CHEMISTRY
A European Journal

Supporting Information

α-Hydroxy Ketones as Masked Ester Donors in Brønsted Base Catalyzed Conjugate Additions to Nitroalkenes

Iurre Olaizola,[a] Teresa E. Campano,[a] Igor Iriarte,[a] Silvia Vera,[a] Antonia Mielgo,[a]
Jesús M. García,[b] José M. Odriozola,[b] Mikel Oiarbide,*[a] and Claudio Palomo*[a]

chem_201705968_sm_miscellaneous_information.pdf

Supporting Information

Table of Contents

1. Materials and general techniques

All reactions were carried out under argon atmosphere in flame dried glassware with efficient magnetic stirring. Unless otherwise specified, materials were obtained from commercial sources and used without purification. Methylene chloride (CH_2Cl_2) was distilled from CaH_2, and diethyl ether and tetrahydrofuran were dried by filtration through activated alumina (powder ≈ 150 mesh, pore size 58 Å, basic, Sigma Aldrich) columns. Analytical reagent grade MeOH, CH_3CN and 1,4-dioxane were used without further drying.

Catalyst **C1** and **C2** were obtained from commercial sources and catalyst **C3**[1], **C4**[2], **C5**[3] and **C6**[4] were prepared following the procedures described in the literature. Nitroalkenes **5a-g** were obtained from commercial sources and **5h**, **5i**, **5j** and **5k**, were prepared following the procedure described in the literature.[5]

Reactions were monitored by thin layer chromatography (TLC) using Merck silica gel 60 F254 plates and visualized by fluorescence quenching under UV light. In addition, TLC plates were stained with a solution of potassium permanganate (1 g) in 100 ml of water (limited lifetime), followed by heating. ^1H NMR and ^{13}C NMR spectra were recorded at 300 MHz and 75 MHz respectively. The chemical shifts are reported in ppm relative to $CDCl_3$ (d = 7.26) and CD_3OD (d = 3.31) for ^1H NMR and relative to the central resonances of $CDCl_3$ (d = 77.0) and CD_3OD (d = 49.2) for ^{13}C NMR. Purification of reaction products was carried out by flash column chromatography using ROCC silica gel 60 (0.040–0.063mm, 230–400 mesh). Optical rotations were recorded on a Jasco P-2000 polarimeter. Specific rotation ($[\alpha]_D$) are reported in 10^{-1} deg·cm^2·g^{-1}; concentrations (*c*) are quoted in g/100 mL; *D* refers to the D-line of sodium (589 nm). MS spectra were recorded on an ESI-ion trap Mass spectrometer (Agilent 1100 series LC/MSD, SL model) and on an UPLC-DAD-QTOF (Ultra High Performance Liquid Chromatograph-Mass spectrometer; Waters UPLC ACQUITY, Waters PDA Detector, Waters Synapt G2). Analytical high performance liquid chromatography (HPLC) was performed on Waters-600E, equipped with 2996 and 2998 photodiode array UV detector, using Daicel Chiralpak AD-H, OD-H, IA, IB and IC columns.

---

[1] W. Yang, M. U. Du *Org. Lett*. **2010**, *12*, 5450-5453.

[2] For the diamine formation, see: a) Y. Gao, Q. Ren, L. Wang, J. Wang *Chem. Eur. J.* **2010**, *16*, 13068-13071. For the coupling reaction and characterization, see: b) K. Hu, A. Lu, Y. Wang, Z. Zhou, C. Tang *Tetrahedron: Asymmetry* **2013**, *24*, 953-957.

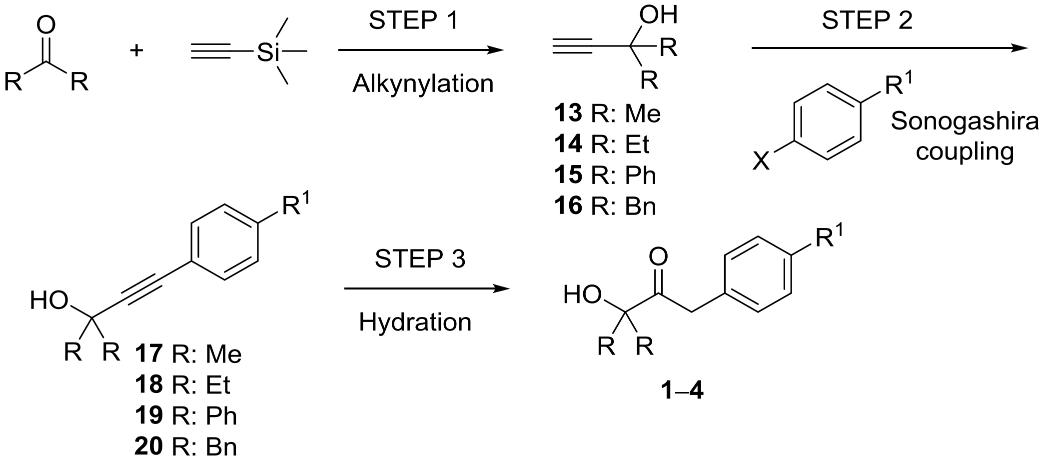
[3] I. Iriarte, O. Olaizola, S. Vera, I. Gamboa, M. Oiarbide, C. Palomo, *Angew. Chem.* **2017**, *129*, 8986-8990; *Angew. Chem. Int. Ed.* **2017**, *56*, 8860-8864

[4] a) S. H. McCooey, S. Connon, *Angew. Chem.* **2005**, *117*, 6525-6528; *Angew. Chem. Int. Ed.* **2005**, *44*, 6367-6370; b) J. Ye, D. J. Dixon, P. S. Hynes, *Chem. Commun.* **2005**, 4481-4483; c) B. Vakulya, S. Varga, A. Csampai, T. Sojs, *Org. Lett.* **2005**, *7*, 1967-1969; d) B.-J. Li, L. Jiang, M. Liu, Y.-C. Chen, L.-S. Ding, Y. Wu, *Synlett* **2005**, 603-606

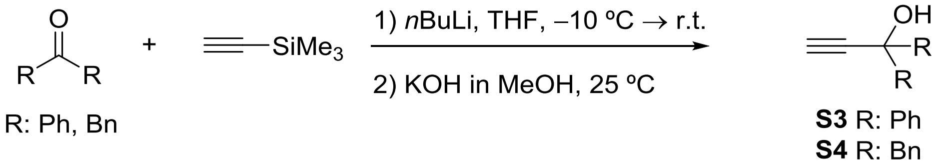
[5] B. M. Trost and Ch. Muller, *J. Am. Chem. Soc*. **2008**, *130*, 2438-2439.

2. Preparation of α-hydroxy ketones 1–4

α-Hydroxy ketones **1**–**4** were prepared by the three-step sequence shown in the scheme.

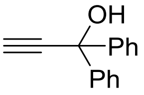


2.1 Step 1: Alkynylation of ketones[6]



*n*BuLi (2.5M in hexane, 2 eq., 4.0 mL, 10 mmol) was added dropwise under N_2 to a solution of ethynyltrimethylsilane (2 eq., 1.4 mL, 10 mmol) in THF (16.7 mL) at –10 ºC. After stirring for 30 min at –10 ºC, benzophenone or dibenzyl ketone (1 eq., 5 mmol) was added. The mixture was stirred at room temperature for 4 h. A solution of potassium hydroxide (5 eq., 1.4 g, 25 mmol) in MeOH (2 mL) was added to the mixture at 0 ºC. Desilylation was complete within 30 min as monitored by TLC. The mixture was poured into a satured solution of NH_4Cl (25 mL) and extracted with EtOAc (3 x 25 mL). The combined organic layers were washed with brine, dried over $MgSO_4$, filtered and the solvent was evaporated under reduced pressure. The residue was purified by flash column chromatography on silica gel (eluting with Hexane/ AcOEt 95:5 → 90:10) to afford the desired product.

1,1-Diphenylprop-2-yn-1-ol (S3)



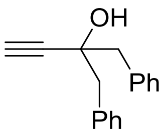
The title compound **S3** was prepared from benzophenone (0.9 g, 5 mmol) according to the general procedure. Colorless oil, yield: 1.01 g, 5 mmol, quantitative. ^1H NMR (300 MHz, $CDCl_3$), δ: 7.61 (d, *J* = 6.9 Hz, 4H), 7.44–

---

[6] Gawel, P.; Dengiz, C.; Finke, A. D.; Trapp, N.; Boudon, C.; Gisselbrecht, J. P.; Diederich, F. *Angew. Chem. Int. Ed.* **2014**, *53*, 4341–4345.

7.27 (m, 6H), 2.88 (s, 1H), 2.77 (s, 1H).

2-Benzyl-1-phenylbut-3-yn-2-ol (S4)

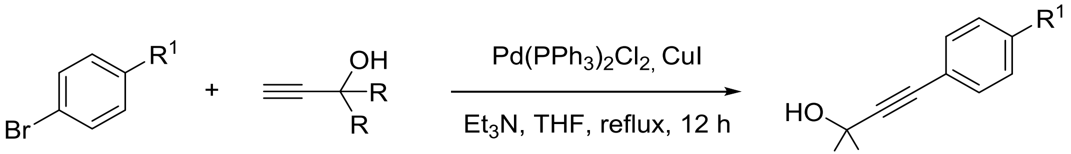


The title compound **S4** was prepared from 1,3-diphenylpropan-2-one (1.1 g, 5 mmol) according to the general procedure. Colorless oil, yield: 1.23 g, 4.3 mmol, 86%. ^{1}H NMR (300 MHz, CDCl$_3$), δ 7.42–7.25 (m, 10H), 3.02 (s, 4H), 2.48 (s, 1H).

Propargylic alcohols **S1** and **S2** are commercially available.

2.2 Step 2: Sonogashira coupling

METHOD A[7] (For R^1: NO$_2$, CN)



A R^1: NO$_2$
B R^1: CN

S1 R: Me
S2 R: Et
S3 R: Ph
S4 R: Bn

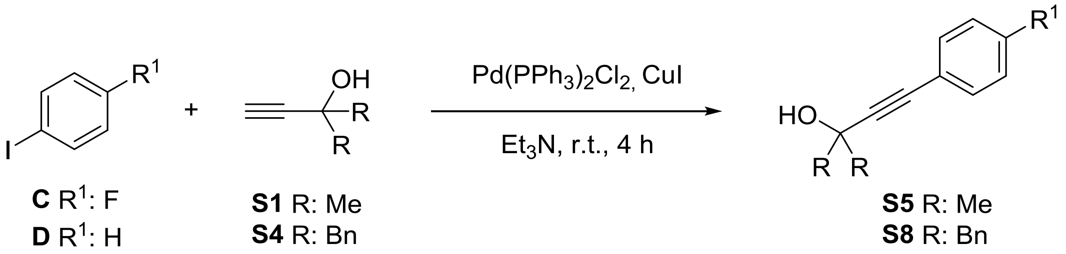
S5 R: Me
S6 R: Et
S7 R: Ph
S8 R: Bn

To a solution of *p*-bromo-nitrobenzene or *p*-bromobenzonitrile (1 eq.) and the corresponding alkyne **S1–S4** (1.3 eq.) in THF (3 mL/mmol) were added Pd(PPh$_3$)$_2$Cl$_2$ (2 mol %) and CuI (4 mol %), and the reaction mixture was degassed with N$_2$. To this solution was added Et$_3$N (2 eq.), and the reaction mixture was stirred under refluxing for 12 h. The solvent was removed under vacuum, and the residue was purified by flash column chromatography on silica gel (eluting with Hexane/ AcOEt 90:10 → 80:20) to afford the desired coupling product.

---

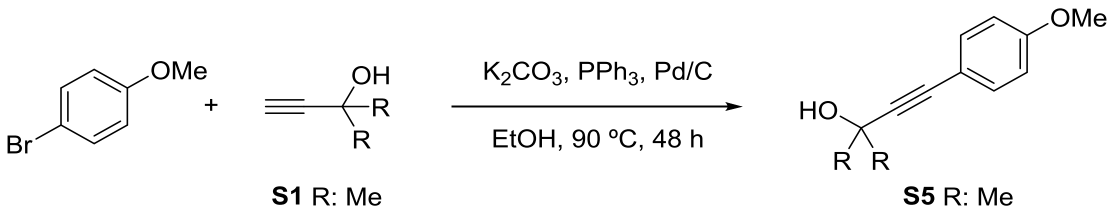
[7] Li, Y.; Zou, H.; Gong, J.; Xiang, J.; Luo, T.; Quan, J.; Wang, G.; Yang, Z. *Org. Lett.* **2007**, *9*, 4057–4060.

METHOD B[8] (For R^1: F, H)



To a solution of Et_3N (3.75 mL), $Pd(PPh_3)_2Cl_2$ (2 mol %), CuI (1 mol %), and iodobenzene or *p*-fluoroiodobenzene (1 eq.) was added the corresponding propargylic alcohol **S1** or **S4** (1.2 eq.) under inert N_2 atmosphere. The mixture was allowed to stir at room temperature for 4 h. After completion, the reaction was quenched with saturated NH_4Cl (20 mL) solution and extracted with EtOAc (3 x 20 mL). The combined organic layers were washed with brine, dried over $MgSO_4$, filtered and the solvent was evaporated under reduced pressure. The residue was purified by flash column chromatography on silica gel (eluting with Hexane/ AcOEt 95:5 → 90:10) to afford the desired product.

METHOD C[9] (For R^1: OMe)



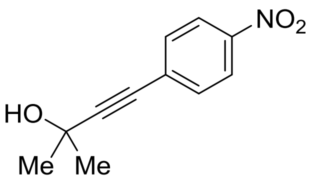
A mixture of K_2CO_3 (2.8 g, 20 mmol, 4 eq.), PPh_3 (26.5 mg, 0.1 mmol, 2 mol%) and 10% palladium on charcoal (53.6 mg, 0.05 mmol, 1 mol%) in EtOH (50 mL) was stirred gently for 30 min, then 1-bromo-4-methoxybenzene (0.63 mL, 5 mmol, 1 eq.) and propargylic alcohol **S1** (0.58 mL, 6 mmol, 1.2 eq.) were added. The mixture was stirred at reflux for 48 h. The resulting precipitate was filtered through a pad of silica gel and the EtOH was evaporated. The residue was purified by flash column chromatography on silica gel (eluting with Hexane/ AcOEt 95:5 → 90:10) to afford the desired product.

---

[8] Hussain, M. K.; Ansari, M. I.; Kant, R.; Hajela, K. *Org. Lett.* **2014**, *16*, 560–563.

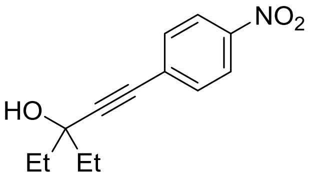
[9] Arsenyan P. et al., *Tetrahedron Letters* **2014**, *54*, 6524–6528.

2-Methyl-4-(4-nitrophenyl)but-3-yn-2-ol (S5A)



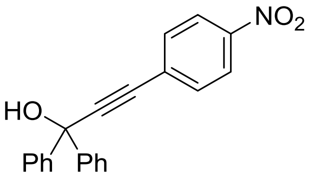
The title compound was prepared from 2-methyl-3-butyn-2-ol (**S1**) (0.6 mL, 6.5 mmol) and 1-bromo-4-nitrobenzene (1.0 g, 5 mmol) according to the general procedure A. Orange oil, yield: 1.02 g, 5 mmol, quantitative. ^{1}H NMR (300 MHz, $CDCl_3$), δ: 8.18 (d, *J* = 8.9 Hz, 2H), 7.56 (d, *J* = 8.9 Hz, 2H), 2.01 (s, 1H), 1.64 (s, 6H).

3-Ethyl-1-(4-nitrophenyl)pent-1-yn-3-ol (S6A)



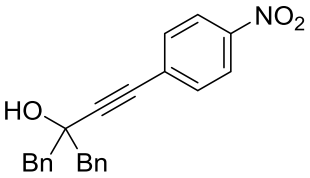
The title compound was prepared from 3-ethylpent-1-yn-3-ol (**S2**) (0.5 mL, 3.9 mmol) and 1-bromo-4-nitrobenzene (0.6 g, 3 mmol) according to the general procedure A. Orange oil, yield: 0.71 g, 3 mmol, quantitative. ^{1}H NMR (300 MHz, $CDCl_3$), δ: 8.18 (d, *J* = 8.9 Hz, 2H), 7.56 (d, *J* = 8.9 Hz, 2H), 1.97 (s, 1H), 1.87–1.74 (m, 4H), 1.11 (t, *J* = 7.4 Hz, 6H).

3-(4-Nitrophenyl)-1,1-diphenylprop-2-yn-1-ol (S7A)



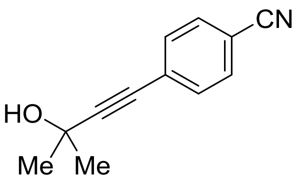
The title compound was prepared from 1,1-diphenylprop-2-yn-1-ol (**S3**) (1.0 g, 5 mmol) and 1-bromo-4-nitrobenzene (0.8 g, 3.8 mmol) according to the general procedure A. Orange solid, yield: 1.30 g, 3.85 mmol, quantitative. ^{1}H NMR (300 MHz, $CDCl_3$), δ: 8.21 (d, *J* = 8.9 Hz, 2H), 7.72–7.60 (m, 4H), 7.43–7.26 (m, 8H), 2.87 (s, 1H).

2-Benzyl-4-(4-nitrophenyl)-1-phenylbut-3-yn-2-ol (S8A)



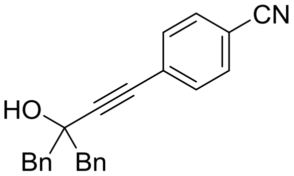
The title compound was prepared from 2-benzyl-1-phenylbut-3-yn-2-ol (**S4**) (1.2 g. 4.3 mmol) and 1-bromo-4-nitrobenzene (0.7 g, 3.3 mmol) according to the general procedure A. Orange oil, yield: 1.14 g, 3 mmol, quantitative. ^{1}H NMR (300 MHz, $CDCl_3$), δ: 8.19 (d, *J* = 9.0 Hz, 2H), 7.55–7.20 (m, 12H), 3.16 (s, 4H), 2.22 (s, 1H).

4-(3-Hydroxy-3-methylbut-1-yn-1-yl)benzonitrile (S5B)



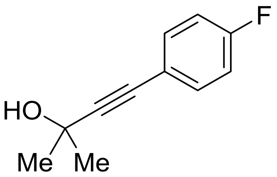
The title compound was prepared from 2-methyl-3-butyn-2-ol (**S1**) (0.6 mL, 6.5 mmol) and 4-bromobenzonitrile (0.9 g, 5 mmol) according to the general procedure A. Orange oil, yield: 0.95 g, 4.9 mmol, 97%. ^{1}H NMR (300 MHz, $CDCl_3$), δ: 7.63 (d, *J* = 8.6Hz, 2H), 7.53 (d, *J* = 8.6Hz, 2H), 2.05 (s,1H), 1.66 (s, 6H).

4-(3-Benzyl-3-hydroxy-4-phenylbut-1-yn-1-yl)benzonitrile (S8B)



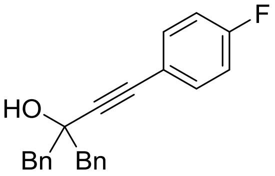
The title compound was prepared from 2-benzyl-1-phenylbut-3-yn-2-ol (**S4**) (1.0 g, 4.2 mmol) and 4-bromobenzonitrile (0.6 g, 3.3 mmol) according to the general procedure A. Orange solid, yield: 1.03 g, 3.0 mmol, 92%. ^{1}H NMR (300 MHz, CDCl$_3$), δ: 7.60 (d, *J* = 8.6Hz, 2H), 7.47–7.31 (m, 12H), 3.15 (s, 4H).

4-(4-Fluoropheny)-2-methylbut-3-yn-2-ol (S5C)



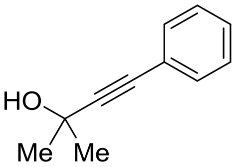
The title compound was prepared from 2-methyl-3-butyn-2-ol (**S1**) (0.6 mL, 6 mmol) and 1-fluoro-4-iodobenzene (0.6 mL, 5.0 mmol) according to the general procedure B. Orange oil, yield: 0.87 g, 4.9 mmol, 97%. ^{1}H NMR (300 MHz, CDCl$_3$), δ: 7.48–7.35 (m, 2H), 7.07–6.96 (m, 2H), 2.34 (s, 1H), 1.64 (s, 6H).

2-Benzyl-4-(4-fluorophenyl)-1-phenylbut-3-yn-2-ol (S8C)



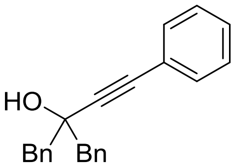
The title compound was prepared from 2-benzyl-1-phenylbut-3-yn-2-ol (**S4**) (0.9 g, 3.8 mmol) and 1-fluoro-4-iodobenzene (0.4 mL, 3.2 mmol) according to the general procedure B. Orange oil, yield: 1.04 g, 3.2 mmol, 99%. ^{1}H NMR (300 MHz, CDCl$_3$), δ: 7.54–7.23 (m, 12H), 7.09–6.94 (m, 2H), 3.14 (s, 4H), 2.16 (s, 1H).

2-Methyl-4-phenylbut-3-yn-2-ol (S5D)



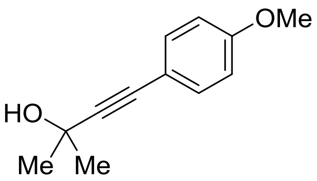
The title compound was prepared from 2-methyl-3-butyn-2-ol (**S1**) (0.5 mL, 5 mmol) and iodobenzene (0.5 mL, 4.1 mmol) according to the general procedure B. Orange oil, yield: 0.62 g, 4.1 mmol, quantitative. ^{1}H NMR (300 MHz, CDCl$_3$), δ: 7.47–7.36 (m, 2H), 7.35–7.27 (m, 3H), 2.00 (s, 1H), 1.62 (s, 6H).

2-Benzyl-1,4-diphenylbut-3-yn-2-ol (S8D)



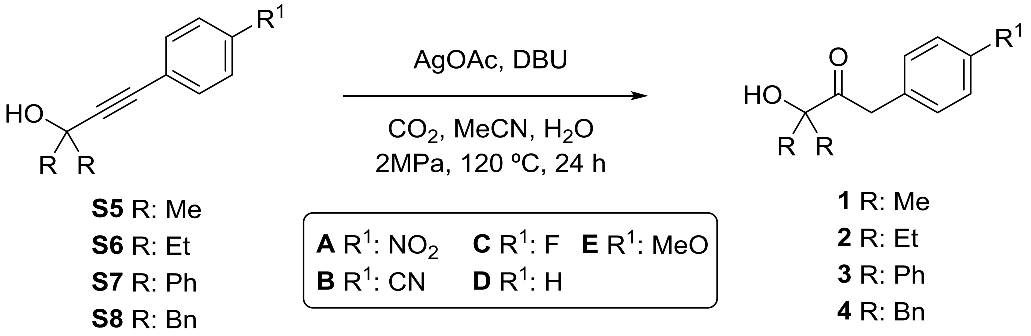
The title compound was prepared from 2-benzyl-1-phenylbut-3-yn-2-ol (**S4**) (1.2 g, 5 mmol) and iodobenzene (0.5 mL, 4.1 mmol) according to the general procedure B. Orange oil, yield: 1.21 g, 3.8 mmol, 96%. ^{1}H NMR (300 MHz, CDCl$_3$), δ: 7.81–7.04 (m, 15H), 3.15 (s, 4H), 2.16 (s, 1H).

4-(4-methoxyphenyl)-2-methylbut-3-yn-ol (S5E)



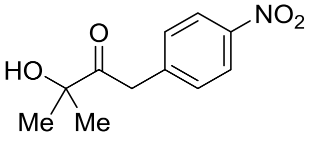
The title compound was prepared from 1-bromo-4-methoxybenzene (0.63 mL, 5 mmol) and propargylic alcohol **S1** (0.58 mL, 6 mmol) according to the general procedure C. Orange oil, yield: 0.76 g, 4 mmol, 80%. ^{1}H NMR (300 MHz, $CDCl_3$), δ: 7.39 (d, *J* = 8.9Hz, 2H), 6.87 (d, *J* = 8.9Hz, 2H), 3.84 (s, 3H), 2.02 (s, 1H), 1.65 (s, 6H).

2.1 Step 3: Alkyne hydration[10]



To a pressure reactor, the mixture of the corresponding propargylic alcohol **S5–S8** (1 eq.), AgOAc (10 mol %), DBU (0.5 eq.), H_2O (0.6 mL/mmol) and MeCN (2 mL/mmol) was added successively. The reactor was filled up with dry ice (CO_2), closed and stirred for 24 h at 120 ºC and 30-40 bar. Then the reaction mixture was cooled and the pressure was released slowly to atmospheric pressure. The residual material was diluted with diethyl ether and MeCN, dried over $MgSO_4$, filtered and the solvent was evaporated under reduced pressure. The residue was purified by flash column chromatography on silica gel (eluting with Hexane/ AcOEt 90:10 → 80:20) to afford the desired product.

3-Hydroxy-3-methyl-1-(4-nitrophenyl)butan-2-one (1A)

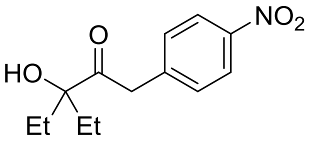


The title compound **1A** was prepared from 2-methyl-4-(4-nitrophenyl)but-3-yn-2-ol (**S5A**) (0.9 g, 4.5 mmol) according to the general procedure. Orange solid, yield: 0.77 g, 3.5 mmol, 77%. M.p. 103–104 ºC. ^{1}H NMR (300 MHz, $CDCl_3$), δ: 8.20 (d, *J* = 8.8 Hz, 2H), 7.38 (d, *J* = 8.8 Hz, 2H), 4.02 (s, 2H), 3.20 (s, 1H), 1.47 (s, 6H). All the spectroscopic data were consistent with those previously reported.[10]

3-Ethyl-3-hydroxy-1-(4-nitrophenyl)pentan-2-one (2A)

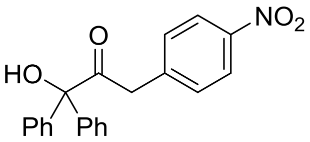
---

[10] He, H.; Qi, C.; Hu, X.; Guan, Y.; Jiang, H. *Green Chem.* **2014**, *16*, 3729–3733.



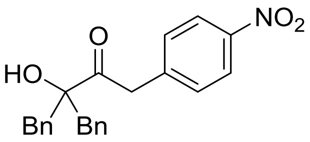
The title compound **2A** was prepared from 3-ethyl-1-(4-nitrophenyl)pent-1-yn-3-ol (**S6A**) (0.7 g, 3 mmol) according to the general procedure. M.p. 81–82 ºC. Yellow solid, yield: 0.48 g, 1.9 mmol, 64%. ^{1}H NMR (300 MHz, $CDCl_3$), δ: 8.12 (d, *J* = 8.6 Hz, 2H), 7.34 (d, *J* = 8.3 Hz, 2H), 3.90 (s, 2H), 3.50 (s, 1H), 1.94–1.60 (m, 4H), 0.78 (t, *J* = 6.8 Hz, 6H). ^{13}C NMR (75 MHz, $CDCl_3$), δ: 210.6, 146.9, 141.0, 123.4, 82.6, 42.6, 31.2, 7.5. UPLC-DAD-QTOF: $C_{13}H_{16}NO_4$ $[M–H]^-$ calcd.: 250.1079, found: 250.1070.

1-Hydroxy-3-(4-nitrophenyl)-1,1-diphenylpropan-2-one (3A)



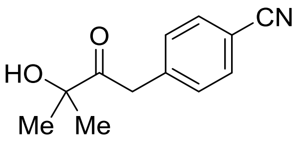
The title compound **3A** was prepared from 3-(4-nitrophenyl)-1,1-diphenylprop-2-yn-1-ol (**S7A**) (1.2 g, 3.5 mmol) according to the general procedure. M.p. 98–99 ºC. Orange solid, yield: 0.45 g, 1.3 mmol, 37%. ^{1}H NMR (300 MHz, $CDCl_3$), δ: 8.07 (d, *J* = 8.7 Hz, 2H), 7.53–7.17 (m, 10H), 7.12 (d, *J* = 8.7 Hz, 2H), 4.02 (s, 2H). ^{13}C NMR (75 MHz, $CDCl_3$), δ: 206.8, 141.2, 140.5, 130.3, 128.8, 128.5, 128.5, 128.0, 123.3, 86.1, 44.2. UPLC-DAD-QTOF: $C_{21}H_{16}NO_4$ $[M–H]^-$ calcd.: 346.1079, found: 346.1070.

3-Benzyl-3-hydroxy-1-(4-nitrophenyl)-4-phenylbutan-2-one (4A)



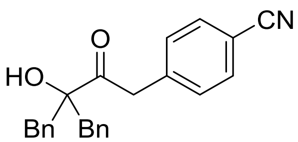
The title compound **4A** was prepared from 2-benzyl-4-(4-nitrophenyl)-1-phenylbut-3-yn-2-ol (**S8A**) (1.1 g, 3 mmol) according to the general procedure. Orange solid, yield: 0.94 g, 2.5 mmol, 83%. M.p. 133–134 ºC. ^{1}H NMR (300 MHz, $CDCl_3$), δ: 8.04 (d, *J* = 8.7 Hz, 2H), 7.49–7.04 (m, 10H), 6.83 (d, *J* = 8.6 Hz, 2H), 3.41 (s, 2H), 3.29 (d, *J* = 13.5 Hz, 2H), 2.97 (d, *J* = 13.6 Hz, 2H), 2.66 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$), δ: 211.3, 146.7, 141.2, 135.1, 130.5, 130.3, 128.6, 127.2, 123.2, 83.4, 46.2, 45.5. UPLC-DAD-QTOF: $C_{23}H_{20}NO_4$ $[M–H]^-$ calcd.: 374.1392, found: 374.1382.

4-(3-Hydroxy-3methyl-2-oxobutyl)benzonitrile (1B)



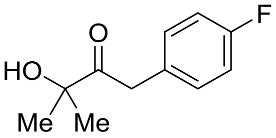
The title compound **1B** was prepared from 4-(3-hydroxy-3-methylbut-1-yn-1-yl)benzonitrile (**S5B**) (0.9 g, 5 mmol) according to the general procedure. Yellow oil, yield: 0.91 g, 4.5 mmol, 90%. ^{1}H NMR (300 MHz, $CDCl_3$), δ: 7.65 (d, *J* = 8.3 Hz, 2H), 7.35 (d, *J* = 8.3 Hz, 2H), 4.00 (s, 2H), 1.48 (s, 6H). All the spectroscopic data were consistent with those previously reported.[10]

4-(3-Benzyl-3-hydroxy-2-oxo-4-phenylbutyl)benzonitrile (4B)



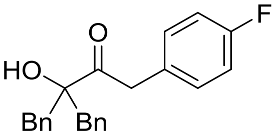
The title compound **4B** was prepared from 4-(3-benzyl-3-hydroxy-4-phenylbut-1-yn-1-yl)benzonitrile (**S8B**) (0.6 g, 1.8 mmol) according to the general procedure. White solid, yield: 0.36 g, 1.0 mmol, 56%. M.p. 131–132 ºC. ^{1}H NMR (300 MHz, $CDCl_3$), δ: 7.49 (d, *J* = 8.3 Hz, 2H), 7.38–7.29 (m, 6H), 7.23–7.20 (m, 4H), 6.80 (d, *J* = 8.2 Hz, 2H), 3.38 (s, 2H), 3.29 (d, *J* = 13.6 Hz, 2H), 2.97 (d, *J* = 13.6 Hz, 2H), 2.64 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$), δ: 211.9, 139.4, 135.6, 132.3, 130.9, 130.7, 129.0, 127.7, 119.2, 111.0, 83.8, 46.8, 45.9. UPLC-DAD-QTOF: $C_{24}H_{21}NO_2Na$ $[M+Na]^+$ calcd.: 378.1470, found: 378.1477.

1-(4-Fluorophenyl)-3-hydroxy-3-methylbutan-2-one (1C)



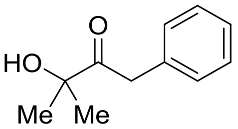
The title compound **1C** was prepared from 4-(4-fluoropheny)-2-methylbut-3-yn-2-ol (**S5C**) (0.9 g, 5 mmol) according to the general procedure. Yellow oil, yield: 0.43 g, 2.2 mmol, 44 %. ^{1}H NMR (300 MHz, $CDCl_3$), δ: 7.20 (dd, *J* = 8.6, 5.4 Hz, 2H), 7.06 (t, *J* = 8.7 Hz (s, 2H), 3.89 (s, 2H), 1.48 (s, 6H). All the spectroscopic data were consistent with those previously reported.[10]

3-Benzyl-1-(4-fluorophenyl)-3-hydroxy-4-phenylbutan-2-one (4C)



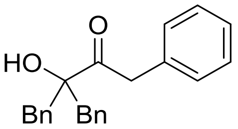
The title compound **4C** was prepared from 2-methyl-4-phenylbut-3-yn-2-ol (**S8C**) (1.0 g, 3.1 mmol) according to the general procedure. White solid, yield: 0.66 g, 1.9 mmol, 60%. M.p. 121–122 ºC. ^{1}H NMR (300 MHz, $CDCl_3$), δ: 7.43–7.21 (m, 11H), 7.01–6.90 (m, 2H), 6.82–6.72 (m, 2H), 3.44 (s, 2H), 3.32 (d, *J* = 13.6 Hz, 2H), 3.03 (d, *J* = 13.6 Hz, 2H), 2.86 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$), δ: 212.4,163.7, 135.7, 131.5, 131.4, 130.7, 128.9, 127.5, 115.6, 115.3, 83.6, 45.7, 45.5. UPLC-DAD-QTOF: $C_{23}H_{22}O_2F$ $[M+H]^+$ calcd.: 349.1604, found: 349.1605.

3-Hydroxy-3-methyl-1-phenylbutan-2-one (1D)



The title compound **1D** was prepared from 2-methyl-4-(4-phenyl)but-3-yn-2-ol (**S5D**) (0.6 g, 4 mmol) according to the general procedure. Colorless oil, yield: 0.23 g, 1.3 mmol, 43%. ^{1}H NMR (300 MHz, $CDCl_3$), δ: 7.42–7.12 (m, 5H), 3.88 (s, 2H), 1.45 (s, 6H). All the spectroscopic data were consistent with those previously reported.[10]

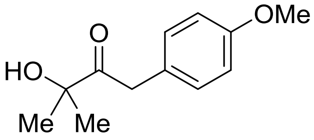
3-Benzyl-3-hydroxy-1,4-diphenylbutan-2-one (4D)



The title compound **4D** was prepared from 2-benzyl-1,4-diphenylbut-3-yn-2-ol (**S8D**) (1.1 g, 3.5 mmol) according to the general procedure. White solid, yield: 0.74 g, 2.1 mmol, 60%. M.p. 101–102 ºC. ^{1}H NMR (300 MHz, $CDCl_3$), δ: 7.42–7.10 (m, 13H), 6.83 (dd, *J* = 6.8, 2.7 Hz, 2H), 3.49 (s, 2H), 3.29 (d, *J* = 13.6 Hz, 2H), 3.02 (d, *J* = 13.6 Hz, 2H), 2.89 (s,1H). ^{13}C NMR (75 MHz, $CDCl_3$), δ:

212.3, 135.8, 130.7, 130.1, 128.9, 128.7, 127.5, 127.2, 83.5, 46.2, 45.6. UPLC-DAD-QTOF: $C_{23}H_{23}O_2$ $[M+H]^+$ calcd.: 331.1698, found: 331.1703.

3-Hydroxy-1-(4-methoxyphenyl)-3-methylbutan-2-one (1E)



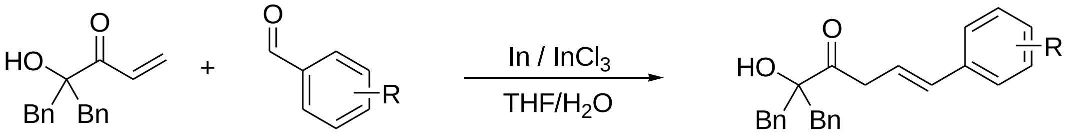
The title compound **1E** was prepared from 4-(4-methoxyphenyl)-2-methylbut-3-yn-ol) (0.65 g, 3.4 mmol) according to the general procedure. Orange oil, yield: 0.37 g, 1.8 mmol, 52%. ^{1}H NMR (300 MHz, $CDCl_3$), δ: 7.16 (d, *J* = 8.7 Hz, 2H), 6.91 (d, *J* = 8.7 Hz, 2H), 3.85 (s, 2H), 3.83 (s, 3H), 1.47 (s, 6H). All the spectroscopic data were consistent with those previously reported.[11]

---

[11] He, H.; Qi, C.; Hu, X.; Guan, Y.; Jiang, H. *Green Chem*. **2014**, *16*, 3729–3733.

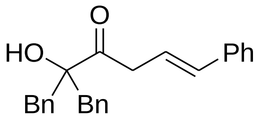
3. Preparation of alkenyl hydroxyketones 16-18.

Method A:



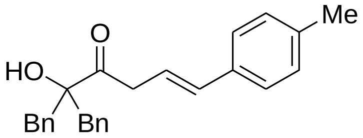
A mixture of the corresponding aldehyde (3.0 mmol, 3 equiv.), In powder (230 mg, 2 mmol, 2 equiv.), $InCl_3$ (110 mg, 0.5 mmol, 0.5 equiv.) and 4-benzyl-4-hydroxy-5-phenylpent-1-en-3-one (266 mg, 1 mmol, 1 equiv.) in THF/H_2O (1: 1,8 mL) was stirred at room temperature for 8h. After the addition of 1M HCl (15 mL), the resulting mixture was stirred for 30 min and extracted with ethyl acetate (15 mL x 4). The combined organic phase was washed with brine and dried with $MgSO_4$. After filtration, the solvent was evaporated under reduced pressure and the crude product war purified by flash column chromatography (hexane/ethyl acetate 90/10).

(E)-2-Benzyl-2-hydroxy-1,6-diphenylhex-5-en-3-one (16)



Prepared according to the general procedure starting from benzaldehyde (0.3 mL, 3 mmol) .The title compound was isolated as a white solid. Yield: 278 mg (78%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33 – 7.22 (m, 15H), 6.23 (d, *J* = 16.0 Hz, 1H), 6.03 (dt, *J* = 16.0 Hz, *J'* = 6.8 Hz, 1H), 3.26 (d, *J* = 13.6 Hz, 2H), 3.20 (dd, *J* = 6.8 Hz, *J'* = 1.2 Hz, 2H), 3.02 (d, *J* = 13.6 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 212.3, 136.9, 135.4, 133.6, 130.3, 128.4, 127.5, 127.1, 126.3, 121.4, 83.1, 45.0, 42.8.

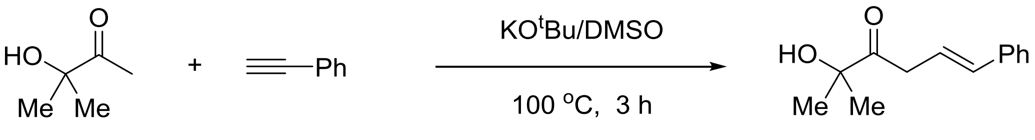
(E)-2-Benzyl-2-hydroxy-1-phenyl-6-*p*-tolylhex-5-en-3-one (17)



Prepared according to the general procedure starting from 4-methylbenzaldehyde (0.35 mL, 3 mmol). The title compound was isolated as a white solid. Yield: 304 mg (82%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32–7.11 (m, 14H), 6.21 (d, *J* = 16.0 Hz, 1H), 5.97 (dt, *J* = 16.0 Hz, *J'* = 6.8 Hz, 1H), 3.25 (d, *J* = 14.0 Hz, 2H), 3.19 (dd, *J* = 6.8 Hz, *J'* = 1.2 Hz, 2H), 3.02 (d, *J* = 14.0 Hz, 2H), 2.35 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 212.4, 137.3, 135.6, 135.4, 133.4, 130.3, 129.1, 128.4, 127.1, 126.1, 120.3, 83.1, 45.0, 42.8, 21.2.

Method B:[12]

2-Hydroxy-2-methyl-6-phenylhex-5-en-3-one (18)



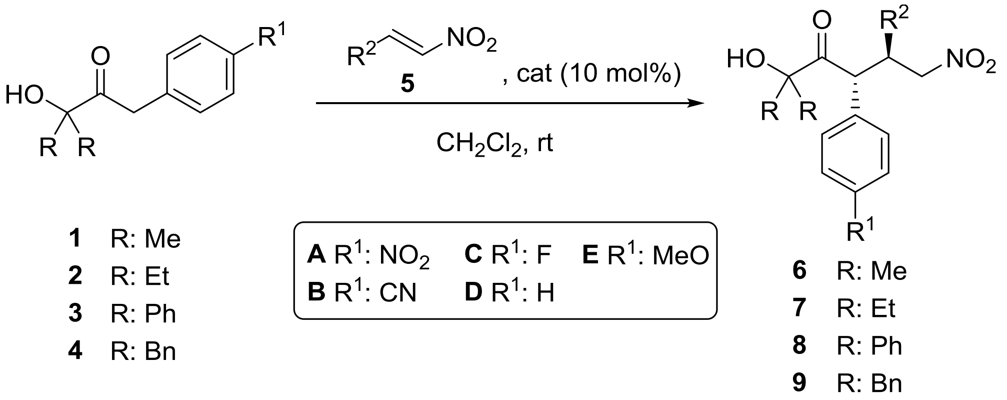
18

A mixture of commercial 3-hydroxy-3-methyl-2-butanone (3 eq., 1.6 mL , 15 mmol), phenylacetylene (1 eq., 0.6 mL, 5 mmol) and KO^{t}Bu (1.4 eq., 0.78 g, 7 mmol) in DMSO (12.5 mL) was heated (100 ^{o}C) and stirred for 3 hours. The reaction mixture, after cooling, was diluted with H_2O, neutralized with NH_4Cl, and extracted with Et_2O. The organic extract was washed with H_2O and dried dried over $MgSO_4$, filtered and the solvent was evaporated. The residue was purified by flash column chromatography on silica gel (eluting hexane/ EtAcO 95:5). Yellow oil, yield: 0.41 g, 2 mmol, 40%. ^{1}H NMR (300 MHz, $CDCl_3$), δ: 7.45–7.23 (m, 5H), 6.53 (d, *J* = 16.0 Hz, 1H), 6.37 (dt, *J* = 15.9, 6.7 Hz, 1H), 3.55 (d, *J* = 7.9 Hz, 2H), 1.47 (s, 6H). ^{13}C NMR (75 MHz, $CDCl_3$), δ: 212.6, 137.1, 134.1, 128.9, 128.0, 126.6, 121.9, 76.8, 40.1, 26.9. UPLC-DAD-QTOF: $C_{13}H_{17}O_2$ $[M+H]^+$ calcd.: 205.1229, found: 205.1230.

---

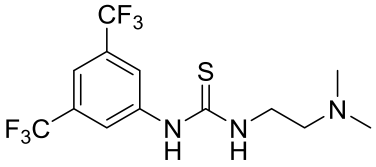
[12] Adapted from: J. Org. Chem. **2012**, *77*, 6880-6886

4. Catalytic conjugate addition of α-hydroxy ketones 1-4 to nitroalkenes



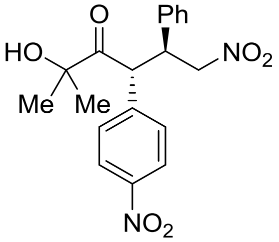
To a mixture of the corresponding α-hydroxyketone **1-4** (1 eq., 0.1 mmol) and the nitroalkene **5** (2.0 eq., 0.2 mmol for aromatic nitroalkenes; 3.0 eq., 0.3 mmol for aliphatic nitroalkenes), in dichloromethane (0.3 mL) at room temperature (or cooled to the corresponding temperature), catalyst **C1**–**C6** (10 mol %) was added. The resulting suspension was stirred at the same temperature, until consumption of the α-hydroxyketone as monitored by ^{1}H NMR. The mixture was quenched with HCl 2M (1 mL) and extracted with CH_2Cl_2 (3 x 2 mL). The combined organic layers were dried over $MgSO_4$, filtered and the solvent was evaporated under reduced pressure. The residue was purified by flash column chromatography on silica gel (eluting with Hexane/ AcOEt 95:5 → 90:10) to afford the desired product.

The corresponding racemic compounds were prepared following the above procedure at room temperature, but using as catalyst either TEA, DBU or achiral thiourea **S9**[13](10 mol%).



S9

2-Hydroxy-2-methyl-6-nitro-4-(4-nitrophenyl)-5-phenylhexan-3-one (6Aa)



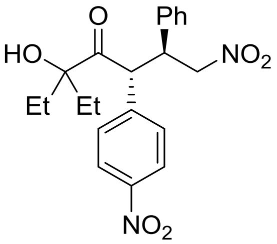
The title compound **6Aa** was prepared from 3-hydroxy-3-methyl-1-(4-nitrophenyl)butan-2-one (**1A**) (22.3 mg, 0.1 mmol) and nitrostyrene (**5a**) (29.8 mg, 0.2 mmol) according to the general procedure. White solid, yield: 36.8 mg, 0.098 mmol, 98%. m.p. 170–172 ºC. ^{1}H NMR (300 MHz, $CDCl_3$), δ: 8.25 (d, J = 8.8 Hz, 2H), 7.67 (d, J = 8.8 Hz,

---

[13] Synthesis adapted from: R. C. Pratt, B. G. Lohmeijer, D. A. Long, P. N. Lundberg, A. P. Dove, H. B. Li, C. G. Wade, R. M. Waymouth, J. L. Hedrick, *Macromolecules*, **2006**, *39*, 7863–7871.

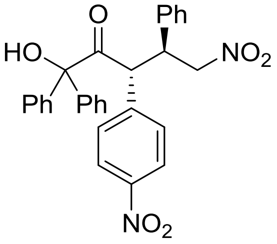
2H), 7.44–7.16 (m, 5H), 4.95 (d, *J* = 11.5 Hz, 1H), 4.53 (dd, *J* = 12.5, 10.1 Hz, 1H), 4.43–4.28 (m, 1H)4.19 (dd, *J* = 12.5, 4.3 Hz, 1H), 0.89 (s, 3H), 0.80 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$), δ: 210.5, 147.9, 142.3, 136.9, 129.8, 129.0, 128.5, 128.3, 124.5, 77.8, 77.8, 55.0, 47.1, 26.6, 25.9. UPLC-DAD-QTOF: $C_{19}H_{19}N_2O_6$ [M–H]$^-$ calcd.: 371.1243, found: 371.1239. The enantiomeric purity of the major diastereomer was determined by HPLC analysis (Daicel Chiralpak OD-H, hexane/isopropanol 90/10, flow rate = 1.0 mL/min, retention times: 24.6 min (minor) and 30.1 min (major)).

5-Ethyl-5-hydroxy-1-nitro-3-(4-nitrophenyl)-2-phenylheptan-4-one (7Aa)



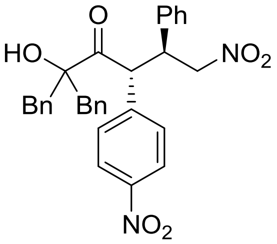
The title compound **7Aa** was prepared from 3-ethyl-3-hydroxy-1-(4-nitrophenyl)pentan-2-one (**2A**) (25.1 mg, 0.1 mmol) and nitrostyrene (**5a**) (29.8 mg, 0.2 mmol) according to the general procedure. White solid, yield: 39.6 mg, 0.097 mmol, 97%. m.p. 166–167 ºC. ^{1}H NMR (300 MHz, $CDCl_3$), δ: 8.26 (d, *J* = 8.7 Hz, 2H), 7.66 (d, *J* = 8.7 Hz, 2H), 7.45–7.23 (m, 5H), 5.00 (d, *J* = 11.3 Hz, 1H), 4.49 (dd, *J* = 12.2, 10.4 Hz, 1H), 4.43–4.31 (m, 1H), 4.16 (dd, *J* = 12.3, 4.1 Hz, 1H), 1.86 (s, 1H), 1.46–1.24 (m, 2H), 1.25–1.10 (m, 2H), 0.27 (t, *J* = 7.5 Hz, 3H), 0.17 (t, *J* = 7.5 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$), δ: 209.8, 147.8, 142.0, 137.1, 130.1, 129.0, 128.5, 128.5, 124.4, 83.4, 78.3, 46.9, 29.73, 29.6, 6.8, 6.6. UPLC-DAD-QTOF: $C_{21}H_{23}N_2O_6$ [M–H]$^-$ calcd.: 399.1556, found: 399.1551. The enantiomeric purity of the major diastereomer was determined by HPLC analysis (Daicel Chiralpak AD-H, hexane/isopropanol 90/10, flow rate = 1.0 mL/min, retention times: 25.8 min (major) and 33.4 min (minor)).

1-Hydroxy-5-nitro-3-(4-nitrophenyl)-1,1,4-triphenylpentan-2-one (8Aa)



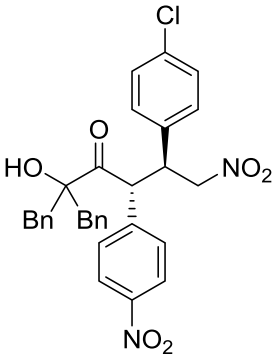
The title compound **8Aa** was prepared from 1-hydroxy-3-(4-nitrophenyl)-1,1-diphenylpropan-2-one (**3A**) (34.7 mg, 0.1 mmol) and nitrostyrene (**5a**) (29.8 mg, 0.2 mmol) according to the general procedure. White solid, yield: 43.2 mg, 0. 087 mmol, 87%. m.p. 186–188 ºC. ^{1}H NMR (300 MHz, $CDCl_3$), δ: 8.13 (d, *J* = 8.8 Hz, 2H), 7.50 (d, *J* = 8.7 Hz, 2H), 7.42–7.25 (m, 8H), 7.19–7.09 (m, 3H), 6.91 (d, *J* = 12.3 Hz, 2H), 6.71 – 6.62 (m, 2H), 5.21 (d, *J* = 11.3 Hz, 1H), 4.54–4.43 (m, 1H), 4.40–4.31 (m, 1H), 4.18 (dd, *J* = 12.1, 3.8 Hz, 1H), 2.36 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$), δ: 206.5, 147.4, 142.8, 140.2, 140.0, 136.7, 129.8, 128.8, 128.6, 128.4, 128.3, 128.2, 128.2, 128.0, 127.4, 127.4, 124.0, 86.4, 78.3, 55.3, 47.0. UPLC-DAD-QTOF: $C_{29}H_{23}N_2O_6$ [M–H]$^-$ calcd.:495.1556, found: 495.1540. The enantiomeric purity of the major diastereomer was determined by HPLC analysis (Daicel Chiralpak IA, hexane/isopropanol 70/30, flow rate = 1.0 mL/min, retention times: 7.2 min (major) and 13.1 min (minor)).

