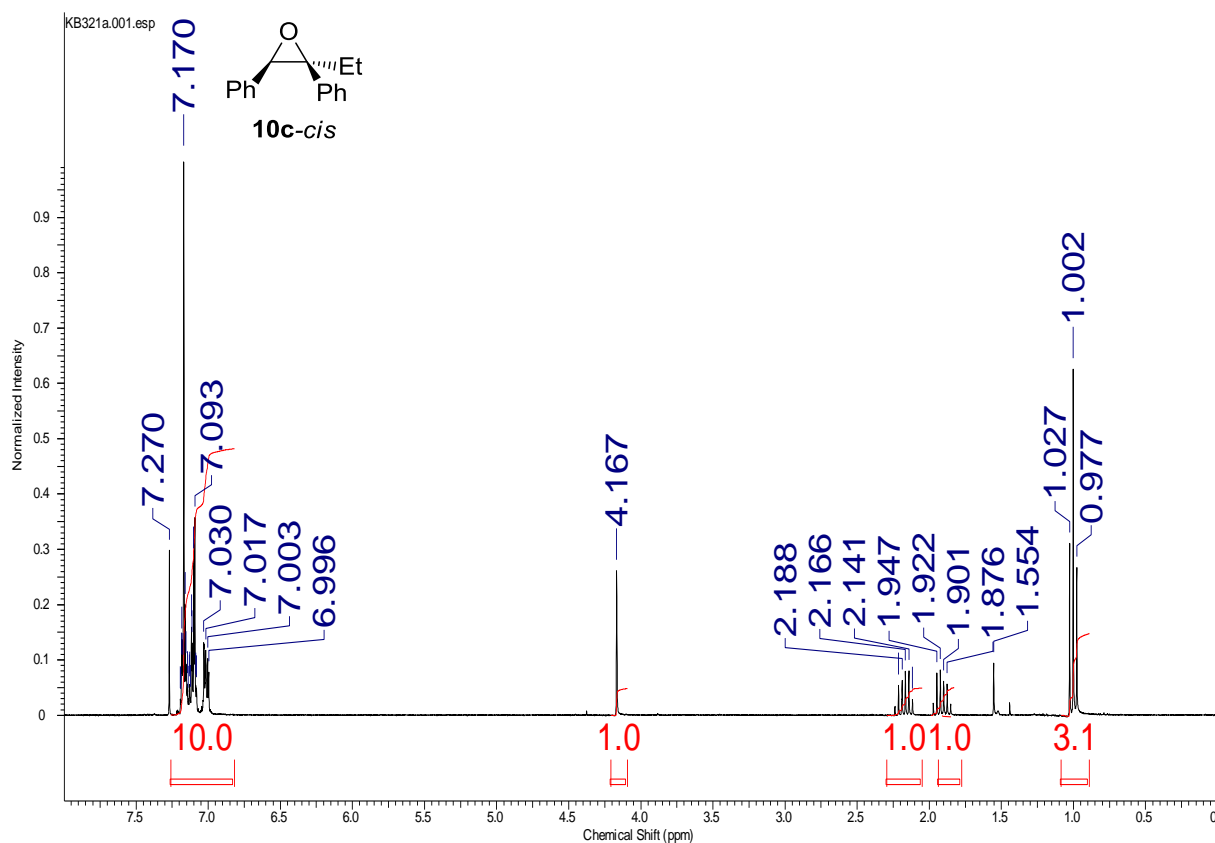




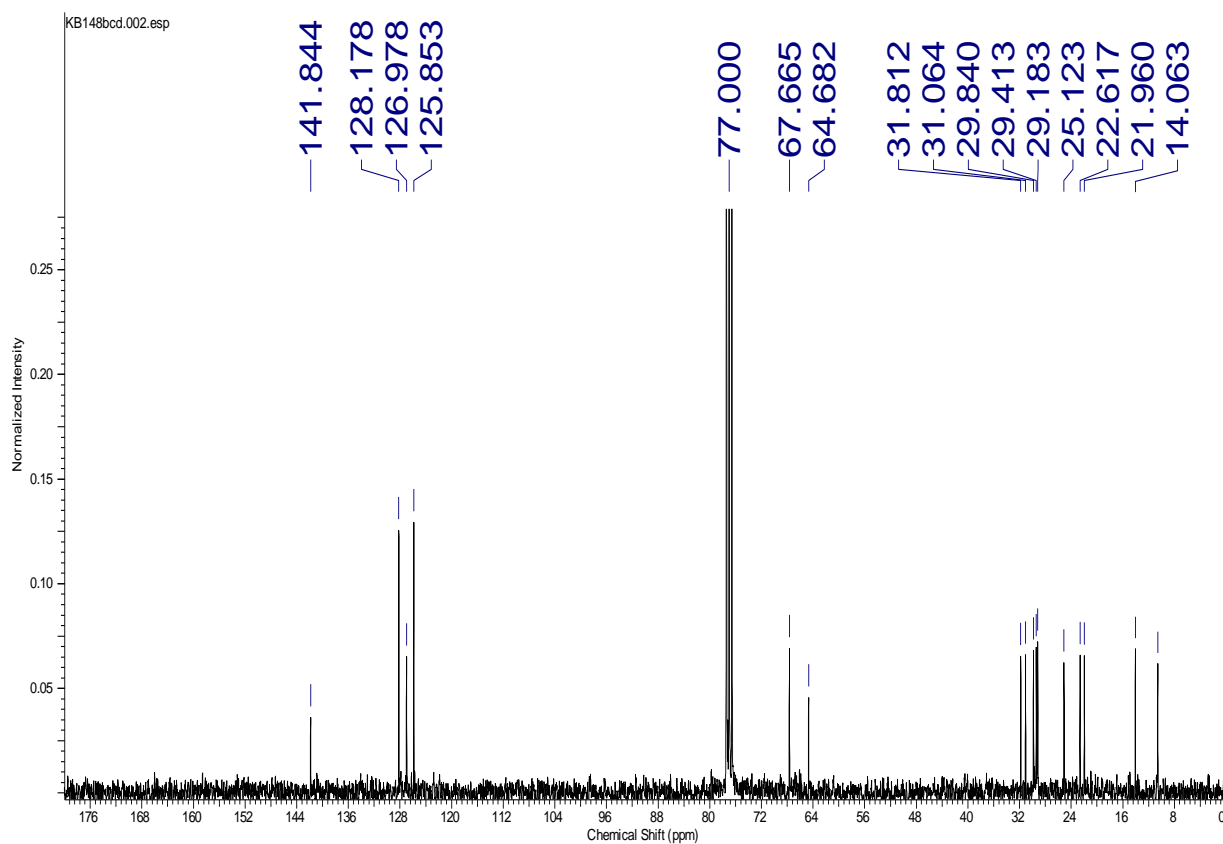