2-Benzyl-2-hydroxy-6-nitro-4-(4-nitrophenyl)-1,5-diphenylhexan-3-one (9Aa)



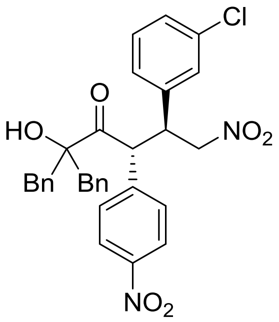
The title compound **9Aa** was prepared from 3-benzyl-3-hydroxy-1-(4-nitrophenyl)-4-phenylbutan-2-one (**4A**) (37.5 mg, 0.1 mmol) and nitrostyrene (**5a**) (29.8 mg, 0.2 mmol) according to the general procedure. White solid, yield: 51.9 mg, 0. 099 mmol, 99%. $[\alpha]_D^{25}$= –97.0 (c= 0.54, 99% *ee*, CH_2Cl_2). m.p. 187–188 ºC. ^{1}H NMR (300 MHz, $CDCl_3$), δ: 7.86 (d, *J* = 8.7 Hz, 2H), 7.42–7.24 (m, 8H), 7.16 (d, *J* = 9.3 Hz, 2H), 7.00–6.88 (m, 3H), 6.86–6.75 (m, 2H), 6.58 (d, *J* = 7.1 Hz, 2H), 5.00 (d, *J* = 11.0 Hz, 1H), 4.43 (dd, *J* = 12.0, 10.3 Hz, 1H), 4.28 (dd, *J* = 11.0, 4.0 Hz, 1H), 4.17 (dd, *J* = 12.1, 4.0 Hz, 1H), 3.01 (d, *J* = 13.5 Hz, 1H), 2.27 (dd, *J* = 28.1, 13.6 Hz, 2H), 1.95 (d, *J* = 13.7 Hz, 1H), 1.75 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$), δ: 208.9, 147.2, 139.9, 137.4, 134.6, 134.2, 130.8, 130.1, 129.8, 129.1, 128.8, 128.5, 128.5, 128.1, 127.3, 126.5, 124.0, 83.4, 78.1, 55.5, 46.2, 42.8, 42.4. UPLC-DAD-QTOF: $C_{31}H_{27}N_2O_6$ $[M–H]^–$ calcd.: 523.1869, found: 523.1880. The enantiomeric purity of the major diastereomer was determined by HPLC analysis (Daicel Chiralpak IA, hexane/isopropanol 90/10, flow rate = 1.0 mL/min, retention times: 16.7 min (major) and 22.7 min (minor)).

2-Benzyl-5-(4-chlorophenyl)-2-hydroxy-6-nitro-4-(4-nitrophenyl)-1-phenylhexan-3-one (9Ab)



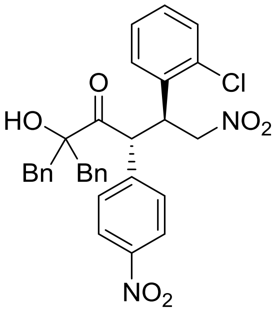
The title compound **9Ab** was prepared from 3-benzyl-3-hydroxy-1-(4-nitrophenyl)-4-phenylbutan-2-one (**4A**) (37.5 mg, 0.1 mmol) and 4-chloronitrostyrene (**5b**) (36.7 mg, 0.2 mmol) according to the general procedure. White solid, yield: 48.1 mg, 0. 086 mmol, 86%. $[\alpha]_D^{25}$= –12.27 (c = 1, 99% *ee*, CH_2Cl_2). m.p. 236–238 ºC. ^{1}H NMR (300 MHz, Acetone-d_6), δ: 7.89 (d, *J* = 8.8 Hz, 2H), 7.52 (d, *J* = 8.5 Hz, 2H), 7.43 (d, *J* = 8.6 Hz, 2H), 7.28 (d, *J* = 8.8 Hz, 2H),7.25–7.18 (m, 3H), 7.04–6.65 (m, 7H), 5.29 (d, *J* = 11.2 Hz, 1H), 4.77 (dd, *J* = 13.0, 11.3 Hz, 1H), 4.34 (dd, *J* = 13.1, 4.2 Hz, 1H), 4.23 (td, *J* = 11.2, 4.2 Hz, 1H), 4.17 (s, 1H), 2.91 (d, *J* = 13.5 Hz, 1H), 2.52 (d, *J* = 13.5 Hz, 1H), 2.40 (d, *J* = 13.5 Hz, 1H), 2.26 (d, *J* = 13.5 Hz, 1H).^{13}C NMR (75 MHz, Acetone-d_6), δ: 210.4, 148.5, 142.4, 139.2, 137.4, 136.6, 134.8, 132.5, 132.3, 132.1, 131.8, 130.2, 129.5, 128.9, 128.2, 127.3, 125.0, 85.1, 79.7, 56.5, 47.5, 45.9, 44.5. UPLC-DAD-QTOF: $C_{13}H_{27}ClN_2O_6Na$ $[M+Na]^+$ calcd.: 581.1455, found: 581.1454. The enantiomeric purity of the major diastereomer was determined by HPLC analysis (Daicel Chiralpak IA, hexane/isopropanol 90/10, flow rate = 1.0 mL/min, retention times: 16.4 min (major) and 21.5 min (minor)).

2-Benzyl-5-(3-chlorophenyl)-2-hydroxy-6-nitro-4-(4-nitrophenyl)-1-phenylhexan-3-one (9Ac)



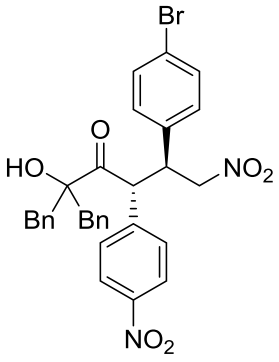
The title compound **9Ac** was prepared from 3-benzyl-3-hydroxy-1-(4-nitrophenyl)-4-phenylbutan-2-one (**4A**) (37.5 mg, 0.1 mmol) and 3-chlronitrostyrene (**5c**) (36.7 mg, 0.2 mmol) according to the general procedure. White solid, yield: 45.3 mg, 0. 081 mmol, 81%. $[\alpha]_D^{25}$= –101.6 (c = 0.52, 99% *ee*, CH_2Cl_2). m.p. 176–177 ºC. ^1H NMR (300 MHz, $CDCl_3$), δ: 7.86 (d, *J* = 8.7 Hz, 2H), 7.35–7.21 (m, 6H), 7.21–7.07 (m, 3H), 7.07–6.88 (m, 3H), 6.83 (t, *J* = 7.5 Hz, 2H), 6.60 (d, *J* = 7.4 Hz, 2H), 4.92 (d, *J* = 10.4 Hz, 1H), 4.47–4.30 (m, 1H), 4.30–4.12 (m, 2H), 3.01 (d, *J* = 13.6 Hz, 1H), 2.48 – 2.23 (m, 2H), 2.22–2.00 (m, 1H),), 1.80 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$), δ: 208.8, 147.2, 139.6, 139.4, 135.0, 134.5, 134.0, 131.95, 130.8, 130.3, 130.1, 129.8, 128.7, 128.6, 128.2, 127.5, 126.7, 126.6, 124.0, 83.4, 77.70, 55.3, 45.6, 43.3, 42.8. UPLC-DAD-QTOF: $C_{31}H_{26}N_2O_6Cl$ $[M–H]^–$ calcd.: 557.1479, found: 557.1478. The enantiomeric purity of the major diastereomer was determined by HPLC analysis (Daicel Chiralpak IA, hexane/isopropanol 90/10, flow rate = 1.0 mL/min, retention times: 16.6 min (major) and 22.8 min (minor)).

2-Benzyl-5-(2-chlorophenyl)-2-hydroxy-6-nitro-4-(4-nitrophenyl)-1-phenylhexan-3-one (9Ad)



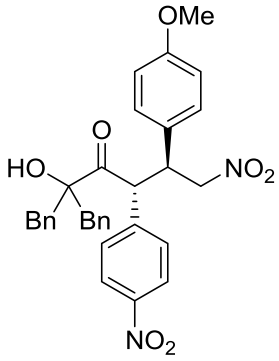
The title compound **9Ad** was prepared from 3-benzyl-3-hydroxy-1-(4-nitrophenyl)-4-phenylbutan-2-one (**4A**) (37.5 mg, 0.1 mmol) and 2-chlronitrostyrene (**5d**) (36.7 mg, 0.2 mmol) according to the general procedure. White solid, yield: 43.0 mg, 0. 077 mmol, 77%. $[\alpha]_D^{25}$= –94.6 (c = 0.52, 99% *ee*, CH_2Cl_2). m.p. 155–156 ºC. ^1H NMR (300 MHz, $CDCl_3$), δ: 7.86 (d, *J* = 8.9 Hz, 2H), 7.48–7.13 (m, 8H), 7.09–6.93 (m, 4H), 6.90 – 6.79 (m, 2H), 6.62 (d, *J* = 7.3 Hz, 2H), 4.84–4.61 (m, 2H), 4.46–4.16 (m, 2H), 3.01 (d, *J* = 13.5 Hz, 2H), 2.33 (d, *J* = 13.5 Hz, 2H), 1.82 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$), δ: 208.9, 147.2, 139.7, 134.6, 134.6, 134.0, 130.8, 130.8, 130.1, 130.1, 129.7, 128.5, 128.5, 128.1, 127.4, 126.6, 123.9, 83.4, 76.2, 54.0, 53.5, 43.2, 42.3. UPLC-DAD-QTOF: $C_{31}H_{26}N_2O_6Cl$ $[M–H]^–$ calcd.: 557.1479, found: 557.1487. The enantiomeric purity of the major diastereomer was determined by HPLC analysis (Daicel Chiralpak IA, hexane/isopropanol 90/10, flow rate = 1.0 mL/min, retention times: 14.4 min (major) and 18.4 min (minor)).

2-Benzyl-5-(4-bromophenyl)-2-hydroxy-6-nitro-4-(4-nitrophenyl)-1-phenylhexan-3-one (9Ae)



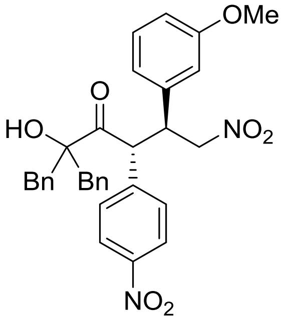
The title compound **9Ae** was prepared from 3-benzyl-3-hydroxy-1-(4-nitrophenyl)-4-phenylbutan-2-one (**4A**) (37.5 mg, 0.1 mmol) and 4-bromonitrostyrene (**5e**) (45.6 mg, 0.2 mmol) according to the general procedure. White solid, yield: 56.1 mg, 0. 093 mmol, 93%. $[\alpha]_D^{25}$= –84.6 (c = 0.49, 99% *ee*, CH_2Cl_2). m.p. 212–214 ºC. ^{1}H NMR (300 MHz, $CDCl_3$), δ: 7.88 (d, *J* = 8.8 Hz, 2H), 7.46 (d, *J* = 8.4 Hz, 2H), 7.33–7.24 (m, 4H), 7.13 (dd, *J* = 8.6, 2.9 Hz, 4H), 7.03–6.95 (m, 2H), 6.87 (t, *J* = 7.4 Hz, 2H), 6.63 (d, *J* = 7.2 Hz, 2H), 4.89 (d, *J* = 10.4 Hz, 1H), 4.34 (dd, *J* = 13.5, 11.7 Hz, 1H), 4.26–4.10 (m, 2H), 2.98 (d, *J* = 13.6 Hz, 1H), 2.38–2.26 (m, 3H), 1.77 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$), δ: 208.7, 147.2, 139.7, 136.4, 134.5, 134.0, 132.2, 130.7, 130.1, 130.0, 129.8, 128.6, 128.2, 127.4, 126.7, 124.0, 122.5, 83.5, 77.8, 55.4, 45.5, 43.4, 42.8. UPLC-DAD-QTOF: $C_{13}H_{26}N_2O_6Br$ $[M–H]^-$ calcd.: 601.0974, found: 601.0972. The enantiomeric purity of the major diastereomer was determined by HPLC analysis (Daicel Chiralpak IA, hexane/isopropanol 90/10, flow rate = 1.0 mL/min, retention times: 18.5 min (major) and 24.6 min (minor)).

2-Benzyl-2-hydroxy-5-(4-methoxyphenyl)-6-nitro-4-(4-nitrophenyl)-1-phenylhexan-3-one (9Af)



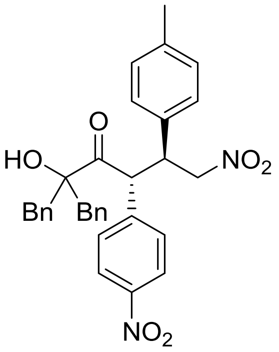
The title compound **9Af** was prepared from 3-benzyl-3-hydroxy-1-(4-nitrophenyl)-4-phenylbutan-2-one (**4A**) (37.5 mg, 0.1 mmol) and 4-methoxynitrostyrene (**5f**) (35.8 mg, 0.2 mmol) according to the general procedure. White solid, yield: 51.0 mg, 0. 092 mmol, 92%. $[\alpha]_D^{25}$= –112.6 (c = 0.50, 99% *ee*, CH_2Cl_2). m.p. 223–224 ºC. ^{1}H NMR (300 MHz, $CDCl_3$), δ: 7.86 (d, *J* = 8.8 Hz, 2H), 7.43–7.05 (m, 8H), 7.01–6.73 (m, 6H), 6.59 (d, *J* = 8.4 Hz, 2H), 4.97 (d, *J* = 11.0 Hz, 1H), 4.45–4.29 (m, 1H), 4.28–4.06 (m, 2H), 3.74 (s, 3H), 3.01 (d, *J* = 13.4 Hz, 1H), 2.46–1.95 (m, 3H),), 1.75 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$), δ: ^{13}C NMR (75 MHz, $CDCl_3$) δ 209.0, 159.5, 147.14, 140.1, 134.6, 134.2, 130.8, 130.1, 129.8, 129.5, 128.5, 128.1, 127.3, 126.5, 124.0, 114.9, 114.4, 83.4, 78.34, 55.5, 55.2, 45.6, 43.0, 42.5. UPLC-DAD-QTOF: $C_{33}H_{31}N_2O_9$ $[M+HCOOH–H]^-$ calcd.: 599.2030, found: 599.2028. The enantiomeric purity of the major diastereomer was determined by HPLC analysis (Daicel Chiralpak IA, hexane/isopropanol 90/10, flow rate = 1.0 mL/min, retention times: 21.5 min (major) and 28.4 min (minor)).

2-Benzyl-2-hydroxy-5-(3-methoxyphenyl)-6-nitro-4-(4-nitrophenyl)-1-phenylhexan-3-one (9Ag)



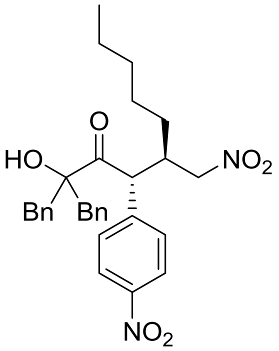
The title compound **9Ag** was prepared from 3-benzyl-3-hydroxy-1-(4-nitrophenyl)-4-phenylbutan-2-one (**4A**) (37.5 mg, 0.1 mmol) and 3-methoxynitrostyrene (**5g**) (35.8mg, 0.2 mmol) according to the general procedure. White solid, yield: 44.4 mg, 0. 080 mmol, 80%. $[\alpha]_D^{25}$= –114.8 (c = 0.46, 99% *ee*, CH_2Cl_2). m.p. 201–202 ºC. ^1H NMR (300 MHz, $CDCl_3$), δ: 7.86 (d, *J* = 8.8 Hz, 2H), 7.38–7.21 (m, 4H), 7.15 (d, *J* = 8.8 Hz, 2H), 7.03–6.74 (m, 8H), 6.58 (d, *J* = 7.1 Hz, 2H), 5.01 (d, *J* = 10.9 Hz, 1H), 4.49–4.32 (m, 1H), 4.33–4.09 (m, 2H), 3.80 (s, 3H), 3.01 (d, *J* = 13.5 Hz, 1H), 2.32 (t, *J* = 13.3 Hz, 2H), 2.20–1.96 (m, 1H),), 1.78 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$), δ: 208.9, 160.0, 147.2, 140.0, 138.9, 134.6, 134.2, 130.8, 130.1, 130.1, 129.8, 128.5, 128.1, 127.3, 126.5, 124.0, 120.4, 115.1, 113.4, 83.4, 78.2, 55.3, 55.2, 46.2, 42.9, 42.6. UPLC-DAD-QTOF: $C_{33}H_{31}N_2O_9$ $[M+HCCOH–H]^{-}$ calcd.: 599.2030, found: 599.2015. The enantiomeric purity of the major diastereomer was determined by HPLC analysis (Daicel Chiralpak IA, hexane/isopropanol 90/10, flow rate = 1.0 mL/min, retention times: 23.6 min (major) and 35.4 min (minor)).

2-Benzyl-2-hydroxy-6-nitro-4-(4-nitrophenyl)-1-phenyl-5-(p-tolyl)hexan-3-one (9Ah)



The title compound **9Ah** was prepared from 3-benzyl-3-hydroxy-1-(4-nitrophenyl)-4-phenylbutan-2-one (**4A**) (37.5 mg, 0.1 mmol) and 4-methylnitrostyrene (**5h**) (32.6 mg, 0.2 mmol) according to the general procedure. White solid, yield: 45.8 mg, 0. 085 mmol, 85%. $[\alpha]_D^{25}$= –46.6 (c = 0.47, 99% *ee*, CH_2Cl_2). m.p. 214–215 ºC. ^1H NMR (300 MHz, $CDCl_3$), δ: 7.86 (d, *J* = 8.7 Hz, 2H), 7.28–7.26 (m, 3H), 7.21–7.14 (m, 6H), 6.95–6.91 (m, 3H), 6.84–6.79 (m, 2H), 6.59 (d, *J* = 7.2 Hz, 2H), 4.99 (d, *J* = 11.0 Hz, 1H), 4.47–4.32 (m, 1H), 4.29–4.08 (m, 2H), 3.00 (d, *J* = 13.5 Hz, 1H), 2.46–2.01 (m, 3H), 1.75 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$), δ: 208.9, 147.1, 140.1, 138.3, 134.6, 134.3, 134.2, 130.8, 130.1, 129.8, 129.7, 128.5, 128.3, 128.1, 127.3, 126.5, 124.0, 83.4, 78.3, 55.4, 45.9, 43.0, 42.5, 21.1. UPLC-DAD-QTOF: $C_{33}H_{31}N_2O_8$ $[M+HCOOH–H]^{-}$ calcd.: 583.2080, found: 583.2075. The enantiomeric purity of the major diastereomer was determined by HPLC analysis (Daicel Chiralpak IA, hexane/isopropanol 90/10, flow rate = 1.0 mL/min, retention times: 18.0 min (major) and 20.1 min (minor)).

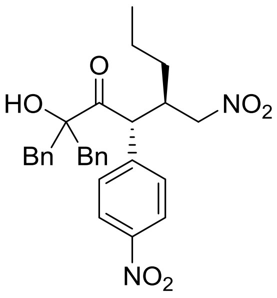
2-Benzyl-2-hydroxy-5-(nitromethyl)-4-(4-nitrophenyl)-1-phenyldecan-3-one (9Ai)



The title compound **9Ai** was prepared from 3-benzyl-3-hydroxy-1-(4-nitrophenyl)-4-phenylbutan-2-one (**4A**) (37.5 mg, 0.1 mmol) and 1-nitrohept-1-ene (**5i**) (42.9 mg, 0.3 mmol) according to the general procedure. White solid, yield: 38.9 mg, 0. 075 mmol, 75%. $[\alpha]_D^{25}$= –

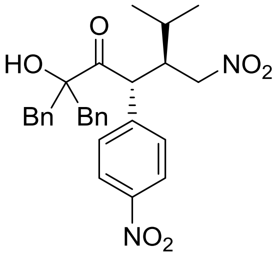
47.3 (c = 0.73, 96% *ee*, CH_2Cl_2). m.p. 122–123 ºC. ^{1}H NMR (300 MHz, $CDCl_3$), δ: 7.90 (d, *J* = 8.8 Hz, 2H), 7.41–7.30 (m, 5H), 7.16–6.98 (m, 5H), 6.79 (d, *J* = 6.9 Hz, 2H), 4.62 (d, *J* = 10.0 Hz, 1H), 4.37 (dd, *J* = 12.9, 4.3 Hz, 1H), 3.81 (dd, *J* = 12.9, 5.3 Hz, 1H), 3.10 (dd, *J* = 18.9, 13.5 Hz, 1H), 2.83 (d, *J* = 13.5 Hz, 1H), 2.79–2.69 (m,1H), 2.57 (d, *J* = 13.5 Hz, 1H), 1.95 (s, 1H), 1.41–1.17 (m, 8H), 0.93 (t, *J* = 6.9 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$), δ: 211.5, 147.3, 141.4, 135.0, 131.2, 130.6, 129.0, 128.8, 127,8, 127.3, 124.1, 84.2, 75.8, 69.0, 54.8, 45.1, 44.0, 40.0, 31.9, 30.2, 26.6, 22.8, 14.4. UPLC-DAD-QTOF: $C_{30}H_{34}N_2O_6Na$ $[M+Na]^+$ calcd.: 541.2315, found: 541.2325. The enantiomeric purity of the major diastereomer was determined by HPLC analysis (Daicel Chiralpak IA, hexane/isopropanol 90/10, flow rate = 1.0 mL/min, retention times: 9.4 min (minor) and 10.9 min (major)).

2-Benzyl-2-hydroxy-5-(nitromethyl)-4-(4-nitrophenyl)-1-phenyloctan-3-one (9Aj)



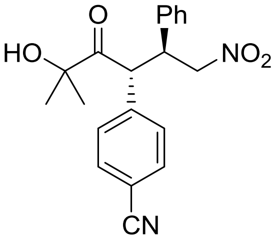
The title compound **9Aj** was prepared from 3-benzyl-3-hydroxy-1-(4-nitrophenyl)-4-phenylbutan-2-one (**4A**) (37.5 mg, 0.1 mmol) and 1-nitropent-1-ene **5j** (34.5 mg, 0.3 mmol) according to the general procedure. White solid, yield: 37.2 mg, 0. 076 mmol, 76%. $[\alpha]_D^{25}$= –41.0 (c = 1.00, 99% *ee*, CH_2Cl_2) m.p. 128–129 ºC. . ^{1}H NMR (300 MHz, $CDCl_3$), δ: 7.91 (d, *J* = 8.8 Hz, 2H), 7.44–7.31 (m, 5H), 7.19–6.96 (m, 5H), 6.79 (d, *J* = 7.0 Hz, 2H), 4.63 (d, *J* = 10.0 Hz, 1H), 4.35 (dd, *J* = 13.0, 4.3 Hz, 1H), 3.81 (dd, *J* = 12.9, 5.3 Hz, 1H), 3.14 (d, *J* = 13.5 Hz, 1H), 3.06 (d, *J* = 13.5 Hz, 1H), 2.83 (d, *J* = 13.6 Hz, 1H), 2.81–2.76 (m, 1H), 2.57 (d, *J* = 13.5 Hz, 1H), 1.94 (s, 1H), 1.43–1.23 (m, 2H), 1.13–1.05 (m, 2H), 0.89 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$), δ: 211.5, 147.4, 141.5, 135.0, 131.3, 130.7, 129.0, 128.8, 127.8, 127.3, 124.1, 84.2, 75.7, 54.9, 45.1, 44.0, 39.8, 32.4, 20.1, 14.3. UPLC-DAD-QTOF: $C_{28}H_{30}N_2O_6Na$ $[M+Na]^+$ calcd.: 513.2002, found: 513.2000. The enantiomeric purity of the major diastereomer was determined by HPLC analysis (Daicel Chiralpak AD–H, hexane/isopropanol 90/10, flow rate = 1.0 mL/min, retention times: 14.2 min (major) and 26.9 min (minor)).

2-Benzyl-2-hydroxy-6-methyl-5-(nitromethyl)-4-(4-nitrophenyl)-1-phenylheptan-3-one (9Ak)



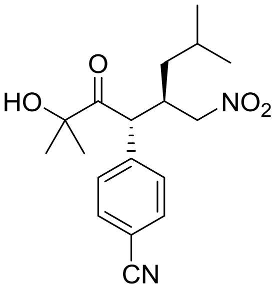
The title compound **9Ak** was prepared from 3-benzyl-3-hydroxy-1-(4-nitrophenyl)-4-phenylbutan-2-one (**4A**) (37.5 mg, 0.1 mmol) and 3-methyl-1-nitrobut-1-ene **5k** (34.5 mg, 0.3 mmol) according to the general procedure. White solid, yield: 22.1 mg, 0. 045 mmol, 45%. $[\alpha]_D^{25}$= –24.2 (c = 0.80, 97% *ee*, CH_2Cl_2). m.p. 159–160 ºC. ^{1}H NMR (300 MHz, $CDCl_3$), δ: 7.92 (d, *J* = 8.8 Hz, 2H), 7.40–7.26 (m, 5H), 7.20 (d, *J* = 8.8 Hz, 2H), 7.13–7.00 (m, 3H), 6.77 (d, *J* = 6.9 Hz, 2H), 4.70 (d, *J* = 10.9 Hz, 1H), 4.18–3.88 (m, 2H), 3.27–3.12 (m, 1H), 3.15 (d, *J* = 13.6, 1H), 2.92 (d, *J* = 13.5 Hz, 1H), 2.79 (d, J = 13.5 Hz, 1H), 2.54 (d, J = 13.5 Hz, 1H), 1.94 (s, 1H), 1.61–1.41 (m, 1H), 0.96 (d, J = 6.9 Hz, 3H), 0.71 (d, J = 7.0 Hz, 3H). ^{13}C NMR (75 MHz, CDCl$_3$), δ: 211.3, 147.5, 141.3, 135.0, 134.8, 131.3, 130.9, 130.6, 129.0, 128.9, 127.8, 127.4, 124.2, 84.1, 74.1, 54.0, 44.8, 44.6, 44.3, 29.4, 21.6, 16.3. UPLC-DAD-QTOF: $C_{28}H_{30}N_2O_6Na$ [M+Na]$^+$ calcd.: 513.2002, found: 513.2001. The enantiomeric purity of the major diastereomer was determined by HPLC analysis (Daicel Chiralpak IA, hexane/isopropanol 99/1, flow rate = 1.0 mL/min, retention times: 84.8 min (major) and 114.7 min (minor)).

4-(5-hydroxy-5-methyl-1-nitro-4-oxo-2-phenylhexan-3-yl)benzonitrile (6Ba)



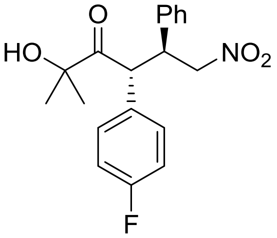
The title compound **6Ba** was prepared from 4-(3-hydroxy-3-methyl-2-oxobutyl)benzonitrile (**1B**) (20.3 mg, 0.1 mmol) and nitrostyrene (17.9 mg, 1.2 mmol) according to the general procedure. White solid, yield: 31.7 mg, 0.089 mmol, 89%. $[\alpha]_D^{25}$= –70.0 (c = 0.19, 82% *ee*, CH$_2$Cl$_2$). m.p. 181–182 ºC. ^{1}H NMR (300 MHz, CDCl$_3$), δ: 7.73 (d, J = 8.5 Hz, 2H), 7.63 (d, J = 8.5 Hz, 2H), 7.40–7.29 (m, 5H), 4.88 (d, J = 11.5 Hz, 1H), 4.54 (dd, J = 12.5, 10.2 Hz, 1H), 4.40–4.28(m, 1H), 4.20 (dd, J = 12.5, 4.3 Hz, 1H), 2.21 (s,1H), 0.91 (s, 3H), 0.83 (s, 3H). ^{13}C NMR (75 MHz, CDCl$_3$), δ: 210.6, 140.3, 136.9, 133.1, 129.7, 129.0, 128.5, 128.3, 118.0, 112.6, 77.9, 47.0, 26.6, 25.9. UPLC-DAD-QTOF: $C_{20}H_{20}N_2O_4Na$ [M+Na]$^+$ calcd.: 375.1321, found: 375.1327. The enantiomeric purity of the major diastereomer was determined by HPLC analysis (Daicel Chiralpak IA, hexane/isopropanol 90/10, flow rate = 1.0 mL/min, retention times: 21.5min (major) and 26.5 min (minor)).

4-(2-Hydroxy-2,7-dimethyl-5-(nitromethyl)-3-oxooctan-4-yl)benzonitrile (6Bk)



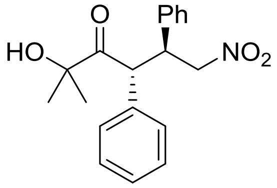
The title compound **6Bk** was prepared from 4-(3-hydroxy-3-methyl-2-oxobutyl)benzonitrile (**1B**) (20.3 mg, 0.1 mmol) and 4-methyl-1-nitropent-1-ene (38.7 mg, 0.3 mmol) according to the general procedure. Colorless oil, yield: 21.3 mg, 0. 064 mmol, 64%. ^{1}H NMR (300 MHz, CDCl$_3$), δ: 7.68 (d, J = 8.4 Hz, 2H), 7.53 (d, J = 8.4 Hz, 2H), 4.69 (d, J = 10.6 Hz, 1H), 4.44 (dd, J = 13.2, 4.6 Hz, 1H), 3.91(dd, J = 13.2, 3.3 Hz, 1H), 2.92–2.86 (m, 1H), 1.80–1.70 (m, 1H), 1.45–1.37 (m, 1H), 1.35 (s, 3H), 1.21 (s,3H), 1.12–1.03 (m, 1H), 0.95 (t, J = 6.6 Hz, 6H). ^{13}C NMR (75 MHz, CDCl$_3$), δ: 213.0, 141.4, 133.2, 130.5, 118.5, 112.7, 78.2, 75.3, 54.4, 39.8, 39.6, 27.5, 27.1, 25.7, 24.1, 21.3. UPLC-DAD-QTOF: $C_{18}H_{24}N_2O_4Na$ [M+Na]$^+$ calcd.: 355.1634, found: 355.1639. The enantiomeric purity of the major diastereomer was determined by HPLC analysis (Daicel Chiralpak IC, hexane/isopropanol 95/5, flow rate = 1.0 mL/min, retention times: 26.5 min (minor) and 33.1 min (major)).

4-(4-Fluorophenyl)-2-hydroxy-2-methyl-6-nitro-5-phenylhexan-3-one (6Ca)



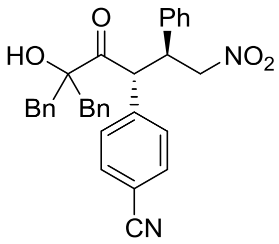
The title compound **6Ca** was prepared from 1-(4-fluorophenyl)-3-hydroxy-3-methylbutan-2-one (**1C**) (19.6 mg, 0.1 mmol) and nitrostyrene (44.7 mg, 0.3 mmol) according to the general procedure. White solid, yield: 24.2 mg, 0.070 mmol, 70%. m.p. 135–136 ºC. ^{1}H NMR (300 MHz, $CDCl_3$), δ: 7.49–7.42 (m, 2H), 7.40–7.26 (m, 5H), 7.20–7.08 (m, 2H), 4.70 (d, *J* = 11.3 Hz, 1H), 4.56 (dd, *J* = 12.3, 10.3 Hz, 1H), 4.41–4.28 (m, 1H), 4.24 (dd, *J* = 12.3, 4.3 Hz, 1H), 2.53 (s,1H) 0.89 (s, 6H). ^{13}C NMR (75 MHz, $CDCl_3$), δ: 211.2, 164.3, 161.0, 137.4, 130.5, 130.4, 128.9, 128.3, 116.7, 116.5, 78.1, 77.5, 54.8, 47.1, 26.4, 25.9. UPLC-DAD-QTOF: $C_{19}H_{20}FNO_4Na$ $[M+Na]^+$ calcd.: 368.1274, found: 368.1271. The enantiomeric purity of the major diastereomer was determined by HPLC analysis (Daicel Chiralpak IA, hexane/isopropanol 90/10, flow rate = 1.0 mL/min, retention times: 9.3 min (major) and 11.0 min (minor)).

2-Hydroxy-2-methyl-6-nitro-4,5-diphenylhexan-3-one (6Da)



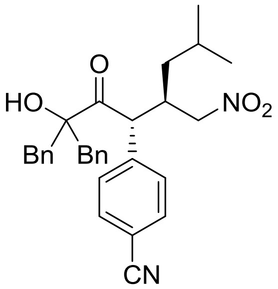
The title compound **6Da** was prepared from 3-hydroxy-3-methyl-1-phenylbutan-2-one (**1D**) (17.8 mg, 0.1 mmol) and nitrostyrene (**5a**) (29.8 mg, 0.2 mmol) according to the general procedure. White solid, yield: 12.1 mg, 0. 037 mmol, 37%. m.p. 128–130 ºC. ^{1}H NMR (300 MHz, $CDCl_3$), δ: 7.58–7.10 (m, 10H), 4.62 (d, *J* = 11.3 Hz, 1H), 4.57–4.50 (m, 1H), 4.42–4.28 (m, 1H), 4.18 (dd, *J* = 12.5, 4.2 Hz, 1H), 2.63 (s, 1H), 0.87 (s, 3H), 0.85 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$), δ: 211.1, 137.7, 134.7, 129.6, 128.9, 128.7, 128.7, 128.3, 128.1, 78.3, 75.9, 55.9, 47.0, 26.4, 25.9. UPLC-DAD-QTOF: $C_{19}H_{20}NO_4$ $[M–H]^–$ calcd.: 326.1392, found: 326.1380. The enantiomeric purity of the major diastereomer was determined by HPLC analysis (Daicel Chiralpak IA, hexane/isopropanol 90/10, flow rate = 1.0 mL/min, retention times: 10.4 min (major) and 13.0 min (minor)).

4-(5-Benzyl-5-hydroxy-1-nitro-4-oxo-2,6-diphenylhexan-3-yl)benzonitrile (9Ba)



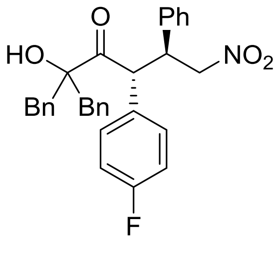
The title compound **9Ba** was prepared from 4-(3-benzyl-3-hydroxy-2-oxo-4-phenylbutyl)benzonitrile **(4B)** (35.5 mg, 0.1 mmol) and nitrostyrene (17.9 mg, 1.2 mmol) according to the general procedure. White solid, yield: 35.3 mg, 0. 070 mmol, 70%. $[\alpha]_D^{25}$= – 66.1 (c = 1.00, 99% *ee*, CH_2Cl_2). m.p. 220–221 ºC. ^{1}H NMR (300 MHz, $CDCl_3$), δ: 7.42–7.21 (m, 10H), 7.13 (d, *J* = 8.3 Hz, 2H), 7.04 (t, *J* = 7.4 Hz, 1H), 6.96 (dd, *J* = 6.5, 2.9 Hz, 2H), 6.89 (t, *J* = 7.6 Hz, 2H), 6.60 (d, *J* = 7.1 Hz, 2H), 4.94 (d, *J* = 11.0 Hz, 1H), 4.50–4.35 (m, 1H), 4.32 –4.13 (m, 2H), 3.03 (d, *J* = 13.5 Hz, 1H), 2.34 (d, *J* = 13.5 Hz, 1H), 2.22 (d, *J* = 13.7 Hz, 1H), 1.99 (d, *J* = 13.7 Hz, 1H), 1.75 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$), δ: 209.0, 138.0, 137.4, 134.5, 134.2, 132.6, 130.8, 130.0, 129.6, 129.0, 128.5, 128.4, 128.1, 127.2, 126.6, 118.2, 111.5, 83.4, 78.1, 55.6, 46.1, 42.7, 42.3. UPLC-DAD-QTOF: $C_{32}H_{28}N_2O_4Na$ [M+Na]$^+$ calcd.: 527.1947, found: 527.1942. The enantiomeric purity of the major diastereomer was determined by HPLC analysis (Daicel Chiralpak IA, hexane/isopropanol 90/10, flow rate = 1.0 mL/min, retention times: 15.1 min (major) and 18.6 min (minor)).

4-(2-Benzyl-2-hydroxy-7-methyl-5-(nitromethyl)-3-oxo-1-phenyloctan-4-yl)benzonitrile (9Bk)



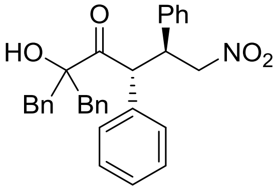
The title compound **9Bk** was prepared from 4-(3-benzyl-3-hydroxy-2-oxo-4-phenylbutyl)benzonitrile **(4B)** (35.5 mg, 0.1 mmol) and 4-methyl-1-nitropent-1-ene **5k** (38.7 mg, 0.3 mmol) according to the general procedure. White solid, yield: 17.4 mg, 0. 036 mmol, 36%. $[\alpha]_D^{25}$= –61.9° (c = 0.21, 99% *ee*, CH_2Cl_2). M.p. 121-122 ºC. ^{1}H NMR (300 MHz, $CDCl_3$), δ: 7.41–7.24 (m, 7H), 7.21–7.00 (m, 5H), 6.80 (d, *J* = 7.1 Hz, 2H), 4.56 (d, *J* = 9.9 Hz, 1H), 4.36 (dd, *J* = 13.0, 4.5 Hz, 1H), 3.75 (dd, *J* = 13.0, 4.2 Hz, 1H), 3.12 (d, *J* = 13.5 Hz, 1H), 3.00 (d, *J* = 13.5 Hz, 1H), 2.84–2.69 (m, 2H), 2.56 (d, *J* = 13.5 Hz, 1H), 1.91 (s, 1H), 1.06–0.96 (m, 2H), 0.92 (d, *J* = 6.5 Hz, 3H), 0.82 (d, *J* = 6.6 Hz, 3H).^{13}C NMR (75 MHz, $CDCl_3$), δ: 211.6, 139.7, 135.1, 135.0, 132.7, 131.3, 130.7, 129.0, 128.9, 127.8, 127.4, 118.8, 111.7, 84.1, 75.7, 55.5, 44.9, 44.1, 39.4, 37.8, 25.5, 24.0, 21.5. UPLC-DAD-QTOF: $C_{30}H_{32}N_2O_4Na$ [M+Na]$^+$ calcd.: 507.2260, found: 507.2263. The enantiomeric purity of the major diastereomer was determined by HPLC analysis (Daicel Chiralpak IA, hexane/isopropanol 98/2, flow rate = 1.0 mL/min, retention times: 29.4 min (minor) and 32.0 min (major)).

2-Benzyl-4-(4-fluorophenyl)-2-hydroxy-6-nitro-1,5-diphenylhexan-3-one (9Ca)



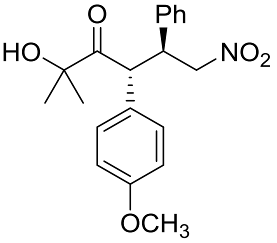
The title compound **9Ca** was prepared from 3-benzyl-1-(4-fluorophenyl)3-hydroxy-4-phenylbutan-2-one (**4C**) (34.8 mg, 0.1 mmol) and nitrostyrene (44.7 mg, 0.3 mmol) according to the general procedure. White solid, yield: 24.4 mg, 0. 049 mmol, 49%. $[\alpha]_D^{25}$= –65.7° (c = 1, 96% *ee*, CH_2Cl_2). M.p. 198-199 ºC. ^{1}H NMR (300 MHz, $CDCl_3$), δ: 7.41–7.22 (m, 8H) 7.08–6.90 (m, 7H), 6.79 (t, *J* = 8.7 Hz, 2H), 6.66 (d, *J* = 7.0 Hz, 2H), 4.83 (d, *J* = 10.7 Hz, 1H), 4.60–4.35 (m, 1H), 4.33–4.15 (m, 2H), 3.05 (d, *J* = 13.4 Hz, 1H), 2.36 (d, *J* = 13.4 Hz, 1H), 2.27–2.09 (m, 2H), 1.77 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$), δ: 210.1, 164.2, 138.4, 135.0, 131.2, 131.0, 130.8, 130.5, 123.3, 128.9, 128.6, 127.4, 127.0, 116.7, 116.4, 83.8, 78.9, 55.4, 46.6, 43.0, 42.5. UPLC-DAD-QTOF: $C_{31}H_{28}FNO_4Na$ [M+Na]$^+$ calcd.: 520.1900, found: 520.1895. The enantiomeric purity of the major diastereomer was determined by HPLC analysis (Daicel Chiralpak IB, hexane/isopropanol 98/2, flow rate = 1.0 mL/min, retention times: 14.1 min (minor) and 15.9 min (major)).

2-Benzyl-2-hydroxy-6-nitro-1,4,5-triphenylhexan-3-one (9Da)



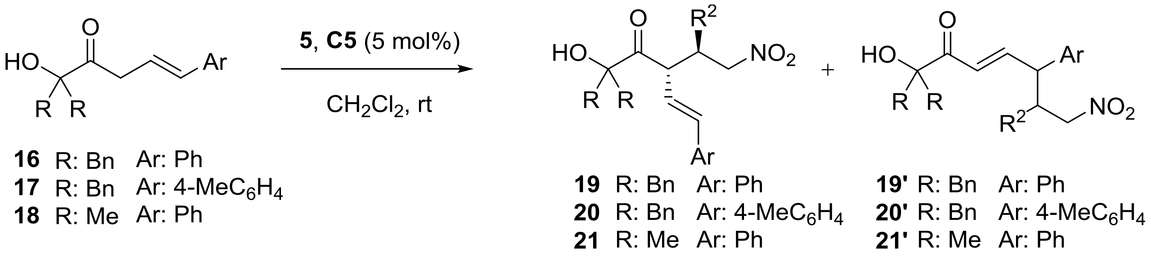
The title compound **9Da** was prepared from 3-benzyl-3-hydroxy-1,4-diphenylbutan-2-one (**4D**) (33.0 mg, 0.1 mmol) and nitrostyrene (44.7 mg, 0.3 mmol) according to the general procedure. White solid, yield: 22.1 mg, 0. 046 mmol, 46%. $[\alpha]_D^{25}$= –98.6° (c= 0.23, 96% *ee*, CH_2Cl_2). M.p. 194–195 ºC. ^1H NMR (300 MHz, $CDCl_3$), δ: 7.41–6.87 (m, 18H), 6.68 (d, *J* = 6.9 Hz, 2H), 4.80 (d, *J* = 10.7 Hz, 1H), 4.54–4.39 (m, 1H), 4.37–4.15 (m, 2H), 3.03 (d, *J* = 13.4 Hz, 1H), 2.38 (d, *J* = 13.4 Hz, 1H) 2.34–2.17 (m, 2H).^{13}C NMR (75 MHz, $CDCl_3$), δ: 210.2, 138.6, 135.2, 135.0, 133.1, 131.2, 130.5, 129.7, 129.3, 128.9, 128.6, 128.6, 128.5, 128.3, 127.3, 127.0, 83.8, 79.1, 56.5, 46.6, 42.9, 42.5. UPLC-DAD-QTOF: $C_{31}H_{29}NO_4Na$ $[M+Na]^+$ calcd.: 502.1994, found: 502.1993. The enantiomeric purity of the major diastereomer was determined by HPLC analysis (Daicel Chiralpak IC, hexane/isopropanol 98/2, flow rate = 1.0 mL/min, retention times: 18.1 min (major) and 21.6 min (minor)).

2-Hydroxy-4-(4-methoxyphenyl)-2-methyl-6-nitro-5-phenylhexan-3-one (6Ea)



The title compound **6Ea** was prepared from 3-hydroxy-1-(4-methoxyphenyl)-3-methylbutan-2-one (**1E**) (20.83 mg, 0.1 mmol) and nitrostyrene (**5a**) (44.7 mg, 0.3 mmol) according to the general procedure. White solid, yield: 16.1 mg, 0.045 mmol, 45%. M.p. 142–143 ºC. ^1H NMR (300 MHz, $CDCl_3$), δ: 7.42–7.25 (m, 7H), 6.96 (d, *J* = 8.8 Hz, 2H), 4.64–4.49 (m, 2H), 4.42–4.20 (m, 2H), 3.85 (s, 3H), 0.91 (s, 3H), 0.88 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$), δ: 210.8, 159.3, 137.4, 129.4, 128.4, 127.8, 127.8, 127.6, 125.9, 114.6, 77.9, 54.9, 54.6, 46.6, 26.0, 25.6. UPLC-DAD-QTOF: $C_{20}H_{23}NO_5Na$ $[M+Na]^+$ calcd.: 380.1474, found: 380.1470. The enantiomeric purity of the major diastereomer was determined by HPLC analysis (Daicel Chiralpak IA, hexane/isopropanol 90/10, flow rate = 1.0 mL/min, retention times: 16.5min (major.) and 21.6 min (min.)).

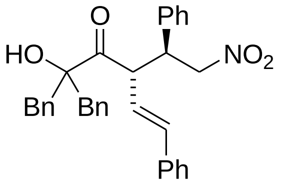
5. Catalytic conjugate addition of alkenyl ketols 16-18 to nitroalkenes.



To a solution of the corresponding hydroxyketone **16–18** (0.2 mmol, 1 equiv.) and trans-β-nitrostyrene (32.8 mg, 0.22 mmol, 1.1 equiv.) in dichloromethane (0.4 mL), catalyst **C5** (11.9 mg, 0.02 mol, 10 mol %) was added at room temperature or –20 °C and the resulting mixture was stirred to completion of the reaction (2–20 h, TLC). Then the reaction mixture was submitted to flash column chromatography (eluent hexane/ethyl acetate 90:10).

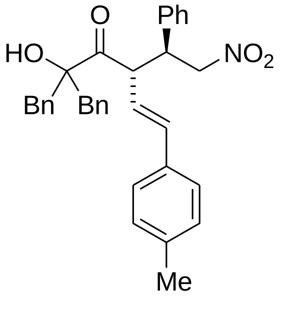
The same procedure was employed for the reactions involving catalyst **C6**, but with a molar ratio of ketone/**5**/catalyst of 1.5:1:0.1.

(E)-2-Benzyl-2-hydroxy-4(*S*)-(2-nitro-1(*S*)-phenylethyl)-1,6-diphenylhex-5-en-3-one (19)



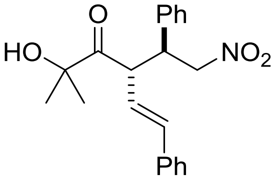
Prepared according to the general procedure starting from **16** (71.3 mg, 0.2 mmol) and **C5** as catalyst. The title compound was purified by flash column chromatography on silicagel (eluting with hexane/ethyl acetate 1/20) and isolated as a white solid. Yield: 63.7 mg (63%). m.p. = 168–171ºC. $[\alpha]_D^{22}$ = –126.7º (c= 0.5, >98% *ee*, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34–7.20 (m, 11H), 7.03–6.92 (m, 8H), 6.84–6.80 (m, 1H), 6.21 (d, *J* = 15.6 Hz, 1H), 5.33 (dd, *J* = 15.6 Hz, *J'* = 10.0 Hz, 1H), 4.76 (dd, *J* = 12.8 Hz, *J'* = 4.8 Hz, 1H), 4.58 (dd, *J* = 12.8 Hz, *J'* = 10.4 Hz, 1H), 4.30 (t, *J* = 10.0 Hz, 1H), 3.97 (td, *J* = 10.2 Hz, *J'* = 4.6 Hz, 1H), 3.20 (d, *J* = 13.2 Hz, 1H), 2.49 (d, *J* = 13.2 Hz, 1H), 2.36 (d, *J* = 13.6 Hz, 1H), 2.28 (d, *J* = 13.6 Hz, 1H), 2.12 (sb, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 210.9, 138.2, 136.9, 135.5, 134.9, 134.8, 130.9, 130.3, 128.8, 128.4, 128.3, 128.0, 127.1, 127.0, 126.6, 121.6, 83.6, 78.2, 54.6, 44.7, 43.0, 42.9. UPLC-DAD-QTOF: $C_{33}H_{32}NO_4$. $[M+H]^+$ calcd.: 506.2331, found: 506.2337.

(E)-2-Benxyl-2-hydroxy-4(*S*)-[2-nitro-1(*S*)-phenylethyl]-1-phenyl-6-*p*-tolylhex-5-en-3-one (20)



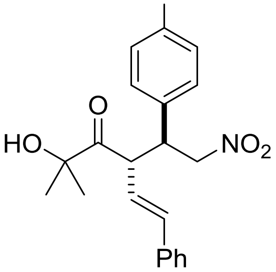
Prepared according to the general procedure starting from (74.1 mg, 0.2 mmol) and **C5** as catalyst. The title compound was purified by flash column chromatography on silicagel (eluting with hexane/ethyl acetate 1:20) and isolated as a white solid. Yield: 72.7 mg (70%). m.p. = 170–173 ºC. $[\alpha]_D^{24}$= –174.5º (c= 0.5, >98% *ee*, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32–6.84 (m, 19H), 6.18 (d, *J* = 15.6 Hz, 1H), 5.25 (dd, *J* = 15.6 Hz, *J'* = 10.0 Hz, 1H), 4.75 (dd, *J* = 13.0 Hz, *J'* = 4.8 Hz, 1H), 4.57 (dd, *J* = 13.0 Hz, *J'* = 10.8 Hz, 1H), 4.25 (t, *J* = 9.6 Hz, 1H), 3.94 (dt, *J* = 10.0 Hz, *J'* = 4.6 Hz, 1H), 3.20 (d, *J* = 13.4 Hz, 1H), 2.49 (d, *J* = 13.4 Hz, 1H), 2.37 (d, *J* = 13.6 Hz, 1H), 2.37 (s, 3H), 2.30 (d, *J* = 13.6 Hz, 1H), 2.13 (sb, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 211.0, 138.3, 138.2, 136.9, 135.0, 134.9, 132.8, 130.8, 130.3, 129.0, 128.8, 128.4, 128.3, 128.0, 127.1, 127.0, 126.6, 120.5, 83.6, 78.2, 54.7, 44.7, 43.0, 42.9, 21.2. UPLC-DAD-QTOF: $C_{34}H_{33}NO_4Na$. $[M+Na]^+$ calcd.: 542.2307, found 542.2315.

(*S*,*E*)-2-hydroxy-2-methyl-4-((*S*)-2-nitro-1-phenylethyl)-6-phenylhex-5-en-3-one (21a)



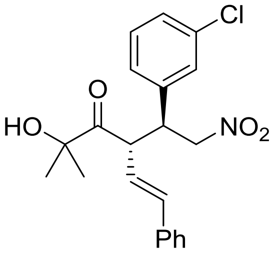
Prepared according to the general procedure starting from 2-hydroxy-2-methyl-6-phenylhex-5-en-3-one **18** (41 mg, 0.2 mmol) and nitroalkene **5a** (32 mg, 0.22 mmol) and **C5** as catalyst. The title compound was isolated as as a white solid. Yield: 60 mg (85 %). m. p.: 143 – 145 °C. $[\alpha]_D^{25}$ = −60.3° (c= 1, 97 % *ee*, CH_2Cl_2). ^{1}H NMR (300 MHz, Chloroform-*d*) δ 7.48 – 7.24 (m, 10H), 6.73 (d, *J* = 15.9 Hz, 1H), 6.10 (dd, *J* = 15.9, 9.5 Hz, 1H), 4.95 – 4.69 (m, 2H), 4.37 – 4.11 (m, 2H), 1.08 (s, 3H), 0.90 (s, 3H). ^{13}C NMR (75 MHz, Chloroform-*d*) δ 211.6, 128.9, 128.8, 128.6, 128.3, 126.5, 124.3, 78.0, 54.5, 45.7, 26.1, 25.9. UPLC-DAD-QTOF: $C_{21}H_{23}NO_4$ $[M+H]^+$ calcd.: 354.1705, found: 354.1707. The enantiomeric purity was determined by HPLC analysis (Daicel Chiralpak IB hexane/isopropanol 90/10, flow rate= 1.0 mL/min; retention times: 17.6 min (minor) and 27.1 min (major)).

(*S*,*E*)-4-((*S*)-1-(4-chlorophenyl)-2-nitroethyl)-2-hydroxy-2-methyl-6-phenylhex-5-en-3-one (21b)



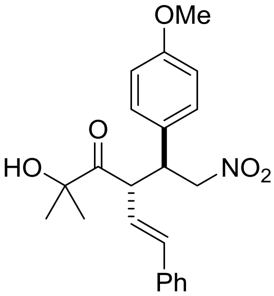
Prepared according to the general procedure starting from 2-hydroxy-2-methyl-6-phenylhex-5-en-3-one **18** (41 mg, 0.2 mmol) and nitroalkene **5b** (40 mg, 0.22 mmol) and **C5** as catalyst. The title compound was isolated as as a white solid. Yield: 64 mg (82 %). m. p.: 166 – 168 °C. $[\alpha]_D^{25}$ = −102.6° (c= 0.5, 95 % *ee*, CH_2Cl_2). ^{1}H NMR (300 MHz, Chloroform-*d*) δ 7.44 – 7.17 (m, 9H), 6.72 (d, *J* = 15.9 Hz, 1H), 6.06 (dd, *J* = 15.9, 9.5 Hz, 1H), 4.86 – 4.60 (m, 2H), 4.28 (dd, *J* = 10.8, 9.5 Hz, 1H), 4.18 (dd, *J* = 10.3, 4.8 Hz, 1H), 1.08 (s, 3H), 0.97 (s, 3H). ^{13}C NMR (75 MHz, Chloroform-*d*) δ 211.1, 136.5, 135.7, 135.1, 133.9, 129.4, 128.8, 128.6, 128.5, 126.3, 123.5, 77.7, 53.9, 44.7, 26.1, 26.0. UPLC-DAD-QTOF: $C_{21}H_{22}ClNO_4$ $[M+H]^+$ calcd.: 388.1316, found: 388.1323. The enantiomeric purity was determined by HPLC analysis (Daicel Chiralpak IB hexane/isopropanol 95/5, flow rate= 1.0 mL/min; retention times: 44.7 min (minor) and 66.2 min (major)).

4-(1-(3-Chlorophenyl)-2-nitroethyl)-2-hydroxy-2-methyl-6-phenylhex-5-en-3-one (21c)



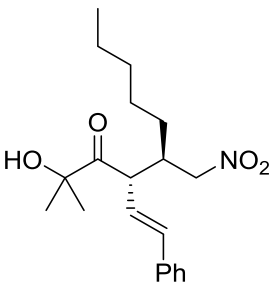
The title compound **21c** was prepared from 2-hydroxy-2-methyl-6-phenylhex-5-en-3-one **18** (40.8 mg, 0.2 mmol) and nitrostyrene (**5c**) (40.4 mg, 0.22 mmol) according to the general procedure for **C5**. White solid, yield: 73.7 mg, 0.19 mmol, 95%. $[\alpha]_D^{25}$= –117.94° (c= 0.5, 96% *ee*, CH_2Cl_2). m.p. 158–160 ºC. ^{1}H NMR (300 MHz, $CDCl_3$), δ: 7.42–7.24 (m, 8H), 7.20–7.12 (m, 1H), 6.73 (d, *J* = 15.9 Hz, 1H), 6.05 (dd, *J* = 15.9, 9.6 Hz, 1H), 4.81 (dd, *J* = 13.2, 4.9 Hz, 1H), 4.68 (dd, *J* = 13.2, 10.0 Hz, 1H), 4.35–4.24 (m, 1H), 4.16 (td, *J* = 10.4, 4.9 Hz, 1H), 2.74 (s, 1H), 1.09 (s, 3H), 0.97 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$), δ: 211.1, 139.5, 136.7, 135.2, 134.6, 130.0, 128.7, 128.6, 128.3, 128.2, 126.5, 126.4, 123.6, 77.7, 54.0, 45.0, 26.2, 26.1. UPLC-DAD-QTOF: $C_{21}H_{22}NO_4ClNa$ $[M+Na]^+$ calcd.: 410.1135, found: 410.1125. The enantiomeric purity of the major diastereomer was determined by HPLC analysis (Daicel Chiralpak IB, hexane/isopropanol 90/10, flow rate = 1.0 mL/min, retention times: 19.5 min (minor) and 25.3 min (major)).

(*S*,*E*)-2-hydroxy-4-((*S*)-1-(4-methoxyphenyl)-2-nitroethyl)-2-methyl-6-phenylhex-5-en-3-one (21f)



Prepared according to the general procedure starting from 2-hydroxy-2-methyl-6-phenylhex-5-en-3-one **18** (41 mg, 0.2 mmol) and nitroalkene **5f** (39 mg, 0.22 mmol) and **C5** as catalyst. The title compound was isolated as as a white solid. Yield: 58 mg (75 %). m. p.: 154 – 156 °C. $[\alpha]_D^{25}$ = −94.1° (c= 1.2, 94 % *ee*, CH_2Cl_2). ^{1}H NMR (300 MHz, Chloroform-*d*) δ 7.42 – 7.29 (m, 4H), 7.24 – 7.13 (m, 2H), 6.90 – 6.83 (m, 2H), 6.70 (d, *J* = 15.9 Hz, 1H), 6.08 (dd, *J* = 15.9, 9.6 Hz, 1H), 4.87 – 4.61 (m, 2H), 4.24 (dd, *J* = 10.8, 9.6 Hz, 1H), 4.12 (td, *J* = 10.4, 5.0 Hz, 1H), 3.79 (s, 3H), 1.00 (d, *J* = 53.0 Hz, 6H). ^{13}C NMR (75 MHz, Chloroform-*d*) δ 212.4, 160.0, 136.9, 136.2, 130.0, 129.8, 129.5, 129.3, 127.2, 125.2, 115.0, 79.0, 55.9, 55.3, 45.7, 26.9, 26.7. UPLC-DAD-QTOF: $C_{22}H_{25}NO_5$ $[M+H]^+$ calcd.: 384.1811, found: 384.1807. The enantiomeric purity was determined by HPLC analysis (Daicel Chiralpak IB hexane/isopropanol 95/5, flow rate= 1.0 mL/min; retention times: 48.8 min (minor) and 76.2 min (major)).

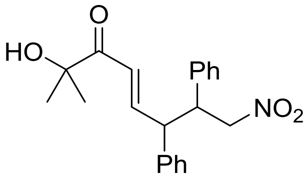
2-Hydroxy-2-methyl-5-(nitromethyl)-4-styryldecan-3-one (21i)



The title compound **21i** was prepared from 2-hydroxy-2-methyl-6-phenylhex-5-en-3-one **18** (40.8 mg, 0.2 mmol) and nitrostyrene (**5i**) (31.5 mg, 0.22 mmol) according to the general procedure for **C5**.

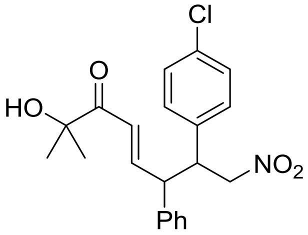
Yellow oil, yield: 65.3 mg, 0.19 mmol, 94%. $[\alpha]_D^{25}$= –64.4° (c = 1, 98% *ee*, CH_2Cl_2). ^1H NMR (300 MHz, $CDCl_3$), δ: 7.40–7.26 (m, 5H), 6.64 (d, *J* = 15.9 Hz, 1H), 6.00 (dd, *J* = 15.9, 9.8 Hz, 1H), 4.67 (dd, *J* = 13.0, 4.6 Hz, 1H), 4.46 (dd, *J* = 13.0, 5.6 Hz, 1H), 4.10 (t, *J* = 9.3 Hz, 1H), 3.36 (s, 1H), 2.72 (s, 1H), 1.44 (s, 3H), 1.40 (s, 3H), 1.37–1.24 (m, 8H), 0.91 (t, *J* = 6.8 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$), δ: 215.6, 138.2, 137.7, 130.7, 130.4, 128.4, 126.2, 79.4, 77.7, 53.4, 41.7, 33.5, 32.1, 28.9, 28.8, 28.3, 24.3, 15.9. UPLC-DAD-QTOF: $C_{20}H_{29}NO_4Na$ $[M+Na]^+$ calcd.: 370.1994, found: 370.1994. The enantiomeric purity of the major diastereomer was determined by HPLC analysis (Daicel Chiralpak IC hexane/isopropanol 95/5, flow rate = 1.0 mL/min, retention times: 9.0 min (minor) and 10.5 min (major)).

2-Hydroxy-2-methyl-8-nitro-6,7-diphenyloct-4-en-3-one (21’a)



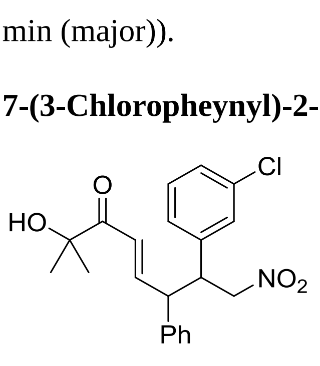
The title compound **21’a** was prepared from 2-hydroxy-2-methyl-6-phenylhex-5-en-3-one **18** (40.8 mg, 0.2 mmol) and nitrostyrene (**5a**) (19.4 mg, 0.13 mmol) according to the general procedure for **C6**. White solid, yield: 7.78 mg, 0.022 mmol, 11%. m.p. 138–139 ºC. ^1H NMR (300 MHz, $CDCl_3$), δ: 7.39–7.15 (m, 7H), 7.07–6.96 (m, 4H), 6.59 (d, *J* = 15.2 Hz, 1H), 4.78–4.63 (m, 2H), 4.00 (td, *J* = 8.8, 6.5 Hz, 1H), 3.82 (t, *J* = 9.6 Hz, 1H), 3.70 (s, 1H), 1.41 (s, 3H), 1.36 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$), δ: 202.9, 149.0, 139.3, 137.4, 129,9, 129.7, 129.0, 128.6, 125.1, 79.4, 76.6, 54.0, 49.8, 27.3. UPLC-DAD-QTOF: $C_{21}H_{23}NO_4Na$ $[M+Na]^+$ calcd.: 376.1525, found: 376.1526.

7-(4-Chloropheynyl)-2-hydroxy-2-methyl-8-nitro-6-phenyloct-4-en-3-one (21’b)



The title compound **21’b** was prepared from 2-hydroxy-2-methyl-6-phenylhex-5-en-3-one **18** (40.8 mg, 0.2 mmol) and nitrostyrene (**5b**) (23.9 mg, 0.13 mmol) according to the general procedure for **C6**. Orange solid, yield: 14.6 mg, 0.04 mmol, 29%. m.p. 145–147 ºC. ^1H NMR (300 MHz, $CDCl_3$), δ: 7.37–7.17 (m, 7H), 7.04 (dd, *J* = 7.8, 1.6 Hz, 2H), 6.95 (d, *J* = 8.5 Hz, 2H), 6.63 (d, *J* = 15.7 Hz, 1H), 4.80–4.60 (m, 2H), 3.99 (td, *J* = 9.3, 5.8 Hz, 1H), 3.79 (t, *J* = 9.7 Hz, 1H) 3.66 (s, 1H), 1.43 (s, 3H), 1.38 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$), δ: 202.9, 148.6, 139.0, 136.0, 134.9, 130.6, 130.1, 130.0, 129.1, 128.8, 125.3, 79.4, 76.6, 53.9, 49.3, 27.3, 27.3 UPLC-DAD-QTOF: $C_{21}H_{22}NO_4ClNa$ $[M+Na]^+$ calcd.: 410.1135, found: 410.1133. The enantiomeric purity of the major diastereomer was determined by HPLC analysis (Daicel Chiralpak IB hexane/isopropanol 90:10, flow rate = 1.0 mL/min, retention times: 17.7 min (minor) and 19.8 min (major)).

7-(3-Chloropheynyl)-2-hydroxy-2-methyl-8-nitro-6-phenyloct-4-en-3-one (21’c)

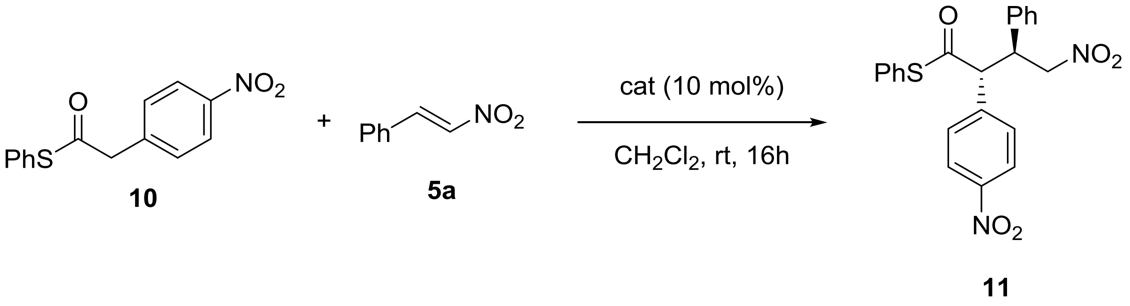


The title compound **21’c** was prepared from 2-hydroxy-2-methyl-6-phenylhex-5-en-3-one **18** (40.8 mg, 0.2 mmol) and nitrostyrene (**5c**)

(23.9 mg, 0.13 mmol) according to the general procedure for **C6**. Yellow oil, yield: 18.2 mg, 0.05 mmol, 36%. ^{1}H NMR (300 MHz, CDCl$_3$), δ: 7.36–7.09 (m, 5H), 7.07–6.99 (m, 2H), 6.89 (d, *J* = 6.8 Hz, 1H), 6.62 (d, *J* = 15.7 Hz, 1H), 4.80–4.60 (m, 2H), 3.97 (td, *J* = 9.2, 6.0 Hz, 1H), 3.79 (t, *J* = 9.7 Hz, 1H), 1.41 (s, 3H), 1.36 (s, 3H). ^{13}C NMR (75 MHz, CDCl$_3$), δ: 201.5, 146.9, 138.3, 137.6, 134.2, 129.6, 128.6, 127.8, 127.7, 127.4, 126.2, 77.7, 75.2, 52.4, 48.1, 25.8. UPLC-DAD-QTOF: $C_{21}H_{22}ClNO_4Na$ [M+Na]$^+$ calcd.: 410.1135, found: 410.1138. The enantiomeric purity of the major diastereomer was determined by HPLC analysis (Daicel Chiralpak IB hexane/isopropanol 90:10, flow rate = 1.0 mL/min, retention times: 19.2 min (minor) and 24.9 min (major)).

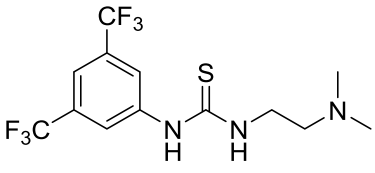
6. Control experiments using as donors 10, 12, and 14

Catalytic conjugate addition of 2-(4-nitrophenyl)ethanethioate to nitrostyrene



To a mixture of phenyl 2-(4-nitrophenyl)ethanethioate **10** (27.3 mg, 1 eq., 0.1 mmol) and nitrostyrene (**5a**) (29.8 mg, 0.2 mmol) in dichloromethane (0.3 mL) at room temperature, catalyst **C5** (5.9 mg, 10 mol %, 0.01 mmol) was added. The resulting solution was stirred at room temperature, until consumption of the phenyl 2-(4-nitrophenyl)ethanethioate as monitored by ^{1}H NMR. The mixture was quenched with HCl 2M (1 mL) and extracted with CH_2Cl_2 (3 x 2 mL). The combined organic layers were dried over $MgSO_4$, filtered and the solvent was evaporated under reduced pressure. The residue was purified by flash column chromatography on silica gel (eluting with Hexane/ AcOEt 80:20) to afford phenyl 4-nitro-2-(4-nitrophenyl)-3-phenylbutanethioate **11** as a 73:27 mixture of diastereomers (50 % *ee*, major; 20% *ee*, minor). Yield: 21.9 mg, 0.052 mmol, 52%. The enantiomeric purity was determined by HPLC analysis (Daicel Chiralpak AD-H, hexane/isopropanol 80/20, flow rate = 1.0 mL/min, retention times: major diastereomer: 13.6 min (minor.) and 17.4 min (major.)); minor diastereomer: 15.6 min (major) and 24.6 min (minor)).

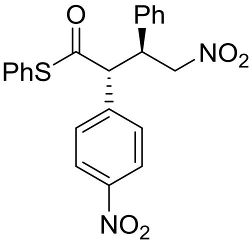
The corresponding racemic compound was prepared following the above procedure at room temperature, but using as catalyst achiral thiourea **S9** (3.6 mg, 10 mol%, 0.01 mmol).[14]



S9

---

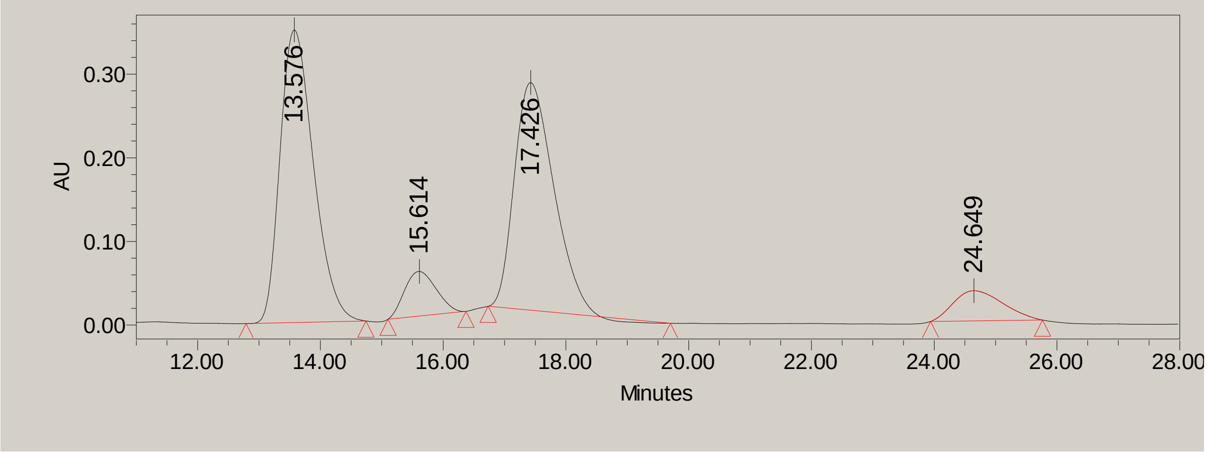
[14] Synthesis adapted from: R. C. Pratt, B. G. Lohmeijer, D. A. Long, P. N. Lundberg, A. P. Dove, H. B. Li, C. G. Wade, R. M. Waymouth, J. L. Hedrick, *Macromolecules*, **2006**, *39*, 7863–7871.



11

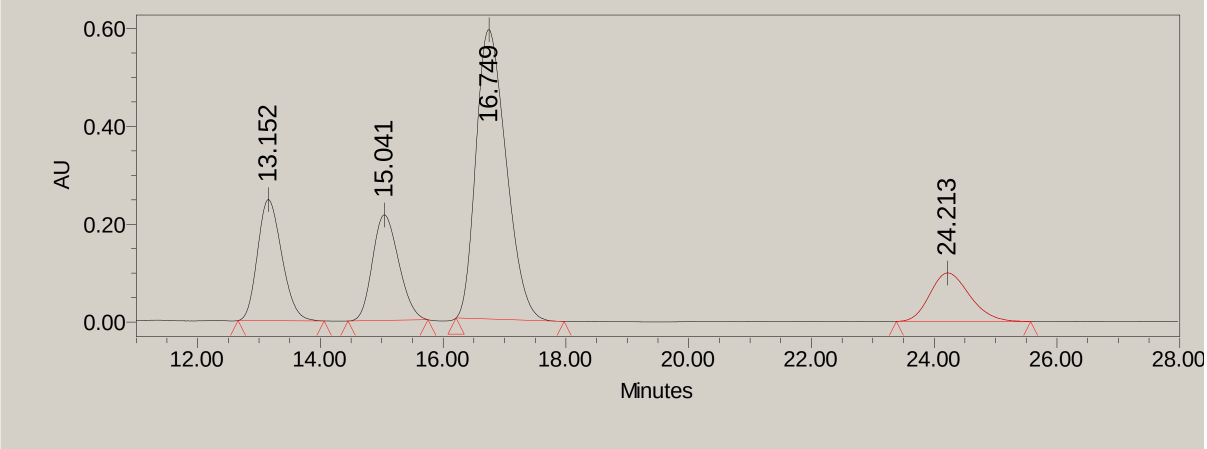
Daicel Chiralpak AD-H, hexane/isopropanol 80/20 flow rate = 1.0 mL/min, λ: 210.0 nm.

Rac-**11**



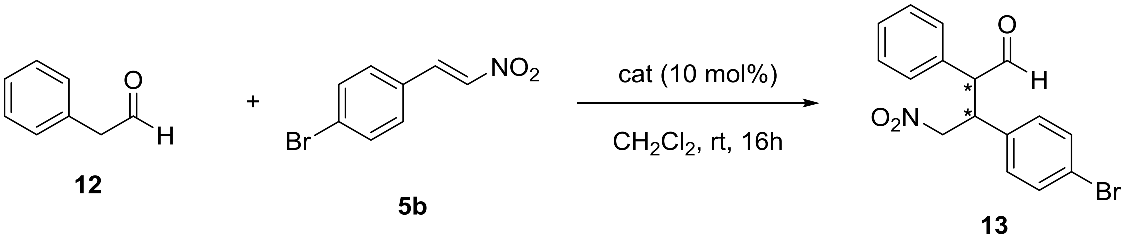
	Retention Time	% Area
1	13.576	44.86
2	15.614	6.44
3	17.426	41.88
4	24.649	6.81

Scalemic **11**



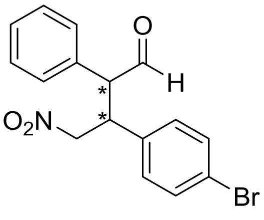
	Retention Time	% Area
1	13.152	18.17
2	15.041	15.79
3	16.749	55.04
4	24.213	11.00

Catalytic conjugate addition of 2-phenylacetaldehyde to 4-bromo nitrostyrene



To a mixture of 2-phenylacetaldehyde **12** (12 mg, 1 eq., 0.1 mmol) and 4-bromonitrostyrene (**5b**) (45.6 mg, 0.2 mmol) in dichloromethane (0.3 mL) at room temperature, catalyst **C5** (5.9 mg, 10 mol %, 0.01 mmol) was added. The resulting solution was stirred at room temperature, until consumption of the 2-phenylacetaldehyde as monitored by ^{1}H NMR. The mixture was quenched with HCl 2M (1 mL) and extracted with CH_2Cl_2 (3 x 2 mL). The combined organic layers were dried over $MgSO_4$, filtered and the solvent was evaporated under reduced pressure. The residue was purified by flash column chromatography on silica gel (eluting with Hexane/ AcOEt 90:10) to afford 3-(4-bromophenyl)-4-nitro-2-phenylbutanal **13** as a diastereomeric mixture dr 59:41, major diastereomer 60 % *ee*, minor diastereomer 40% *ee*. White solid. Yield: 33.0 mg, 0.095 mmol, 95%. m.p. 152–153 ºC. ^{1}H NMR (300 MHz, $CDCl_3$), δ: 9.72 (d, *J* = 1.0 Hz, 1H), 9.55 (d, *J* = 1.7 Hz, 1H), 7.52–7.38 (m, 3H), 7.34–7.21 (m, 5H), 7.15 (d, *J* = 8.4 Hz, 2H), 6.99–6.92 (m, 2H), 6.85 (d, *J* = 8.4 Hz, 2H), 4.91 (dd, *J* = 12.7, 5.5 Hz, 1H), 4.73 (dd, *J* = 12.7, 8.9 Hz, 1H), 4.54–4.38 (m, 2H), 4.33 (dd, *J* = 18.6, 4.8 Hz, 1H), 4.27–4.21 (m, 1H), 4.05 (dd, *J* = 10.1, 1.7 Hz, 1H), 3.98 (d, *J* = 9.2 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$), δ: ^{13}C NMR (75 MHz, $CDCl_3$) δ 197.9, 196.4, 136.2, 135.3, 132.2, 131.7, 130.0, 130.0, 129.8, 129.8, 129.4, 129.2, 129.1, 129.1, 128.4, 128.4, 122.2, 121.8, 78.0, 77.8, 61.5, 60.8, 43.7, 43.6. UPLC-DAD-QTOF: $C_{16}H_{13}BrNO_3$ [M–H]$^-$ calcd.: 346.0079, found: 346.0078.

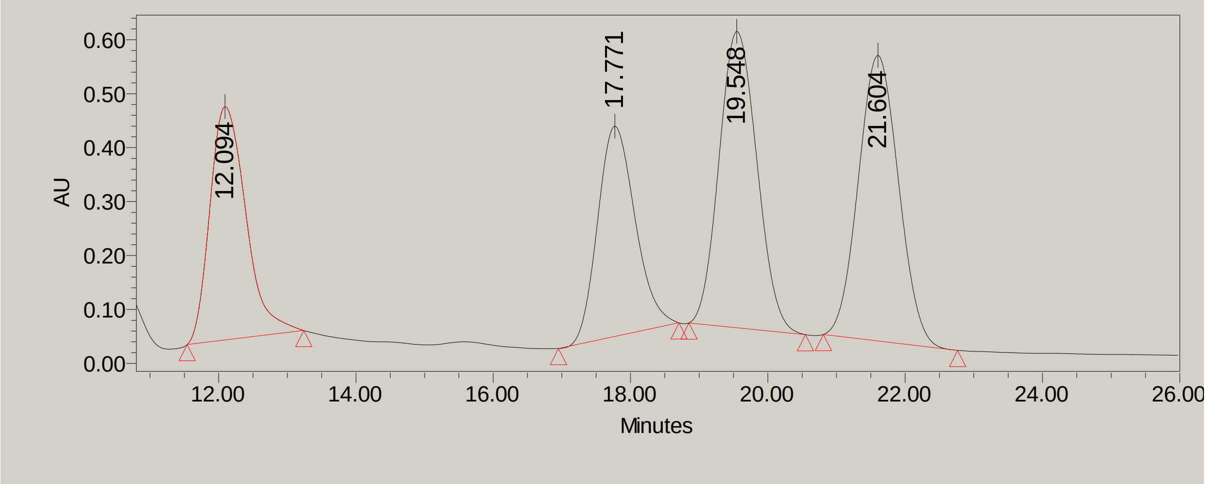
The enantiomeric purity was determined by HPLC analysis (Daicel Chiralpak IC, hexane/isopropanol 90:10, flow rate = 1.0 mL/min, retention times: major diastereomer: 19.5 min (minor) and 21.6 min (major)); minor diastereomer: 12.1 min (major) and 17.8 min (minor)).



13

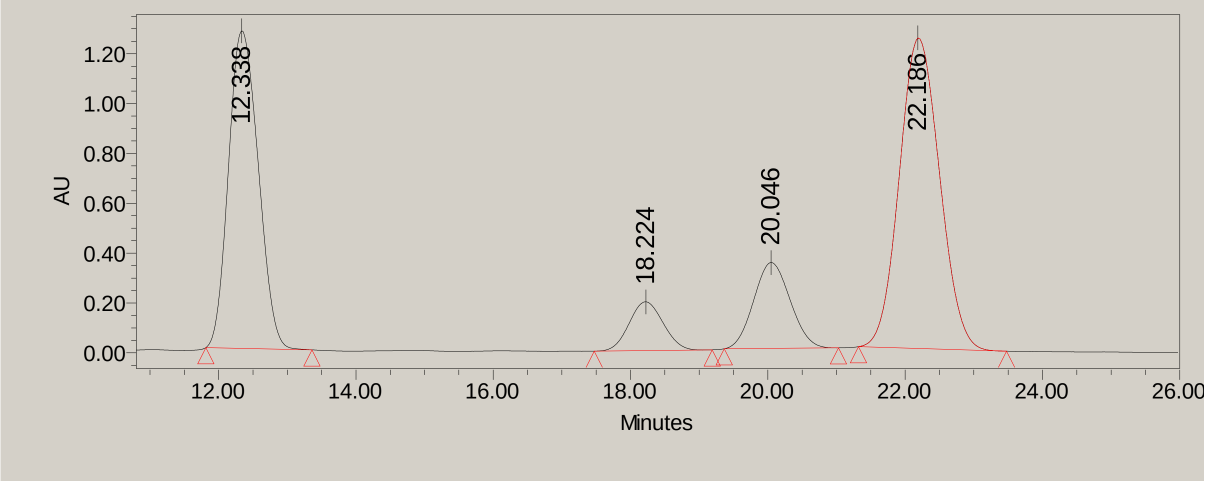
Daicel Chiralpak IC, hexane/isopropanol 90/10 flow rate = 1.0 mL/min, λ: 210.0 nm.

Rac-**13**



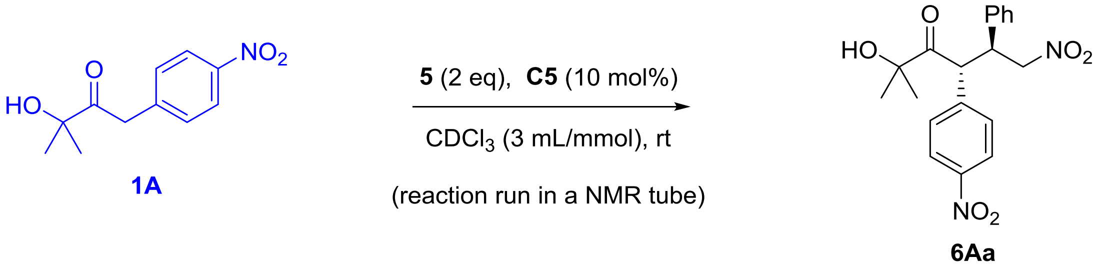
	Retention Time	% Area
1	12.094	21.54
2	17.771	20.21
3	19.548	28.80
4	21.604	29.45

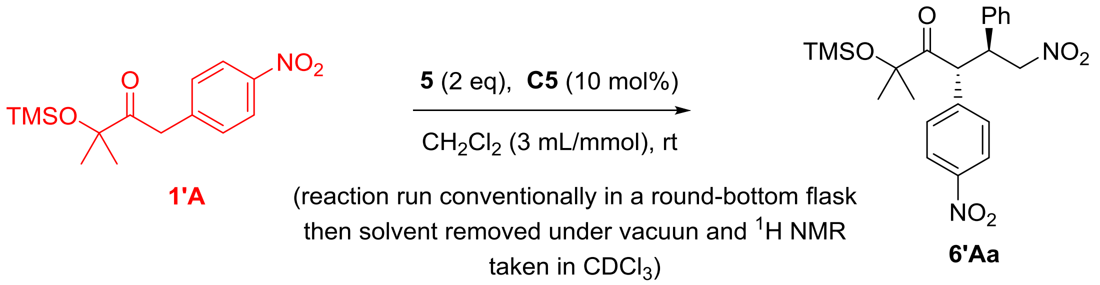
Scalemic **13**

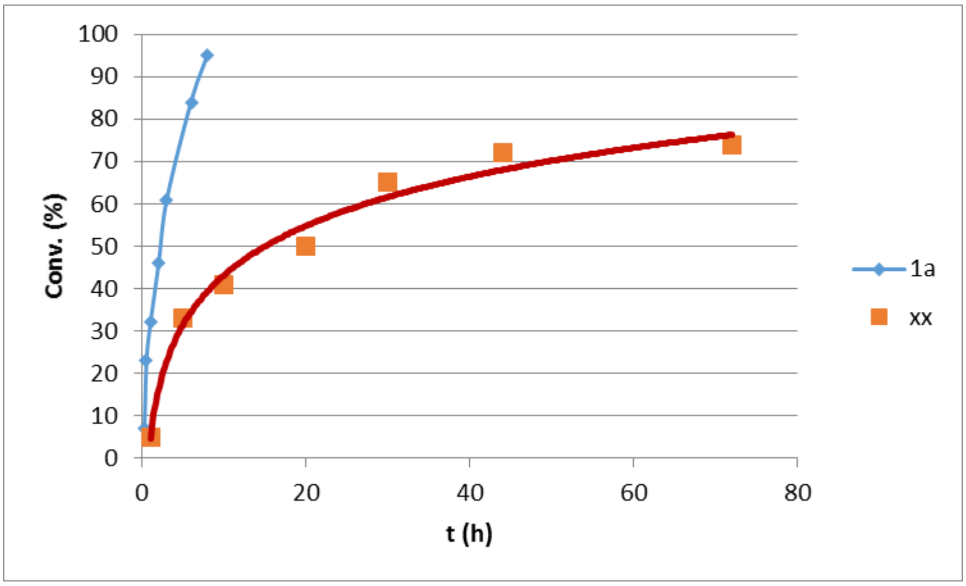


	Retention Time	% Area
1	12.338	35.33
2	18.224	6.19
3	20.046	11.68
4	22.186	46.81

7. Reaction profiles of hydroxy (1A/1B, OH) and silyloxy (1'A/1'B, OSiMe$_3$) ketones





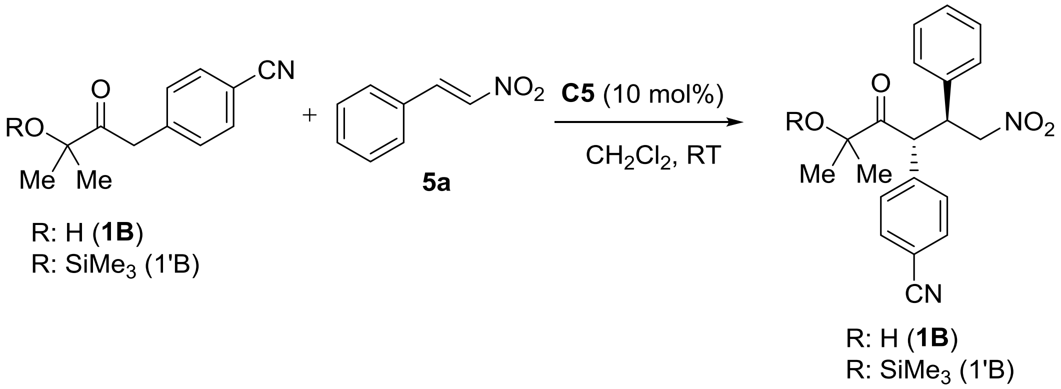


1A

t (h)	Conv (%)
0.25	7
0.5	23
1	32
2	46
3	61
6	84
8	95

1'A

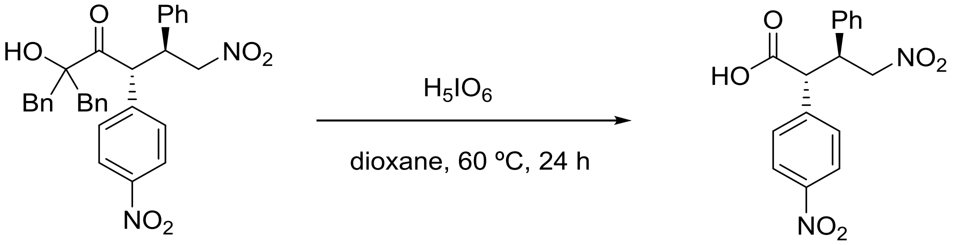
t (h)	Conv (%)
1	5
5	33
10	41
20	50
30	65
44	72
72	74



R	time	conv.	yield	dr	*ee*
H (**1B**)	20 h	>95%	89%	90:10	82%
SiMe$_3$ (**1'B**)	20 h	23%	--	--	--
	44 h	28%	--	--	--

8. Chemical elaboration of adducts

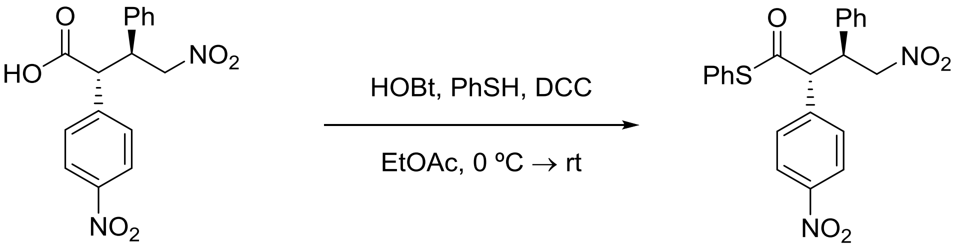
8.1. Ketol cleavage in adduct 9Aa to yield carboxylic acid 22 and conversion to 11



9Aa **22**

To a suspension of **9Aa** (1 eq., 52 mg, 0.1 mmol) in dioxane (3 mL), periodic acid (10 eq., 228 mg, 1 mmol) was added. The resulting mixture was stirred at 60 ºC for 24 h and afterwards the reaction was quenched with water (5 mL) and extracted with ethyl acetate (3 x 5 mL). The combined organic extracts were dried over $MgSO_4$, filtered and the solvent was evaporated. The crude was suspended in dioxane (3 mL), periodic acid (10 eq., 228 mg, 1 mmol) was added. The resulting mixture was stirred at 60 ºC for 24 h and afterwards the reaction was quenched with water (5 mL) and extracted with ethyl acetate (3 x 5 mL). The combined organic extracts were dried over $MgSO_4$, filtered and the solvent was evaporated. The crude was purified by flash column chromatography on silica gel (eluting with hexane/ ethyl acetate 50/50) to give the title compound **22** as a white solid. Yield: 29.4 mg, 0.089 mmol, 89%. $[\alpha]_D^{25}$= –22.0° (c= 1.47, 99% *ee*, MeOH). M.p. 174–176 ºC. ^{1}H NMR (300 MHz, CD_3OD), δ: 8.29 (d, *J* = 8.9 Hz, 2H), 7.81 (d, *J* = 8.9 Hz, 2H), 7.53–7.17 (m, 5H), 4.65 (dd, *J* = 12.8, 9.8 Hz, 1H), 4.44–4.07 (m, 3H). ^{13}C NMR (75 MHz, CD_3OD), δ: 173.5, 149.2, 144.9, 139.0, 131.0, 129.7, 129.5, 129.0, 125.1, 79.3, 56.0, 48.4. UPLC-DAD-QTOF: $C_{16}H_{14}N_2O_6Na$ $[M+Na]^+$ calcd.: 355.0750, found: 353.0739.

Conversion of carboxylic acid 22 into thioester 11[15]



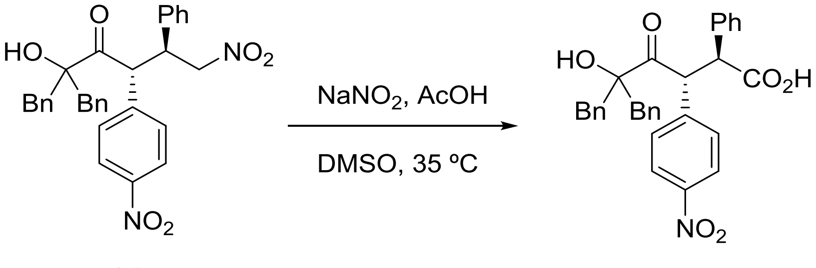
10 **11**

---

[15] E. C. Garnier-Amblard, S. G. Mays, R. F. Arrendale, M. T. Baillie, A. S. Bushnev, D. G. Culver, T. J. Evers, J. J. Holt, R. B. Howard, L. S. Liebeskind, D. S. Menaldino, M. G. Natchus, J. A. Petros, H. Ramaraju, G. P. Reddy, D. C. Liotta, *Med. Chem. Lett.* **2011**, *2*, 438–443.

To a solution of carboxylic acid **22** (1 eq., 33 mg, 0.1 mmol) and 1-hydroxybenzotriazole hydrate (1 eq., 13.5 mg, 0.1 mmol) in ethyl acetate (1 mL) under argon, at 0 ºC, thiophenol (2 eq., 20 µL, 0.2 mmol) was added. After 5 min, dicyclohexylcarbodiimide (1.1 eq., 23 mg, 0.11 mmol) was added. After stirring overnight, a 50% solution of acetic acid in ethyl acetate (0.3 mL) was added. The reaction mixture was filtered throughouth a pad of celite and solvent was removed under vacuum. The residue was purified by flash column chromatography on silica gel (eluting with Hexane/ AcOEt 80:20) to give the title compound **11** as a white solid. Yield: 36.3 mg, 0.086 mmol, 86%. $[\alpha]_D^{25}$= –38.8° (c= 0.5, 98% *ee*, CH_2Cl_2). m.p. 152–153 ºC. ^1H NMR (300 MHz, $CDCl_3$), δ: 8.30 (d, *J* = 8.8 Hz, 2H), 7.70 (d, *J* = 8.7 Hz, 2H), 7.49–7.30 (m, 3H), 7.03–6.93 (m, 2H), 4.58–4.41 (m, 2H), 4.37–4.24 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$), δ: 195.0, 148.2, 141.5, 135.7, 134.1, 129.9, 129.6, 129.3, 129.1, 128.6, 128.2, 126.1, 124.5, 77.8, 62.0, 47.3. UPLC-DAD-QTOF: $C_{22}H_{17}N_2O_5S$ $[M–H]^-$ calcd.: 421.0858, found: 421.0858. The enantiomeric purity was determined by HPLC analysis (Daicel Chiralpak AD-H, hexane/isopropanol 80/20, flow rate = 1.0 mL/min, retention times: major diastereomer: 13.6 min (minor) and 17.4 min (major)); minor diastereomer: 15.6 min (major) and 24.6 min (minor)).

8.2. Nef reaction in adduct 9Aa to yield carboxylic acid 23[16]



9Aa **23**

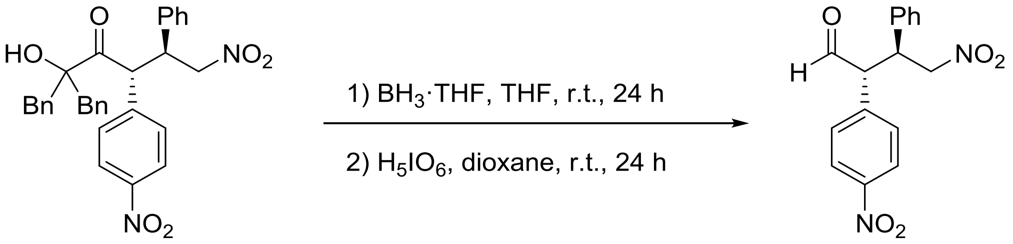
A solution of 2-benzyl-2-hydroxy-6-nitro-4-(4-nitrophenyl)-1,5-diphenylhexan-3-one (**9Aa**) (104.9 mg, 0.2 mmol, 1 eq.), $NaNO_2$ (82.8 mg, 1.2 mmol, 6 eq.) and AcOH (120.1 mg, 2 mmol, 10 eq.) in DMSO (2 mL) was stirred overnight at 35 ºC. The reaction mixture was poured into H_2O (20 mL) and extracted with EtOAc (3 x 20 mL). The combined organic layers were washed successively with brine (20 mL), dried over Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by silica gel chromatography (eluting with hexane/ AcOEt 90:10 → 70:30). Yield 36.7 mg, 0.072 mmol, 36%. $[\alpha]_D^{25}$= –30.3° (c= 0.40, 99% *ee*, CH_2Cl_2). m.p. 169–170 ºC. ^1H NMR (300 MHz, (CD_3OD), δ: 7.77 (d, *J* = 8.8 Hz, 2H), 7.63 (d, *J* = 7.2 Hz, 2H), 7.53–7.28 (m, 4H), 7.27–7.15 (m, 5H), 6.85–6.62 (m,7H), 5.51 (d, *J* = 12.0 Hz, 1H), 4.40 (d, *J* = 12.0 Hz, 1H), 2.82 (d, *J* = 13.5 Hz, 1H), 2.36 (d, *J* =

---

[16] Addapted from: Gong, L., *Adv. Synth. Catal.* **2013**, *355*, 2531-2537

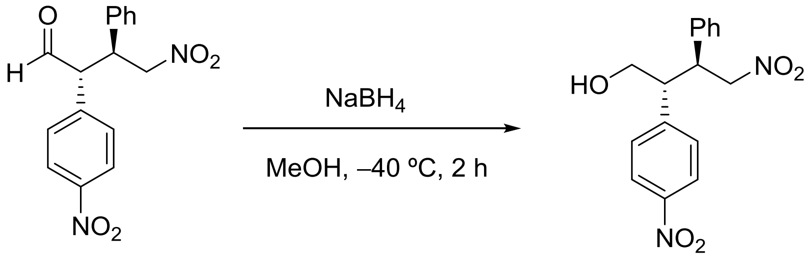
13.5 Hz, 1H), 2.27 (d, *J* = 13.5 Hz, 1H), 2.08 (d, *J* = 13.5 Hz, 1H).^{13}C NMR (75 MHz, CD_3OD), δ: 211.0, 175.1, 147.9, 143.4, 138.8, 137.3, 136.4, 134.0, 132.0, 131.7, 131.4, 130.7, 130.5, 129.8, 129.4, 129.1, 128.9, 128.3, 127.6, 126.6, 123.9, 84.7, 56.6, 56.1, 45.7, 43.7.UPLC-DAD-QTOF: $C_{31}H_{27}NO_6Na$ $[M+Na]^+$ calcd.: 532.1736, found: 532.1732.

8.3 Conversion of 9Aa into aldehyde 24 and alcohol 25



9Aa **24**

To a suspension of **9Aa** (1 eq., 105 mg, 0.2 mmol) in tetrahydrofuran (2 mL), borane tetrahydrofuran solution complex 1.0 M (4 eq., 0.8 mL, 0.8 mmol) was added. The resulting mixture was stirred at room temperature for 24 h and afterwards methanol (1 mL) was added at 0 ºC and the solvent was evaporated. The resulting crude material was suspended in dioxane (4 mL), periodic acid (10 eq., 456 mg, 2 mmol) was added and the mixture was stirred at room temperature for 24 h. The reaction was quenched with water (10 mL) and extracted with ethyl acetate (3 x 10 mL). The combined organic extracts were dried over $MgSO_4$, filtered and the solvent was evaporated. The crude product was crushed with diethyl ether to give the title compound **24** as a white solid. Yield 42.2 mg, 0.13 mmol, 67%. $[\alpha]_D^{25}$= –9.9° (c= 0.40, 99% *ee*, CH_2Cl_2). m.p. 140–142 ºC. ^{1}H NMR (300 MHz, $CDCl_3$), δ: 8.30 (d, *J* = 8.8 Hz, 2H), 7.46 (d, *J* = 8.8 Hz, 2H), 7.42–7.31 (m, 3H), 7.30–7.21 (m, 2H), 4.63–4.40 (m, 2H), 4.34–4.20 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$), δ: 196.2, 148.1, 140.0, 135.8, 130.4, 129.4, 128.7, 128.1, 124.6, 77.8, 60.1, 45.0. UPLC-DAD-QTOF: $C_{16}H_{13}N_2O_5$ $[M–H]^-$ calcd.: 313.0824, found: 313.0821.

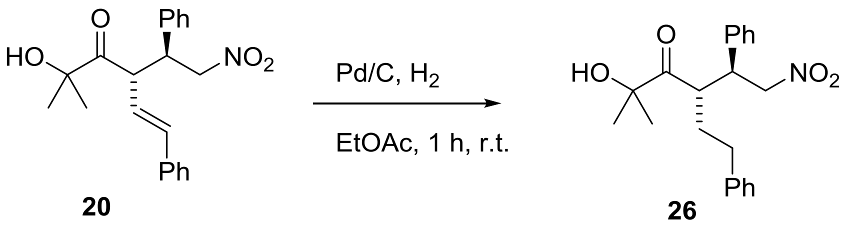


24 **25**

A solution of aldehyde, 4-nitro-2-(4-nitrophenyl)-3-phenylbutanal (**24**) (62.9 mg, 0.2 mmol, 1 eq.), $NaBH_4$ (15.1 mg, 0.4 mmol, 2 eq.) in MeOH (0.4mL) was stirred overnight at –40 ºC during 2 h. Then the reaction was quenched with NH4Cl and extracted with DCM (3 x 2 mL). The combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure. The crude product was purified by silica gel chromatography (eluting with hexane/ AcOEt 90:10). Orange solid, yield 50.6 mg, 0.16 mmol, 80%. $[\alpha]_D^{25}$= +3.21° (c= 0.51, 99% *ee*, CH_2Cl_2). m.p. 128–129 ºC. ^{1}H NMR (300 MHz, (CDCl3), δ: 8.31 (d, *J* = 8.8 Hz, 2H), 7.60 (d, *J* = 8.8 Hz, 2H), 7.48–7.31 (m, 5H), 4.58 (dd, *J* = 12.6, 10.5 Hz, 1H), 4.43–4.31 (m, 1H), 4.00 (td, *J* = 10.6, 4.5 Hz, 1H), 3.68 (d, *J* = 5.6 Hz, 2H), 3.26 (dt, *J* = 10.6, 5.1 Hz, 1H). ^{13}C NMR (75 MHz, CD_3OD), δ: 147.9, 137.3, 129.7, 128.9, 128.3, 124.7, 79.6, 64.5, 51.1, 46.5. UPLC-DAD-QTOF: $C_{16}H_{15}N_2O_5$ [M-H]$^-$ calcd.: 315.0981, found: 315.0976.

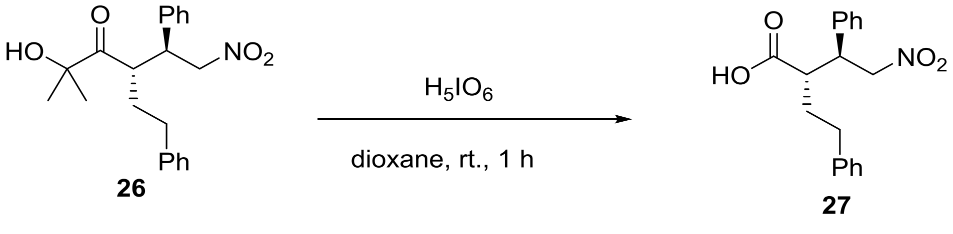
8.4 Hydrogenation of 20 to 26 and subsequent ketol cleavage (27 and 28)

(*S*)-2-hydroxy-2-methyl-4-((*S*)-2-nitro-1-phenylethyl)-6-phenylhexan-3-one (26)



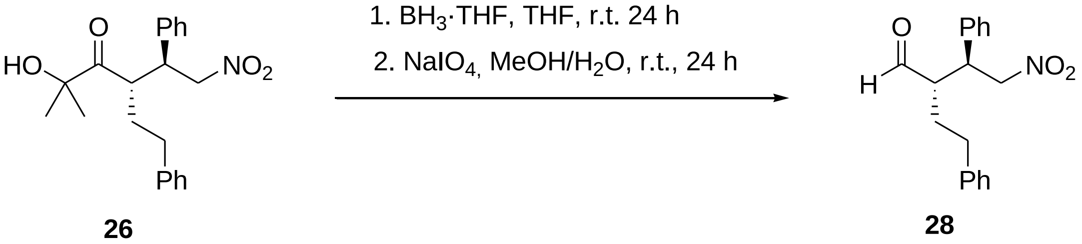
To a solution of (*S*,*E*)-2-hydroxy-2-methyl-4-((*S*)-2-nitro-1-phenylethyl)-6-phenylhex-5-en-3-one **20** (206.6 mg, 0.58 mmol) in dry EtOAc (20 mL), Pd/C (Pd 10% in activated carbon) was added (21 mg). The air was evacuated by vacuum and H_2 was introduced (this process was carried out three times). The reaction mixture was stirred under H_2 atmosphere at room temperature for 1 h. Then, the mixture was filtered over celite and the filtrate was concentrated under reduced pressure to afford the hydrogenated product as a solid.