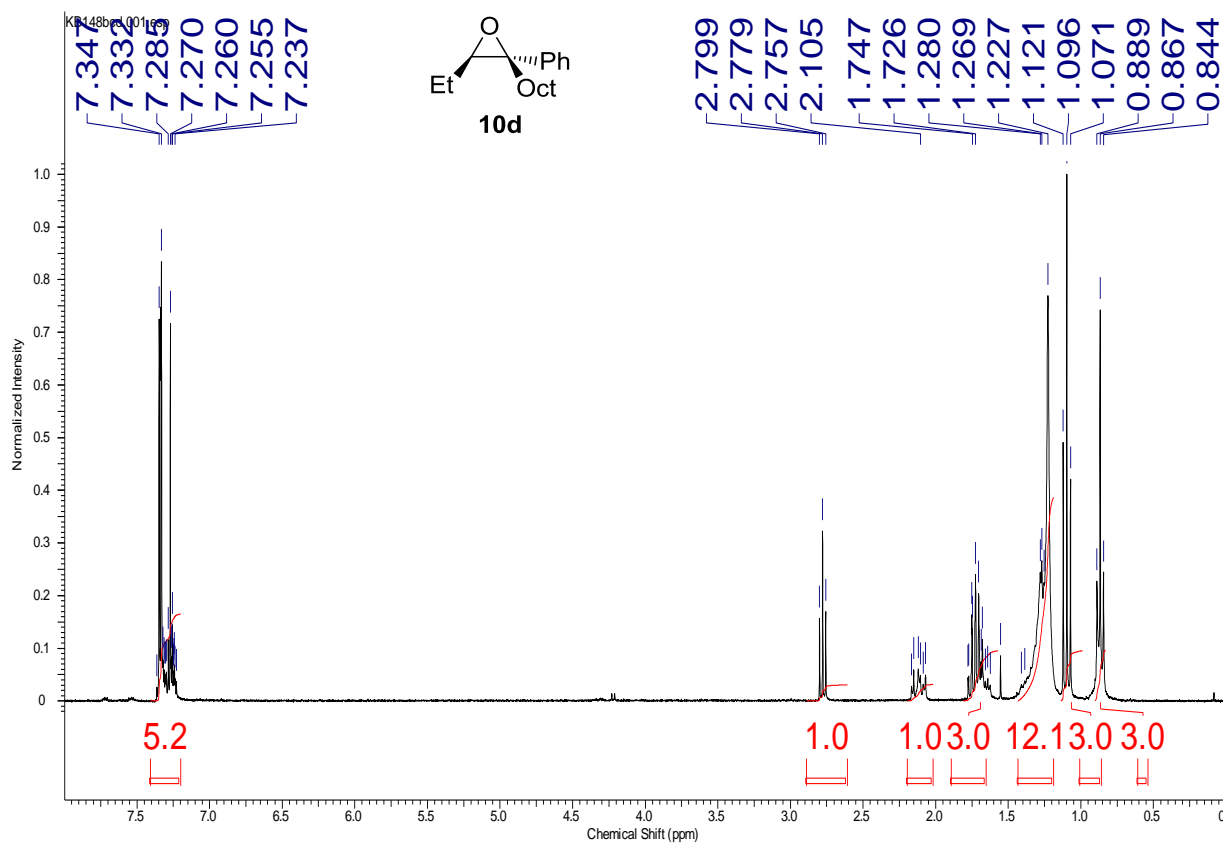


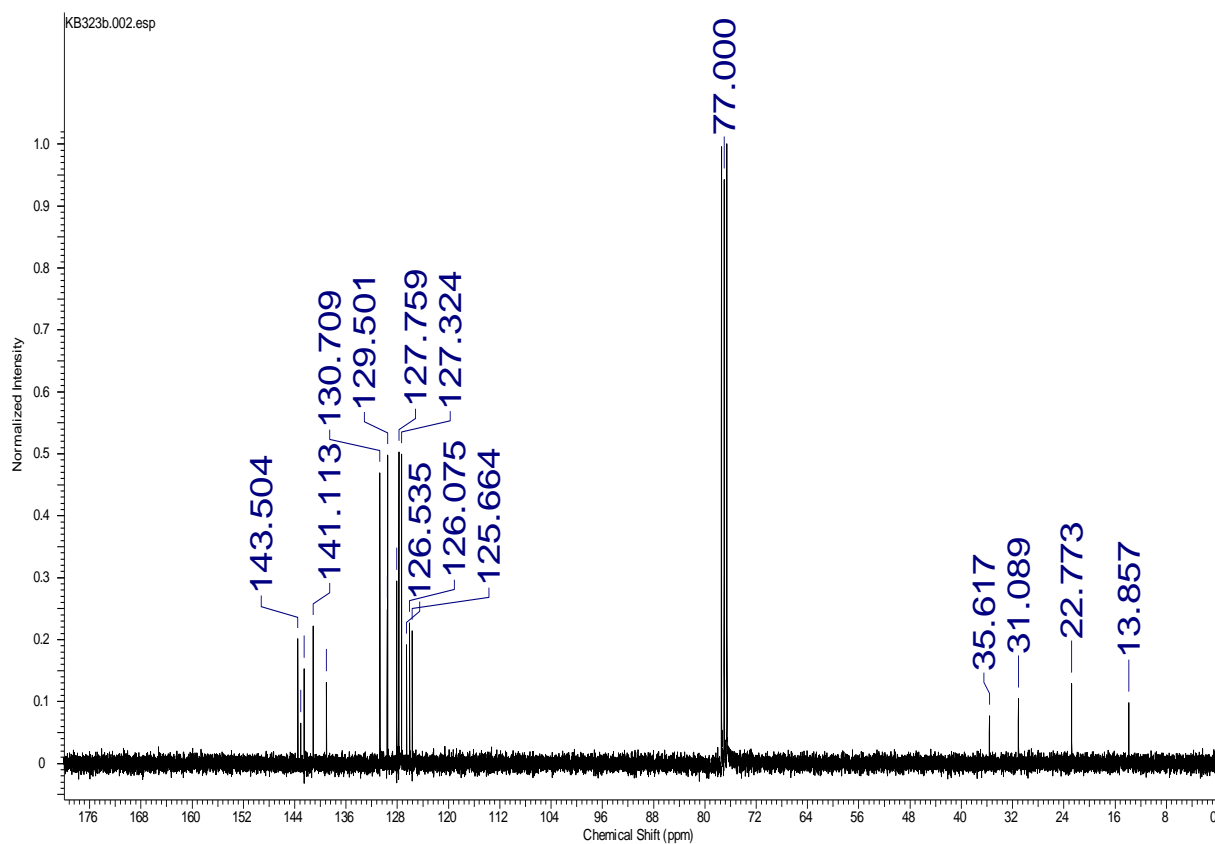