Yield: 196 mg (95%). $[\alpha]_D^{25}$= +5.5° (c= 0.32, 94% *ee*, CH_2Cl_2). m.p. 94–96 ºC. ^{1}H NMR (300 MHz, ($CDCl_3$), δ: 7.41–7.19 (m, 8H), 7.14–7.06 (m, 2H), 4.90–4.76 (m, 2H), 4.09–4.01 (m, 1H), 3.70–3.64 (m, 1H), 2.64–2.39 (m, 2H), 2.12–1.97 (m, 1H), 1.96–1.81 (m, 1H), 1.30 (s, 1H), 1.25 (s, 3H), 1.18 (s, 3H). ^{13}C NMR (75 MHz, CD_3OD), δ: 215.3, 140.6, 138.0, 129.0, 128.6, 128.1, 128.0, 128.0, 126.3, 75.9, 48.7, 44.2, 33.2, 29.8, 26.6. UPLC-DAD-QTOF: $C_{21}H_{25}NO_4Na$ [M+Na]$^+$ calcd.: 378.1681, found: 378.1686.



To a suspension of **26** (1 eq., 49 mg, 0.12 mmol) in dioxane (3 mL), periodic acid (10 eq., 274 mg, 1.2 mmol) was added. The resulting mixture was stirred at room temperature for 1 h and afterwards the reaction was quenched with water (5 mL) and extracted with ethyl acetate (3 x 5 mL). The combined organic extracts were dried over $MgSO_4$, filtered and the solvent was evaporated to give the title compound **27** as an orange oil. Yield: 34.9 mg, 0.11 mmol, 93%.

^{1}H NMR (300 MHz, CD_3OD), δ: 7.38–7.14 (m, 10H), 4.91–4.69 (m, 2H), 3.90–3.82 (m, 1H), 2.92–2.52 (m, 3H), 2.11–1.98 (m, 1H), 1.93–1.82 (m, 1H). ^{13}C NMR (75 MHz, CD_3OD), δ: 177.9, 139.9, 135.8, 128.2, 127.9, 127.7, 127.6, 127.3, 125.7, 77.0, 47.4, 44.9, 32.8, 30.6. UPLC-DAD-QTOF: $C_{18}H_{19}NO_4Na$ $[M+Na]^+$ calcd.: 336.1212, found: 336.1215.



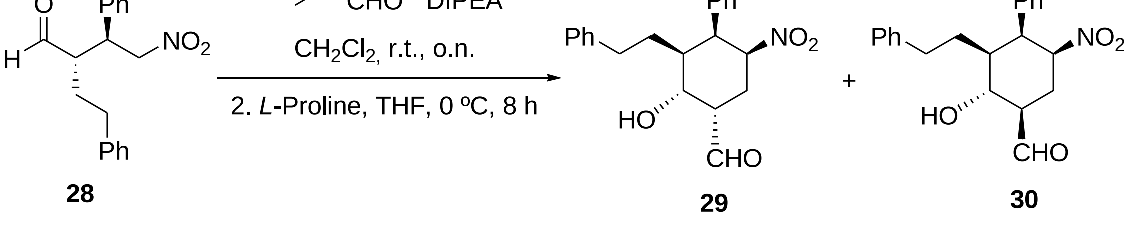
(2*S*, 3*S*)-4-Nitro-2-phenethyl-3-phenylbutanal (28)

BH_3·THF complex (1 M, 1.5 mL, 1.5 mmol) was added to a solution of α-hydroxy ketone **26** (178 mg, 0.5 mmol) in dry THF (1.5 mL) at 0 °C and the resulting solution was stirred at room temperature for 24 h. Then MeOH (2.5 mL) was added and the resulting mixture was stirred at room temperature for 30 min. The solvents were removed under reduced pressure and the residue thus obtained was subjected to oxidative scission by treatment with $NaIO_4$.

A suspension of sodium periodate $NaIO_4$ (535 mg, 2.5 mmol) in water (1.25 mL) was added to a solution of the corresponding diol (0.5 mmol) in methanol (2.5 mL). The mixture was stirred overnight at room temperature. Then the solvent was removed under reduced pressure. Water (4.5 ml) was added to the crude product and the resulting mixture was extracted with Et_2O (3 x 6 mL) and CH_2Cl_2 (2 x 6 mL). The combined organic extracts were dried over $MgSO_4$, filtered and the solvent was evaporated to afford the corresponding aldehyde. The crude product was purified by flash column chromatography on silicagel (eluting with hexane/ethyl acetate 1/20) to afford a colorless oil.

Yield: 110 mg (74%). ^{1}H NMR (400 MHz, ($CDCl_3$)), δ: 9.54 (d, *J* = 2.8 Hz, 1H), 7.36–7.14 (m, 10H), 4.80 (dd, *J* = 6.8, 13.2 Hz, 1H), 4.76 (dd, *J* = 8.4, 13.2 Hz, 1H), 3.85 (dt, *J* = 6.8, 8.4 Hz, 1H), 2.75–2.60 (m, 1H), 2.64–2.39 (m, 3H), 2.06 (m, 1H), 1.90 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$), δ: 202.9, 140.3, 136.0, 135.9, 129.2, 128.7, 128.3, 128.2, 126.5, 77.7, 52.7, 44.5, 33.2, 29.2. UPLC-DAD-QTOF: $C_{18}H_{19}NO_3Na$ $[M+Na]^+$ calcd.: 320.1263, found: 320.1272.

8.5 Michael-aldol reaction of 28 with acrolein (cycloadducts 29 and 30)



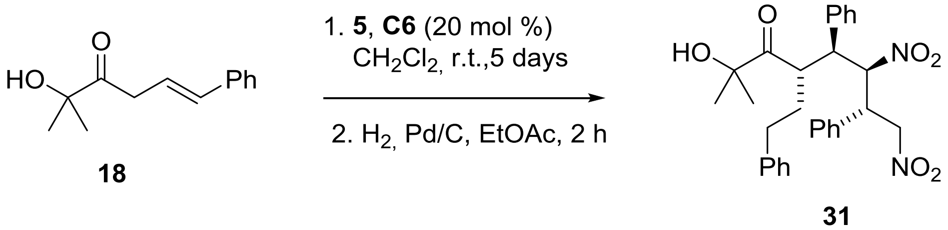
(1*S*,2*R*,3*S*,4*S*,5*S*)-2-Hydroxy-5-nitro-3-phenethyl-4-phenylcyclohexanecarbaldehyde (29)

DIPEA (10.2 μL, 0.06 mmmol) was added to a solution of aldehyde **28** (59.4 mg, 0.2 mmol) and acrolein (26.6 μL, 0.4 mmol) in CH_2Cl_2 (0.8 mL) and the solution was stirred overnight at room temperature. CH_2Cl_2 (5 mL) was added and the mixture was washed with 1 M HCl (5 mL). The organic extract was dried over $MgSO_4$, filtered and the solvent was evaporated to afford the corresponding dialdehyde. The crude product was used in the next step. ^{1}H NMR (400 MHz, ($CDCl_3$), δ: 9.68 (s, 1H), 9.61 (d, J = 2.4 Hz, 1H), 7.40–7.13 (m, 10H), 5.28 (m, 1H), 3.52 (dd, *J* = 5.6, 10.4 Hz, 1H), 2.65 (m, 2H), 2.53 (m, 1H), 2.48 (t, *J* = 6.8 Hz, 2H), 1.94 (m, 1H), 1.90 (t, *J* = 6.8 Hz, 2H), 1.74 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$), δ: 203.0, 199.3, 140.5, 134.4, 129.3, 129.2, 128,6, 128,5, 128,4, 126.4, 88.8, 51.6, 51.0, 39.5, 33.3, 29.6, 24.4.

L-Proline (2.1 mg, 0.02 mmol) was added to a solution of dialdehyde in THF (0.4 mL) at 0 °C and the mixture was stirred at the same temperature for 8 h. CH_2Cl_2 (5 mL) was added and the mixture was washed with water (2 x 5 mL). The organic extract was dried over $MgSO_4$, filtered and the solvent was evaporated to afford the corresponding cyclohexanecarbaldehyde epimers **29** and **30** in a ratio 90:10 respectively. Each isomer was separated as colorless oil by a quick flash column chromatography on silica gel (eluting with hexane/ethyl acetate 1:1). The product was unstable at room temperature and was stored at –30 °C. Yield: 49.5 mg (70%, two steps, both isomers). Major isomer **29**: ^{1}H NMR (400 MHz, ($CDCl_3$), δ: 10.04 (s, 1H), 7.35–6.98 (m, 10H), 4.91 (dt, *J* = 6.0, 11.6 Hz, 1H), 4.50 (dd, *J* = 6.0, 10.8 Hz, 1H), 4.00 (t, *J* = 5.6 Hz, 1H), 3.36 (dt, *J* = 4.4, 5.6 Hz, 1H), 2.67 (m, 1H), 2.60 (m, 2H), 2.50 (m, 1H), 2.15–2.00 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$), δ: 204.5, 141.4, 134.3, 130.4, 128.8, 128.6, 128.4, 128.2, 126.0, 82.8, 70.1, 50.2, 47.7, 44.2, 33.0, 30.5, 23.1. UPLC-DAD-QTOF: $C_{21}H_{23}NO_4Na$ $[M+Na]^+$ calcd.: 376.1525, found: 376.1527. Minor isomer **30**: ^{1}H NMR (400 MHz, ($CDCl_3$), δ: 9.92 (s, 1H), 7.36–7.00 (m, 10H), 4.83 (ddd, *J* = 4.4, 5.6, 12.0 Hz, 1H), 4.33 (t, *J* = 10.4 Hz, 1H), 4.06 (t, *J* = 5.6 Hz, 1H), 2.70–2.66 (m, 1H), 2.57–2.38 (m, 4H), 2.17 (m, 1H), 2.00 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$), δ: 202.7, 141.4, 133.6, 130.6, 128.9, 128.4, 128.3, 128.2, 126.0, 85.6, 68.8, 54.2, 47.9, 45.5, 32.8, 30.2, 23.0. UPLC-DAD-QTOF: $C_{21}H_{23}NO_4Na$ $[M+Na]^+$ calcd.: 376.1525, found: 376.1527.

8.6 Double Michael-Henry approach to cycloadducts 33 and 34 from 18

(4S,5S,6R,7S)-2-Hydroxy-2-methyl-6,8-dinitro-4-phenethyl-5,7-diphenyloctan-3-one (31)



18

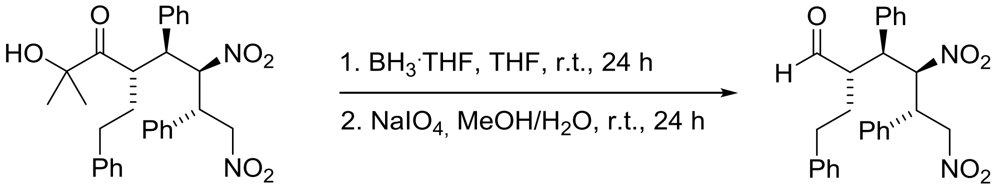
31

1) To a solution of hydroxyketone **18** (40.9 mg, 0.2 mmol, 1 equiv.) and trans-β-nitrostyrene (89.5 mg, 0.6 mmol, 3 equiv.) in dichloromethane (0.4 ml), catalyst **C6** (23.8 mg, 0.04 mmol, 20 mol %) was added at room temperature and the resulting mixture was stirred to completion of the reaction (5 days). When the reaction was finished, the mixture was directly submitted to flash column chromatography (hexane/ethyl acetate 90:10). The organic solvent

evaporation yielded the double addition product 2-hydroxy-2-methyl-6,8-dinitro-5,7-diphenyl-4-(styryl)octan-3-one. White solid, yield: 75.4 mg, 0.15 mmol, 78%. Decomp. temp. 185–187 ºC. ^{1}H NMR (500 MHz, $CDCl_3$), δ: 7.48 (t, *J*= 7.3 Hz, 2H), 7.41 (t, *J*= 7.3 Hz, 1H), 7.36–7.29 (m, 7H), 7.27–7.24 (m, 3H), 7.03–6.95 (m, 2H), 6.65 (d, *J*= 15.8 Hz, 1H), 5.80 (dd, *J*= 15.8, 9.9 Hz, 1H), 5.10 (dd, *J*= 10.6, 4.0 Hz, 1H) 5.00–4.83 (m, 2H), 4.52 (t, *J*= 10.2 Hz, 1H), 4.14 (t, *J*= 10.5 Hz, 1H), 3.77 (dt, *J*= 11.0, 3.6 Hz, 1H), 2.46 (s, 1H), 0.94 (s, 3H), 0.89 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$), δ: 211.2, 136.8, 136.6, 135.6, 134.6, 129.8, 129.3, 129.0, 128.7, 128.8, 128.5, 128.3, 127.1, 126.5, 122.6, 93.7, 77.6, 73.4, 56.6, 47.9, 44.0, 26.8, 26.3. UPLC-DAD-QTOF: $C_{29}H_{30}N_2O_6Na$ $[M+Na]^+$ calcd.: 525.2002, found: 525.2007.

2) This product was dissolved in dry EtOAc (40 ml) and Pd/C (Pd 10% in activated carbon) was added (10.1 mg). The air was evacuated by vacuum and H_2 was introduced (this process was carried out three times). The reaction mixture was stirred under H_2 atmosphere at room temperature for 2 h. Then, the mixture was filtered over celite and the filtrate was concentrated under reduced pressure to afford the hydrogenated product **31** as an oil. Yield: 70.6 mg (70%). $[\alpha]_D^{24} = +13.9^o$ (c= 0.5, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49–7.05 (m, 15H), 5.49 (dd, *J* = 11.2 Hz, 3.6 Hz, 1H), 5.02 (dd, *J*= 14.0, 11.2 Hz, 1H), 4.88 (dd, *J*= 14.0, 3.6 Hz, 1H), 3.93 (dd, *J*= 11.2, 5.2 Hz, 1H), 3.84 (dt, *J*= 10.8, 3.4 Hz, 1H), 3.71–3.67 (m, 1H), 3.00 (sb, 1H), 2.56–2.42 (m, 2H), 2.23–2.12 (m, 1H), 1.87–1.75 (m, 1H), 1.22 (s, 3H), 1.21 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 214.8, 141.0, 136.3, 135.1, 129.5, 129.4, 128.9, 128.7, 128.5, 128.4, 127.2, 126.2, 93.0, 73.5, 48.9, 47.8, 43.9, 33.3, 30.4, 28.1, 27.1. UPLC-DAD-QTOF: $C_{29}H_{36}N_3O_6$. $[M+NH_4]^+$ calcd.: 522.2604, found: 522.2611.

(2S,3S,4R,5S)-4,6-Dinitro-2-phenethyl-3,5-diphenylhexanal (32)



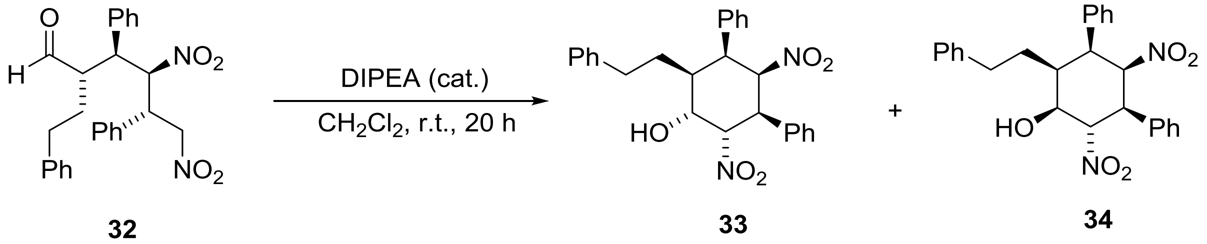
31 **32**

$BH_3\cdot THF$ complex (1 M, 1.5 mL, 1.5 mmol) was added to a solution of α-hydroxy ketone **31** (252 mg, 0.5 mmol) in dry THF (1.5 mL) at 0 °C and the resulting solution was stirred at room temperature for 24 h. Then MeOH (2.5 mL) was added and the resulting mixture was stirred at room temperature for 30 min. The solvents were removed under reduced pressure and the residue thus obtained was subjected to oxidative scission by treatment with $NaIO_4$.

A suspension of sodium periodate $NaIO_4$ (535 mg, 2.5 mmol) in water (1.25 mL) was added to a solution of the corresponding diol (0.5 mmol) in methanol (2.5 mL). The mixture was stirred overnight at room temperature. Then the solvent was removed under reduced pressure. Water (4.5 ml) was added to the crude product and the resulting mixture was extracted with Et_2O (3 x 6 mL) and CH_2Cl_2 (2 x 6 mL). The combined organic extracts were dried over

$MgSO_4$, filtered and the solvent was evaporated to afford the corresponding aldehyde. The crude product was purified by flash column chromatography on silicagel (eluting with hexane/ethyl acetate 1/20) to afford the tittle product as a colorless oil. Yield: 179 mg (80%). $[\alpha]_D^{23}$ = +16.4° (c= 0.5, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$) δ 9.58 (dd, *J* = 2.0 Hz, *J'* = 0.8 Hz, 1H), 7.49–6.98 (m, 15H), 5.62 (dd, *J* = 11.6 Hz, *J'* = 3.6 Hz, 1H), 5.02 (dd, *J* = 14.0 Hz, *J'* = 11.0 Hz, 1H), 4.83 (dd, *J* = 4.2 Hz, 1H), 2.74–2.60 (m, 2H), 2.47–2.42 (m, 1H), 2.01–1.92 (m, 1H), 1.75–1.66 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 203.0, 140.2, 134.9, 133.3, 129.9, 129.5, 129.3, 129.2, 129.0, 128.7, 128.4, 127.1, 126.5, 92.9, 73.6, 51.2, 49.3, 43.5, 33.5, 29.7. UPLC-DAD-QTOF: $C_{26}H_{26}N_2NaO_5$. $[M+Na]^+$ calcd.: 469.1739, found: 469.1730.

(1R,2S,3R,4R,5S,6S)-2,4-Dinitro-6-phenethyl-3,5-diphenylcyclohexanol (33)

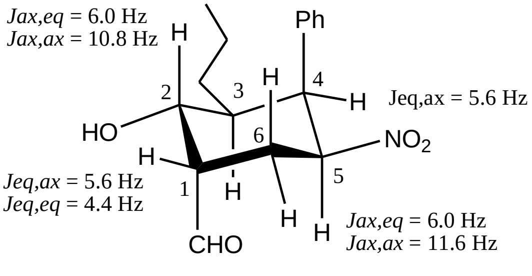


DIPEA (3.5 μL, 0.02 mmol) was added to a solution of aldehyde **32** (44.6 mg, 0.1 mmol) in CH_2Cl_2 (2 mL) at 0 °C and the resulting mixture was stirred at room temperature for 20 h. CH_2Cl_2 (5 mL) was added and the mixture was washed with 1M HCl (5 mL). The organic extract was dried over $MgSO_4$, filtered and the solvent was evaporated to afford the corresponding cyclohexanols epimers **33** and **34** in a ratio 92:8 respectively. The mayor isomer was separated as a white solid by a quick flash column chromatography on silicagel (eluting with hexane/ethyl acetate 20:1). Yield: 37 mg (82%). m.p.= 191–193 ºC. $[\alpha]_D^{25}$ = –38.3° (c= 0.65, CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$) δ 7.38–7.05 (m, 15H), 6.17 (dd, *J* = 12.6 Hz, *J'* = 2.2 Hz, 1H), 5.26 (t, *J* = 5.2 Hz, 1H), 4.74 (t, *J* = 2.4 Hz, 1H), 4.42 (dd, *J* = 12.4 Hz, *J'* = 5.2 Hz, 1H), 4.03 (t, *J* = 5.2 Hz, 1H), 2.81–2.74 (m, 1H), 2.56–2.48 (m, 1H), 2.47–2.42 (m, 1H), 2.22-2.09 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.5, 136.3, 133.8, 129.3, 129.0, 128.8, 128.5, 128.4, 128.3, 127.9, 127.2, 126.2, 91.6, 83.5, 71.1, 45.4, 42.4, 42.1, 35.4, 27.6. UPLC-DAD-QTOF: $C_{26}H_{30}N_3O_5$. $[M+NH_4]^+$ calcd.: 464.2185, found: 464.2190.

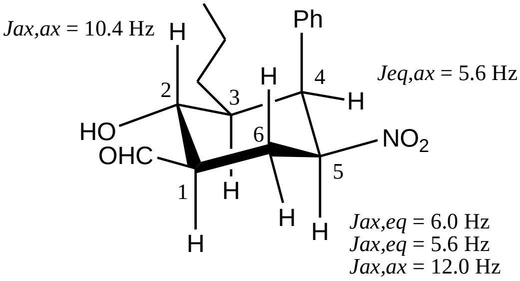
9. Stereochemical determinations

Diastereomeric ratios (*dr*’s) were determined by ^{1}H NMR (300Hz) spectroscopy analysis of the respective crude reaction product. Diastereomeric ratio *dr* ≥ 95:5 denotes that no peaks assignable to any additional stereisomer appear within the ^{1}H NMR limit of detection. Enantioselectivities (*ee*’s) were determined by HPLC using chiral columns as specified for each entry. Both the absolute and relative configurations of adduct **9Ab** were established by X-Ray structure analysis. Configuration of the remaining adducts was assigned by analogy and by assuming a uniform reaction mechanism.

The stereochemistry of cyclic products **29**/**30** and **33**/**34** could be primarily assigned by ^{1}H-NMR taking into account the known configurations *R* and *S* for carbons C3 and C4, respectively, and then the configuration of **33** was unequivocally assigned by X-Ray analysis. Initial assignment was made based on the coupling constants measured among the skeletal protons, applying the following rules for cyclohexane skeleton: $J_{ax,ax}$ = 8–13 Hz, $J_{eq,ax}$ and $J_{eq,eq}$ = 2–6 Hz. Thus, in the spectrum of major isomer **29**, the H2 proton (4.50 ppm) gives a well-resolved doublet of doublet signal with coupling constants (ca. 6 Hz and 11 Hz) referring to a relative 1,2-*diequatorial* relationship for the hydroxyl and phenethyl groups and a relative *axial-equatorial* relationship for the formyl and hydroxyl groups, respectively. In the spectrum of minor isomer **30**, the H2 proton (4.33 ppm) gives a well-resolved triplet signal with coupling constant (ca. 10 Hz) referring to a relative 1,2-*diequatorial* relationship for the hydroxyl group and both phenethyl and formyl groups. On the other hand, a coupling constant of 12 Hz of the proton H5 in both isomers **29** and **30** (4.91 ppm and 4.83 ppm respectively) indicates a relative *equatorial* relationship for the nitro group in both cases. Finally, the two small coupling constants (5.6 and 4.4 Hz) of the H1 signal in **29** (3.36 ppm) fit well with an *axial* position for formyl group. Any other conformation and configuration do not fit well the observed ^{1}H-NMR coupling constants.



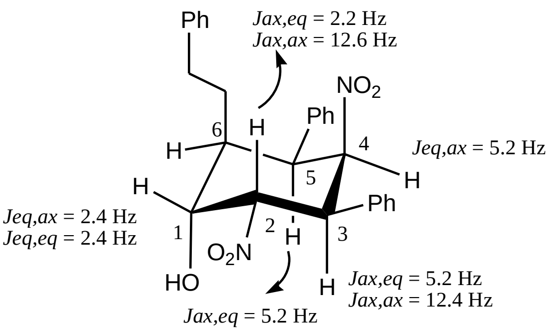
Major isomer 29



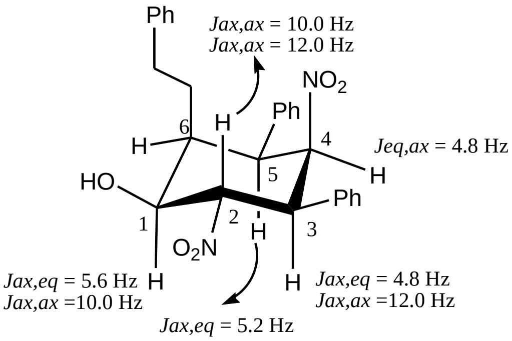
Minor isomer 30

The stereochemistry of major and minor isomers **33** and **34**, respectively, was initially assigned following a similar reasoning, based on the measured coupling constants pattern.

Accordingly, both products **33** and **34** would present a diferente conformational bias as compared with **29**/**30**. Both structures and the relevant coupling constant values are shown below.



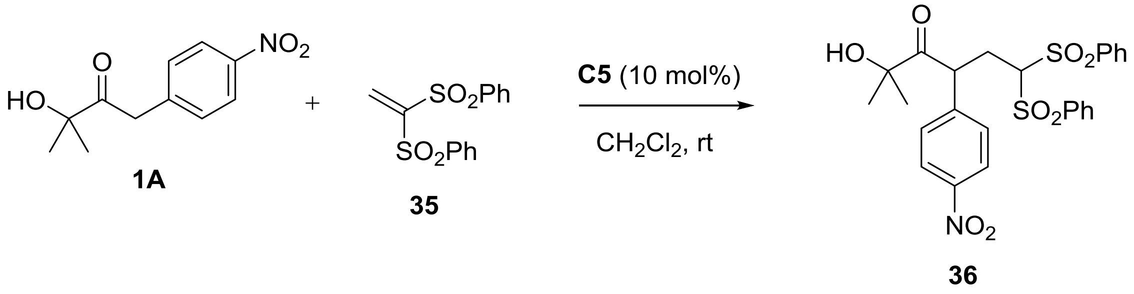
Major isomer 33



Minor isomer 34

The stereochemistry of product **33** was unequivocally determined by a single crystal X-ray structure determination (see section 13, page S137).

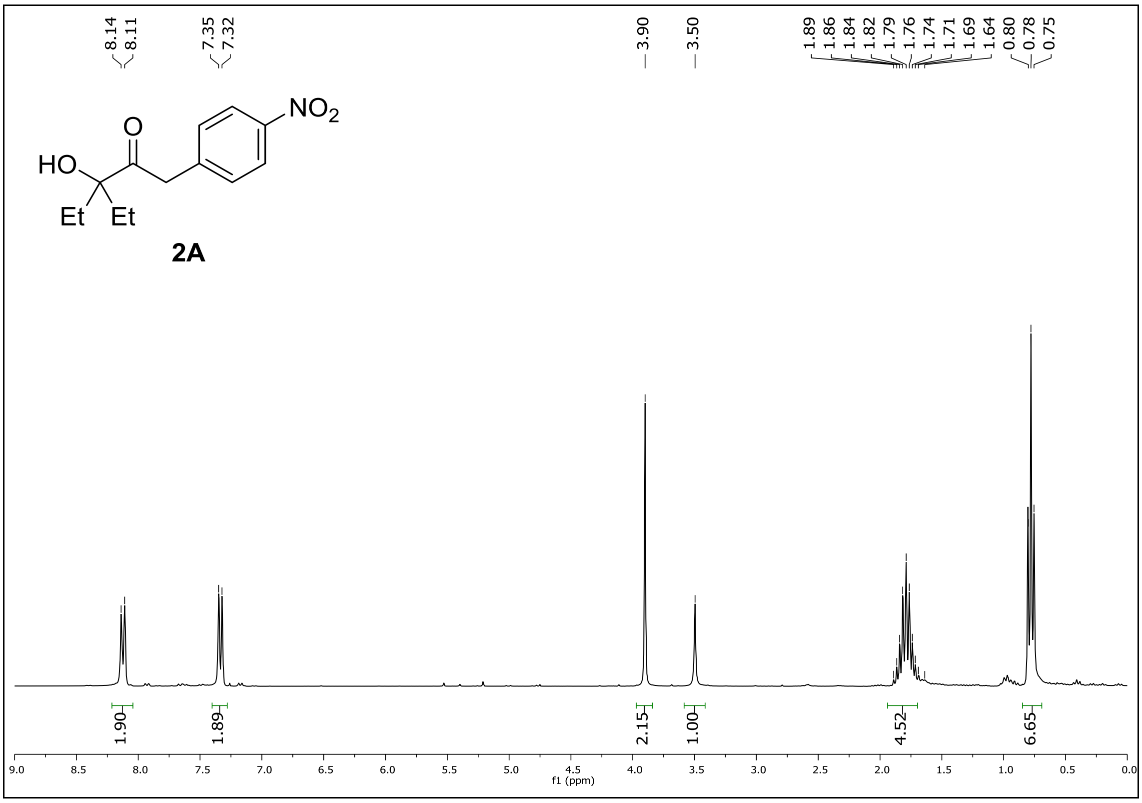
10. Catalytic reaction of α-hydroxy ketone 1A with vinyl 1,1-bis(sulfone) 35.

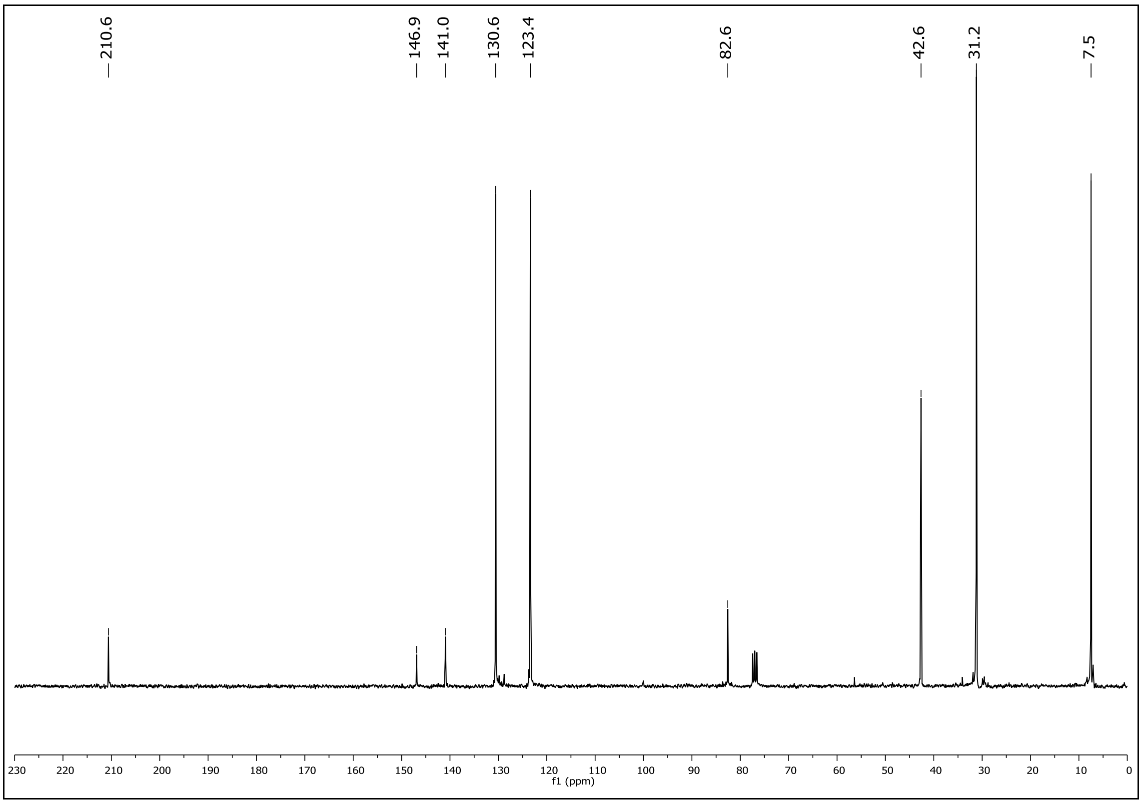


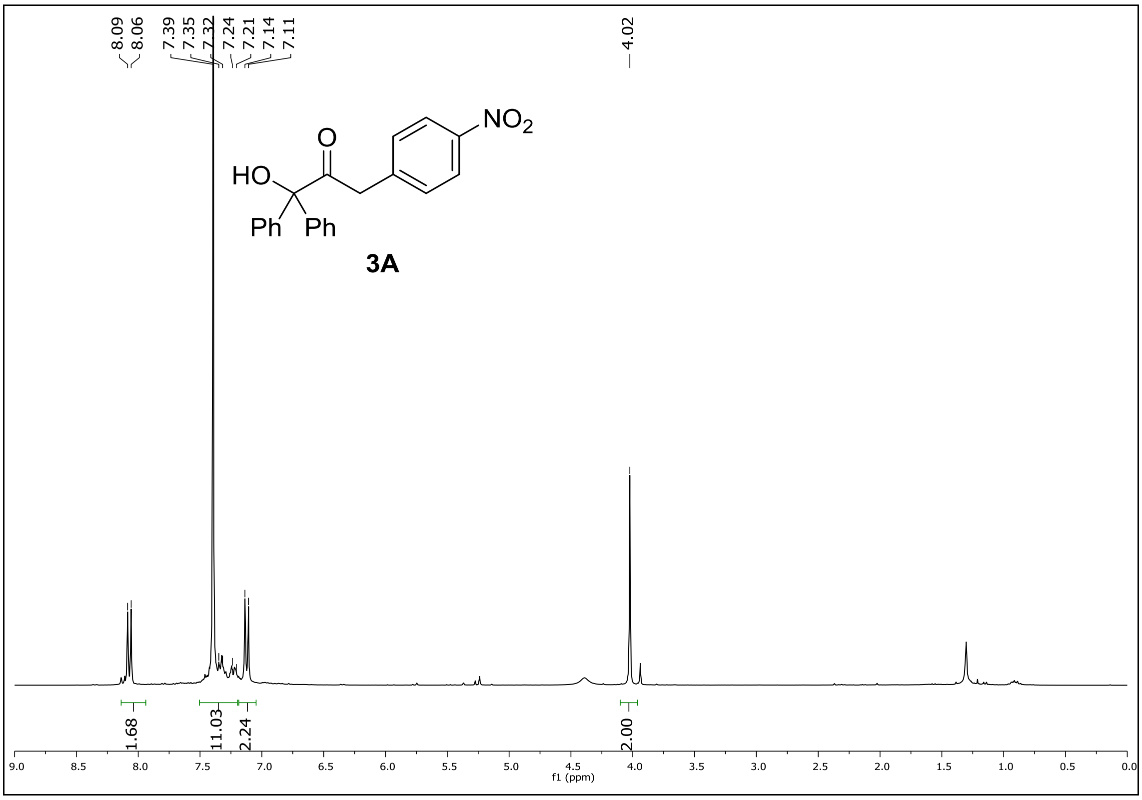
To a mixture of α-hydroxy ketone **1A** (22.3 mg, 0.1 mmol) and 1,1-bis(phenylsulfonyl)ethylene **35** (92.5 mg, 3.0 eq., 0.3 mmol) in dichloromethane (0.3 mL) at room temperature, catalyst **C5** (5.9 mg, 10 mol %, 0.01 mmol) was added. The resulting suspension was stirred at room temperature, until consumption of the α-hydroxyketone as monitored by ^{1}H NMR (40 h). The mixture was quenched with HCl 2M (1 mL) and extracted with CH_2Cl_2 (3 x 2 mL). The combined organic layers were dried over $MgSO_4$, filtered and the solvent was evaporated under reduced pressure. The residue was purified by flash column chromatography on silica gel (eluent Hexane/AcOEt 90:10 → 70:30) to afford the desired product. (2-Hydroxy-2-methyl-4-(4-nitrophenyl)-6,6-bis(phenylsulfonyl)hexan-3-one, **36**). White foam, yield: 47.8 mg, 0.090 mmol, 90%. ^{1}H NMR (300 MHz, $CDCl_3$), δ: 8.08 (d, *J* = 8.8 Hz, 2H), 7.95–7.87 (m, 2H), 7.78–7.68 (m, 4H), 7.63–7.49 (m, 4H), 7.31 (d, *J* = 8.7 Hz, 2H), 5.18 (t, *J* = 7.7 Hz, 1H), 4.13–4.02 (m, 1H), 2.73 (s, 1H), 2.70–2.59 (m, 2H), 1.28 (s, 3H), 1.27 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$), δ: 212.2, 147.5, 143.2, 140.4, 137.6, 137.0, 135.0, 134.9, 129.5, 129.3, 129.3, 128.5, 124.2, 80.2, 77.9, 48.4, 29.8, 27.2, 26.6. UPLC-DAD-QTOF: $C_{25}H_{29}N_2O_8S_2$ $[M+NH_4]^+$ calcd.: 549.1365, found: 549.1368.

The enantiomeric purity was determined to be 38% *ee* by HPLC analysis (Daicel Chiralpak IA, hexane/isopropanol 50/50, flow rate= 1.0 mL/min, retention times: 8.4 min (major) and 10.5 min (minor)).

11. NMR Spectra

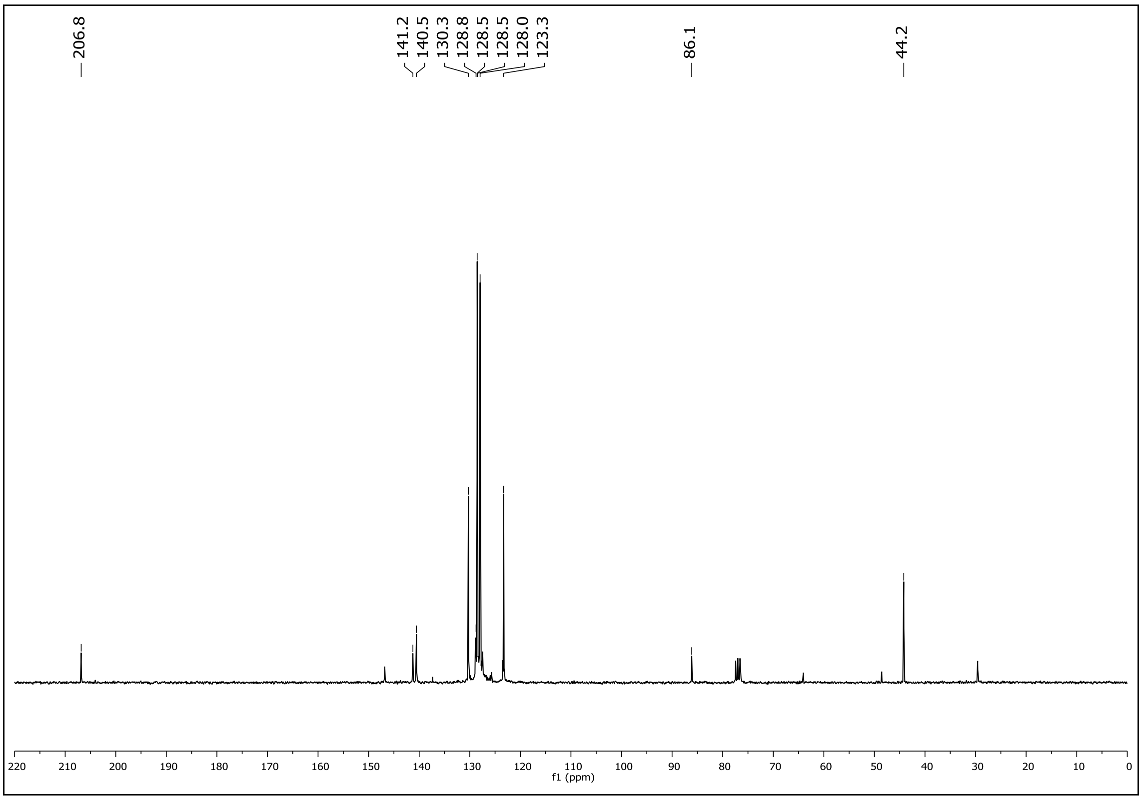




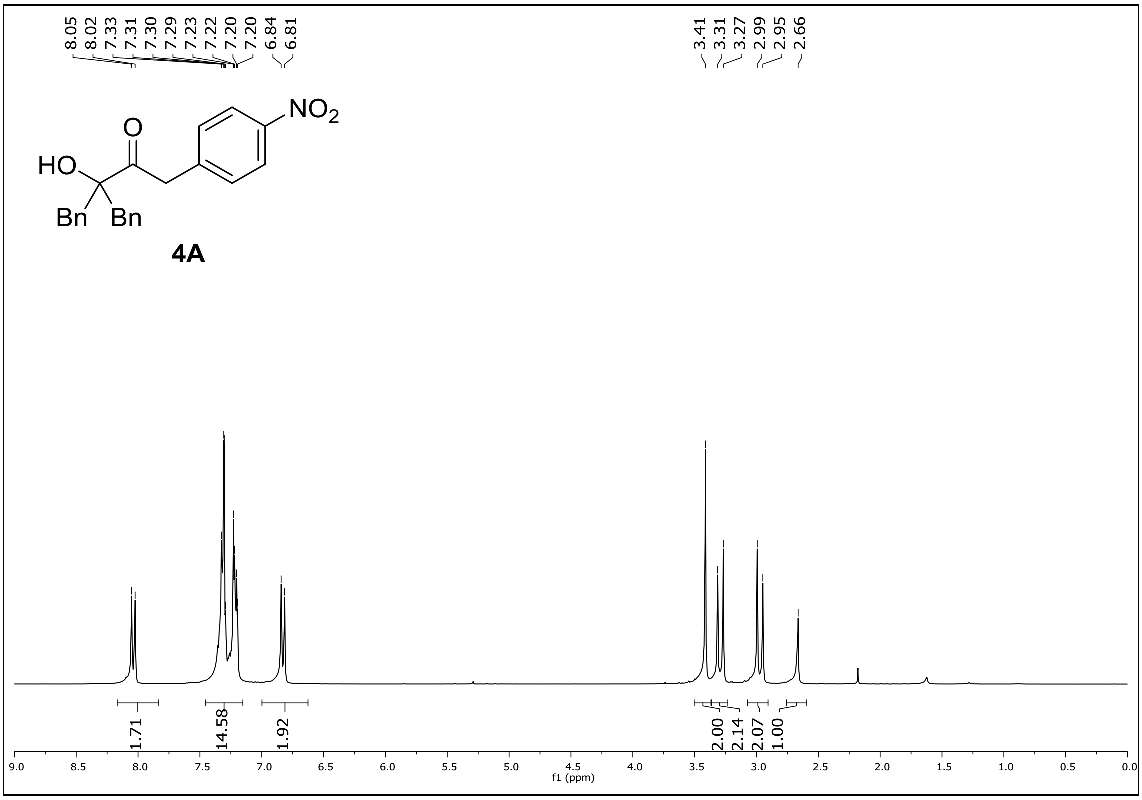


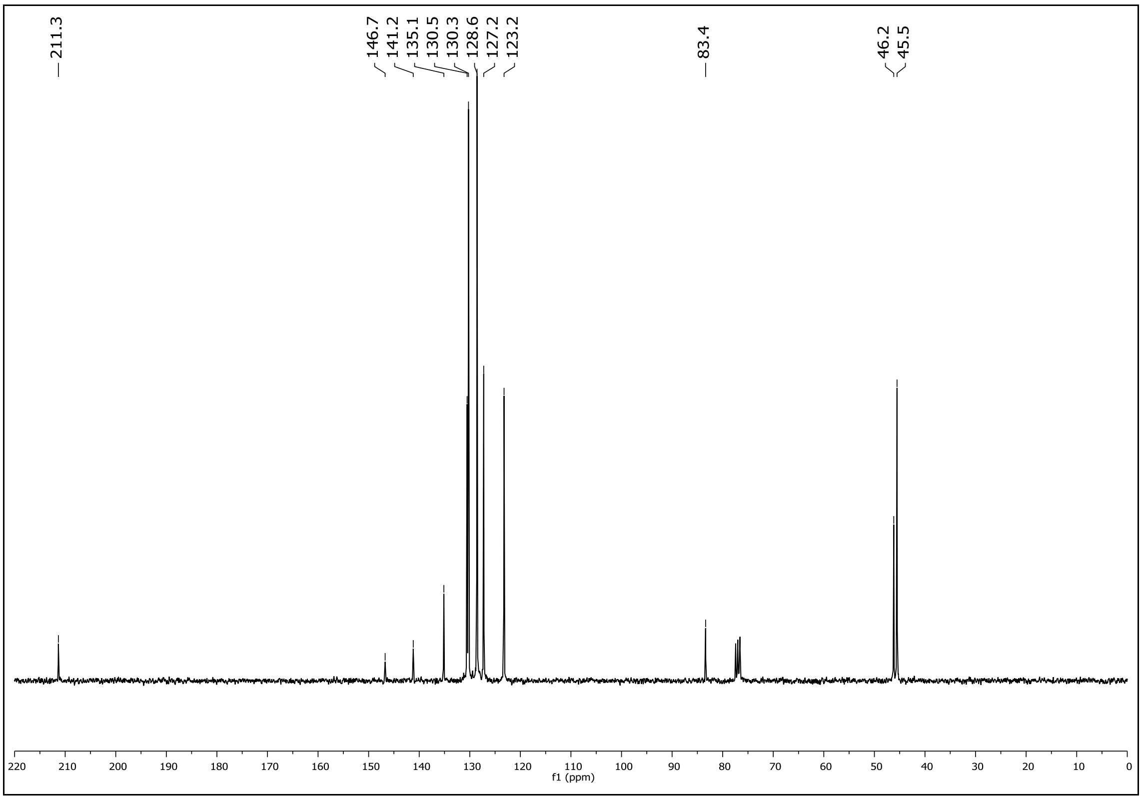
3A

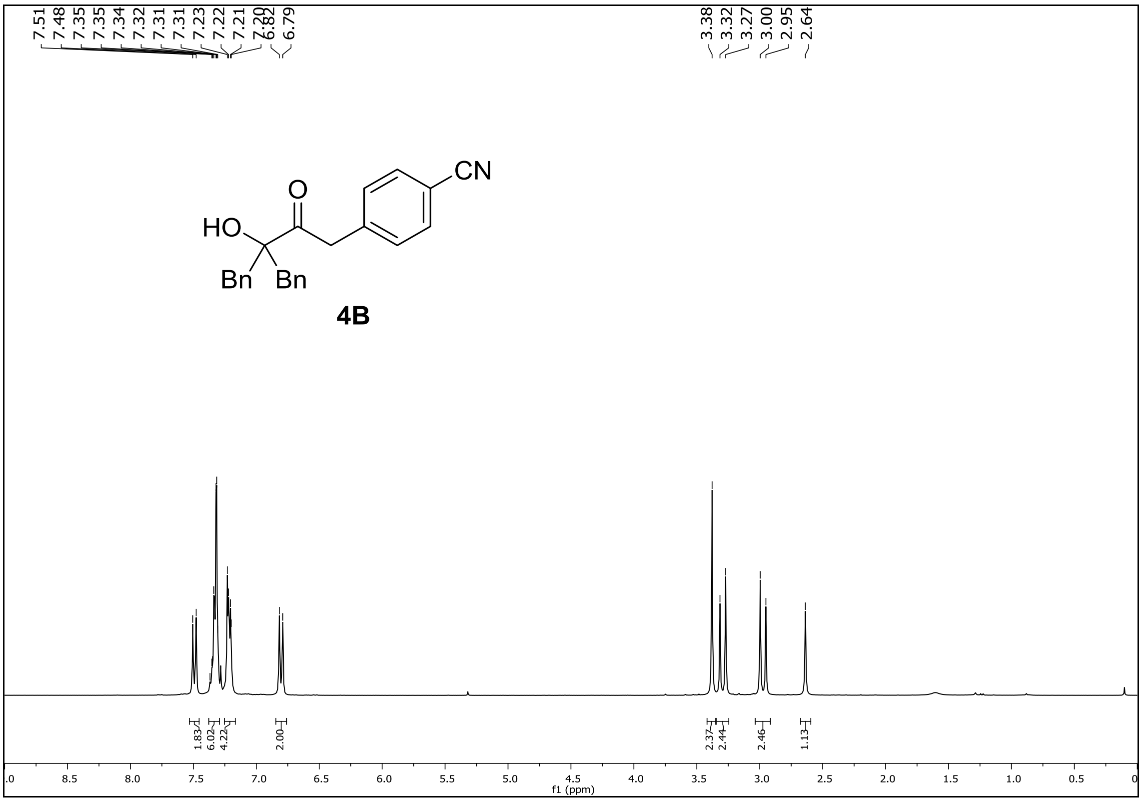
8.09
8.06
7.39
7.35
7.32
7.24
7.21
7.14
7.11
4.02
NO2
O
HO
Ph
Ph
1.68
11.03
2.24
2.00
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

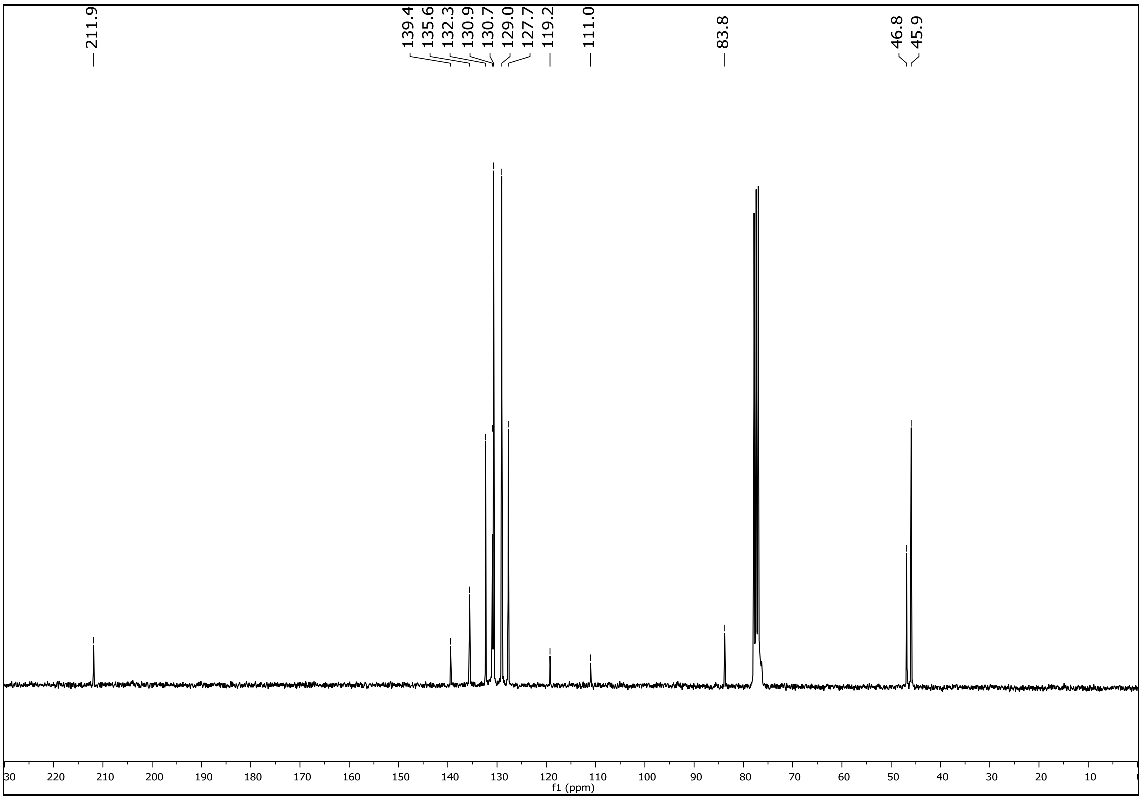


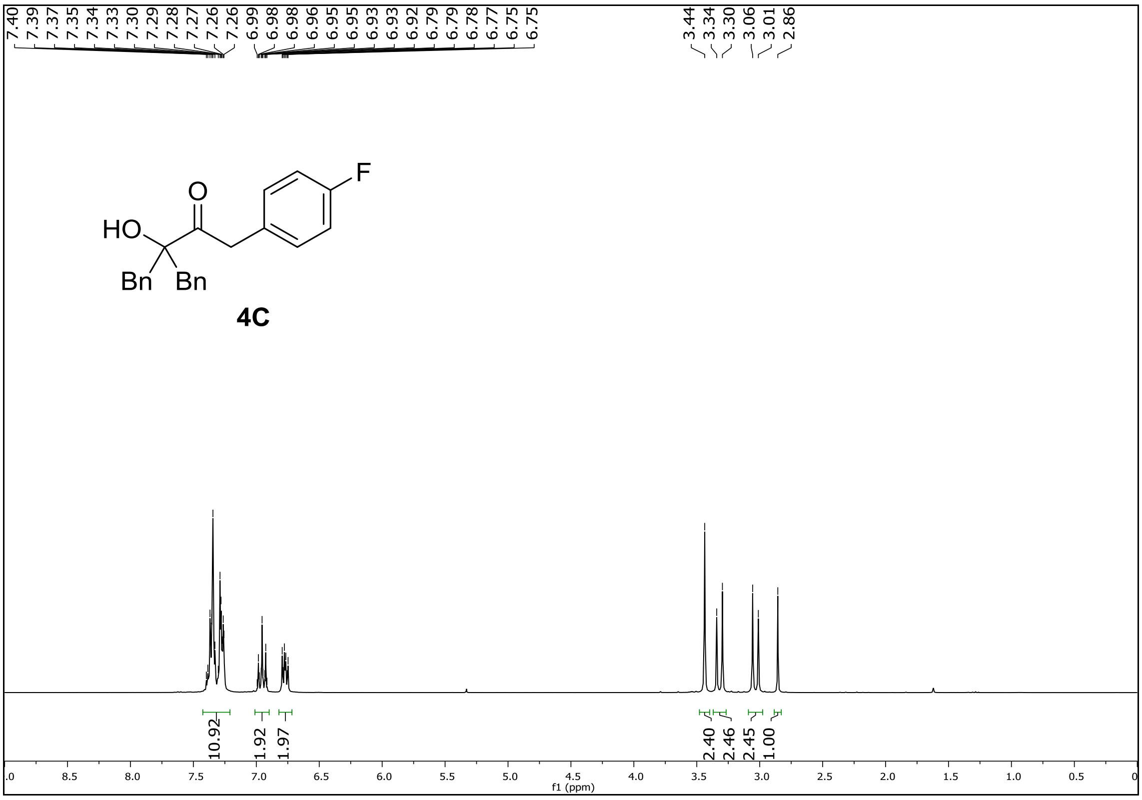
206.8
141.2
140.5
130.3
128.8
128.5
128.5
128.0
123.3
86.1
44.2
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