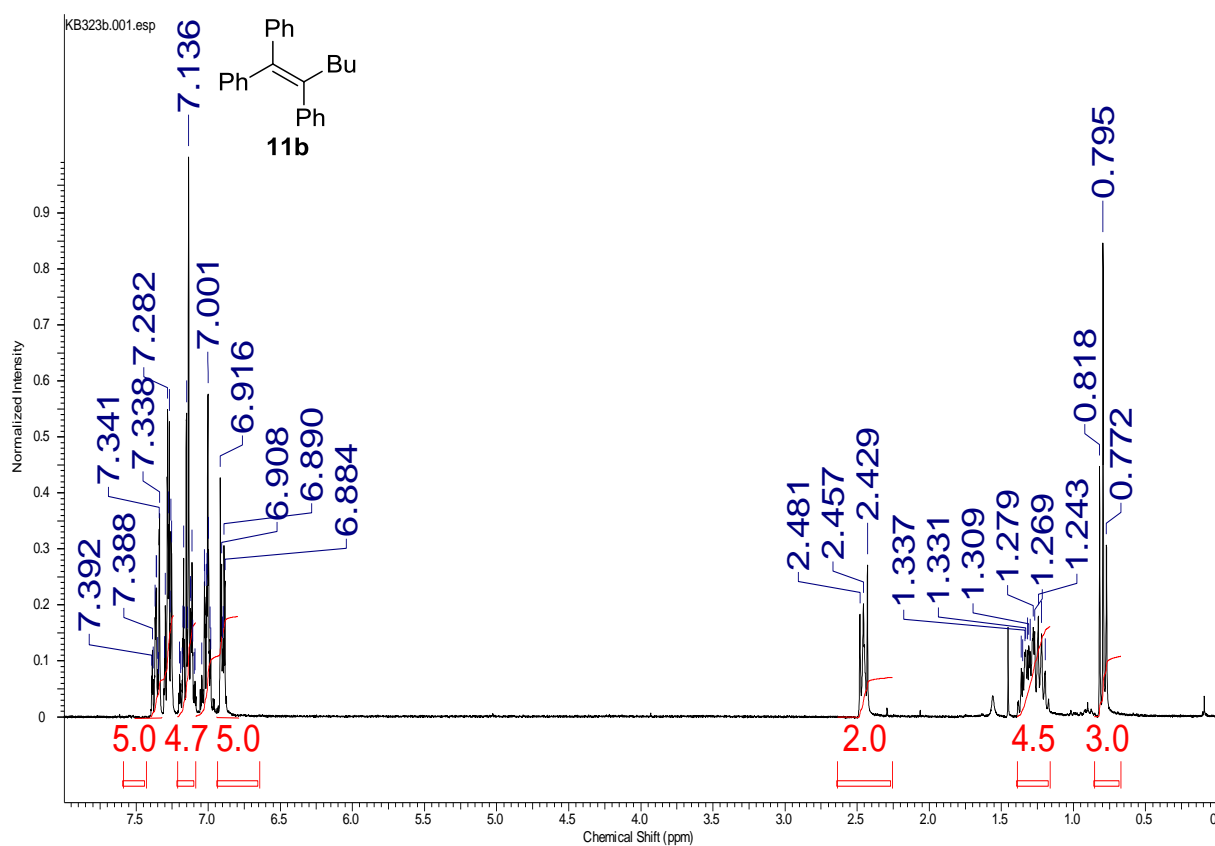


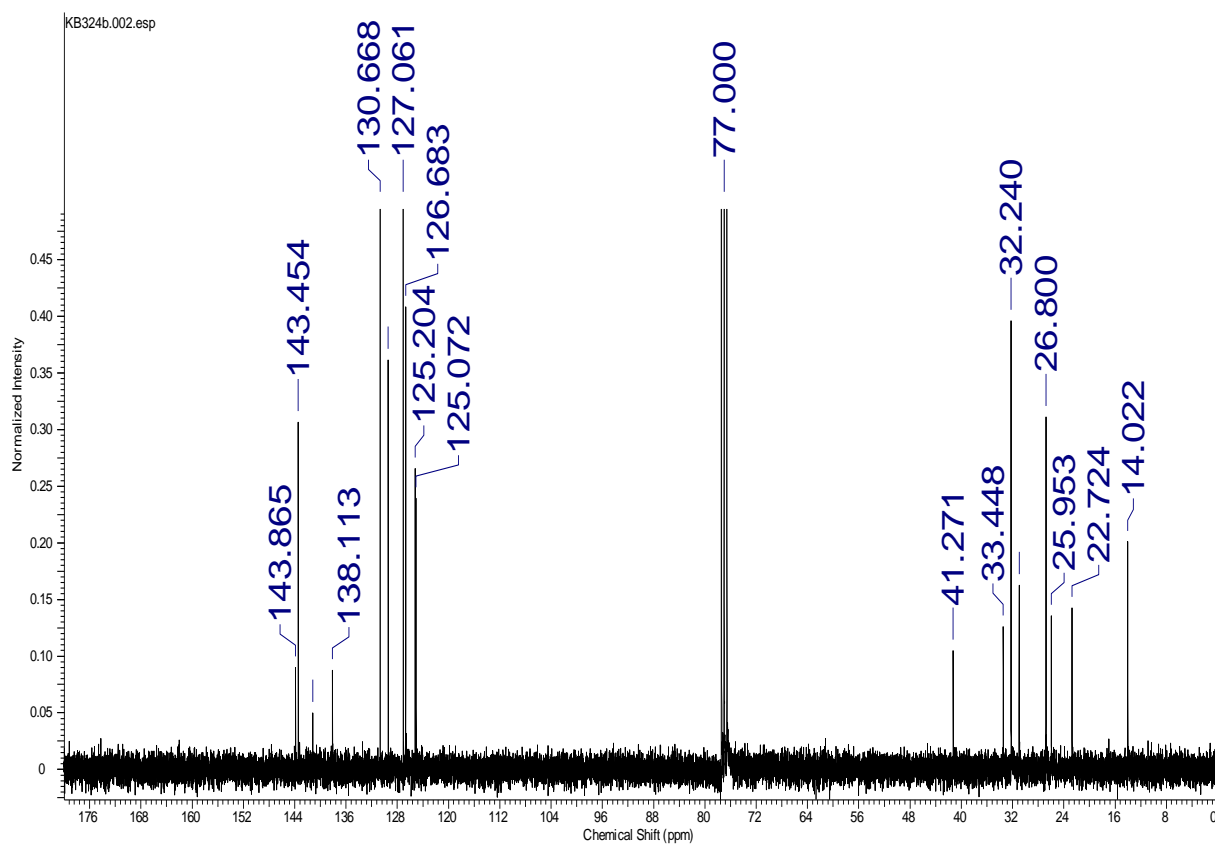