4A
8.05
8.02
7.33
7.31
7.30
7.29
7.23
7.22
7.20
7.20
6.84
6.81
3.41
3.31
3.27
2.99
2.95
2.66
NO2
O
HO
Bn
Bn
1.71
14.58
1.92
2.00
2.14
2.07
1.00
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


211.3
146.7
141.2
135.1
130.5
130.3
128.6
127.2
123.2
83.4
46.2
45.5
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

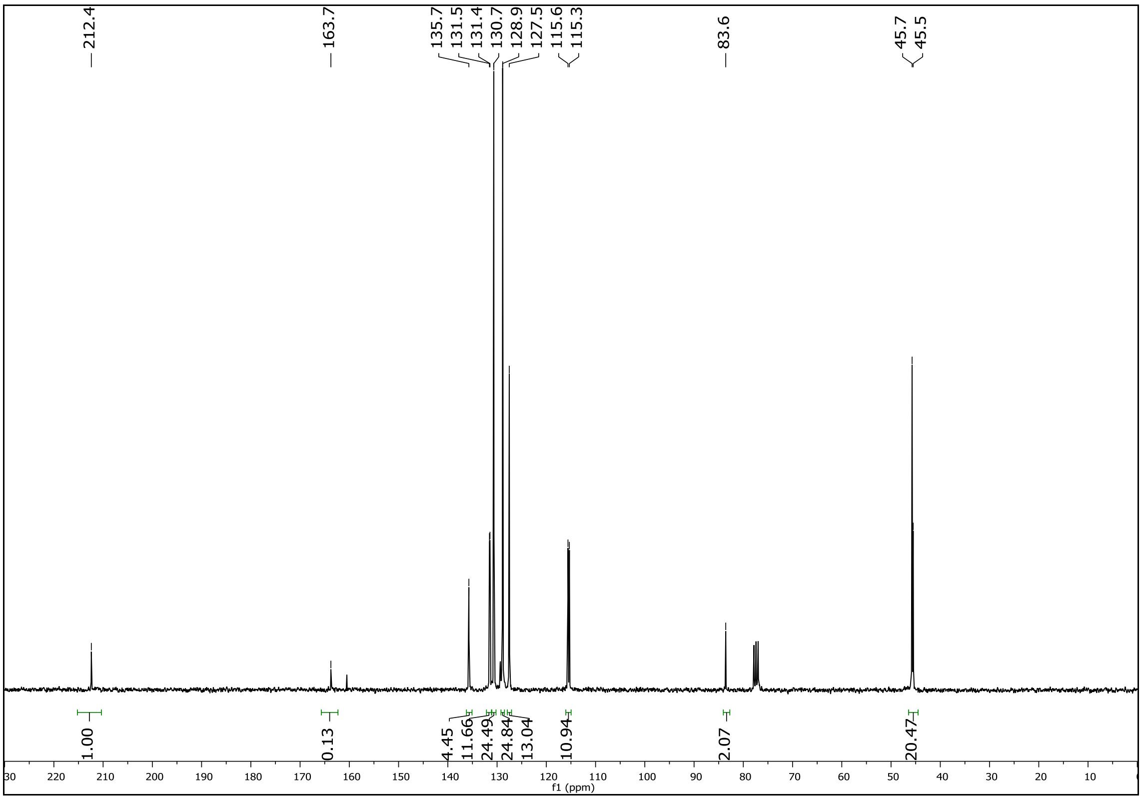

7.51
7.48
7.35
7.35
7.34
7.32
7.31
7.31
7.23
7.22
7.21
7.20
6.82
6.79
3.38
3.32
3.27
3.00
2.95
2.64
CN
O
HO
Bn
Bn
4B
1.83
6.02
4.22
2.00
2.37
2.44
2.46
1.13
.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
f1 (ppm)


211.9
139.4
135.6
132.3
130.9
130.7
129.0
127.7
119.2
111.0
83.8
46.8
45.9
30
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

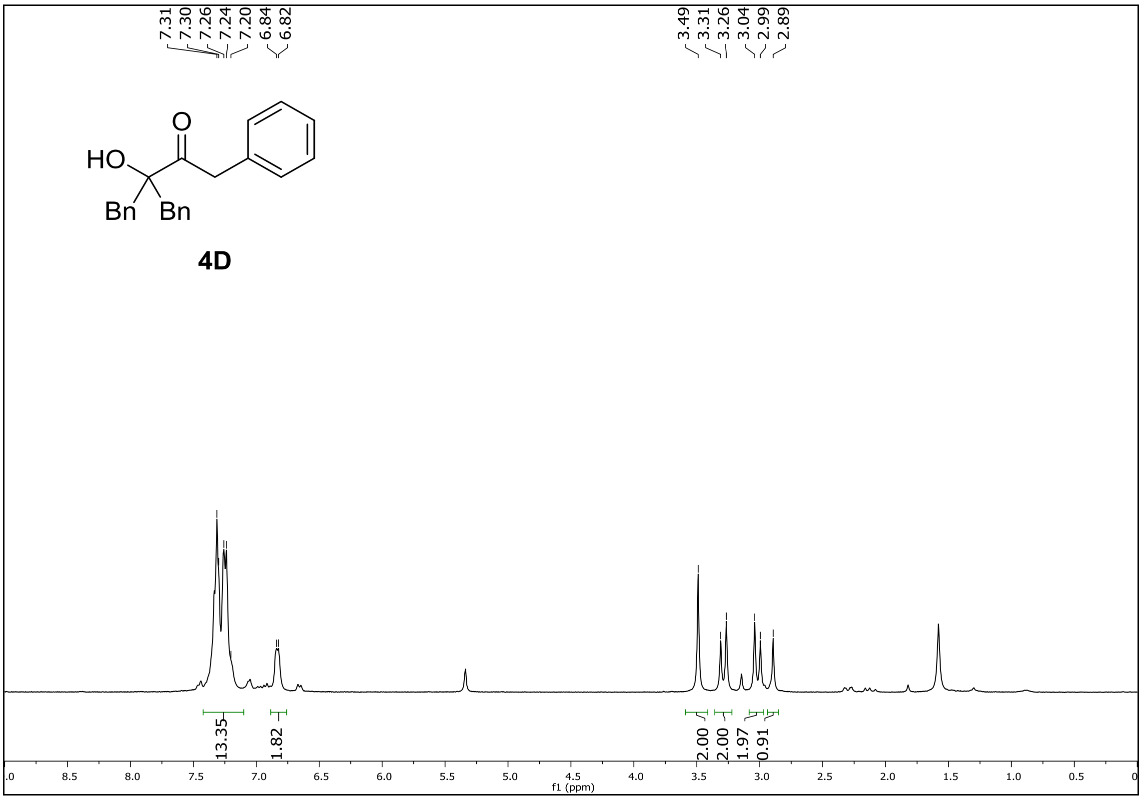


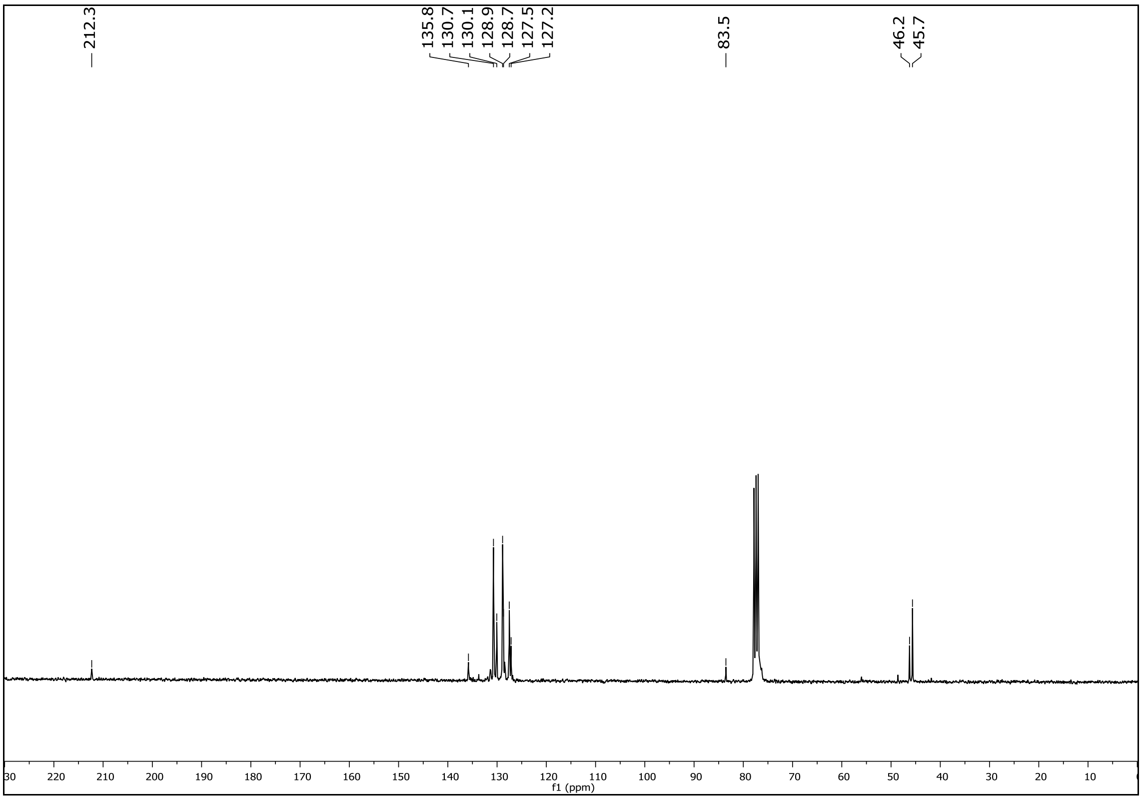
7.40
7.39
7.37
7.35
7.34
7.33
7.30
7.29
7.28
7.27
7.26
7.26
6.99
6.98
6.98
6.96
6.95
6.95
6.93
6.93
6.92
6.79
6.79
6.78
6.77
6.75
6.75
3.44
3.34
3.30
3.06
3.01
2.86
O
F
HO
Bn
Bn
10.92
1.92
1.97
2.40
2.46
2.45
1.00
.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
f1 (ppm)

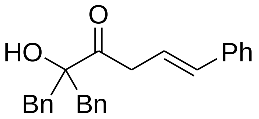
4C



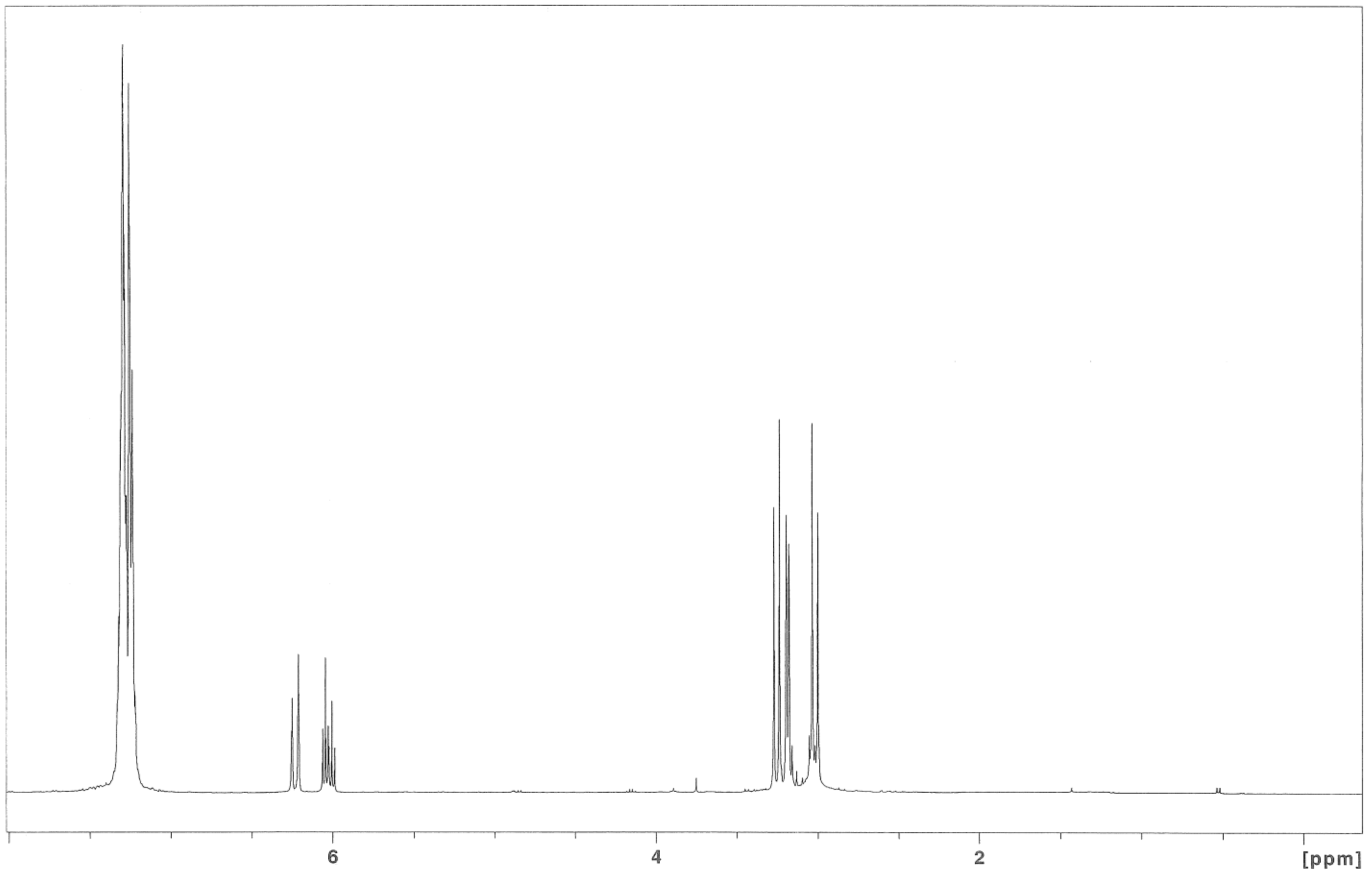
212.4
163.7
135.7
131.5
131.4
130.7
128.9
127.5
115.6
115.3
83.6
45.7
45.5
1.00
0.13
4.45
11.66
24.49
24.84
13.04
10.94
2.07
20.47
30
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

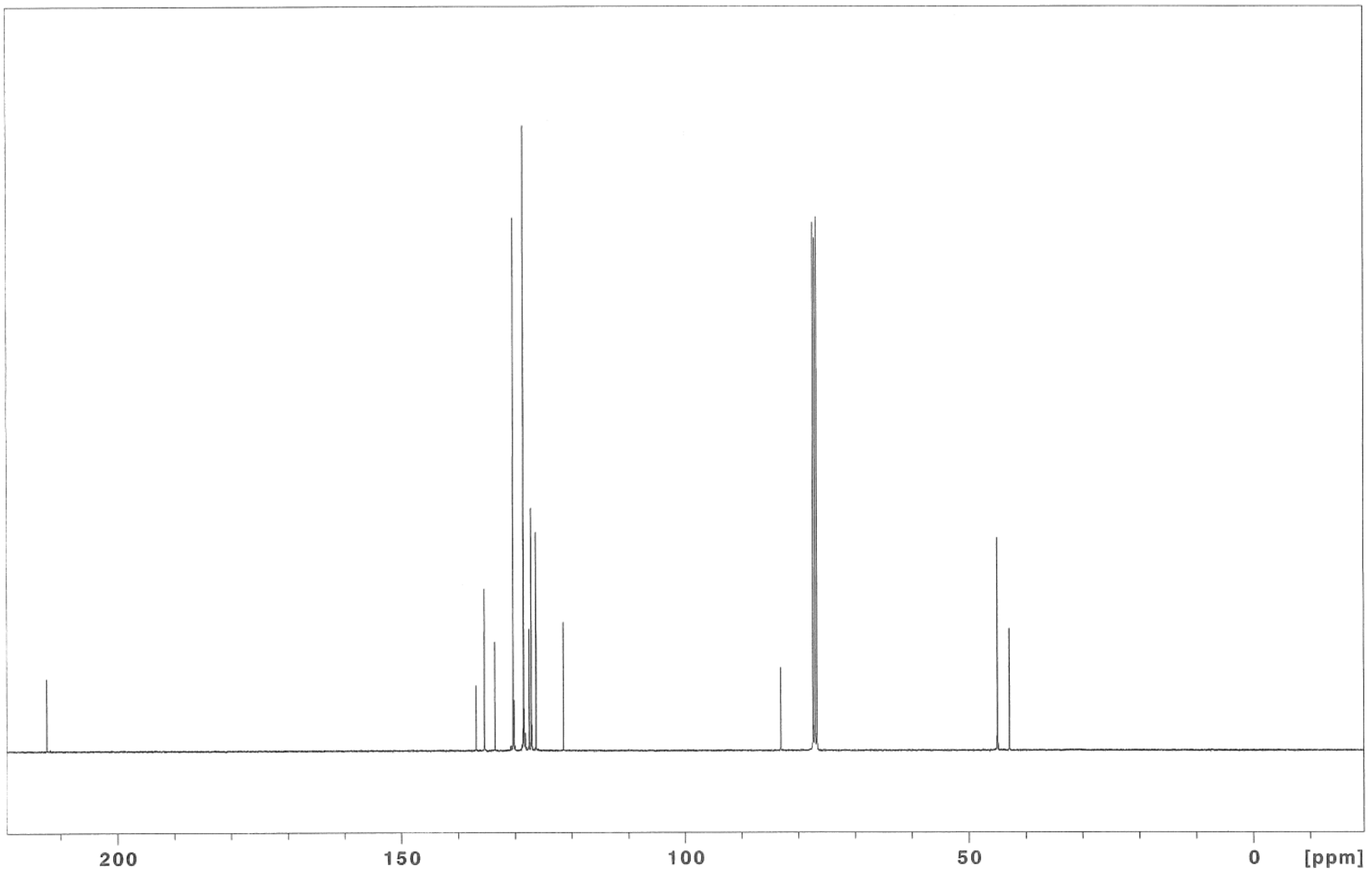

7.31
7.30
7.26
7.24
7.20
6.84
6.82
3.49
3.31
3.26
3.04
2.99
2.89
HO
O
Bn
Bn
4D
13.35
1.82
2.00
2.00
1.97
0.91
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
f1 (ppm)

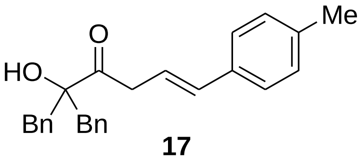

212.3
135.8
130.7
130.1
128.9
128.7
127.5
127.2
83.5
46.2
45.7
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)



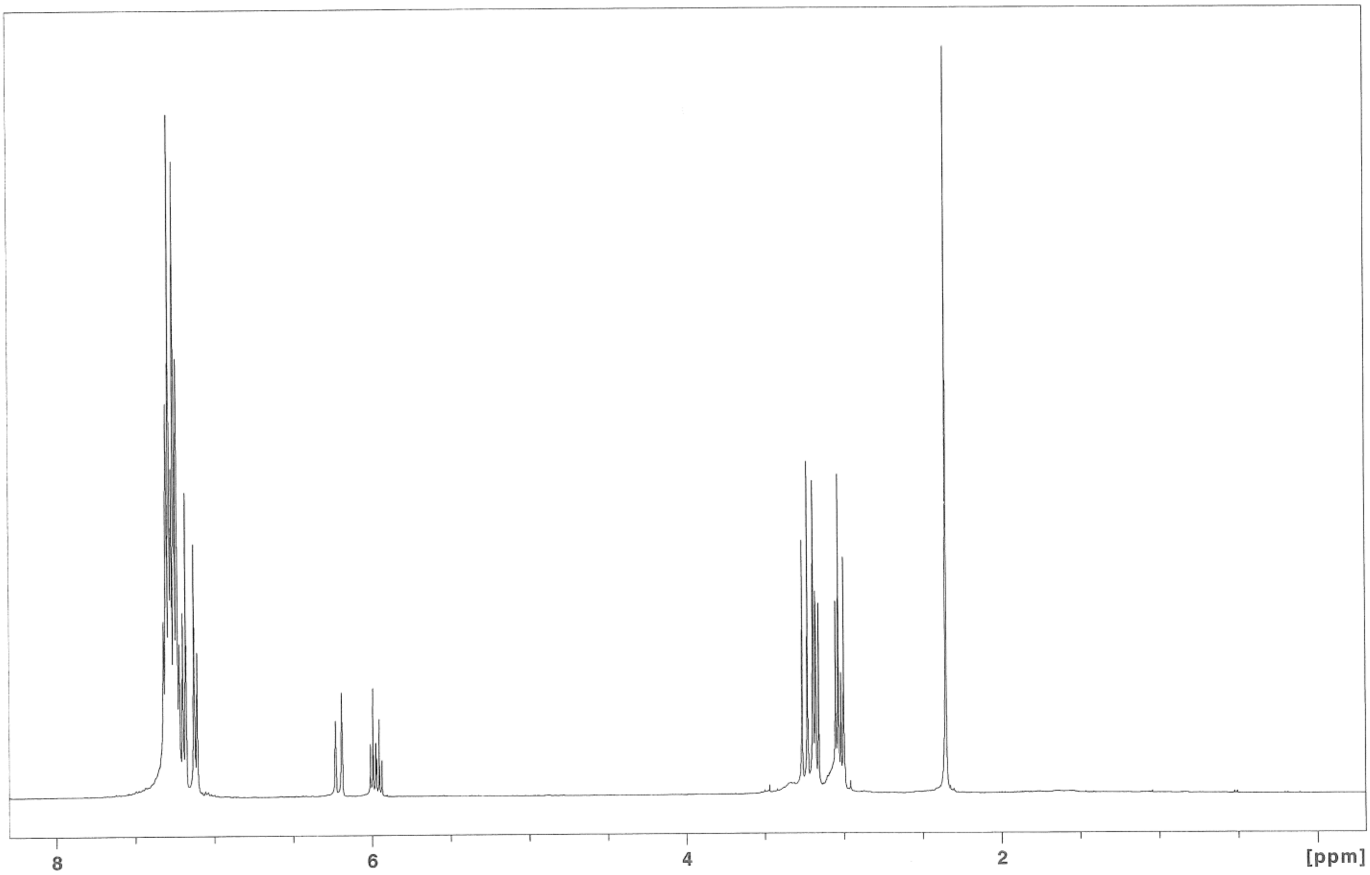
16

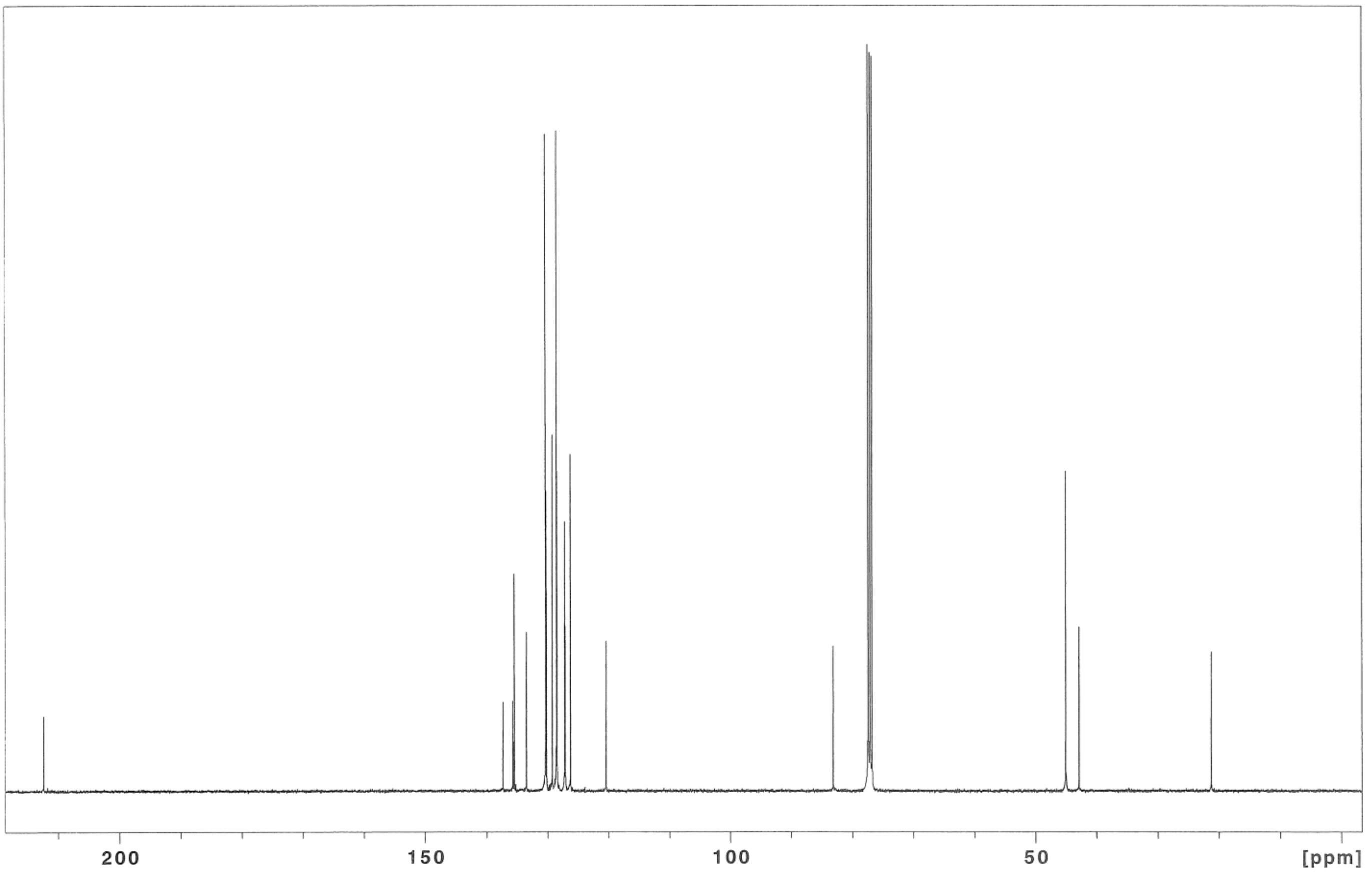


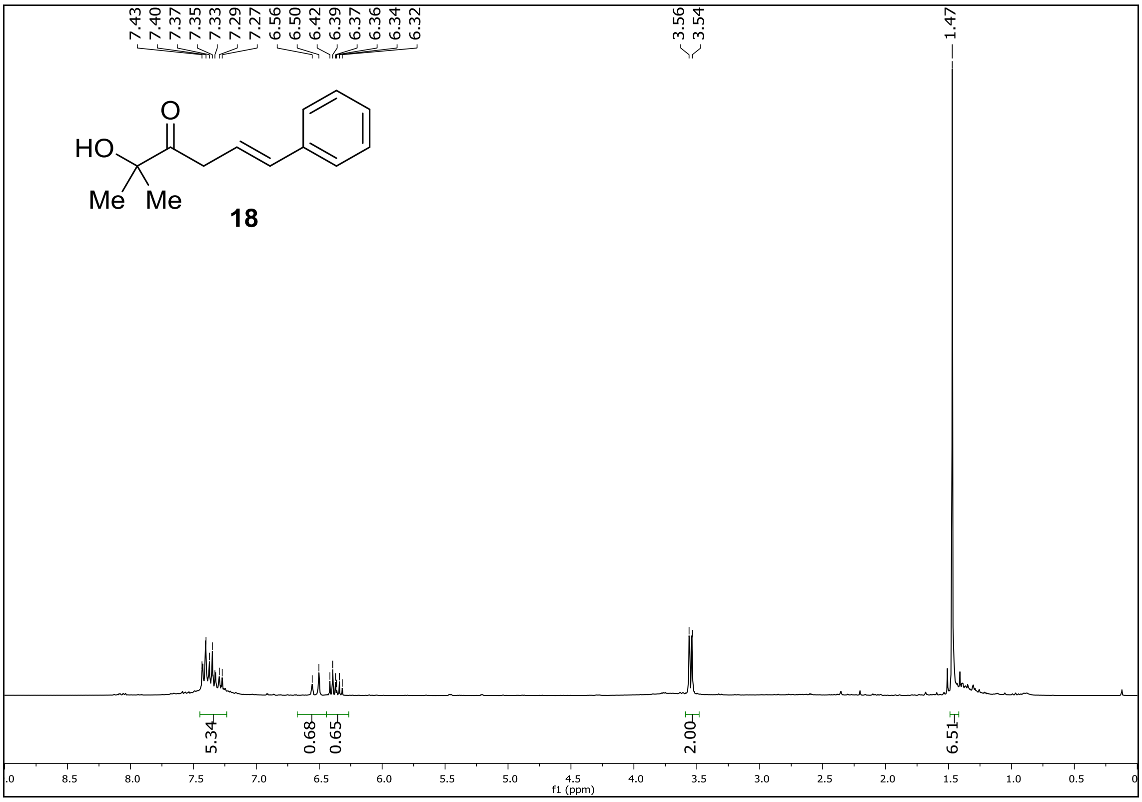


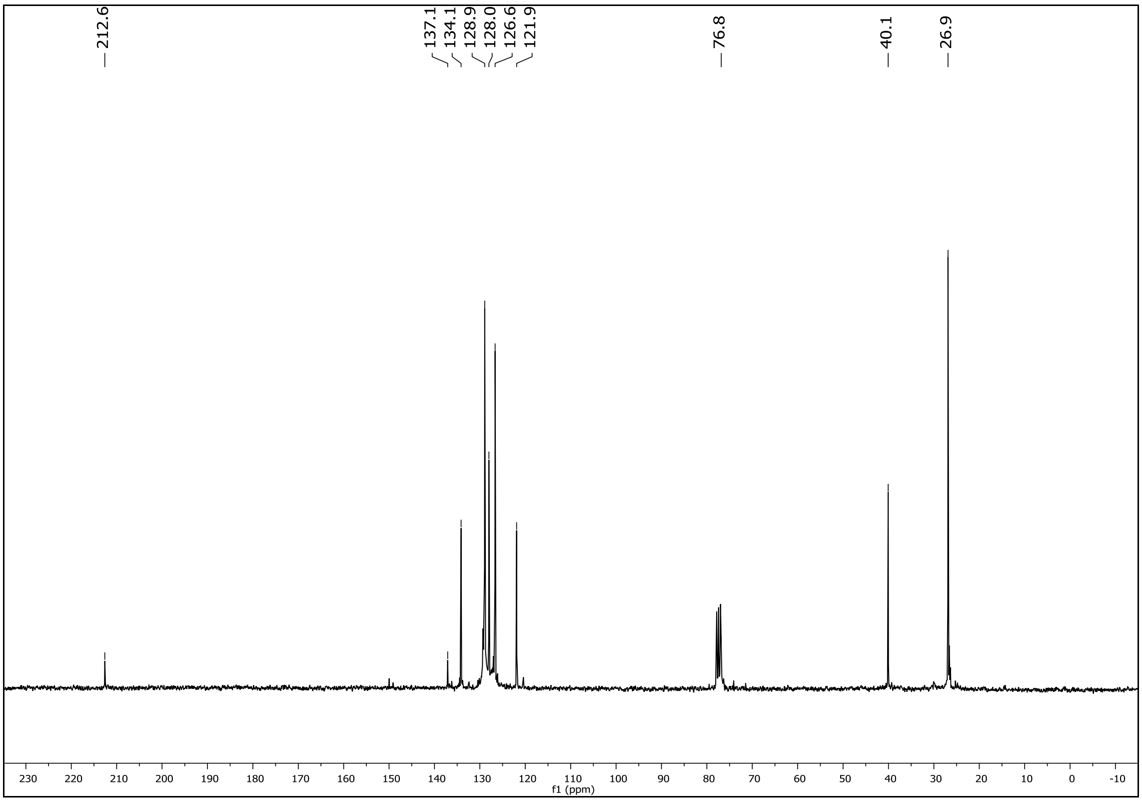


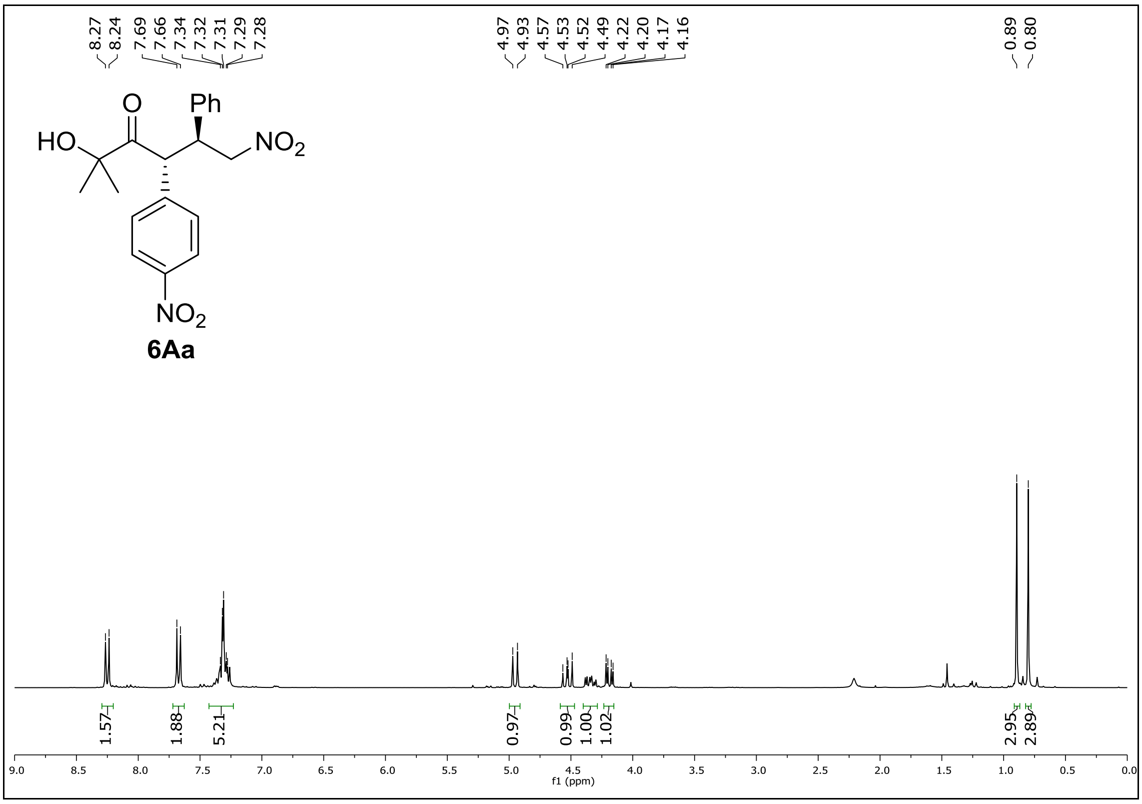
17

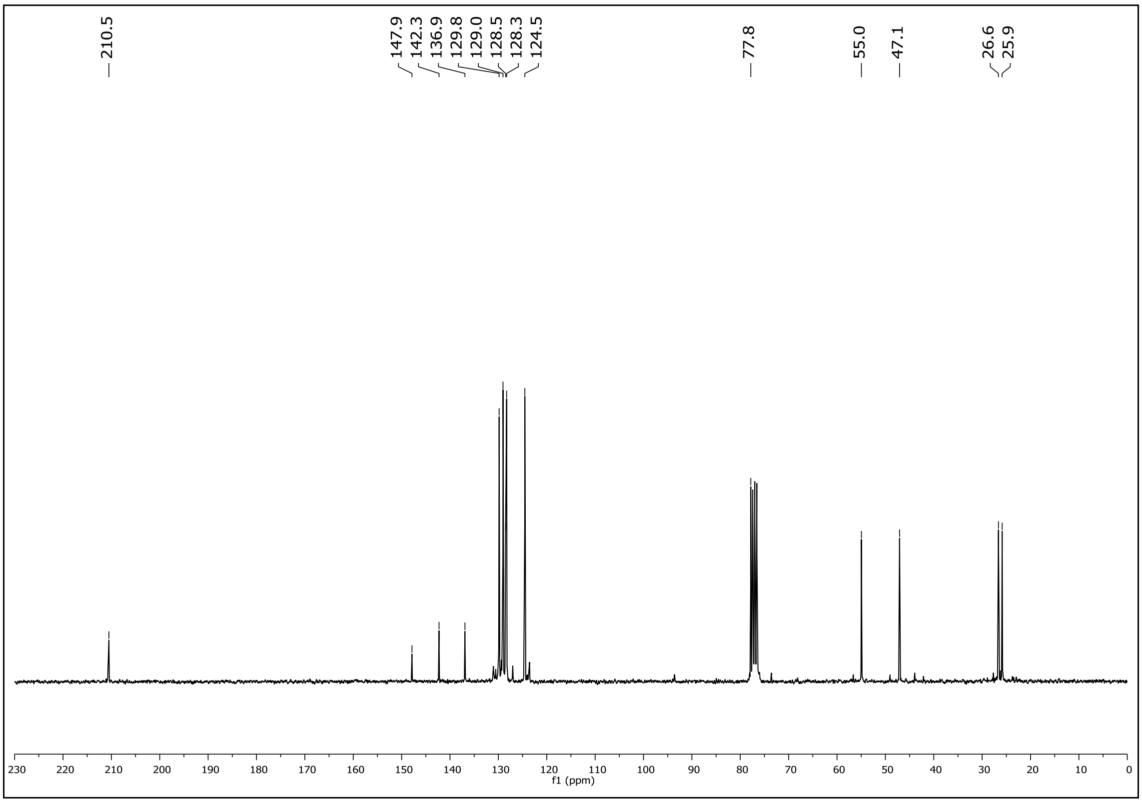


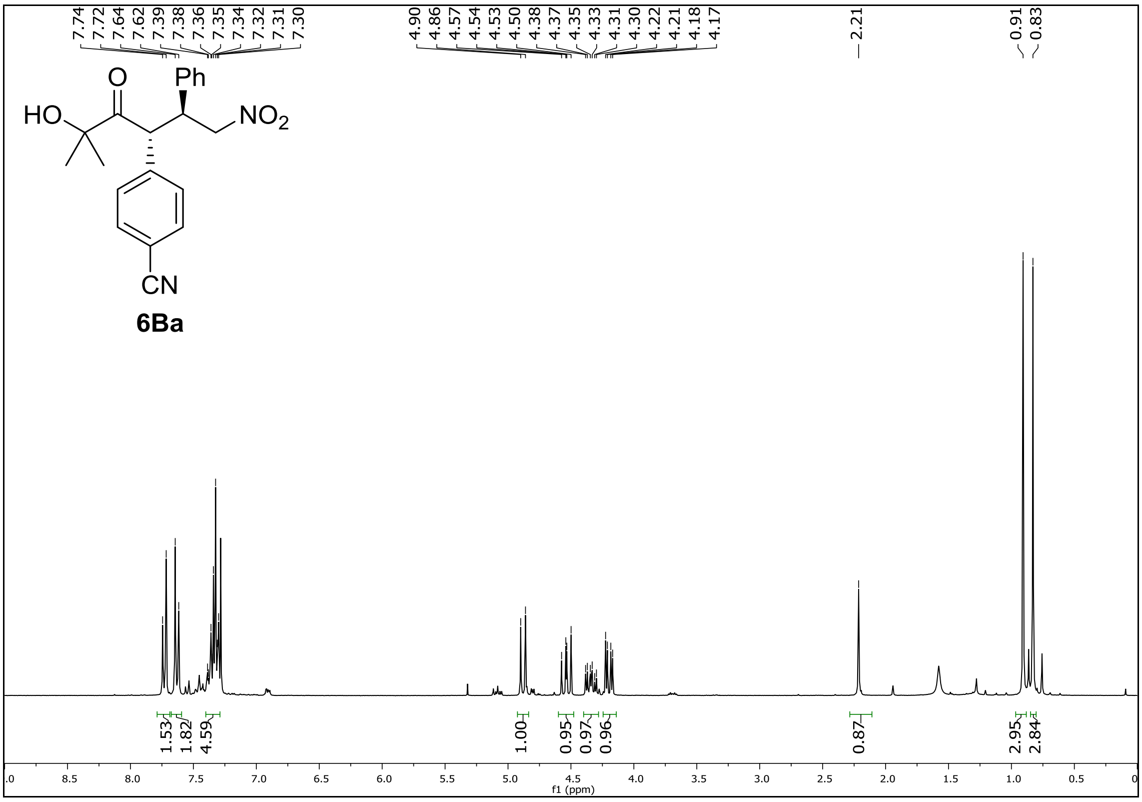



7.43
7.40
7.37
7.35
7.33
7.29
7.27
6.56
6.50
6.42
6.39
6.37
6.36
6.34
6.32
3.56
3.54
1.47
HO
O
Me
Me
18
5.34
0.68
0.65
2.00
6.51
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

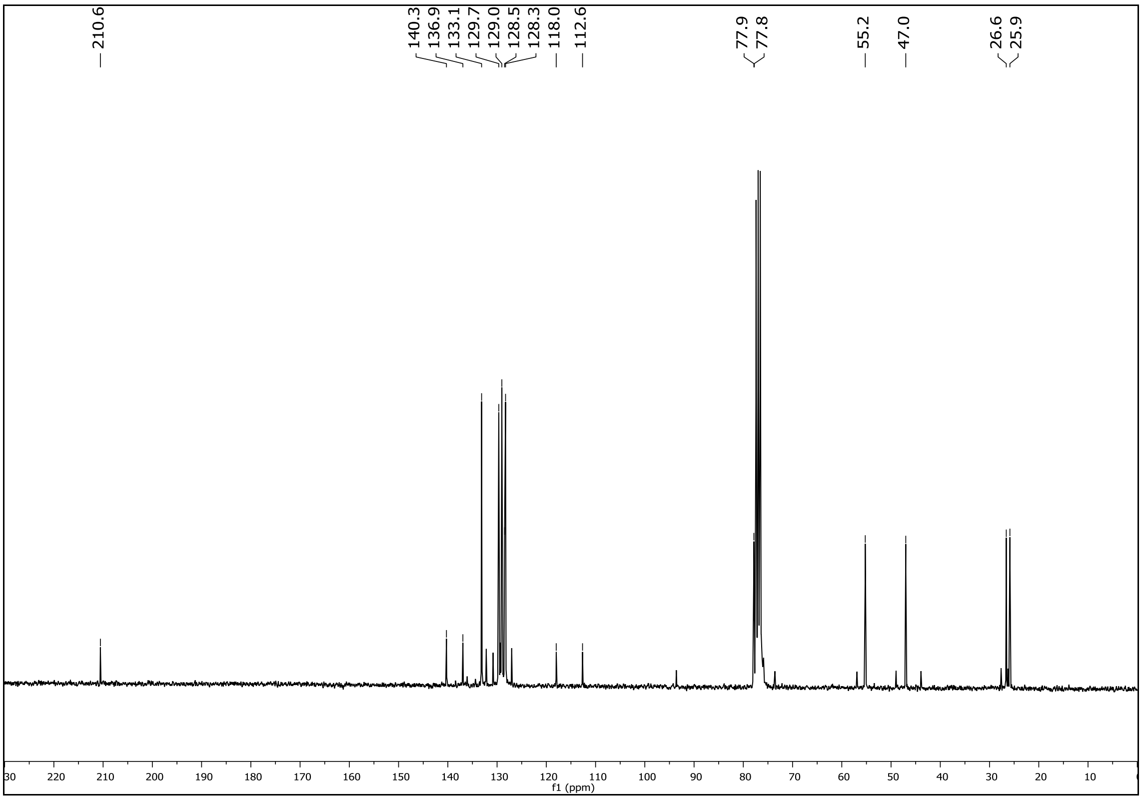

212.6
137.1
134.1
128.9
128.0
126.6
121.9
76.8
40.1
26.9
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


8.27
8.24
7.69
7.66
7.34
7.32
7.31
7.29
7.28
4.97
4.93
4.57
4.53
4.52
4.49
4.22
4.20
4.17
4.16
0.89
0.80
HO
O
Ph
NO2
NO2
6Aa
1.57
1.88
5.21
0.97
0.99
1.00
1.02
2.95
2.89
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

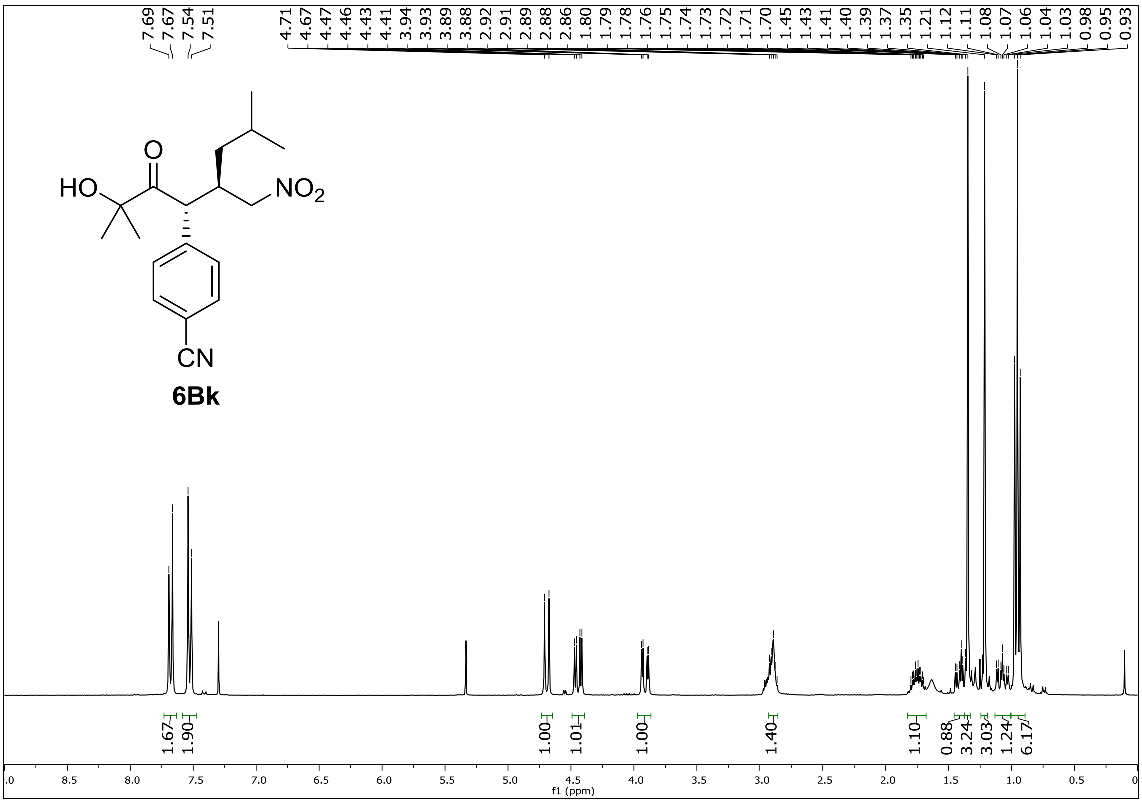

210.5
147.9
142.3
136.9
129.8
129.0
128.5
128.3
124.5
77.8
55.0
47.1
26.6
25.9
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

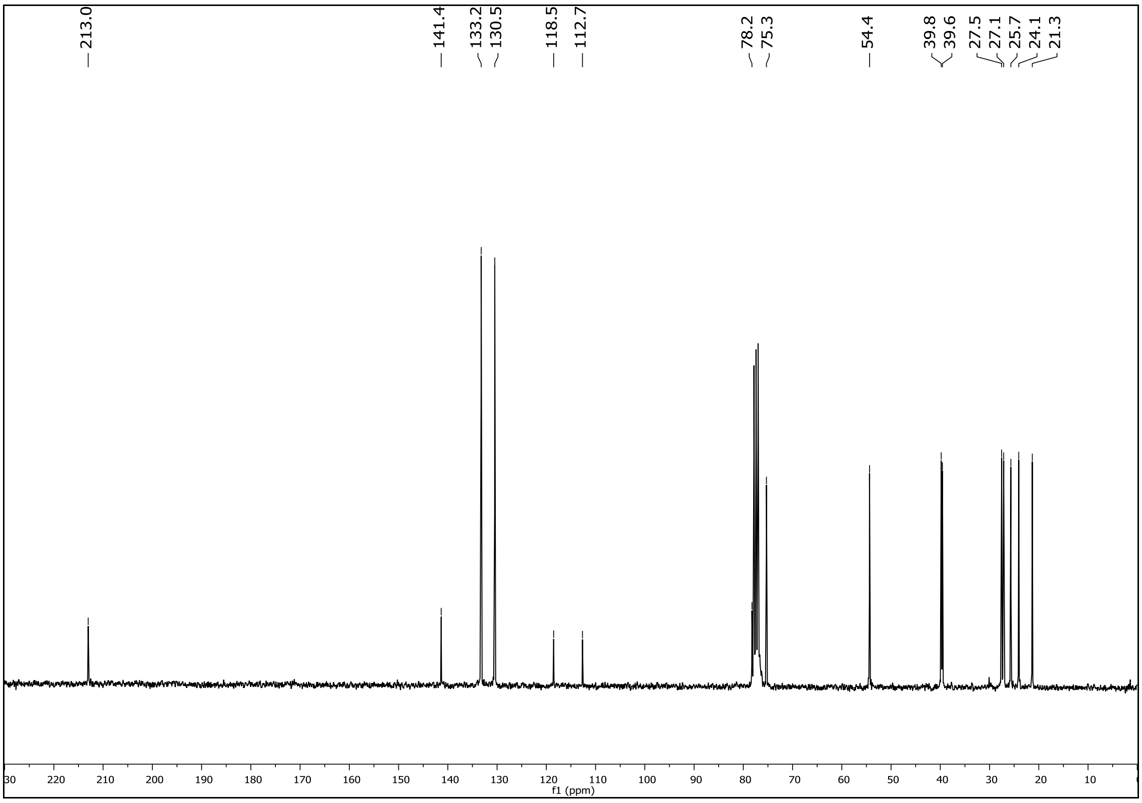

6Ba

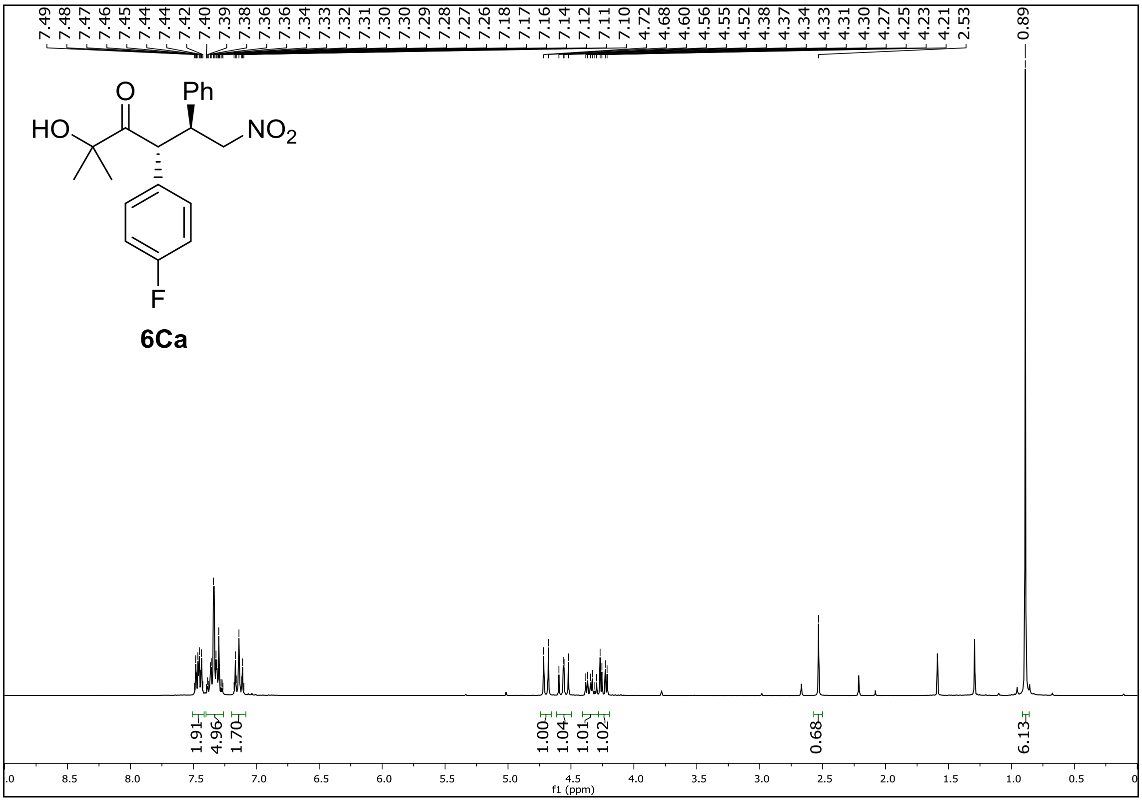
7.74
7.72
7.64
7.62
7.39
7.38
7.36
7.35
7.34
7.32
7.31
7.30
4.90
4.86
4.57
4.54
4.53
4.50
4.38
4.37
4.35
4.33
4.31
4.30
4.22
4.21
4.18
4.17
2.21
0.91
0.83
HO
O
Ph
NO2
CN
1.53
1.82
4.59
1.00
0.95
0.97
0.96
0.87
2.95
2.84
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
f1 (ppm)

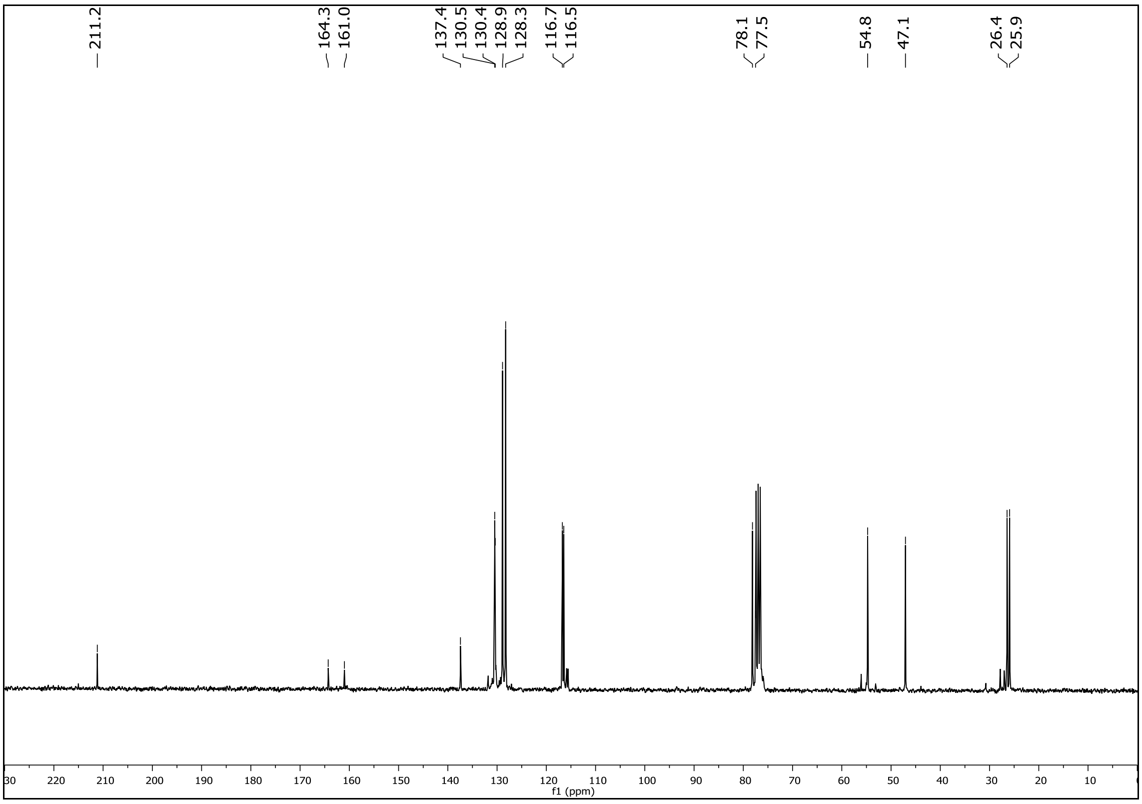


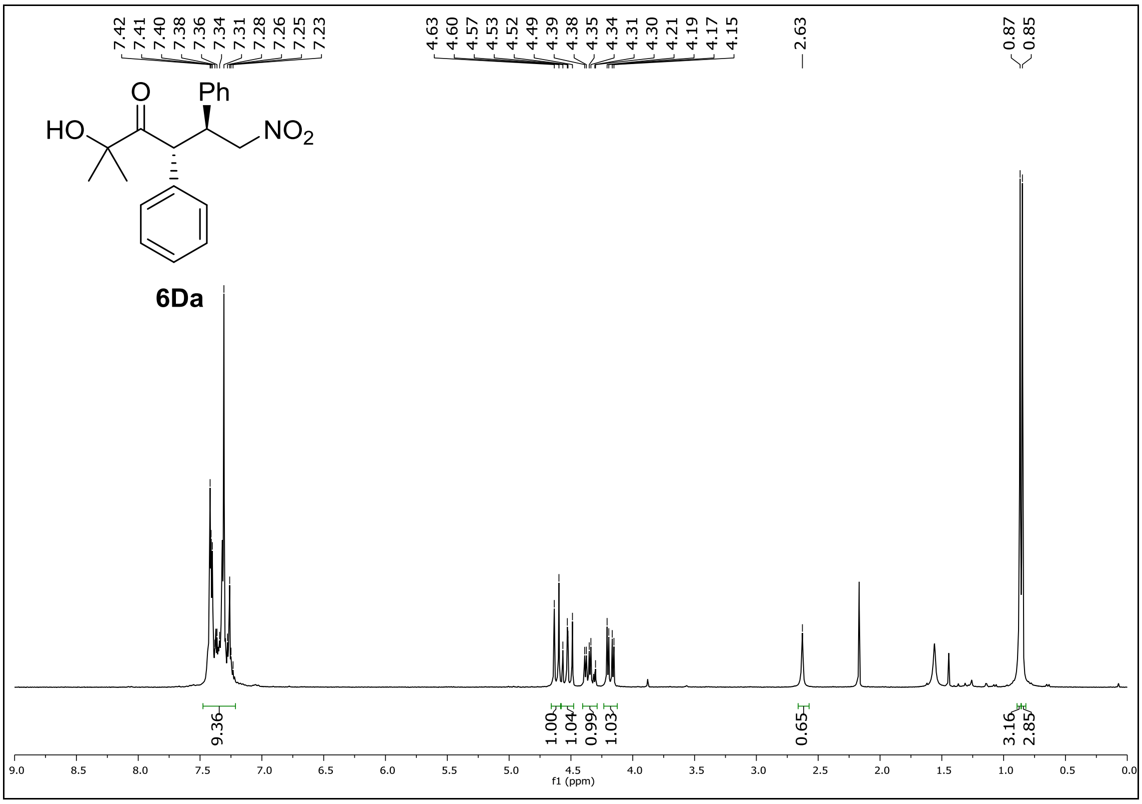
210.6
140.3
136.9
133.1
129.7
129.0
128.5
128.3
118.0
112.6
77.9
77.8
55.2
47.0
26.6
25.9
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

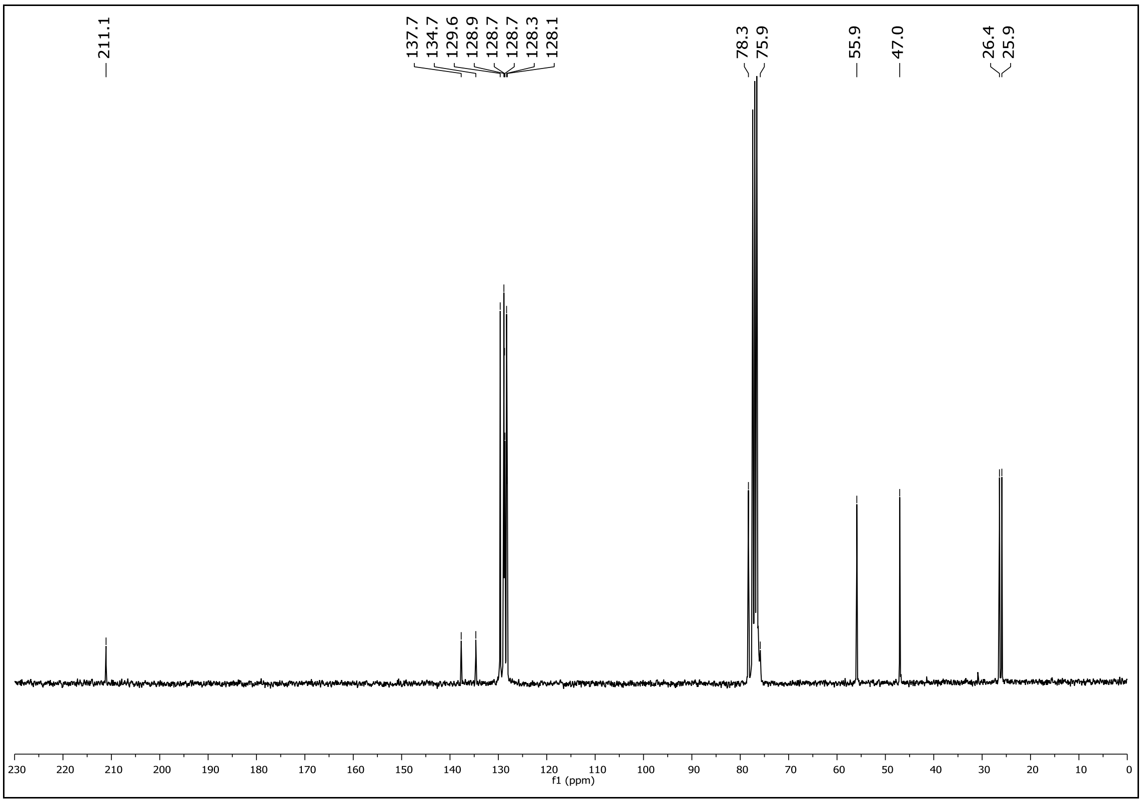

7.69
7.67
7.54
7.51
4.71
4.67
4.47
4.46
4.43
4.41
3.94
3.93
3.89
3.88
2.92
2.91
2.89
2.88
2.86
1.80
1.79
1.78
1.76
1.75
1.74
1.73
1.72
1.71
1.70
1.45
1.43
1.41
1.40
1.39
1.37
1.35
1.21
1.12
1.11
1.08
1.07
1.06
1.04
1.03
0.98
0.95
0.93
HO
O
NO2
CN
6Bk
1.67
1.90
1.00
1.01
1.00
1.40
1.10
0.88
3.24
3.03
1.24
6.17
.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
f1 (ppm)

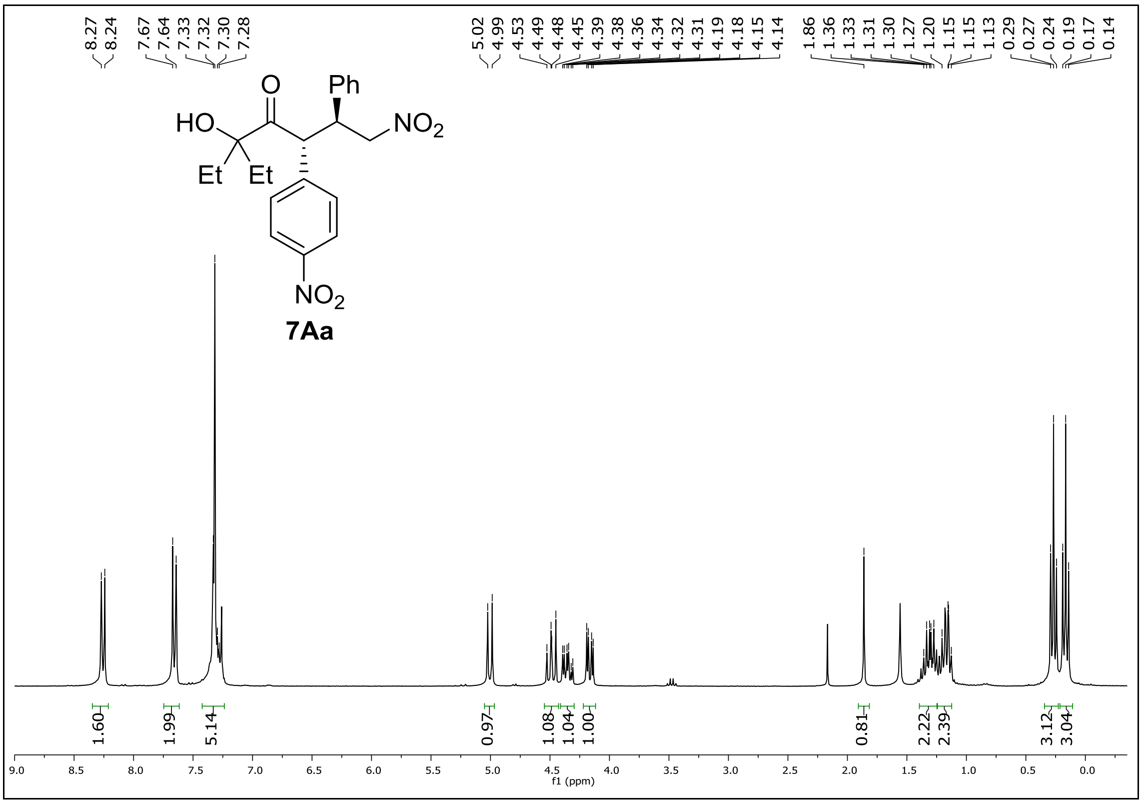

213.0
141.4
133.2
130.5
118.5
112.7
78.2
75.3
54.4
39.8
39.6
27.5
27.1
25.7
24.1
21.3
30
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

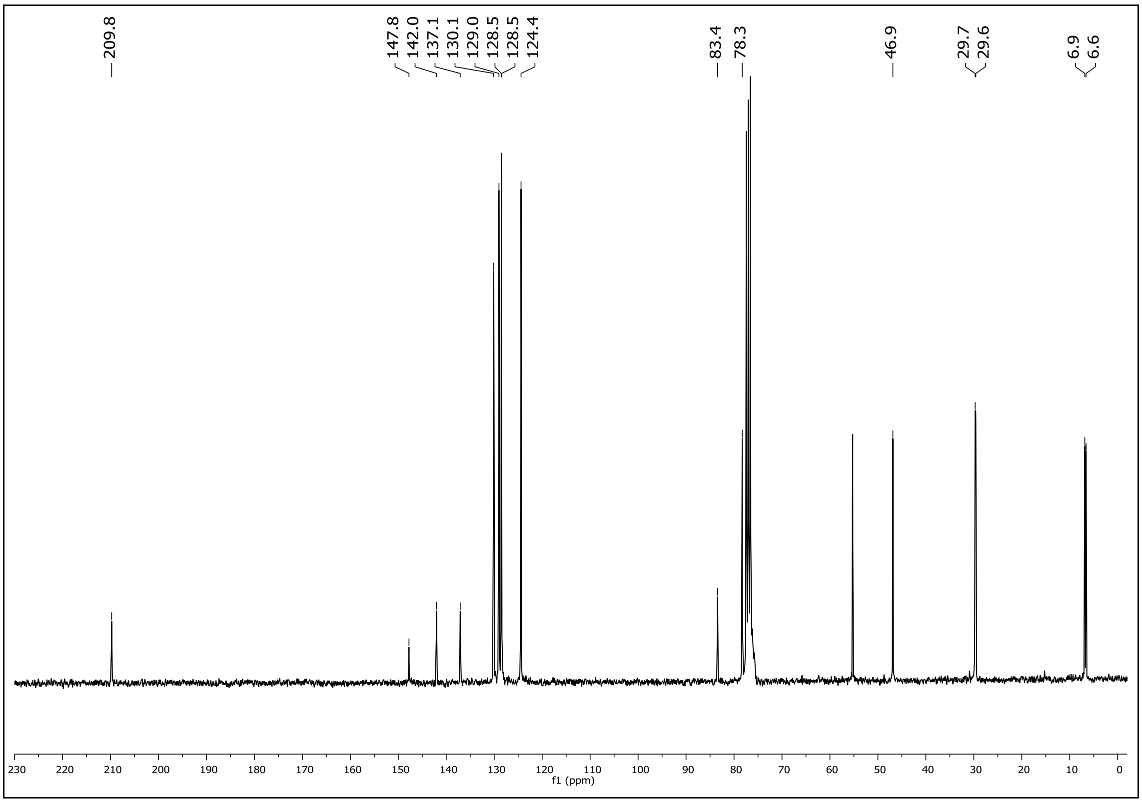

7.49 7.48 7.47 7.46 7.45 7.44 7.44 7.42 7.40 7.39 7.38 7.36 7.36 7.34 7.33 7.32 7.31 7.30 7.30 7.29 7.28 7.27 7.26 7.18 7.17 7.16 7.14 7.12 7.11 7.10 4.72 4.68 4.60 4.56 4.55 4.52 4.38 4.37 4.34 4.33 4.31 4.30 4.27 4.25 4.23 4.21 2.53 0.89
HO
O
Ph
NO2
F
6Ca
1.91
4.96
1.70
1.00
1.04
1.01
1.02
0.68
6.13
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)

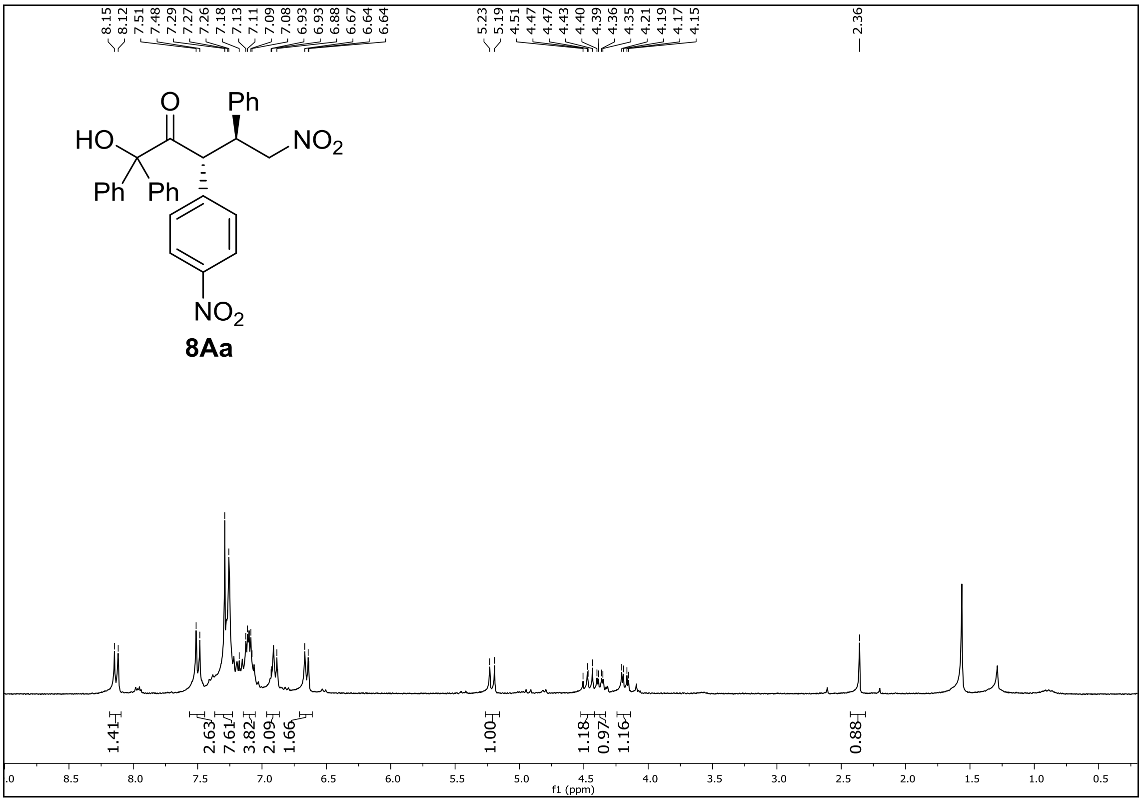

211.2
164.3 161.0
137.4 130.5 130.4 128.9 128.3
116.7 116.5
78.1 77.5
54.8
47.1
26.4 25.9
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)


7.42
7.41
7.40
7.38
7.36
7.34
7.31
7.28
7.26
7.25
7.23
4.63
4.60
4.57
4.53
4.52
4.49
4.39
4.38
4.35
4.34
4.31
4.30
4.21
4.19
4.17
4.15
2.63
0.87
0.85
O
Ph
HO
NO2
6Da
9.36
1.00
1.04
0.99
1.03
0.65
3.16
2.85
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

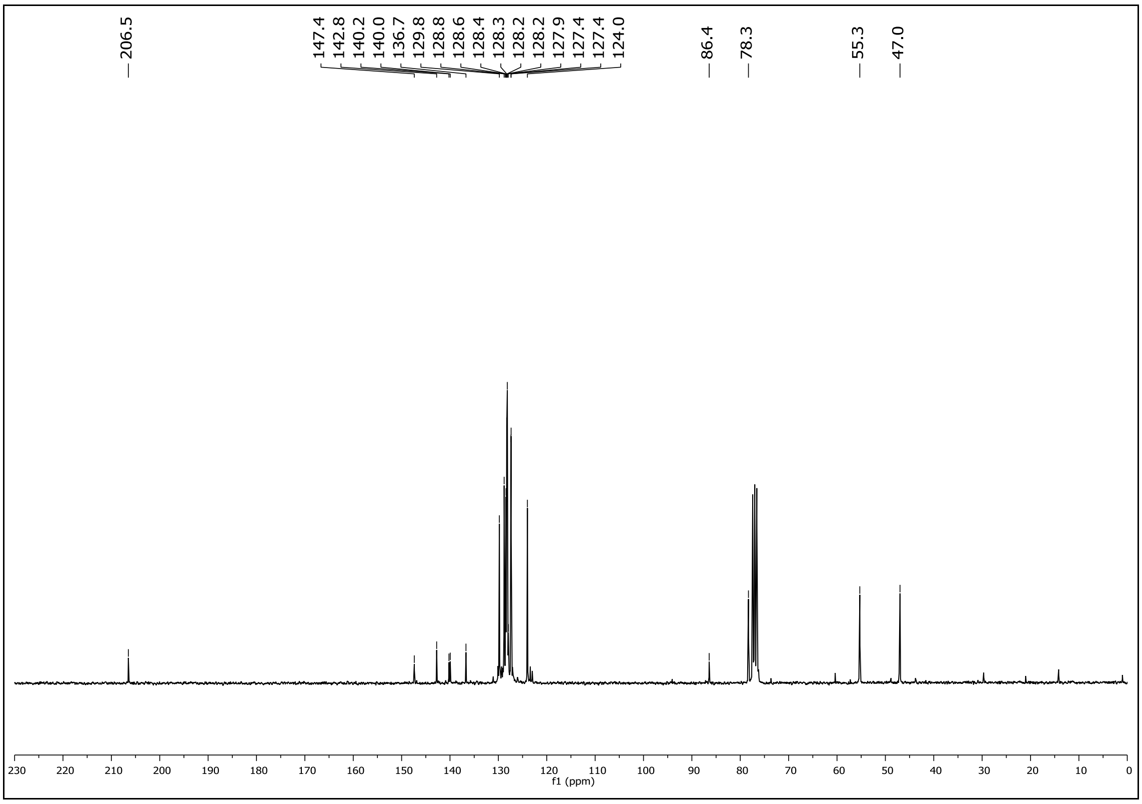

211.1
137.7
134.7
129.6
128.9
128.7
128.7
128.3
128.1
78.3
75.9
55.9
47.0
26.4
25.9
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

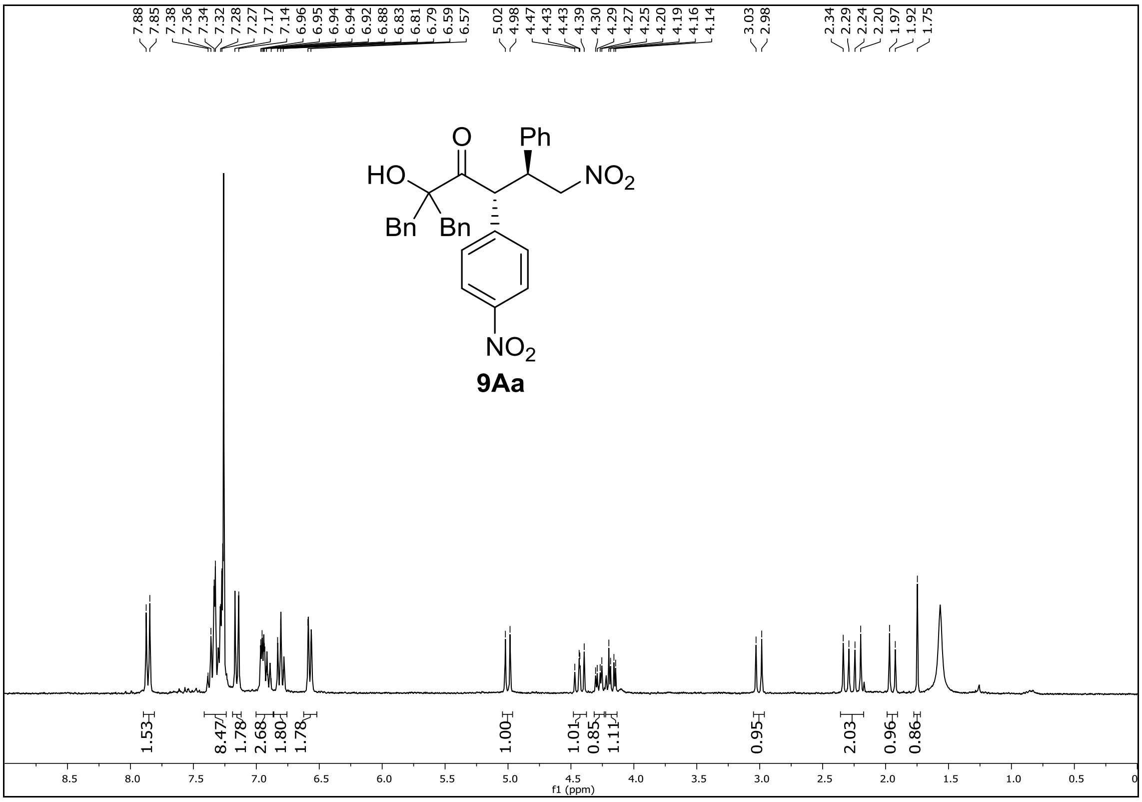

8.27
8.24
7.67
7.64
7.33
7.32
7.30
7.28
5.02
4.99
4.53
4.49
4.48
4.45
4.39
4.38
4.36
4.34
4.32
4.31
4.19
4.18
4.15
4.14
1.86
1.36
1.33
1.31
1.30
1.27
1.20
1.15
1.15
1.13
0.29
0.27
0.24
0.19
0.17
0.14
O
Ph
HO
NO2
Et
Et
NO2
7Aa
1.60
1.99
5.14
0.97
1.08
1.04
1.00
0.81
2.22
2.39
3.12
3.04
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

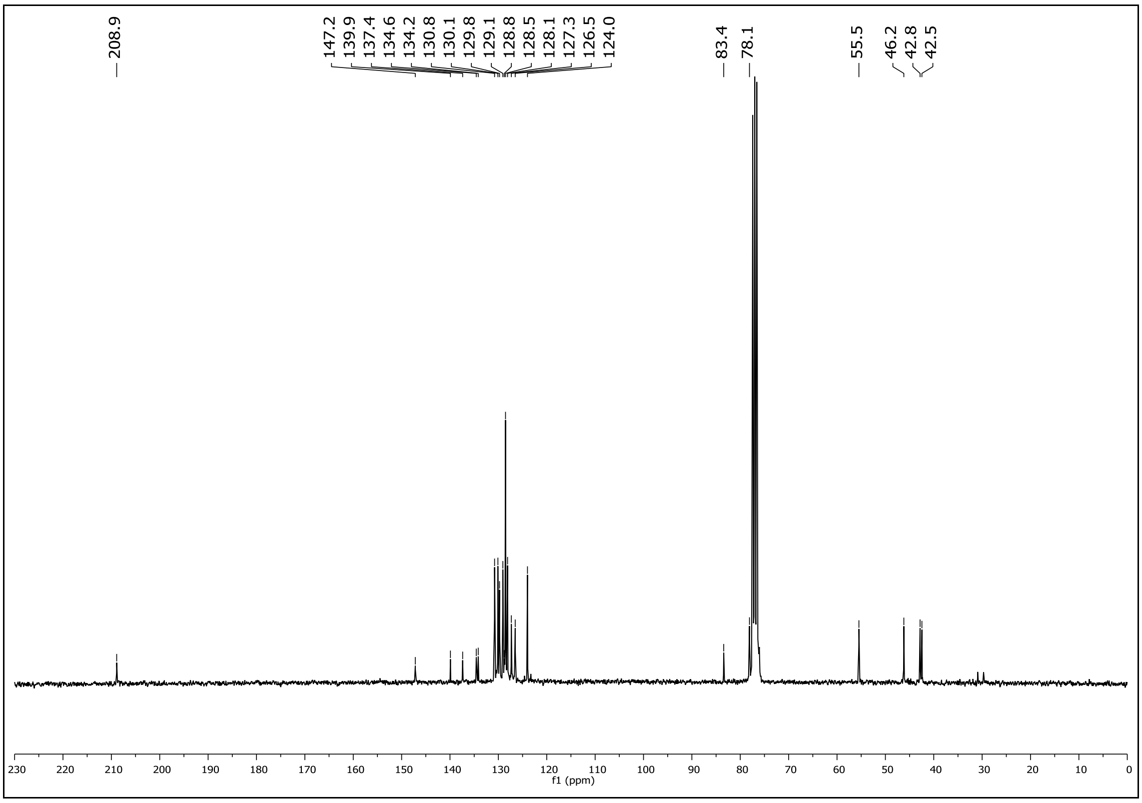

209.8
147.8
142.0
137.1
130.1
129.0
128.5
128.5
124.4
83.4
78.3
46.9
29.7
29.6
6.9
6.6
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

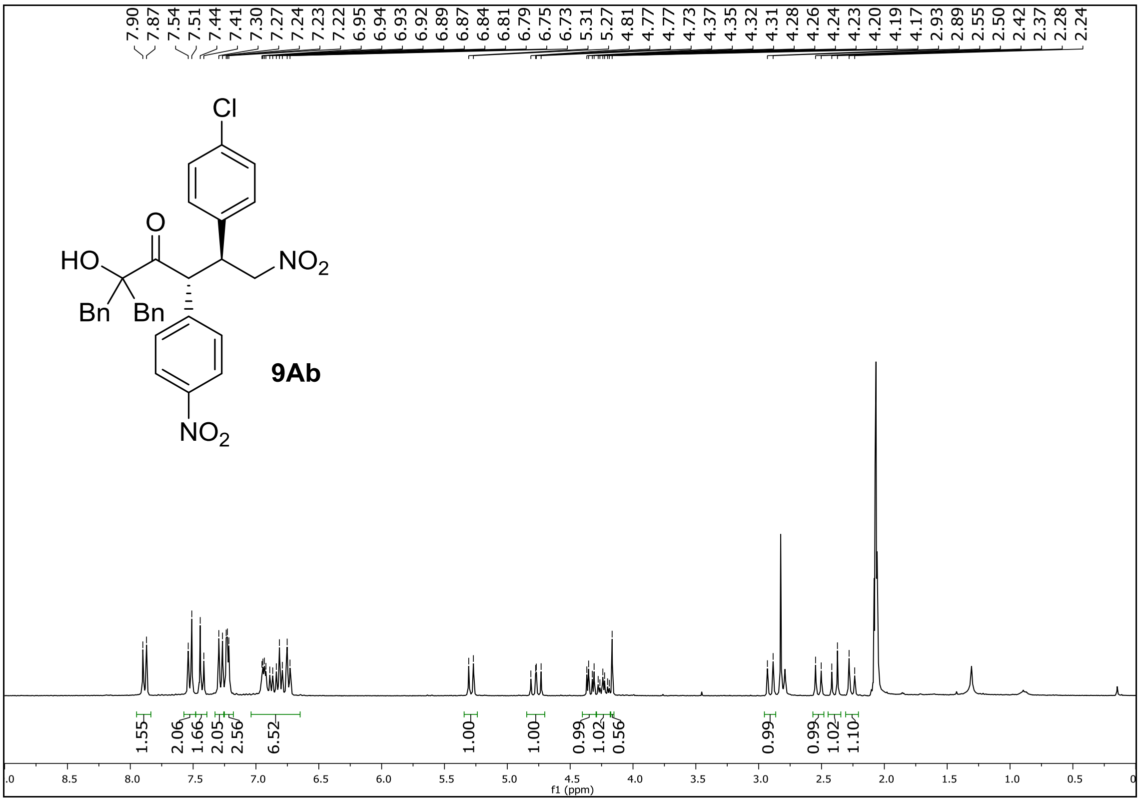

8.15
8.12
7.51
7.48
7.29
7.27
7.26
7.18
7.13
7.11
7.09
7.08
6.93
6.93
6.88
6.67
6.64
6.64
5.23
5.19
4.51
4.47
4.47
4.43
4.40
4.39
4.36
4.35
4.21
4.19
4.17
4.15
2.36
O
Ph
HO
NO2
Ph
Ph
NO2
1.41
2.63
7.61
3.82
2.09
1.66
1.00
1.18
0.97
1.16
0.88
.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

8Aa

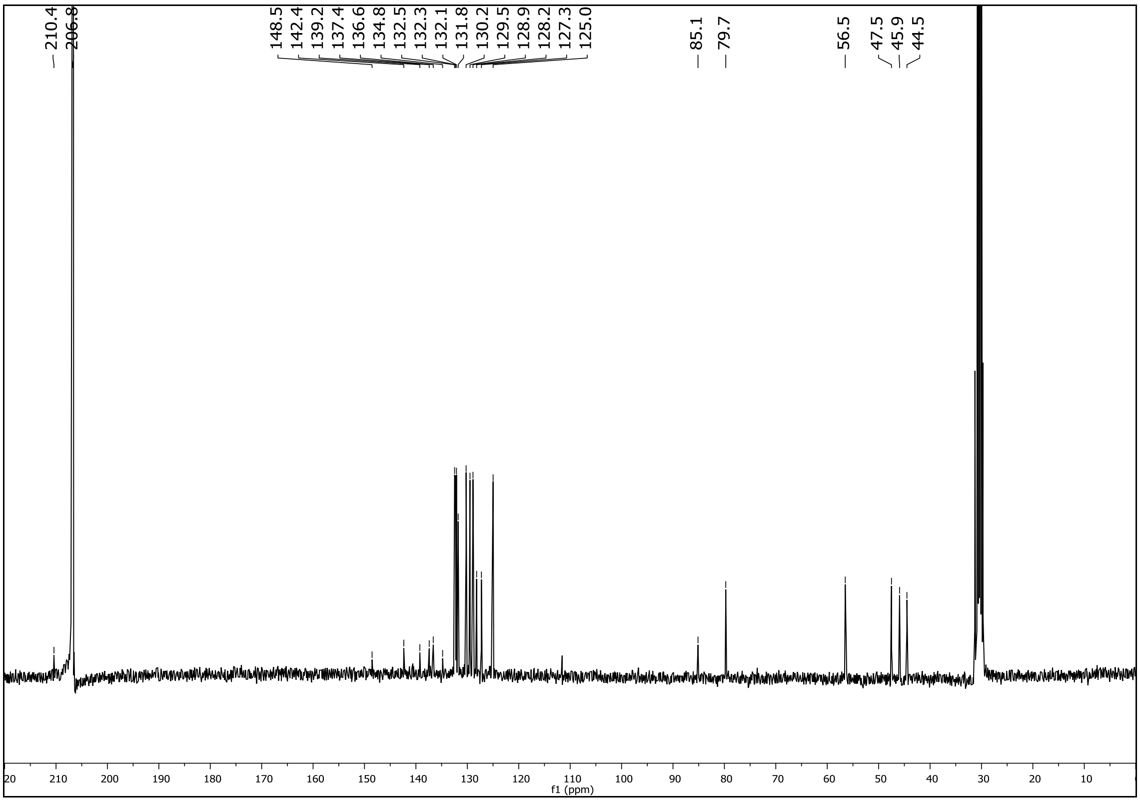

206.5
147.4
142.8
140.2
140.0
136.7
129.8
128.8
128.6
128.4
128.3
128.2
128.2
127.9
127.4
127.4
124.0
86.4
78.3
55.3
47.0
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

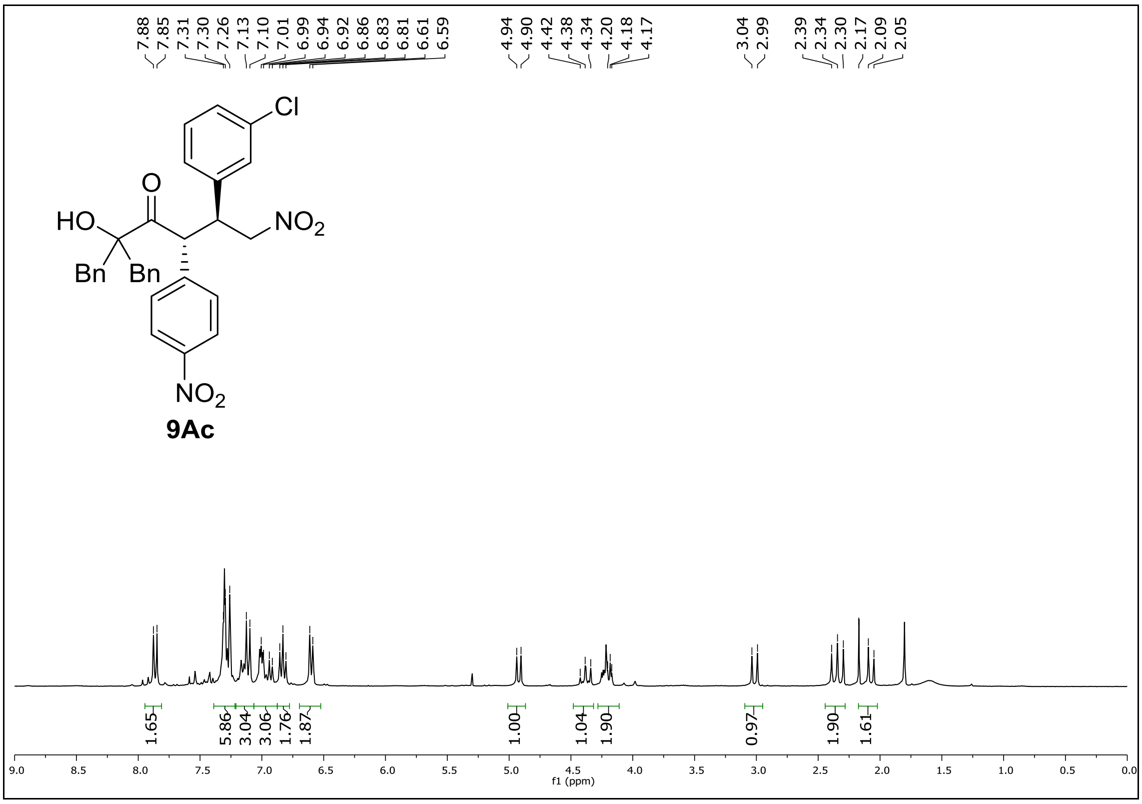

7.88
7.85
7.38
7.36
7.34
7.32
7.28
7.27
7.17
7.14
6.96
6.95
6.94
6.94
6.92
6.88
6.83
6.81
6.79
6.59
6.57
5.02
4.98
4.47
4.43
4.43
4.39
4.30
4.29
4.27
4.25
4.20
4.19
4.16
4.14
3.03
2.98
2.34
2.29
2.24
2.20
1.97
1.92
1.75
O
Ph
HO
NO2
Bn
Bn
NO2
9Aa
1.53
8.47
1.78
2.68
1.80
1.78
1.00
1.01
0.85
1.11
0.95
2.03
0.96
0.86
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
f1 (ppm)

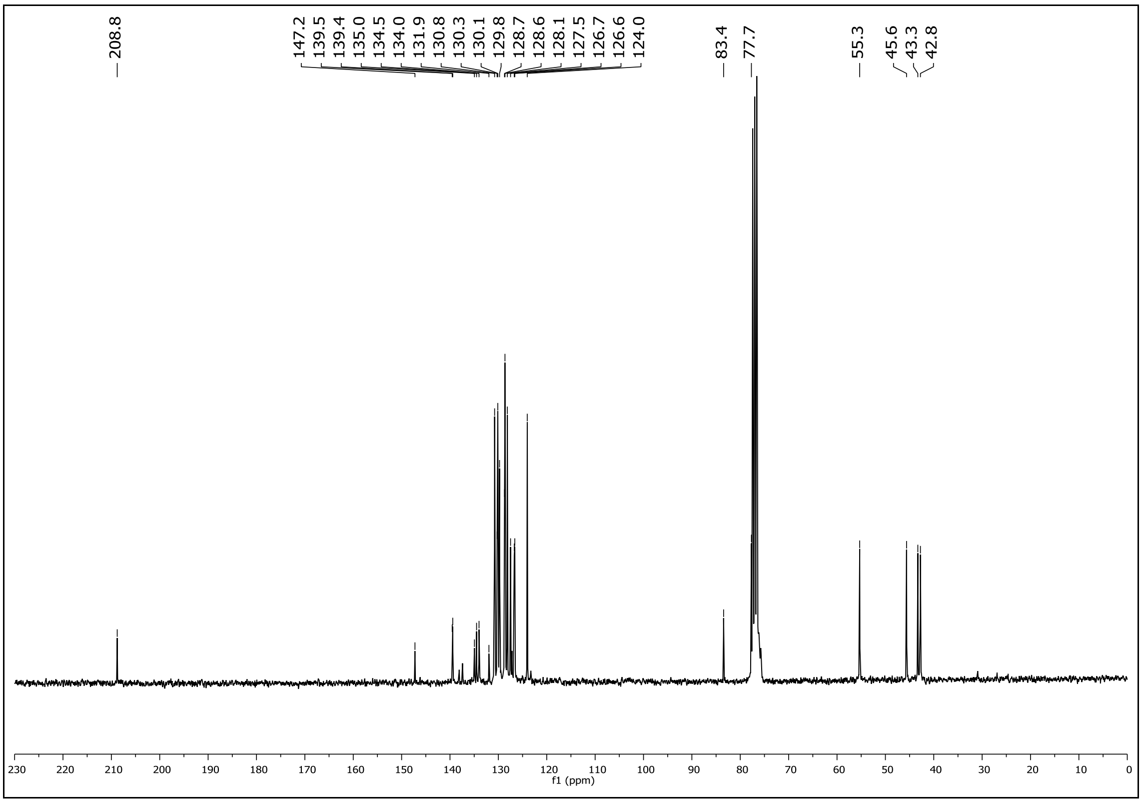

208.9
147.2
139.9
137.4
134.6
134.2
130.8
130.1
129.8
129.1
128.8
128.5
128.1
127.3
126.5
124.0
83.4
78.1
55.5
46.2
42.8
42.5
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

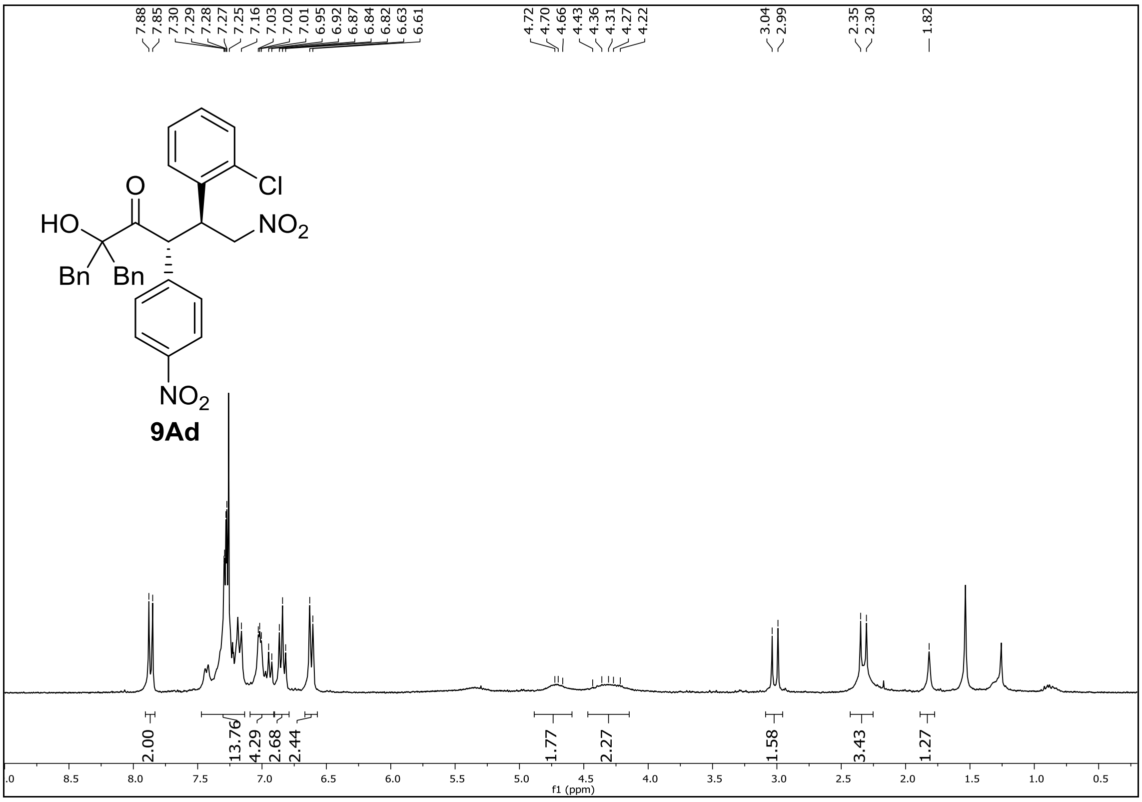

7.90
7.87
7.54
7.51
7.44
7.41
7.30
7.27
7.24
7.23
7.22
6.95
6.94
6.93
6.92
6.89
6.87
6.84
6.81
6.79
6.75
6.73
5.31
5.27
4.81
4.77
4.77
4.73
4.37
4.35
4.32
4.31
4.28
4.26
4.24
4.23
4.20
4.19
4.17
2.93
2.89
2.55
2.50
2.42
2.37
2.28
2.24
Cl
O
HO
NO2
Bn
Bn
NO2
1.55
2.06
1.66
2.05
2.56
6.52
1.00
1.00
0.99
1.02
0.56
0.99
0.99
1.02
1.10
f1 (ppm)