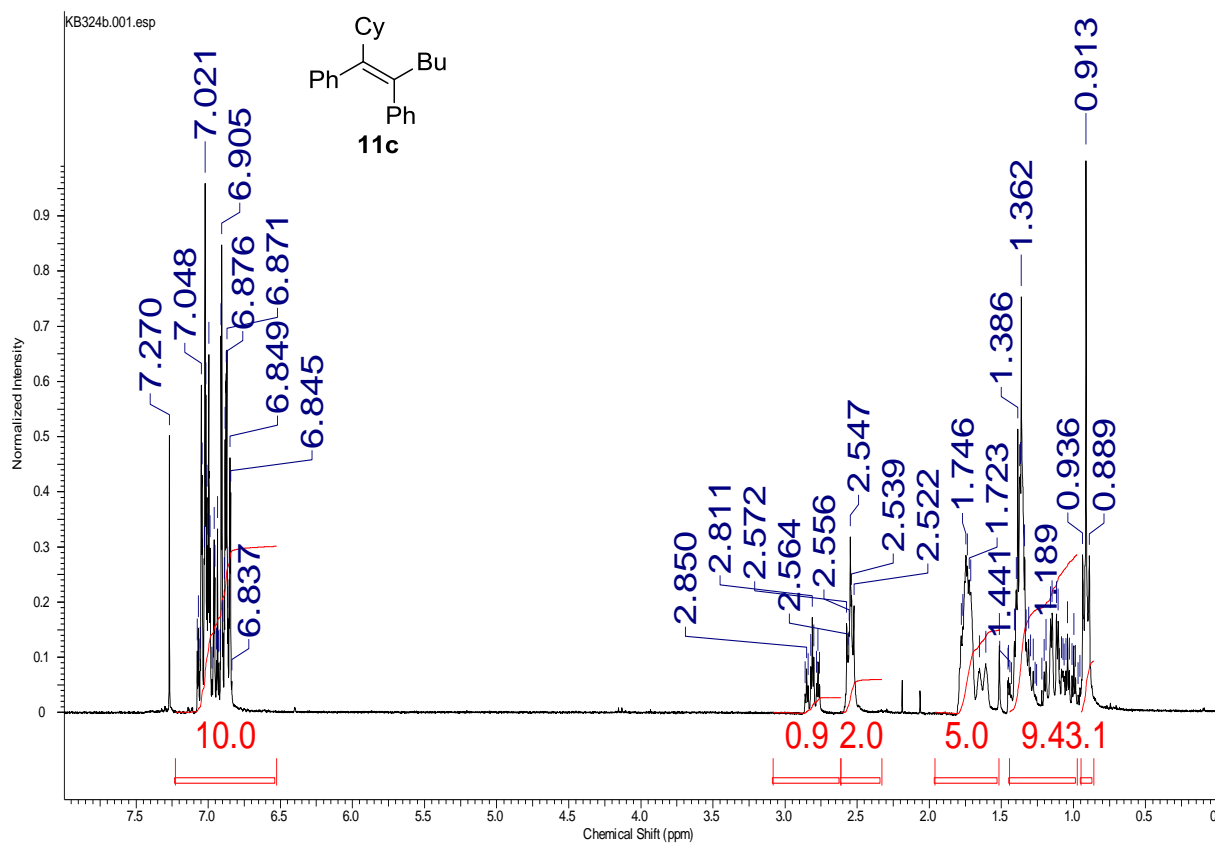




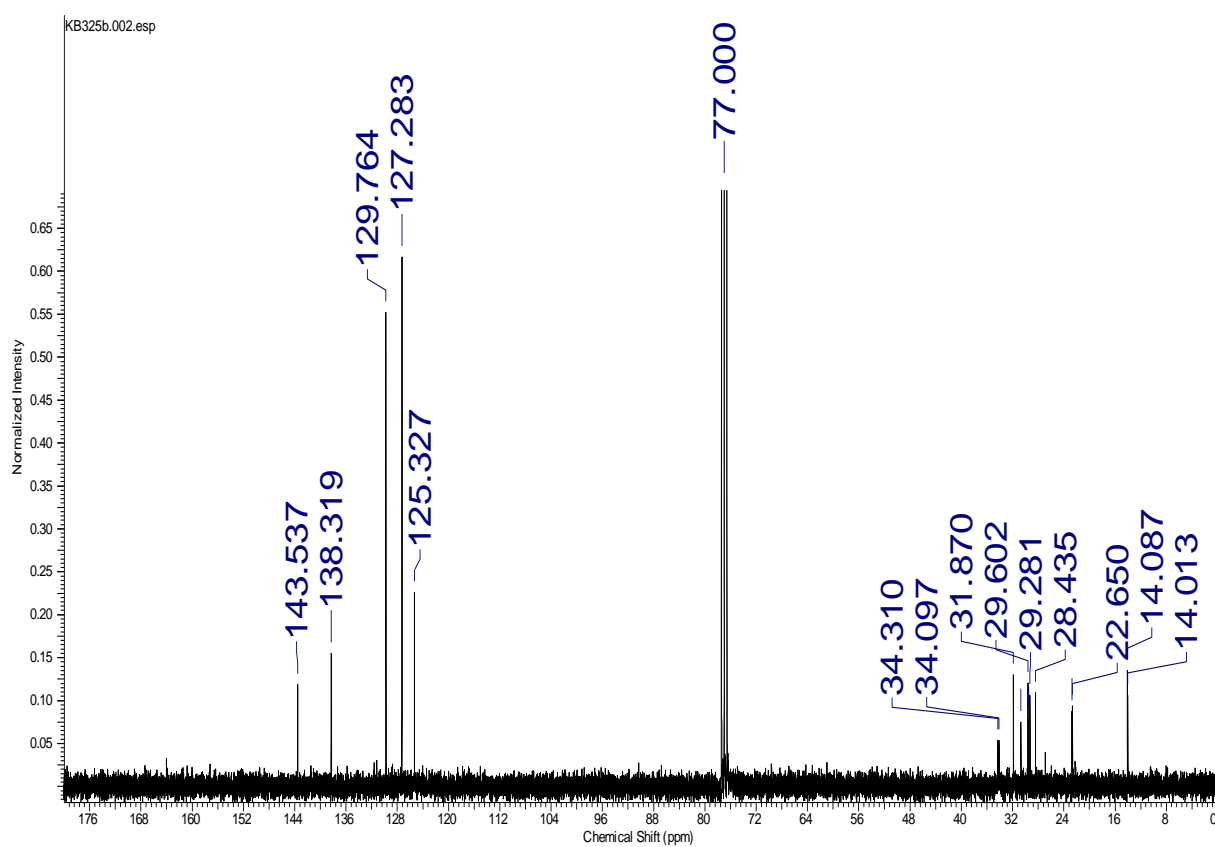