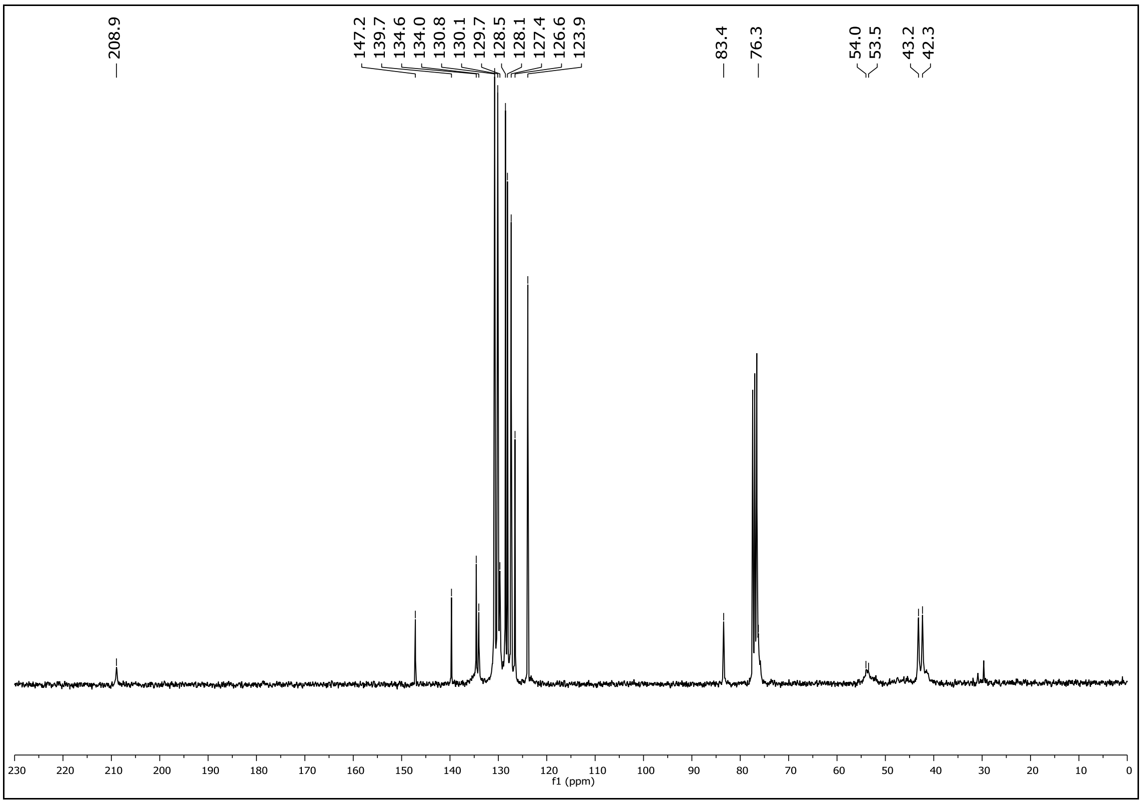
9Ab

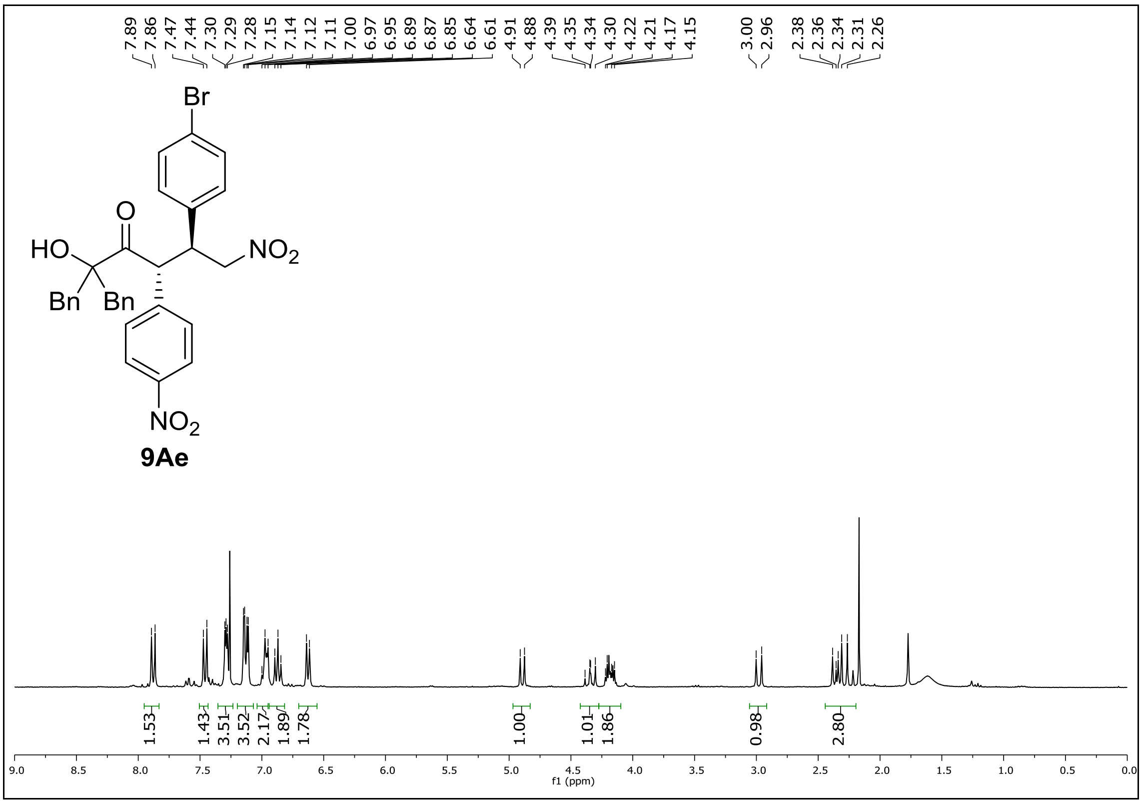

210.4
206.8
148.5
142.4
139.2
137.4
136.6
134.8
132.5
132.3
132.1
131.8
130.2
129.5
128.9
128.2
127.3
125.0
85.1
79.7
56.5
47.5
45.9
44.5
f1 (ppm)


7.88 7.85 7.31 7.30 7.26 7.13 7.10 7.01 6.99 6.94 6.92 6.86 6.83 6.81 6.61 6.59
4.94 4.90 4.42 4.38 4.34 4.20 4.18 4.17
3.04 2.99
2.39 2.34 2.30 2.17 2.09 2.05
Cl
O
HO
NO2
Bn Bn
NO2
9Ac
1.65 5.86 3.04 3.06 1.76 1.87 1.00 1.04 1.90 0.97 1.90 1.61
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


208.8
147.2 139.5 139.4 135.0 134.5 134.0 131.9 130.8 130.3 130.1 129.8 128.7 128.6 128.1 127.5 126.7 126.6 124.0
83.4 77.7
55.3 45.6 43.3 42.8
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

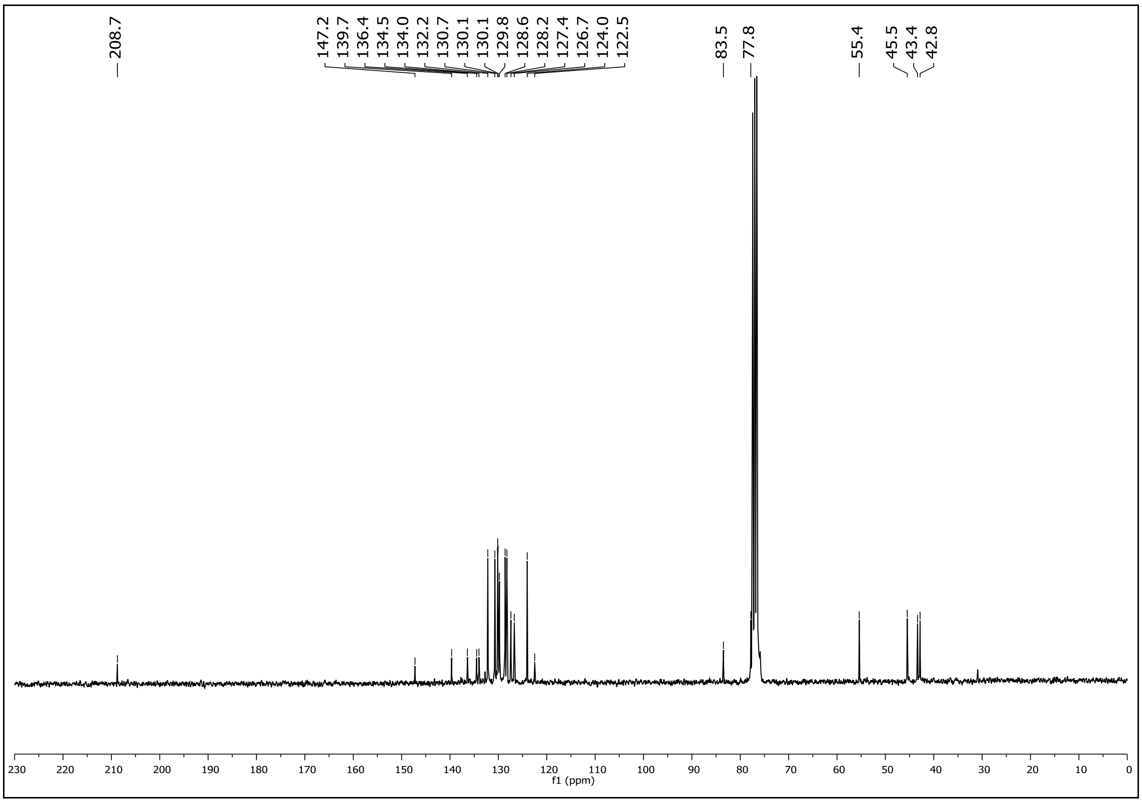

9Ad
7.88
7.85
7.30
7.29
7.28
7.27
7.25
7.16
7.03
7.02
7.01
6.95
6.92
6.87
6.84
6.82
6.63
6.61
4.72
4.70
4.66
4.43
4.36
4.31
4.27
4.22
3.04
2.99
2.35
2.30
1.82
HO
O
Cl
NO2
Bn
Bn
NO2
2.00
13.76
4.29
2.68
2.44
1.77
2.27
1.58
3.43
1.27
f1 (ppm)


208.9
147.2
139.7
134.6
134.0
130.8
130.1
129.7
128.5
128.1
127.4
126.6
123.9
83.4
76.3
54.0
53.5
43.2
42.3
f1 (ppm)

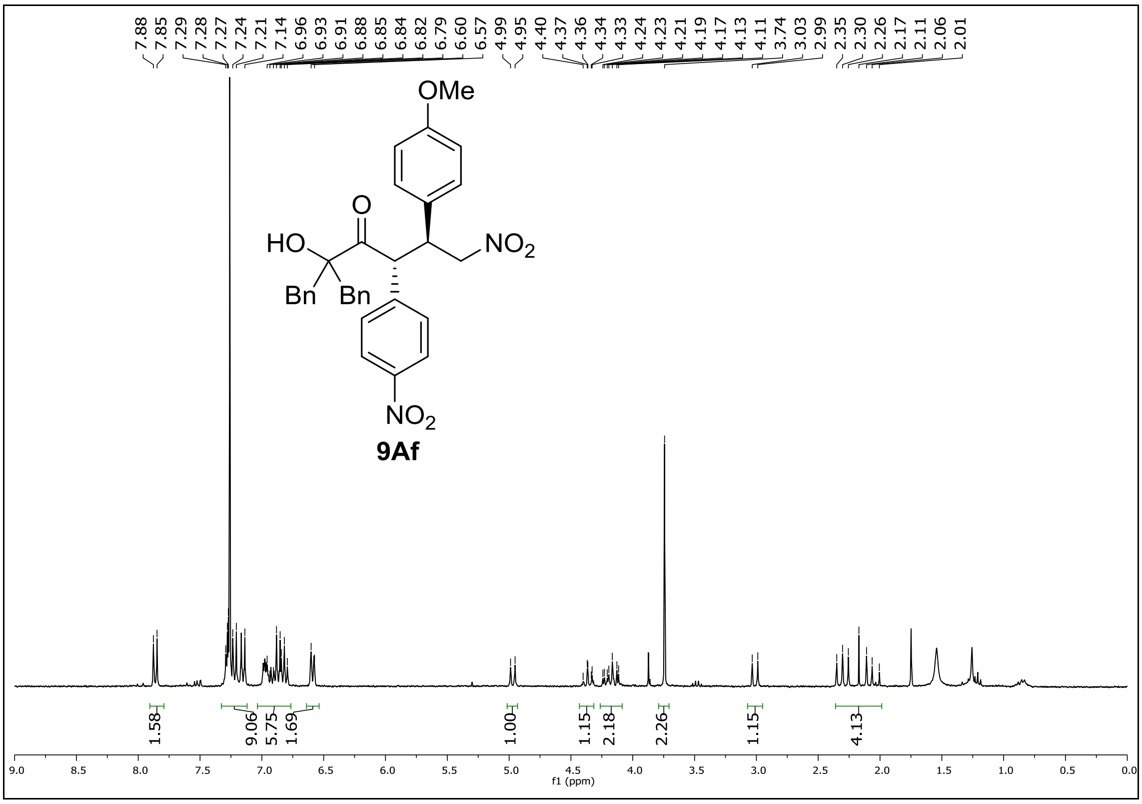


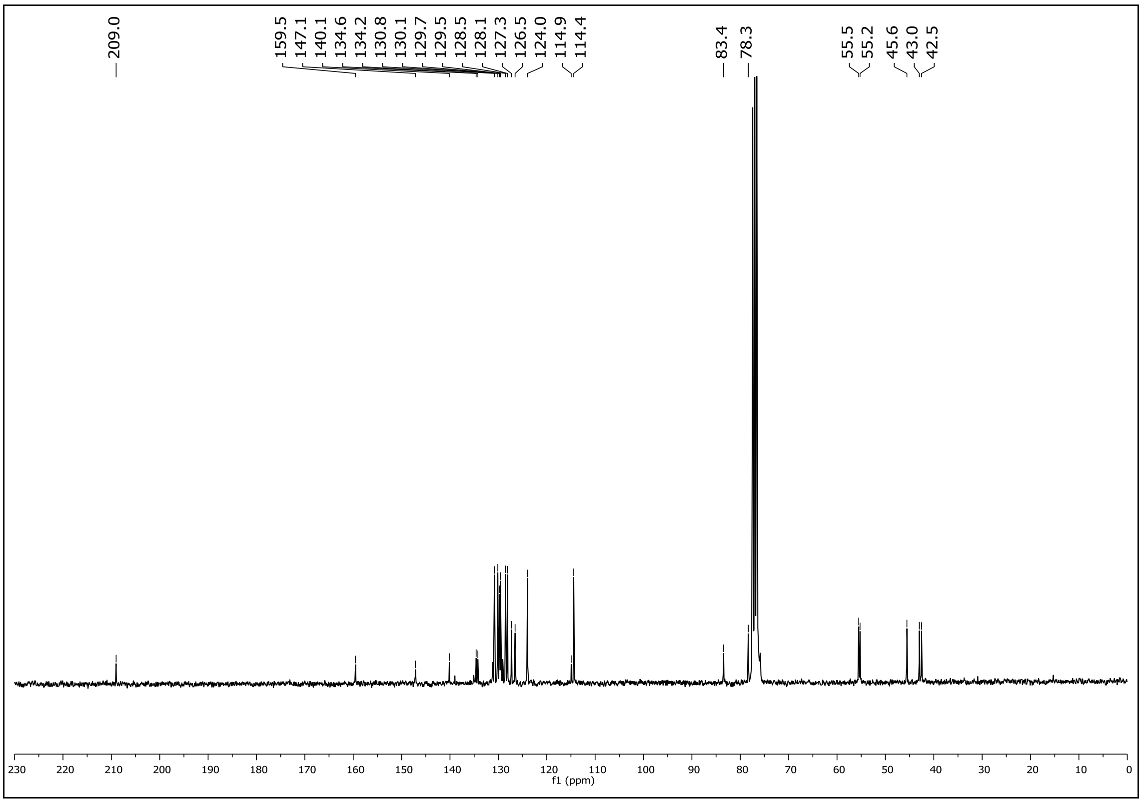
9Ae

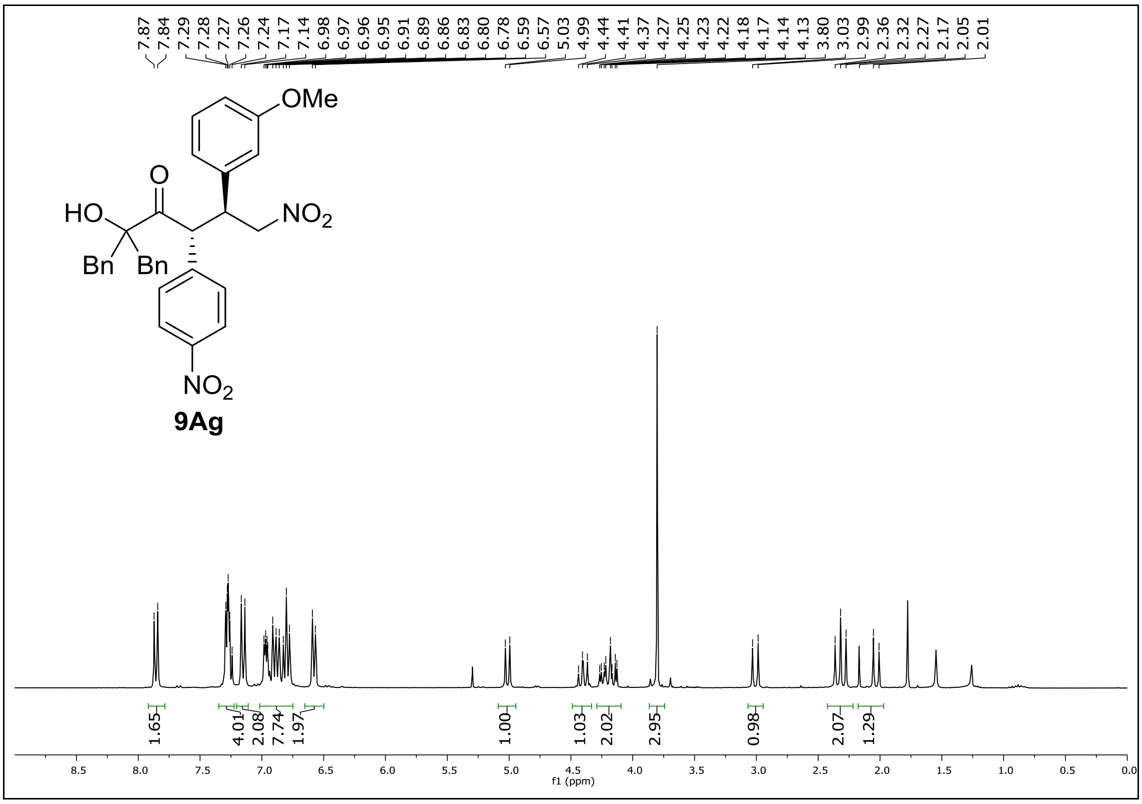
7.89
7.86
7.47
7.44
7.30
7.29
7.28
7.15
7.14
7.12
7.11
7.00
6.97
6.95
6.89
6.87
6.85
6.64
6.61
4.91
4.88
4.39
4.35
4.34
4.30
4.22
4.21
4.17
4.15
3.00
2.96
2.38
2.36
2.34
2.31
2.26
Br
O
HO
NO2
Bn
Bn
NO2
1.53
1.43
3.51
3.52
2.17
1.89
1.78
1.00
1.01
1.86
0.98
2.80
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)



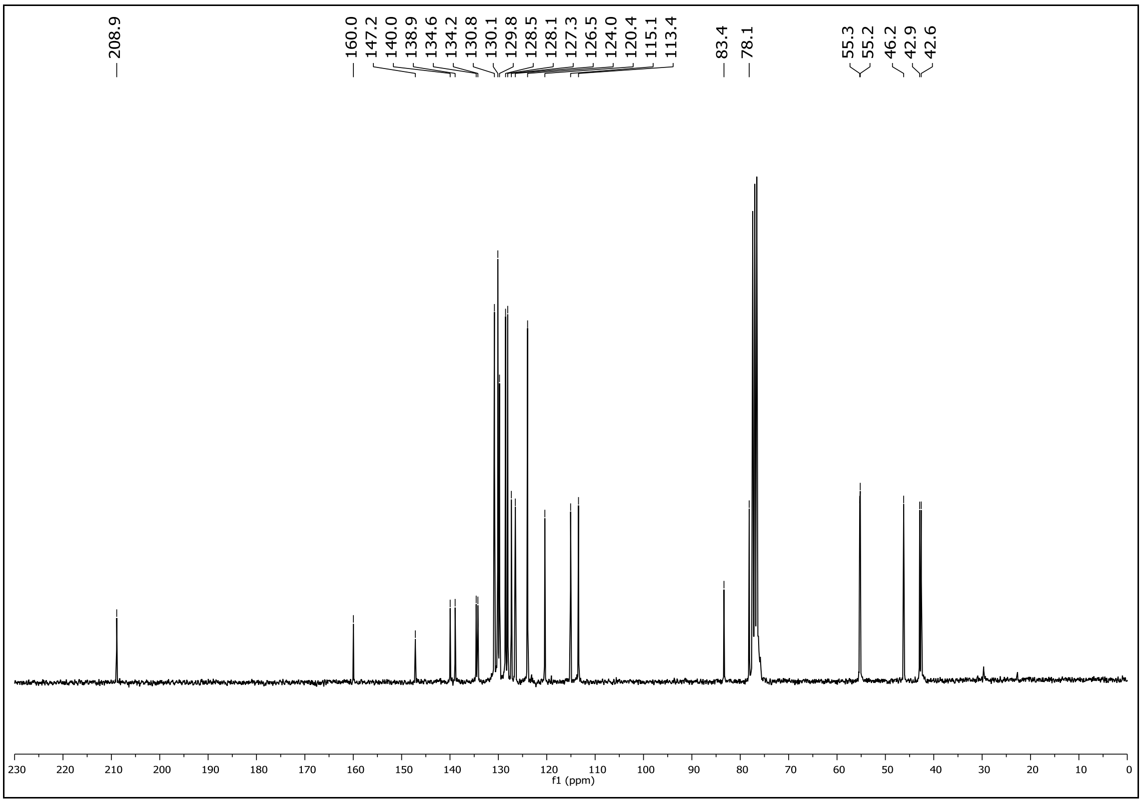
208.7
147.2
139.7
136.4
134.5
134.0
132.2
130.7
130.1
130.1
129.8
128.6
128.2
127.4
126.7
124.0
122.5
83.5
77.8
55.4
45.5
43.4
42.8
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

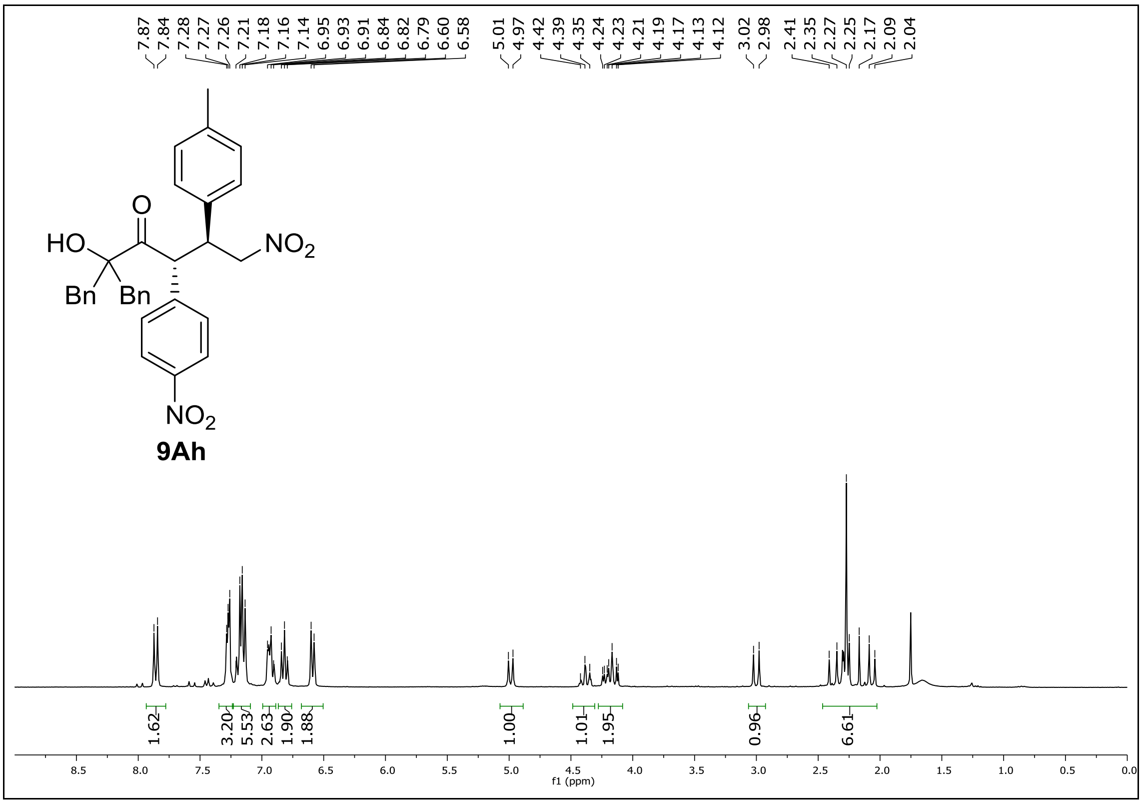

7.88
7.85
7.29
7.28
7.27
7.24
7.21
7.14
6.96
6.93
6.91
6.88
6.85
6.84
6.82
6.79
6.60
6.57
4.99
4.95
4.40
4.37
4.36
4.34
4.33
4.24
4.23
4.21
4.19
4.17
4.13
4.11
3.74
3.03
2.99
2.35
2.30
2.26
2.17
2.11
2.06
2.01
OMe
O
HO
NO2
Bn
Bn
NO2
9Af
1.58
9.06
5.75
1.69
1.00
1.15
2.18
2.26
1.15
4.13
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


209.0
159.5
147.1
140.1
134.6
134.2
130.8
130.1
129.7
129.5
128.5
128.1
127.3
126.5
124.0
114.9
114.4
83.4
78.3
55.5
55.2
45.6
43.0
42.5
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


7.87
7.84
7.29
7.28
7.27
7.26
7.24
7.17
7.14
6.98
6.97
6.96
6.95
6.91
6.89
6.86
6.83
6.80
6.78
6.59
6.57
5.03
4.99
4.44
4.41
4.37
4.27
4.25
4.23
4.22
4.18
4.17
4.14
4.13
3.80
3.03
2.99
2.36
2.32
2.27
2.17
2.05
2.01
OMe
O
HO
NO_2
Bn
Bn
NO_2
1.65
4.01
2.08
7.74
1.97
1.00
1.03
2.02
2.95
0.98
2.07
1.29
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

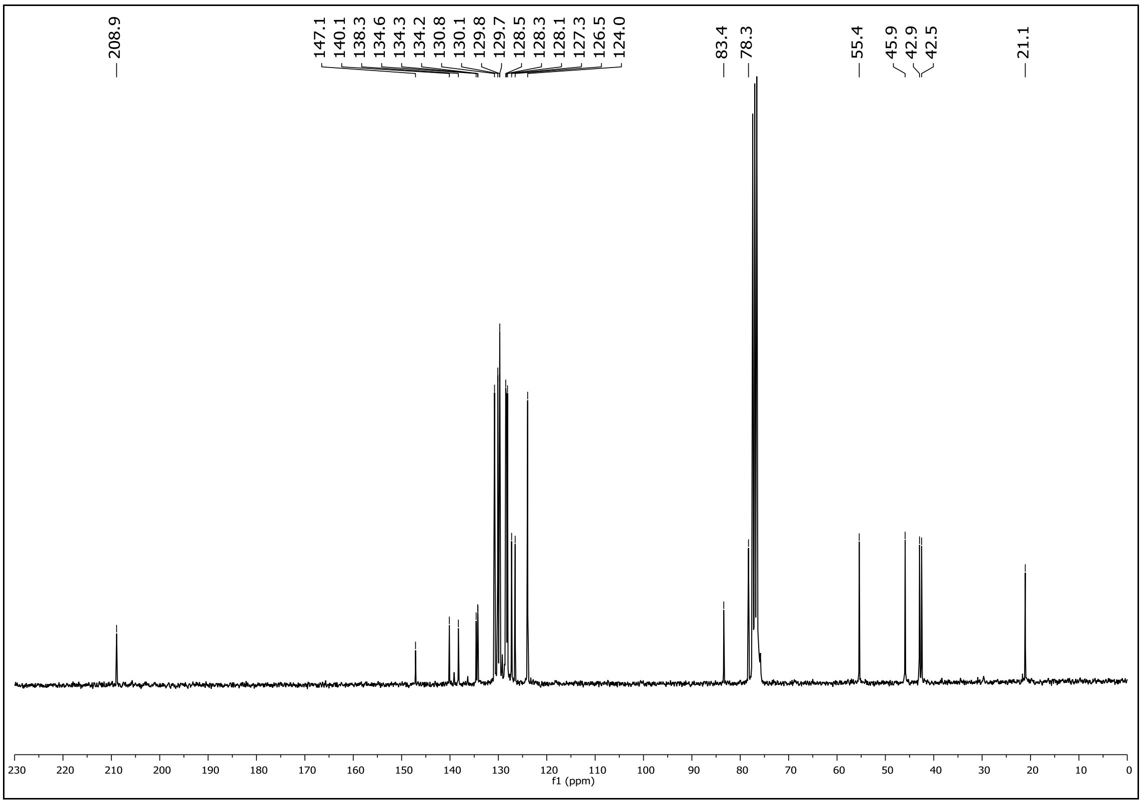
9Ag


208.9
160.0
147.2
140.0
138.9
134.6
134.2
130.8
130.1
129.8
128.5
128.1
127.3
126.5
124.0
120.4
115.1
113.4
83.4
78.1
55.3
55.2
46.2
42.9
42.6
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

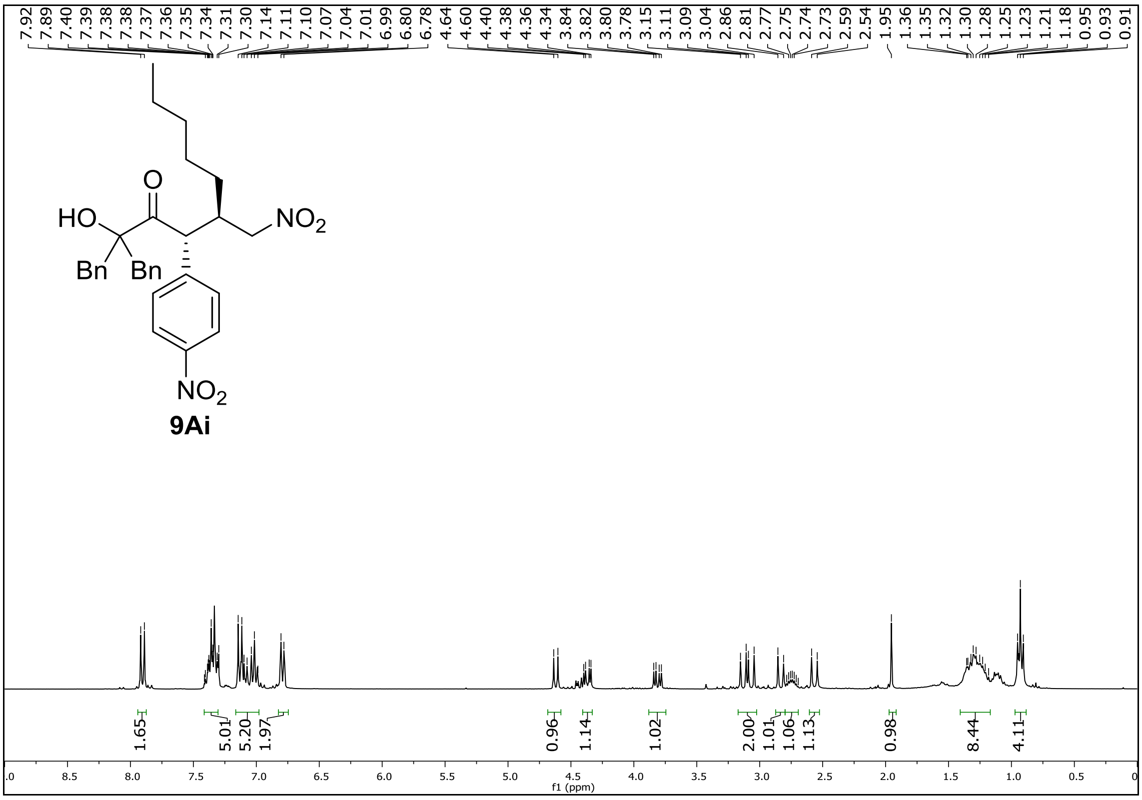


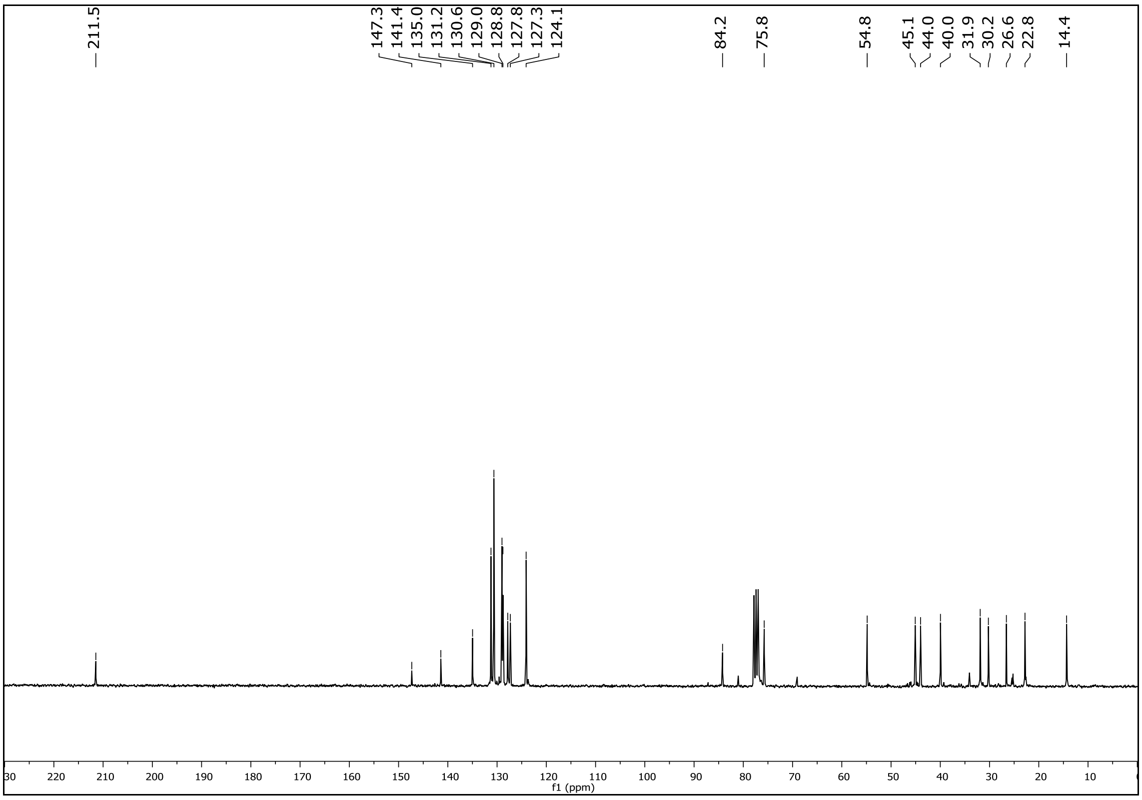
9Ah

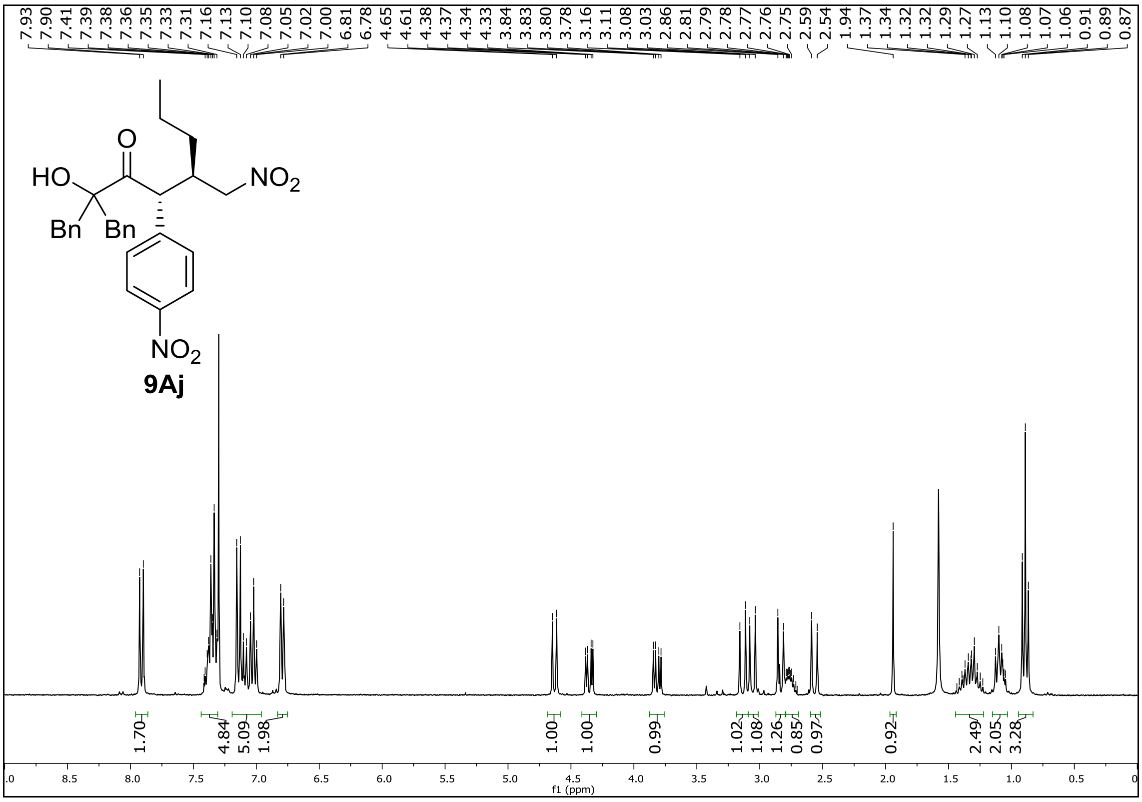
7.87
7.84
7.28
7.27
7.26
7.21
7.18
7.16
7.14
6.95
6.93
6.91
6.84
6.82
6.79
6.60
6.58
5.01
4.97
4.42
4.39
4.35
4.24
4.23
4.21
4.19
4.17
4.13
4.12
3.02
2.98
2.41
2.35
2.27
2.25
2.17
2.09
2.04
HO
O
NO2
Bn
Bn
NO2
1.62
3.20
5.53
2.63
1.90
1.88
1.00
1.01
1.95
0.96
6.61
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

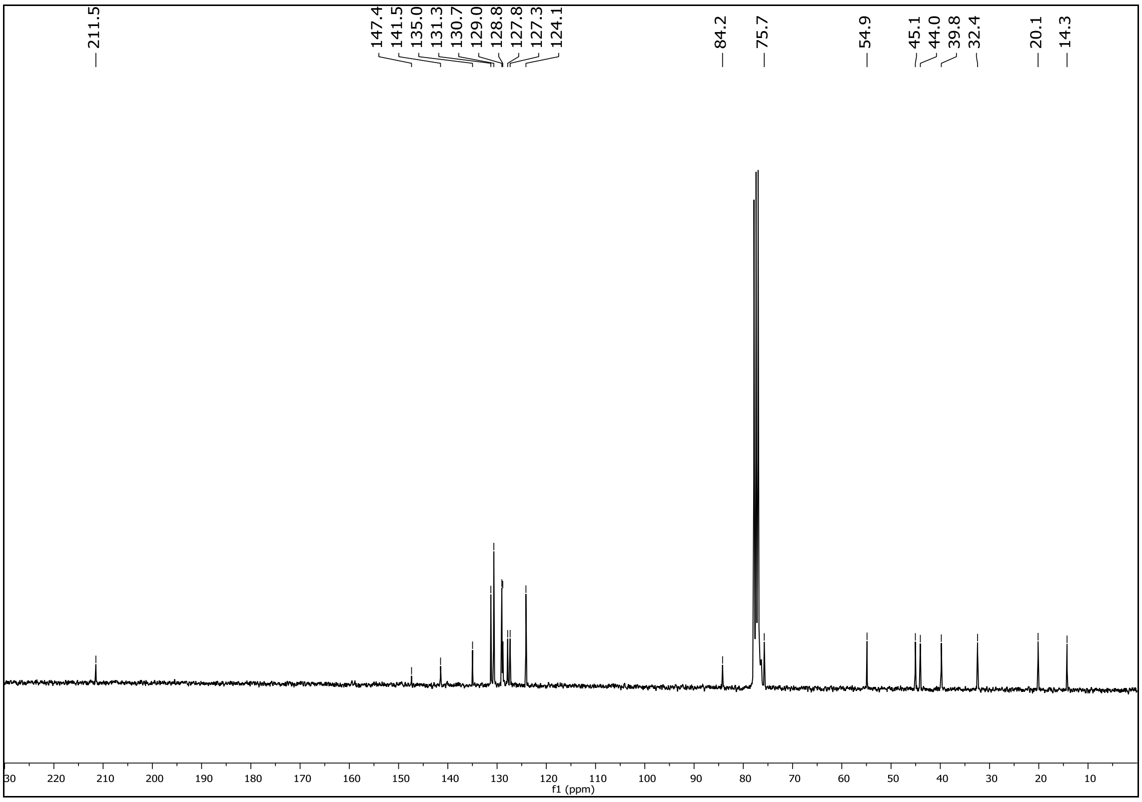


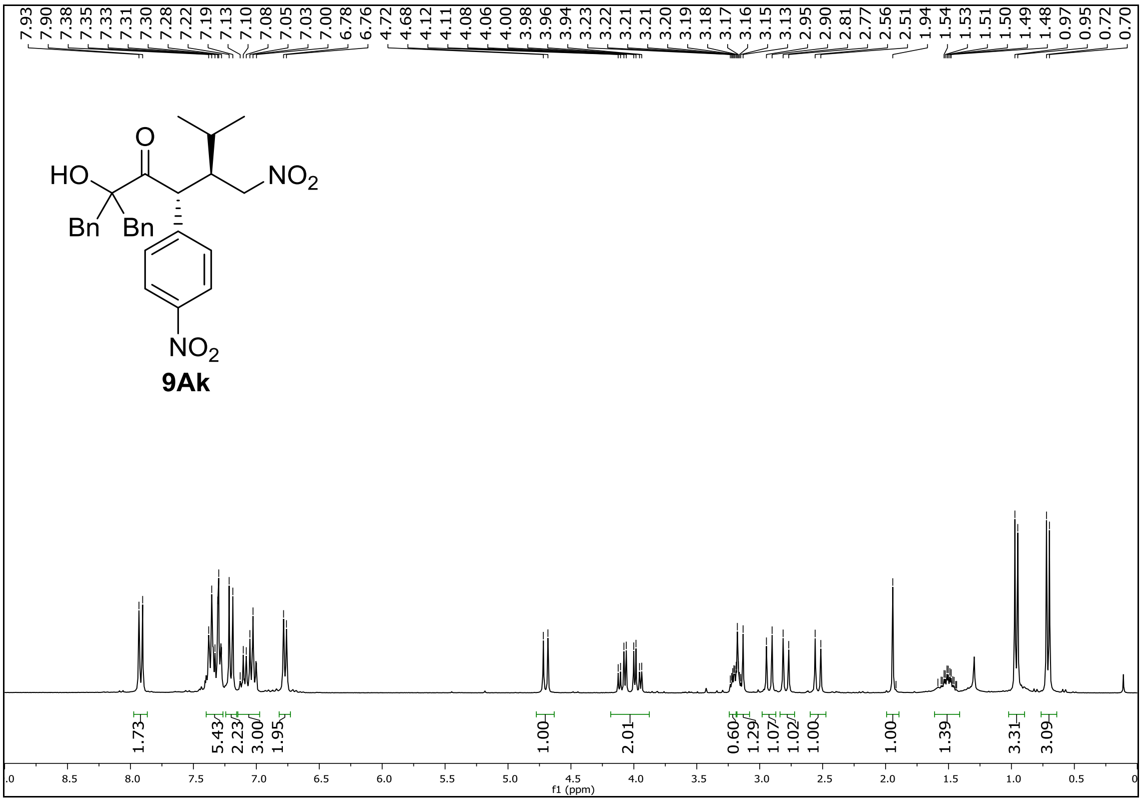
208.9
147.1
140.1
138.3
134.6
134.3
134.2
130.8
130.1
129.8
129.7
128.5
128.3
128.1
127.3
126.5
124.0
83.4
78.3
55.4
45.9
42.9
42.5
21.1
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

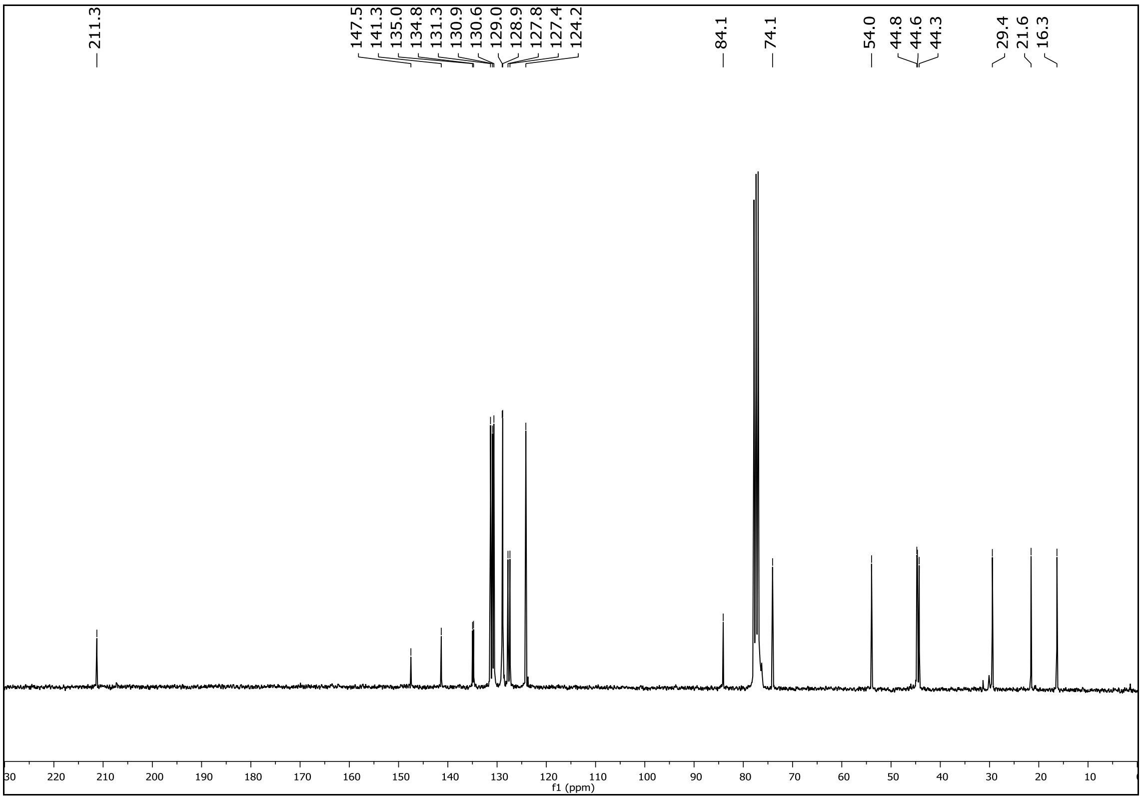

7.92
7.89
7.40
7.39
7.38
7.38
7.37
7.36
7.35
7.34
7.31
7.30
7.14
7.11
7.10
7.07
7.04
7.01
6.99
6.80
6.78
4.64
4.60
4.40
4.38
4.36
4.34
3.84
3.82
3.80
3.78
3.15
3.11
3.09
3.04
2.86
2.81
2.77
2.75
2.74
2.73
2.59
2.54
1.95
1.36
1.35
1.32
1.30
1.28
1.25
1.23
1.21
1.18
0.95
0.93
0.91
O
HO
NO2
Bn
Bn
NO2
9Ai
1.65
5.01
5.20
1.97
0.96
1.14
1.02
2.00
1.01
1.06
1.13
0.98
8.44
4.11
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
f1 (ppm)

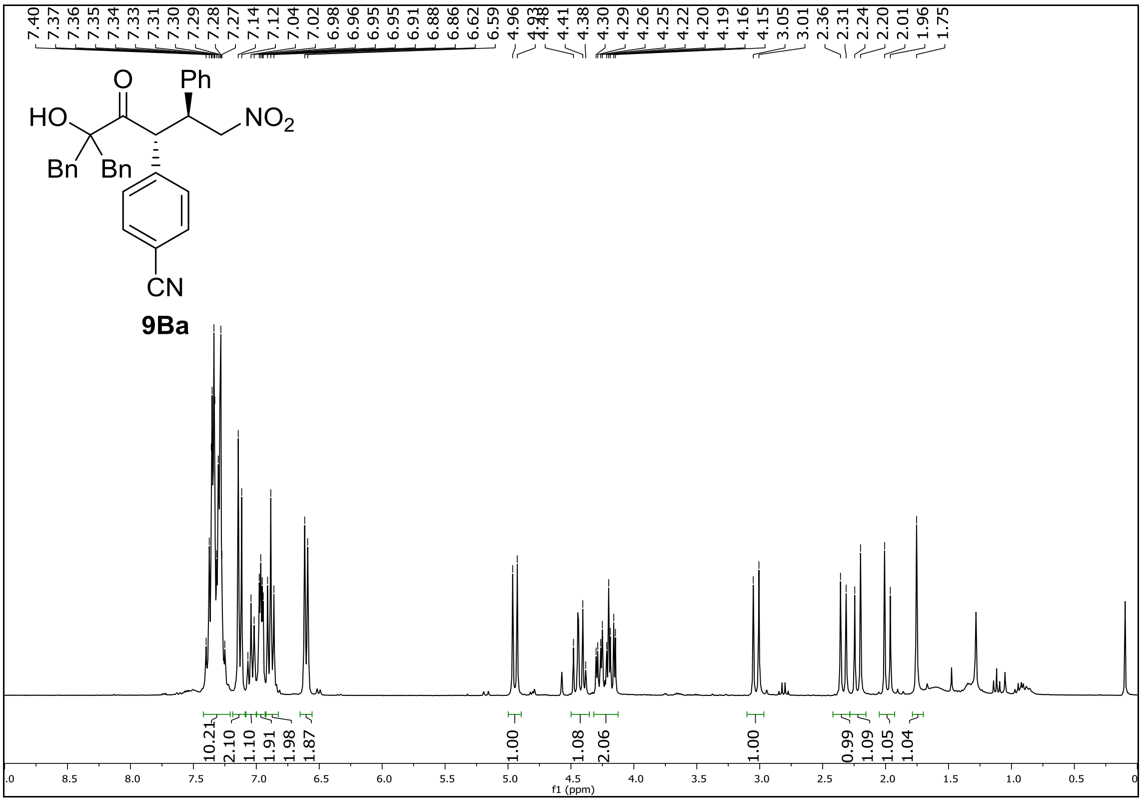

211.5
147.3
141.4
135.0
131.2
130.6
129.0
128.8
127.8
127.3
124.1
84.2
75.8
54.8
45.1
44.0
40.0
31.9
30.2
26.6
22.8
14.4
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