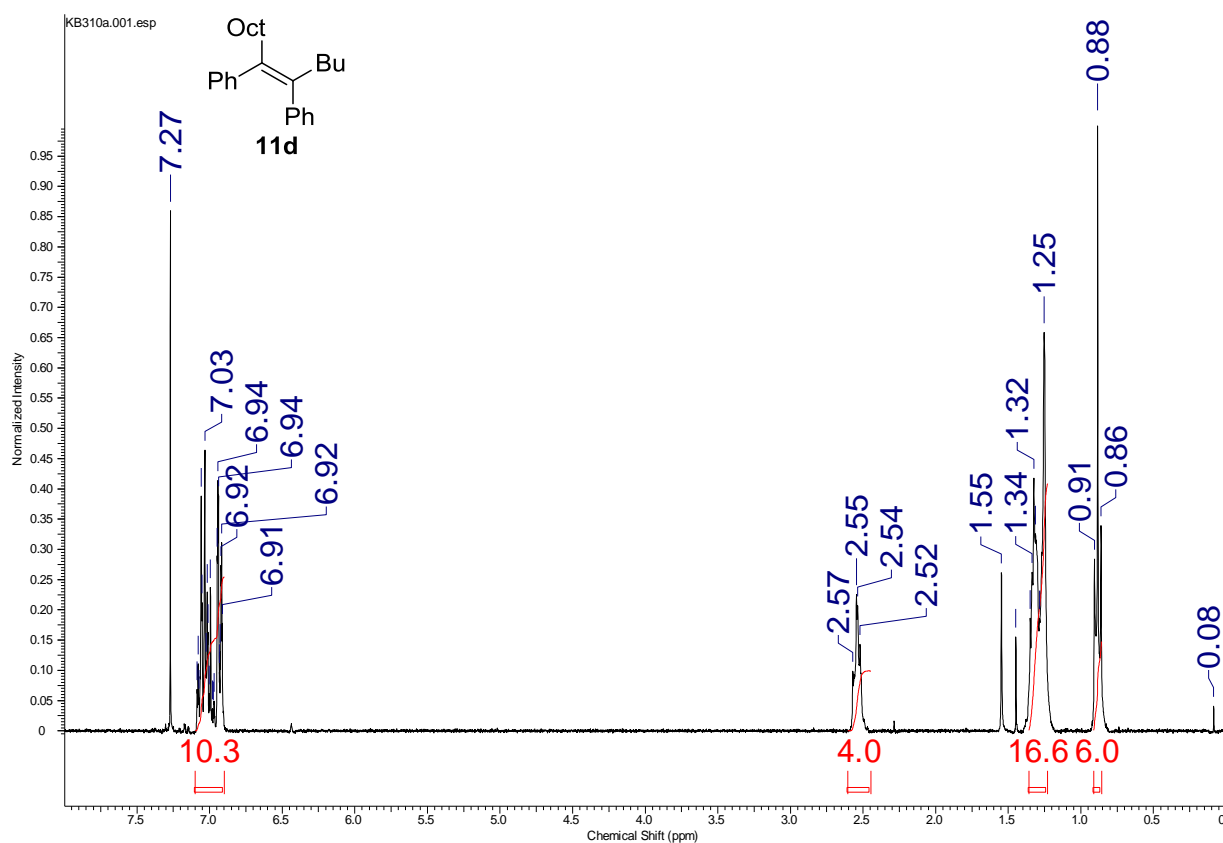
Selected NMR-Spectra

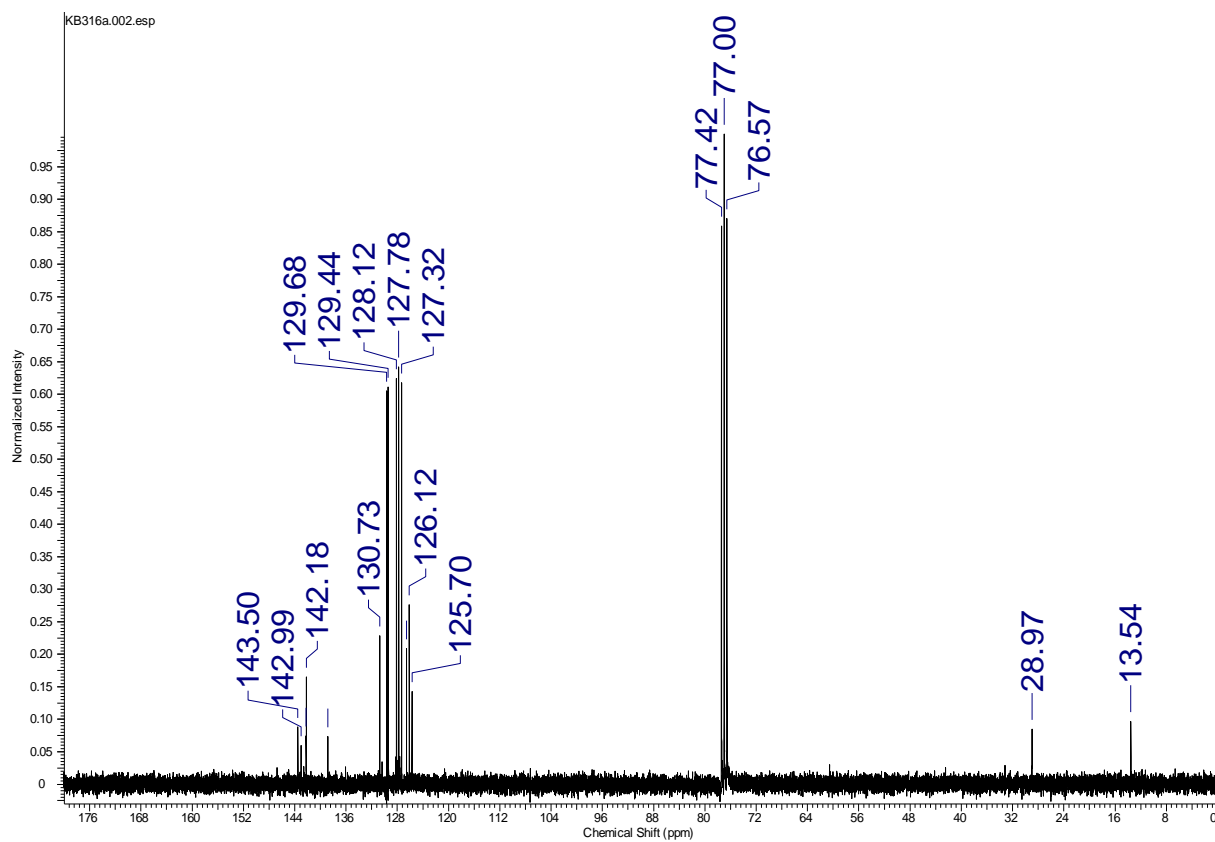
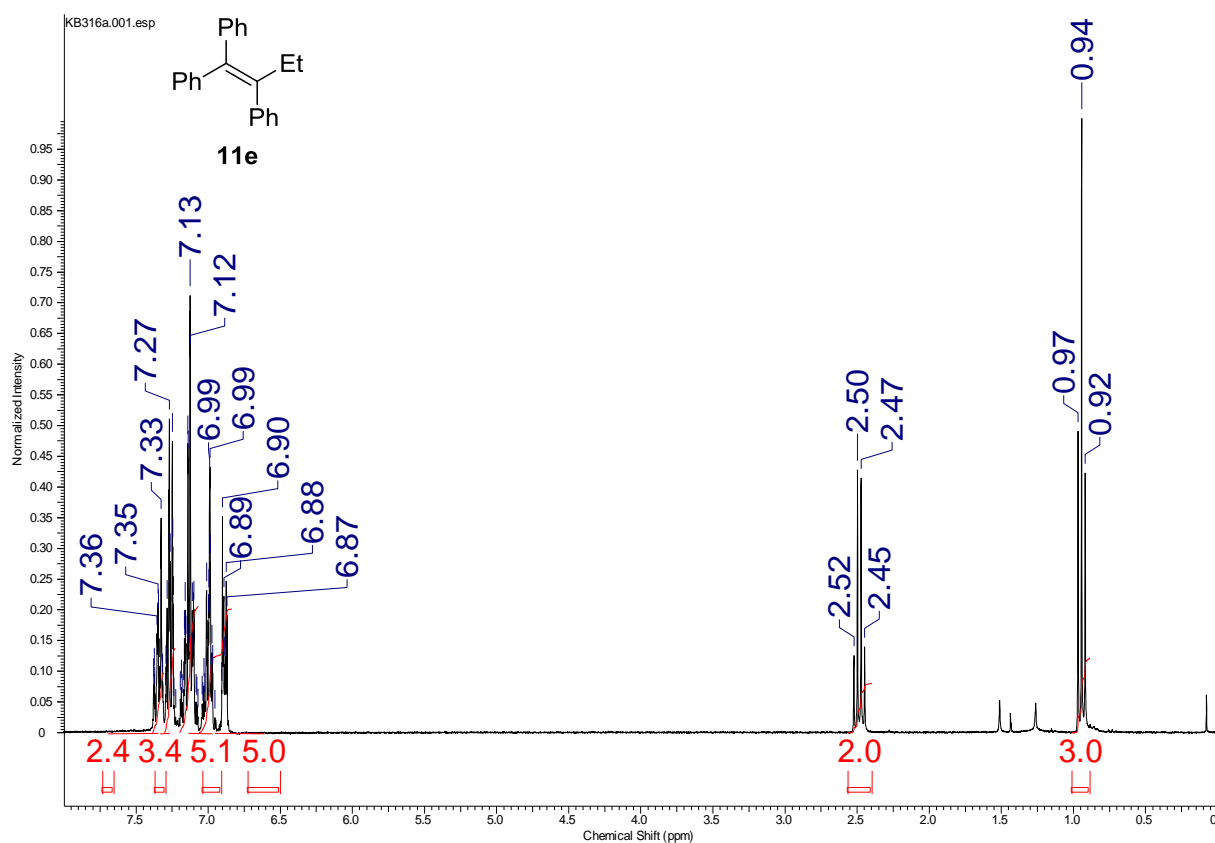




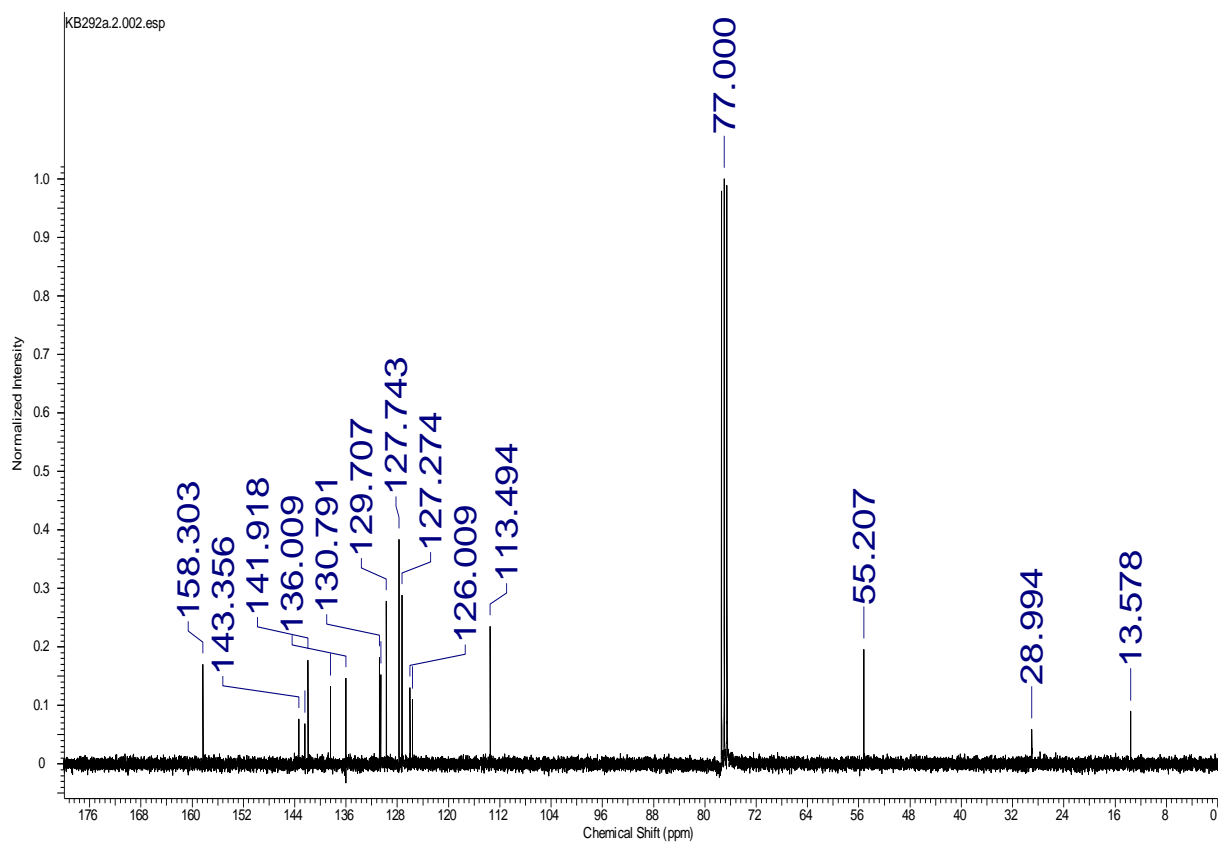
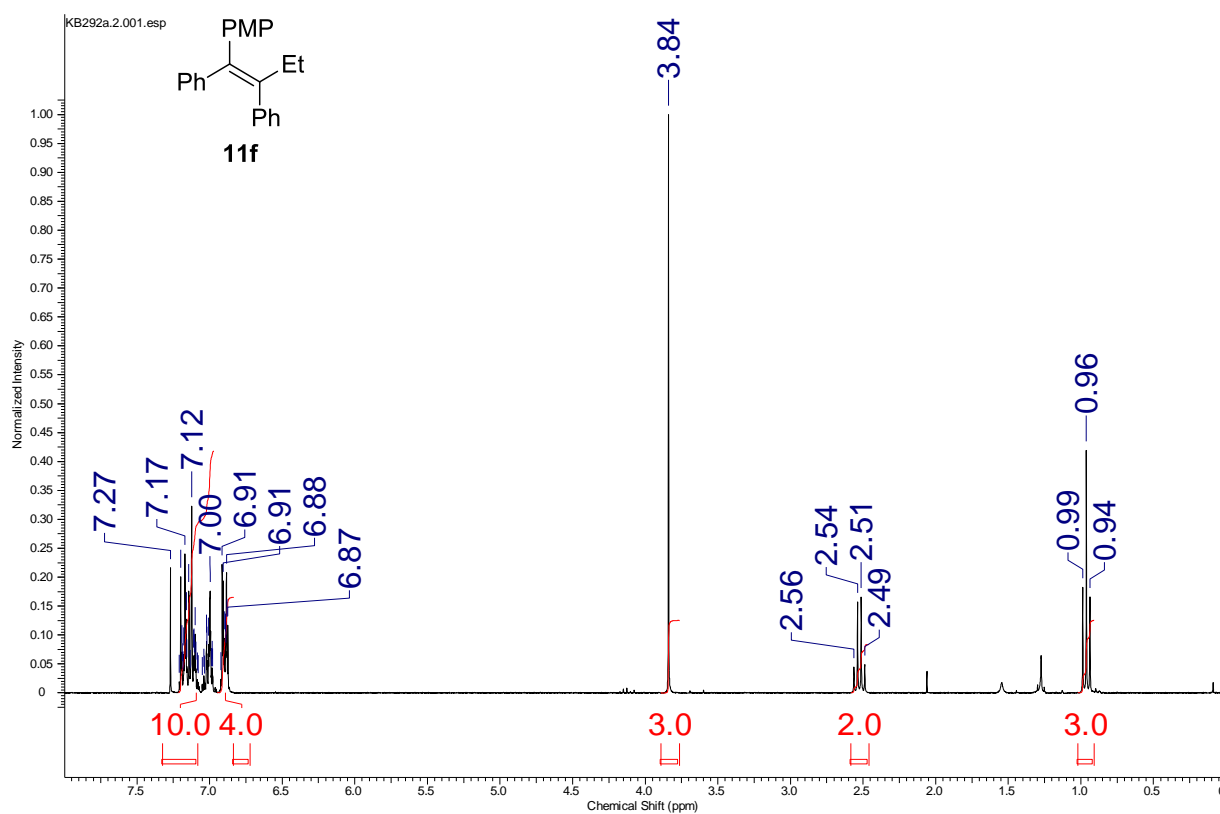


Selected NMR-Spectra





Selected NMR-Spectra



Selected NMR-Spectra