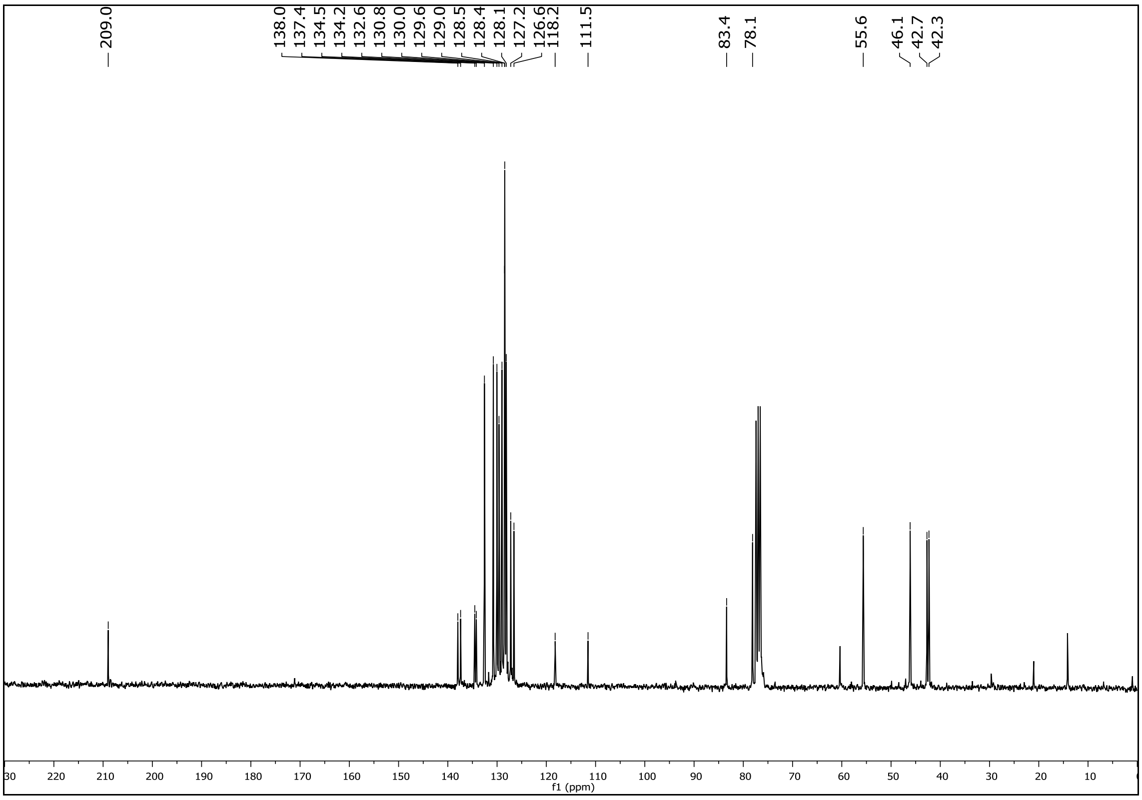

7.93 7.90 7.41 7.39 7.38 7.36 7.35 7.33 7.31 7.16 7.13 7.10 7.08 7.05 7.02 7.00 6.81 6.78 4.65 4.61 4.38 4.37 4.34 4.33 3.84 3.83 3.80 3.78 3.16 3.11 3.08 3.03 2.86 2.81 2.79 2.78 2.77 2.76 2.75 2.59 2.54 1.94 1.37 1.34 1.32 1.32 1.29 1.27 1.13 1.10 1.08 1.07 1.06 0.91 0.89 0.87
O
HO
NO2
Bn
Bn
NO2
9Aj
1.70
4.84
5.09
1.98
1.00
1.00
0.99
1.02
1.08
1.26
0.85
0.97
0.92
2.49
2.05
3.28
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)

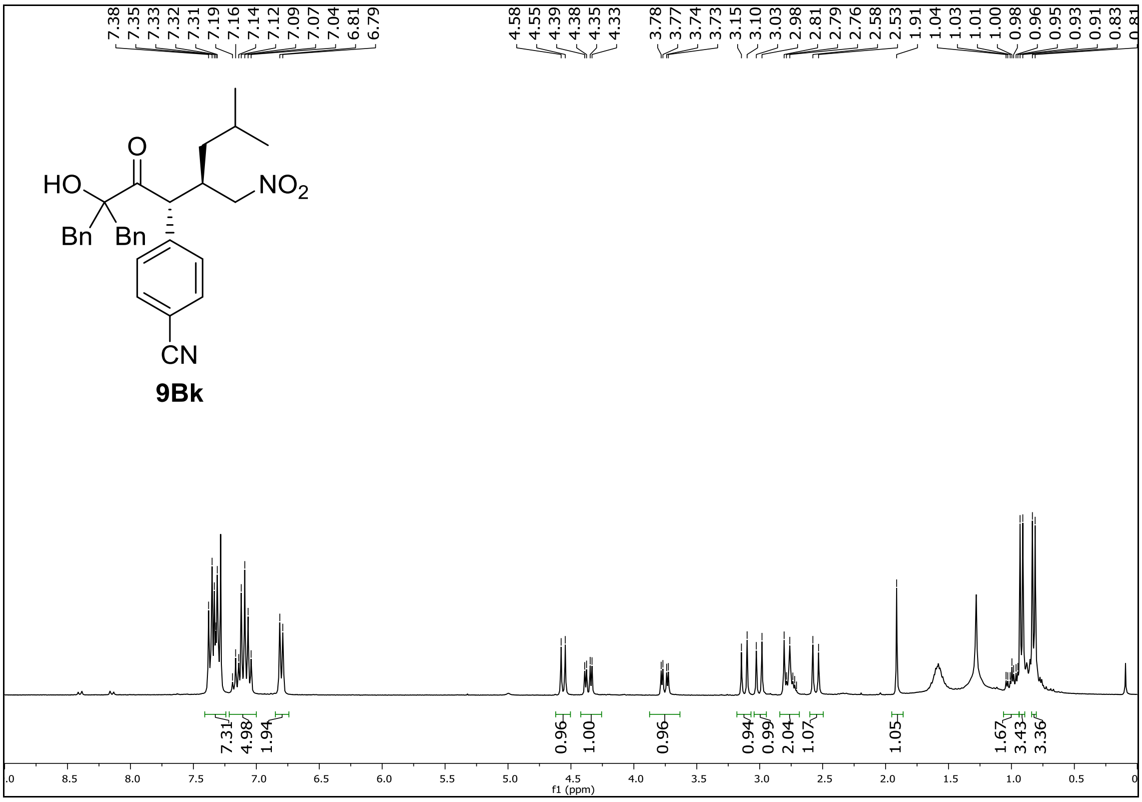

211.5
147.4 141.5 135.0 131.3 130.7 129.0 128.8 127.8 127.3 124.1
84.2
75.7
54.9
45.1 44.0 39.8 32.4
20.1
14.3
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)

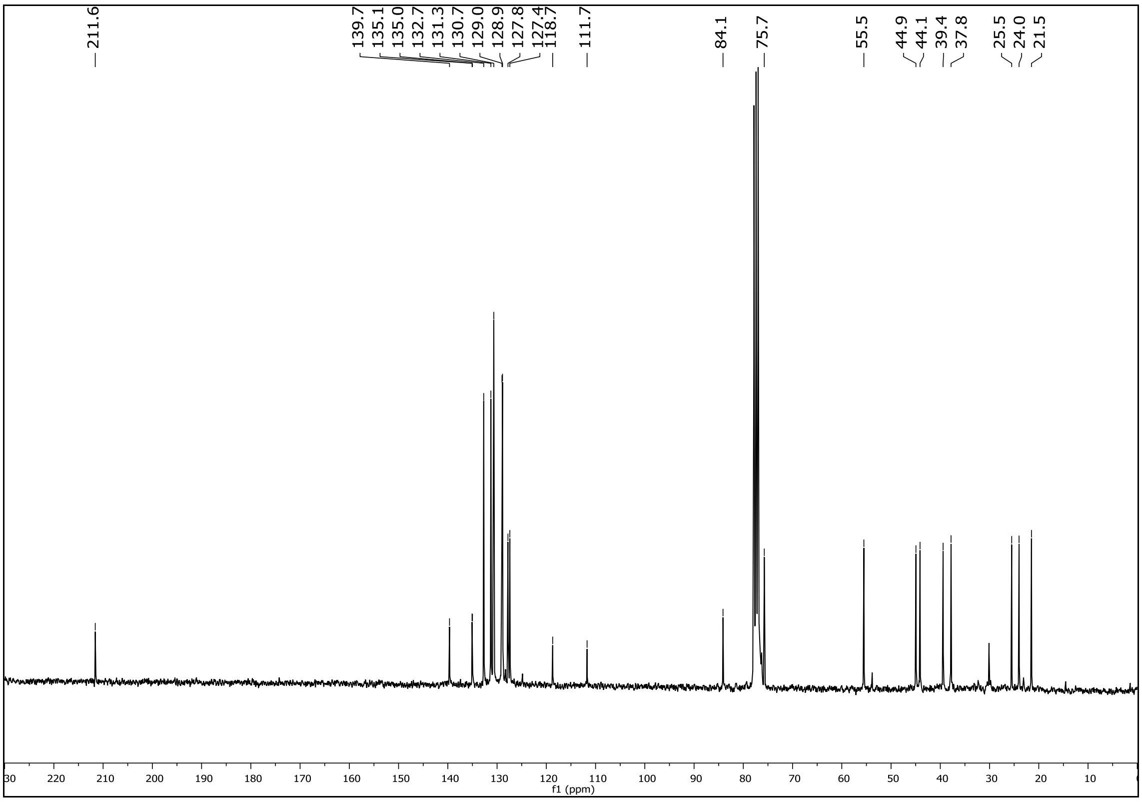

7.93
7.90
7.38
7.35
7.33
7.31
7.30
7.28
7.22
7.19
7.13
7.10
7.08
7.05
7.03
7.00
6.78
6.76
4.72
4.68
4.12
4.11
4.08
4.06
4.00
3.98
3.96
3.94
3.23
3.22
3.21
3.21
3.20
3.19
3.18
3.17
3.16
3.15
3.13
2.95
2.90
2.81
2.77
2.56
2.51
1.94
1.54
1.53
1.51
1.50
1.49
1.48
0.97
0.95
0.72
0.70
O
HO
NO2
Bn
Bn
NO2
9Ak
1.73
5.43
2.23
3.00
1.95
1.00
2.01
0.60
1.29
1.07
1.02
1.00
1.00
1.39
3.31
3.09
.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
f1 (ppm)

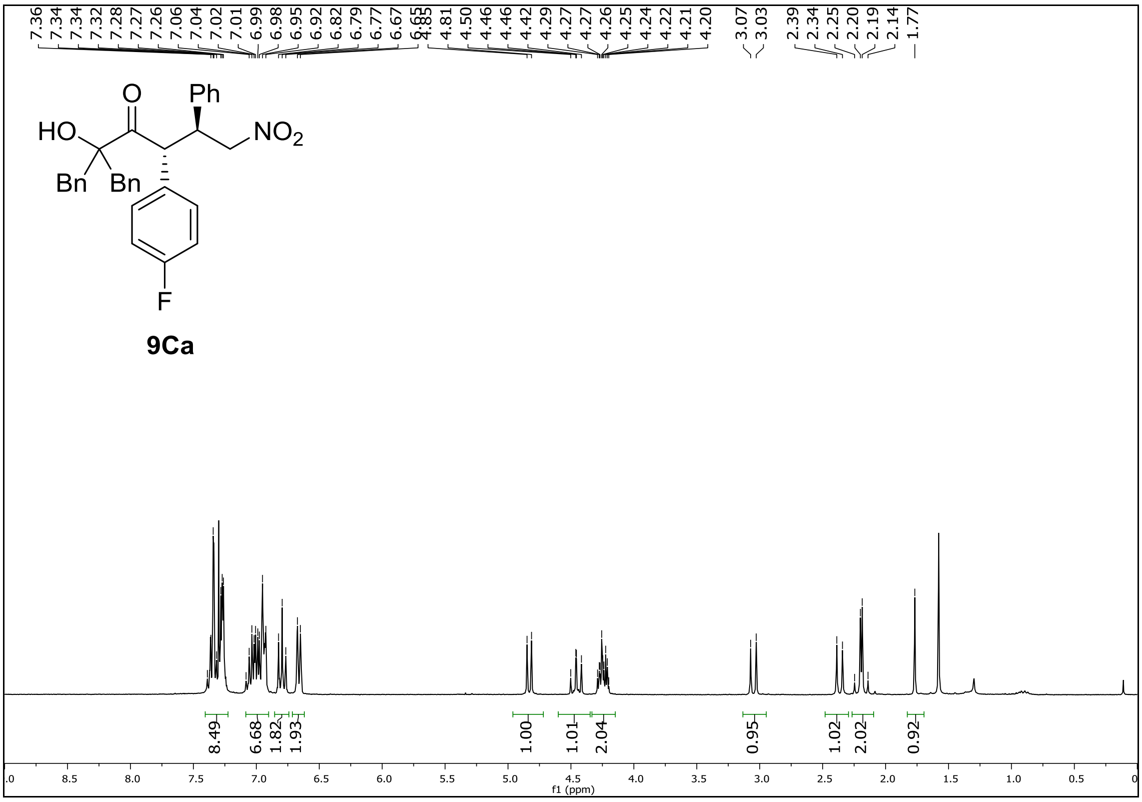

211.3
147.5
141.3
135.0
134.8
131.3
130.9
130.6
129.0
128.9
127.8
127.4
124.2
84.1
74.1
54.0
44.8
44.6
44.3
29.4
21.6
16.3
30
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)


7.40
7.37
7.36
7.35
7.34
7.33
7.31
7.30
7.29
7.28
7.27
7.14
7.12
7.04
7.02
6.98
6.96
6.95
6.95
6.91
6.88
6.86
6.62
6.59
4.96
4.93
4.48
4.41
4.38
4.30
4.29
4.26
4.25
4.22
4.20
4.19
4.16
4.15
3.05
3.01
2.36
2.31
2.24
2.20
2.01
1.96
1.75
O
Ph
HO
NO2
Bn
Bn
CN
9Ba
10.21
2.10
1.10
1.91
1.98
1.87
1.00
1.08
2.06
1.00
0.99
1.09
1.05
1.04
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

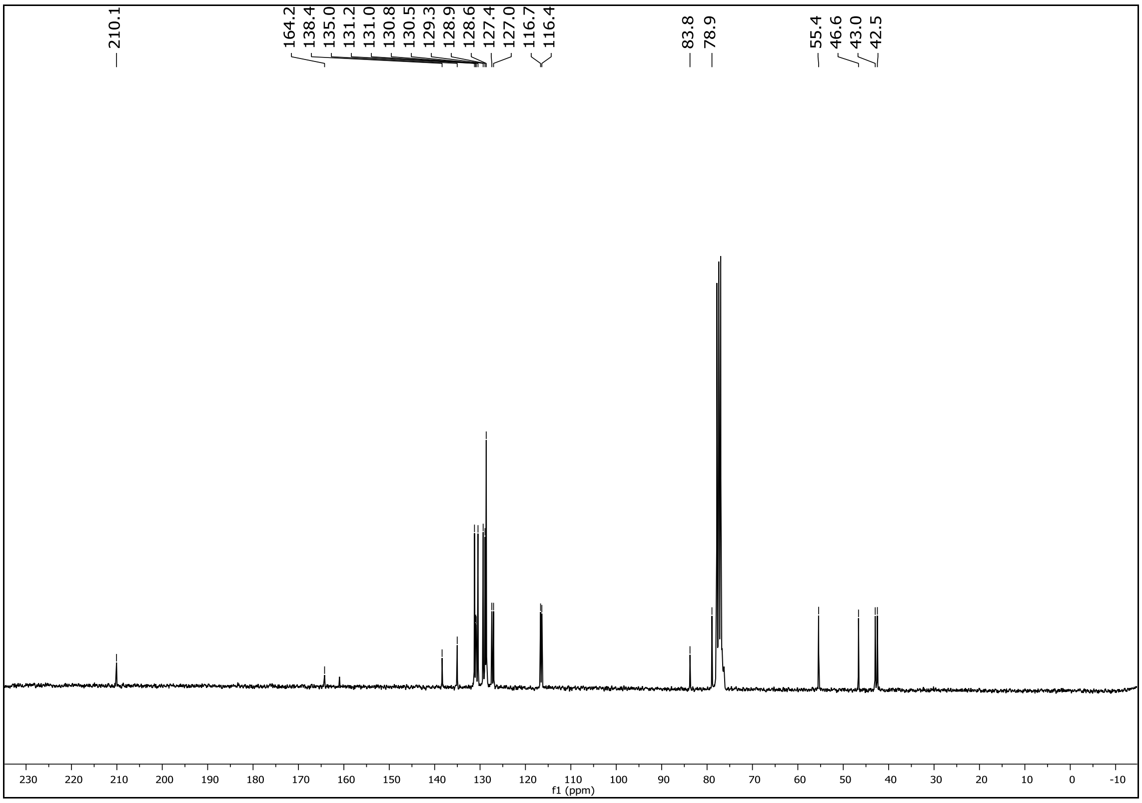

209.0
138.0
137.4
134.5
134.2
132.6
130.8
130.0
129.6
129.0
128.5
128.4
128.1
127.2
126.6
118.2
111.5
83.4
78.1
55.6
46.1
42.7
42.3
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

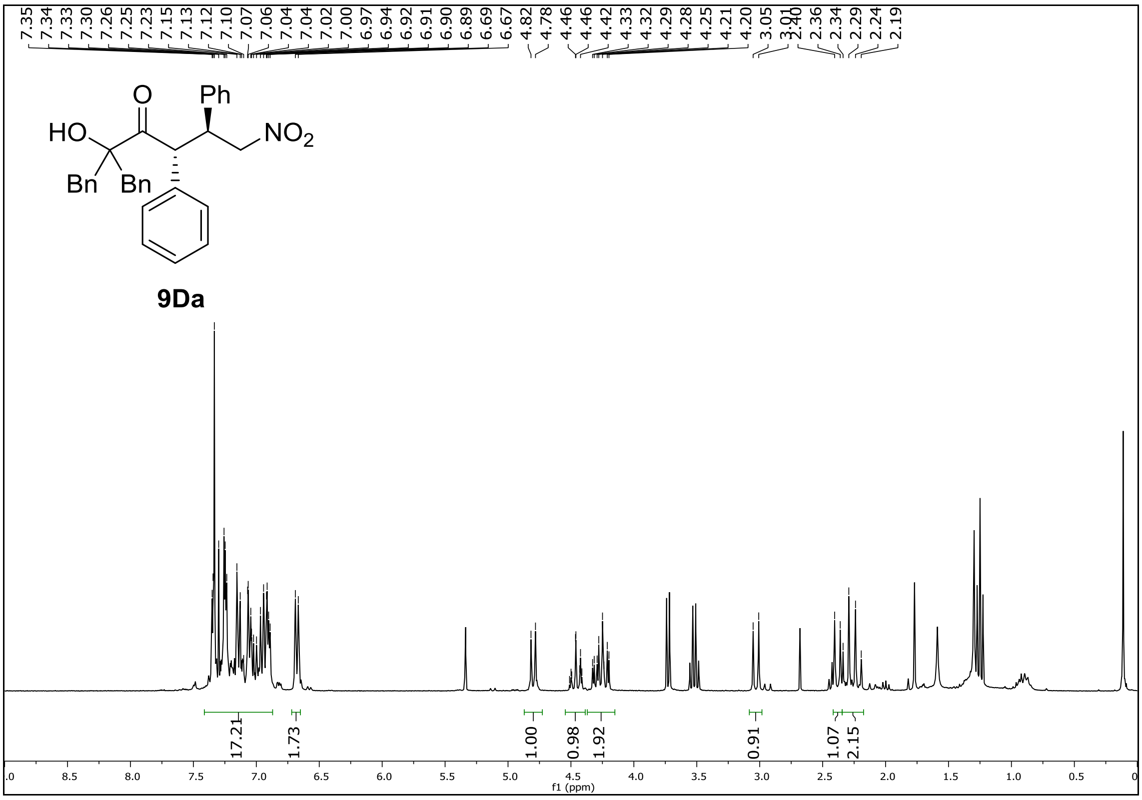

7.38
7.35
7.33
7.32
7.31
7.19
7.16
7.14
7.12
7.09
7.07
7.04
6.81
6.79
4.58
4.55
4.39
4.38
4.35
4.33
3.78
3.77
3.74
3.73
3.15
3.10
3.03
2.98
2.81
2.79
2.76
2.58
2.53
1.91
1.04
1.03
1.01
1.00
0.98
0.96
0.95
0.93
0.91
0.83
0.81
O
HO
NO$_2$
Bn
Bn
CN
9Bk
7.31
4.98
1.94
0.96
1.00
0.96
0.94
0.99
2.04
1.07
1.05
1.67
3.43
3.36
.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
f1 (ppm)


211.6
139.7
135.1
135.0
132.7
131.3
130.7
129.0
128.9
127.8
127.4
118.7
111.7
84.1
75.7
55.5
44.9
44.1
39.4
37.8
25.5
24.0
21.5
30
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

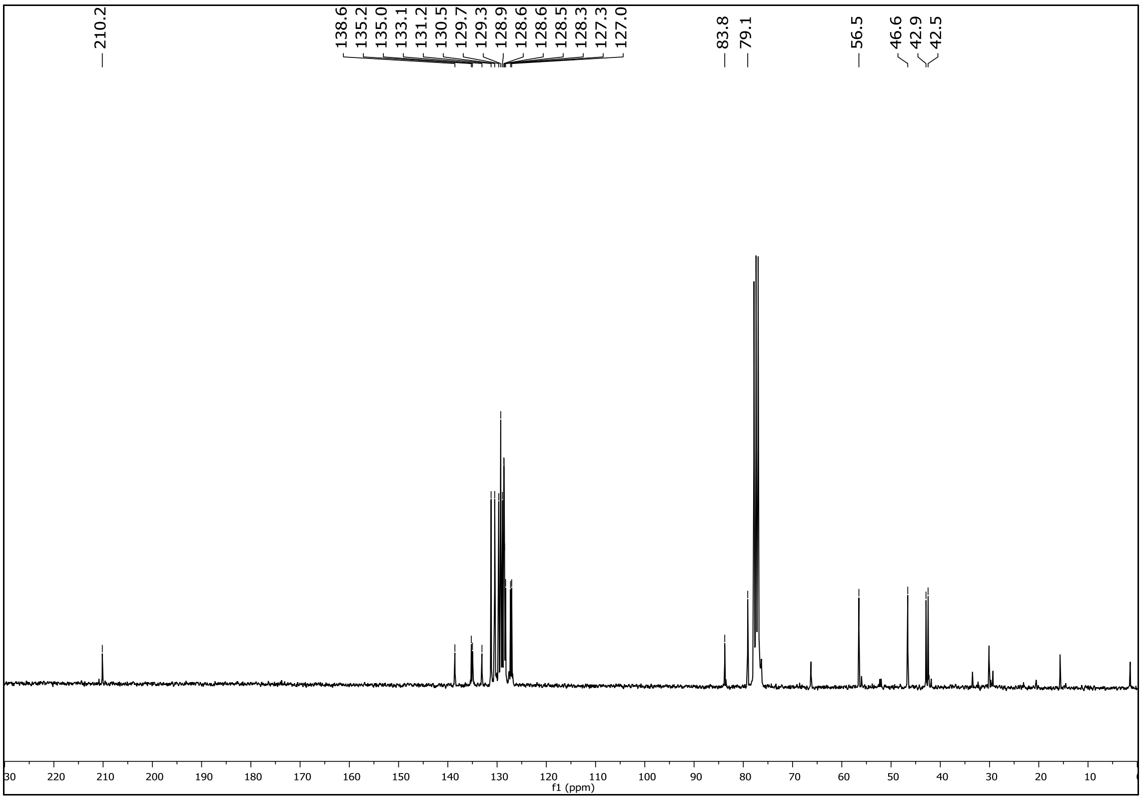

7.36
7.34
7.34
7.32
7.28
7.27
7.26
7.06
7.04
7.02
7.01
6.99
6.98
6.95
6.92
6.82
6.79
6.77
6.67
6.65
4.85
4.81
4.50
4.46
4.46
4.42
4.29
4.27
4.27
4.26
4.25
4.24
4.22
4.21
4.20
3.07
3.03
2.39
2.34
2.25
2.20
2.19
2.14
1.77
O
Ph
HO
NO_2
Bn
Bn
F
8.49
6.68
1.82
1.93
1.00
1.01
2.04
0.95
1.02
2.02
0.92
.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
f1 (ppm)

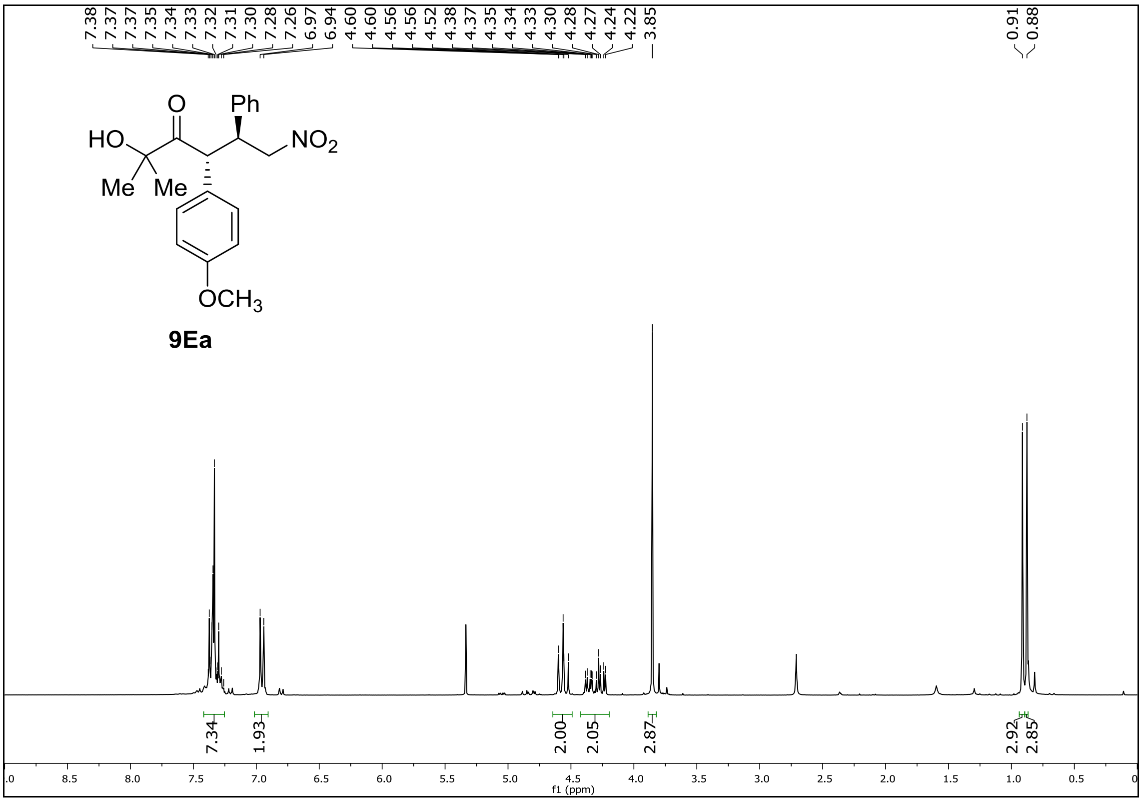
9Ca

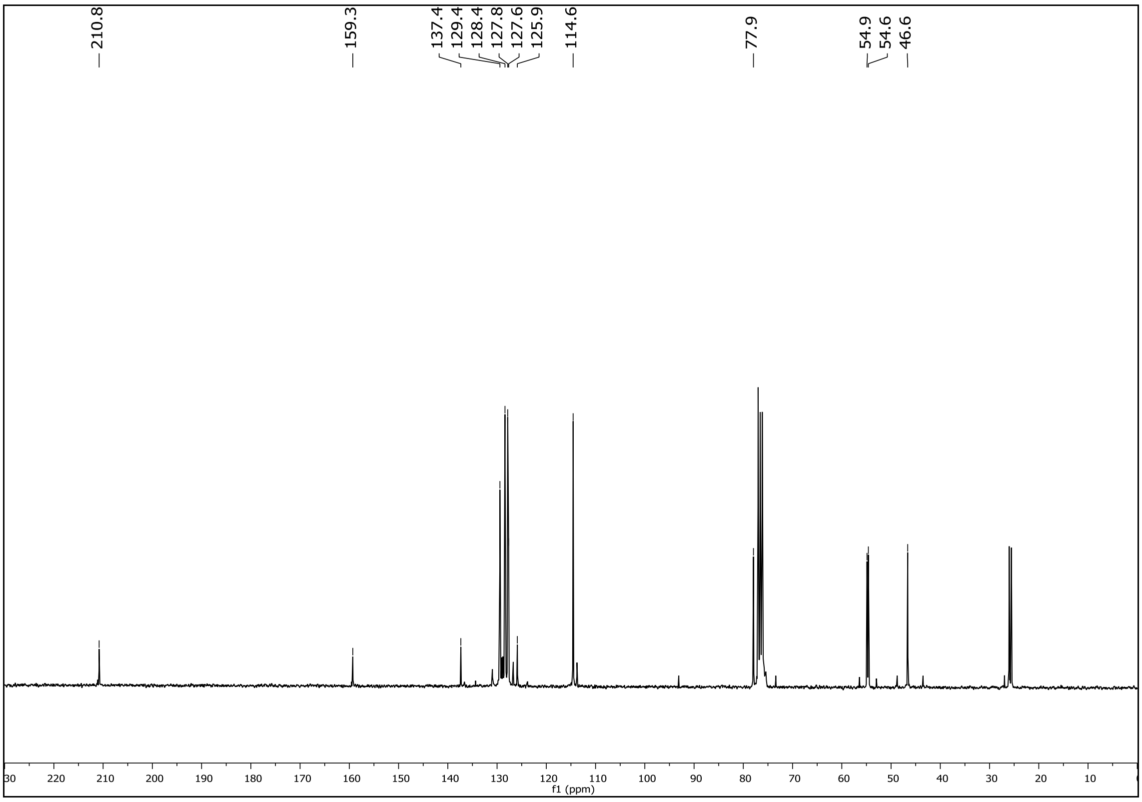

210.1
164.2
138.4
135.0
131.2
131.0
130.8
130.5
129.3
128.9
128.6
127.4
127.0
116.7
116.4
83.8
78.9
55.4
46.6
43.0
42.5
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

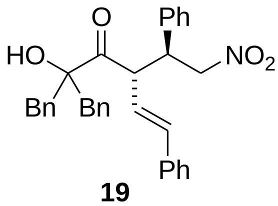

7.35 7.34 7.33 7.30 7.26 7.25 7.23 7.15 7.13 7.12 7.10 7.07 7.06 7.04 7.04 7.02 7.00 6.97 6.94 6.92 6.91 6.90 6.89 6.69 6.67 4.82 4.78 4.46 4.46 4.42 4.33 4.32 4.29 4.28 4.25 4.21 4.20 3.05 3.01 2.40 2.36 2.34 2.29 2.24 2.19
HO
O
Ph
NO2
Bn
Bn
17.21 1.73 1.00 0.98 1.92 0.91 1.07 2.15
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0
f1 (ppm)

9Da

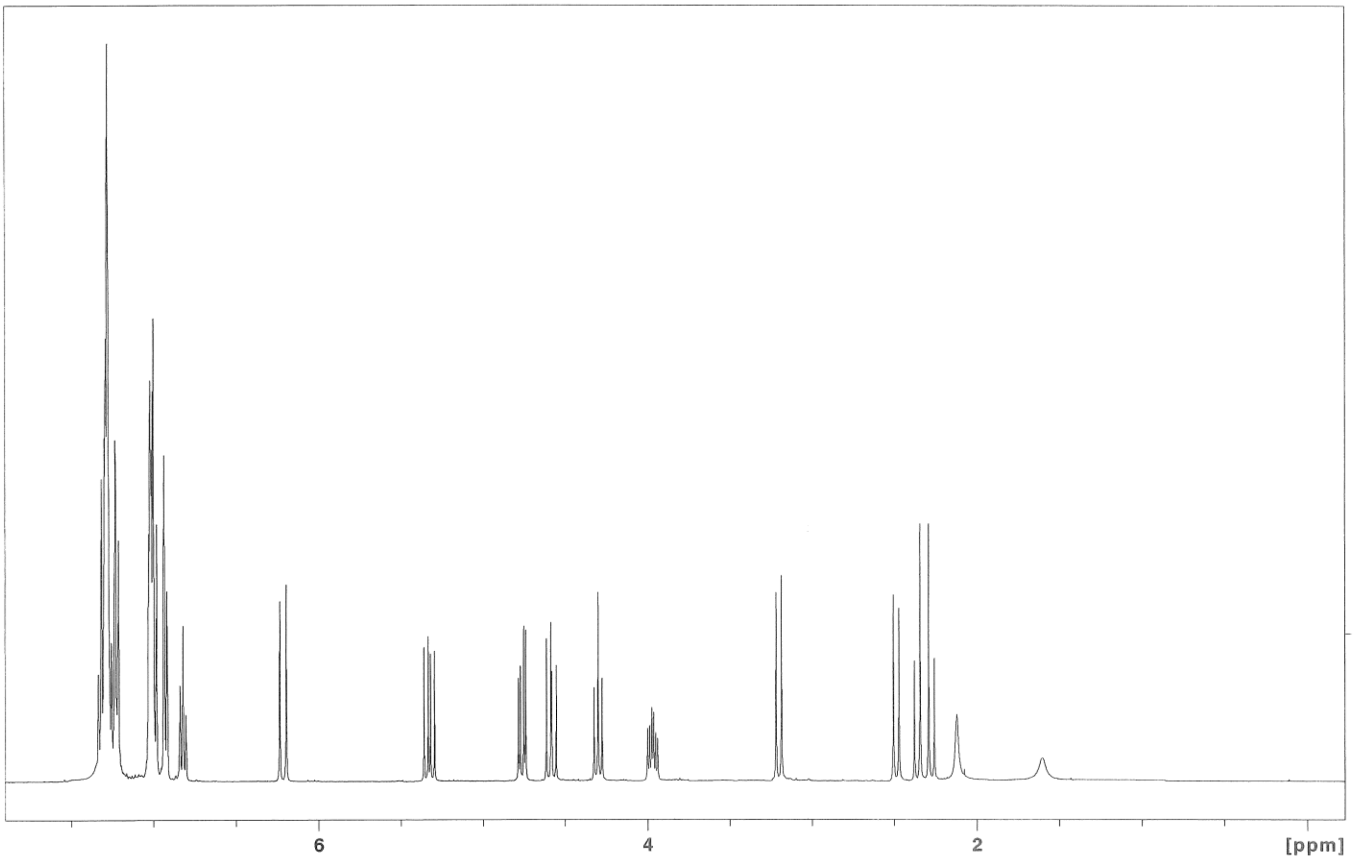

210.2
138.6 135.2 135.0 133.1 131.2 130.5 129.7 129.3 128.9 128.6 128.6 128.5 128.3 127.3 127.0
83.8 79.1
56.5 46.6 42.9 42.5
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

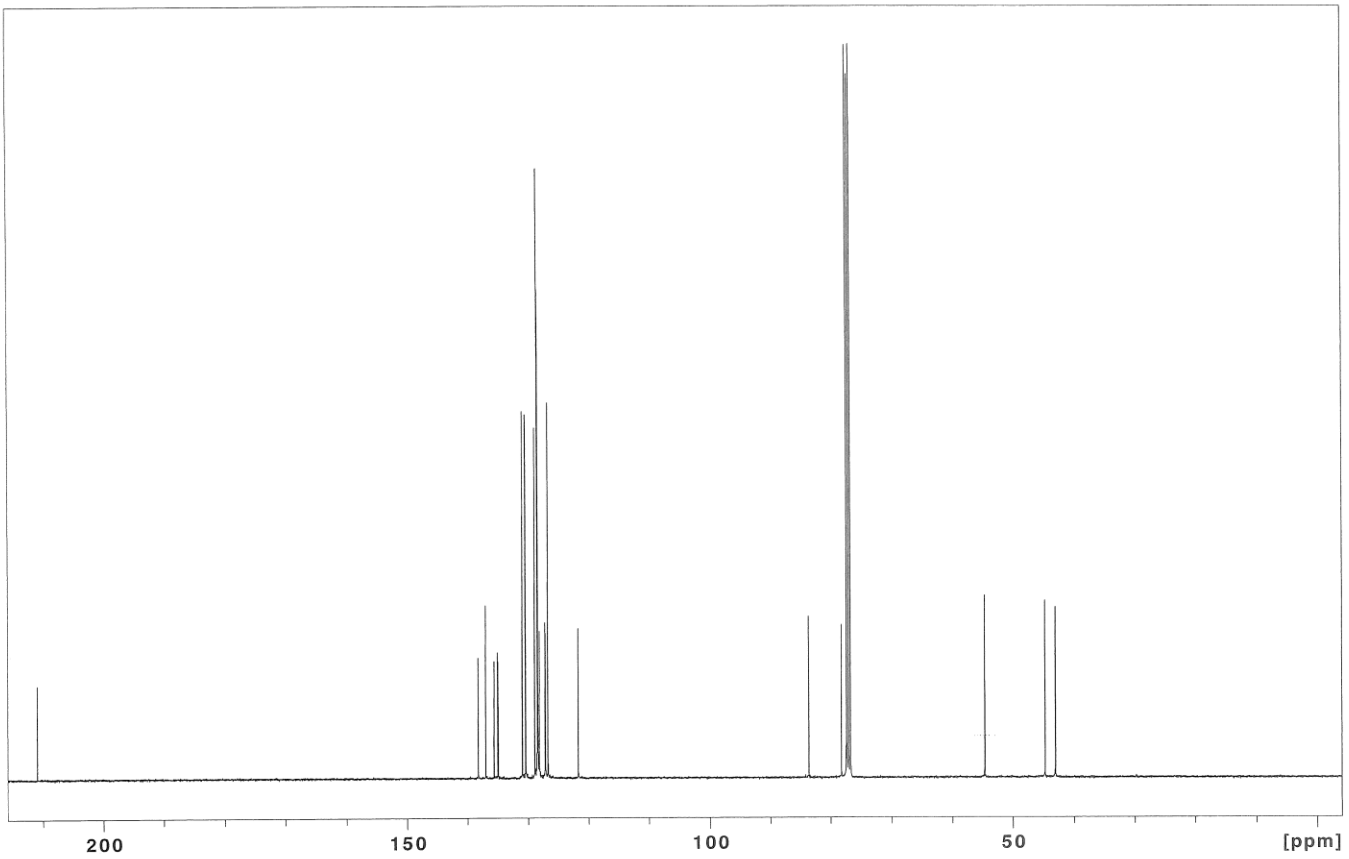

7.38
7.37
7.37
7.35
7.34
7.33
7.32
7.31
7.30
7.28
7.26
6.97
6.94
4.60
4.60
4.56
4.56
4.52
4.38
4.37
4.35
4.34
4.33
4.30
4.28
4.27
4.24
4.22
3.85
0.91
0.88
HO
O
Ph
NO2
Me
Me
OCH3
9Ea
7.34
1.93
2.00
2.05
2.87
2.92
2.85
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

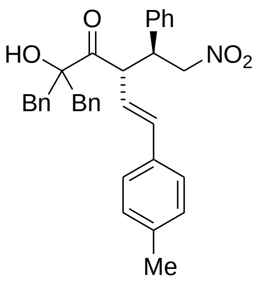

210.8
159.3
137.4
129.4
128.4
127.8
127.6
125.9
114.6
77.9
54.9
54.6
46.6
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)



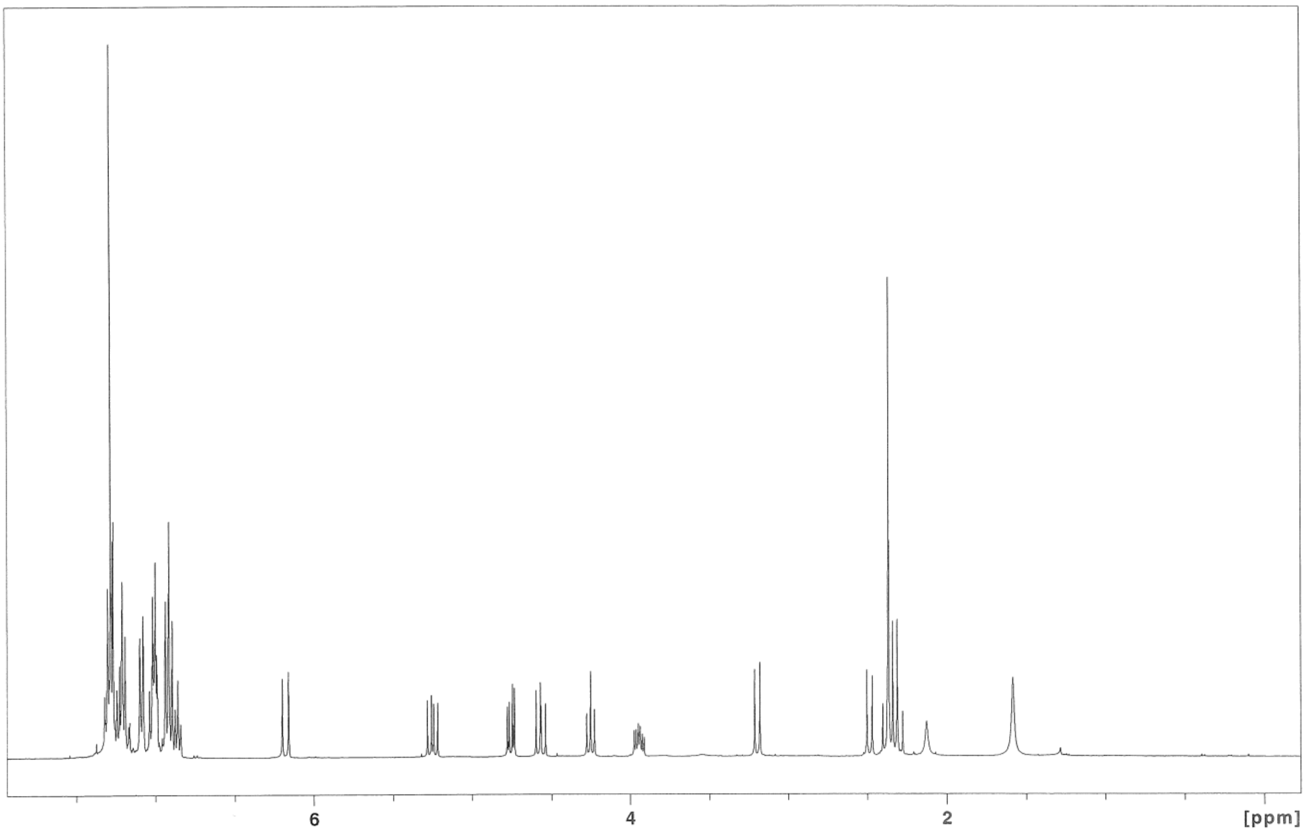
19

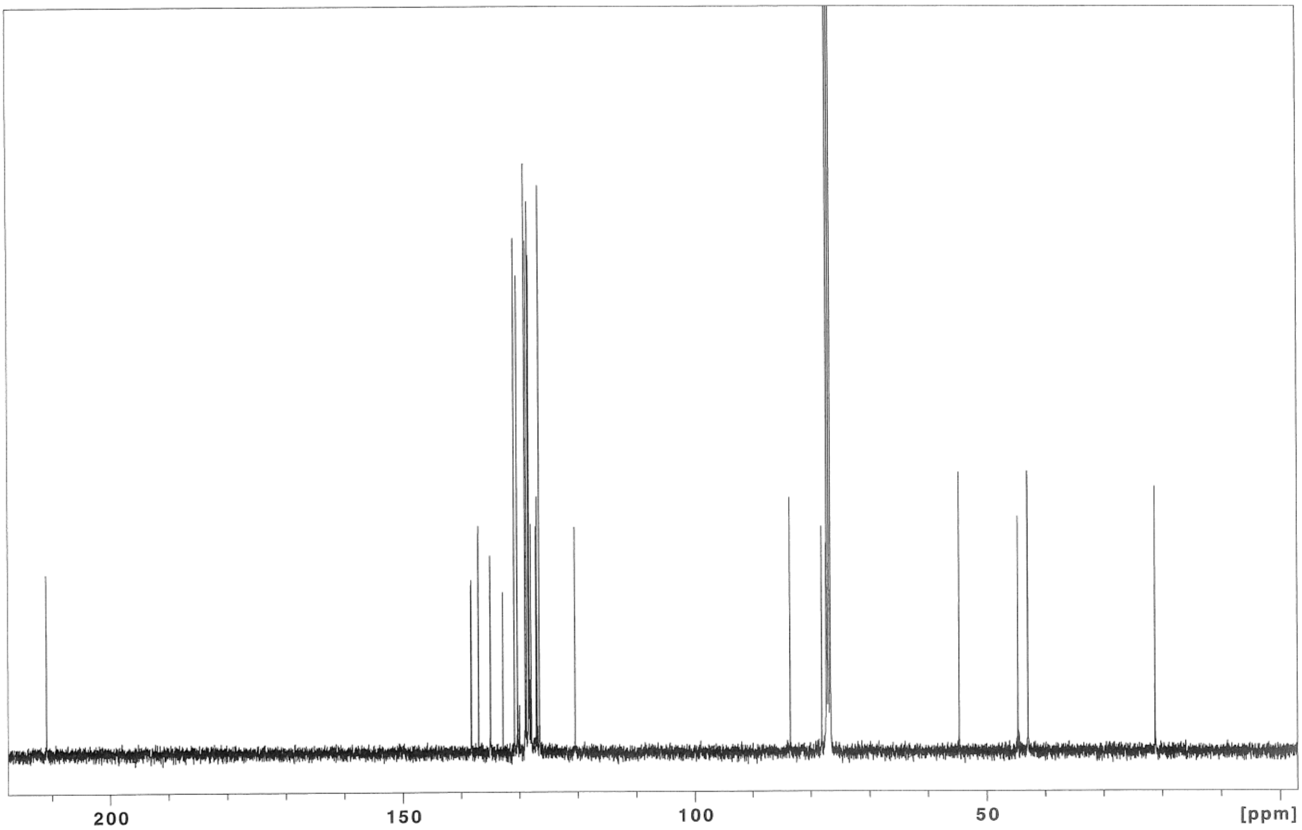


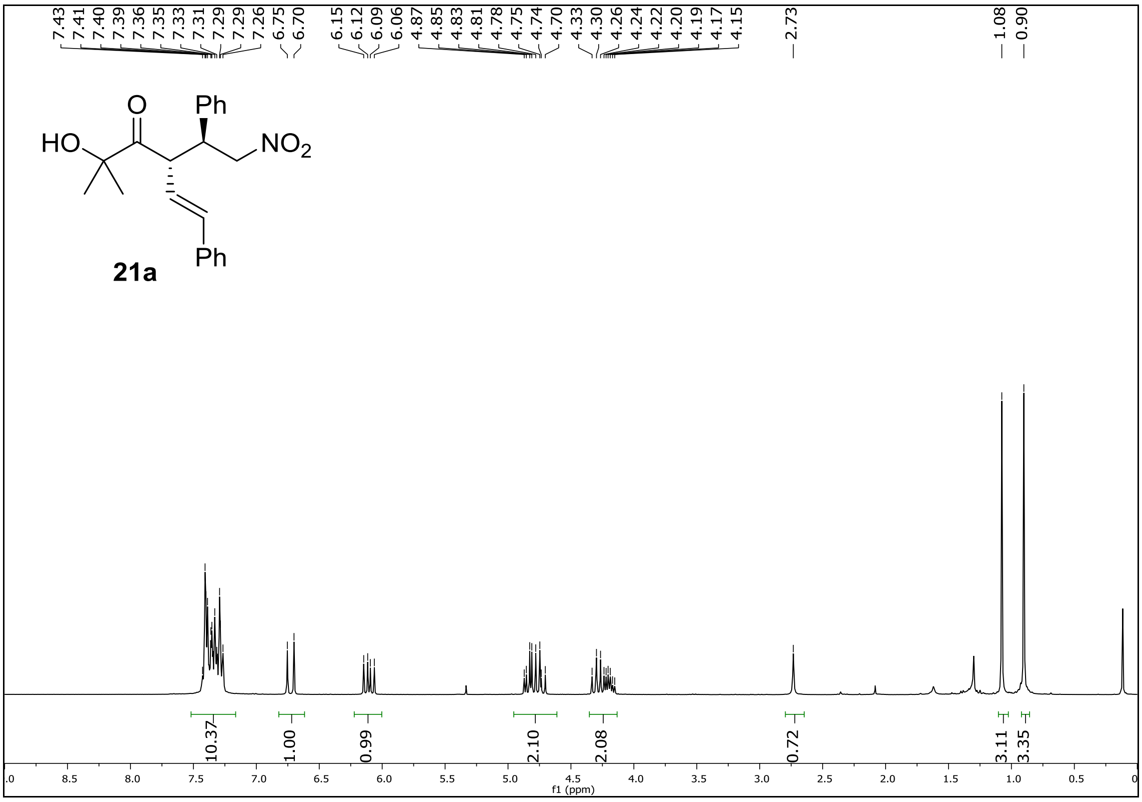


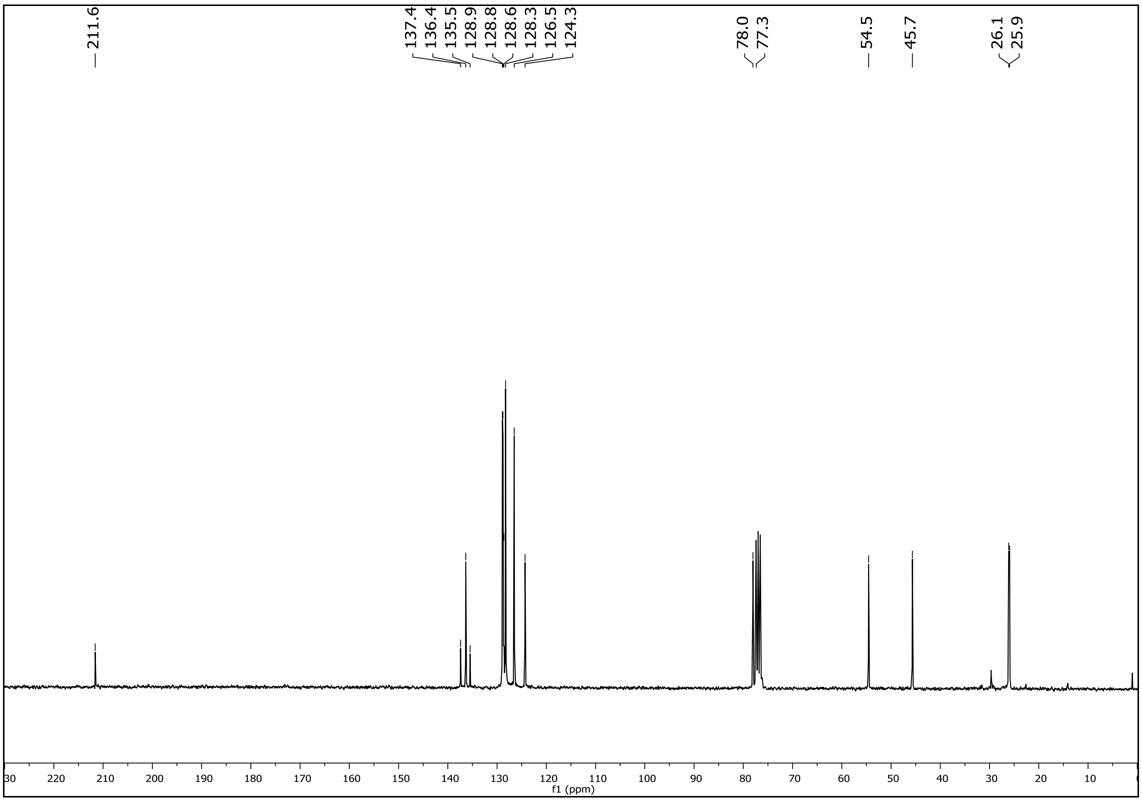


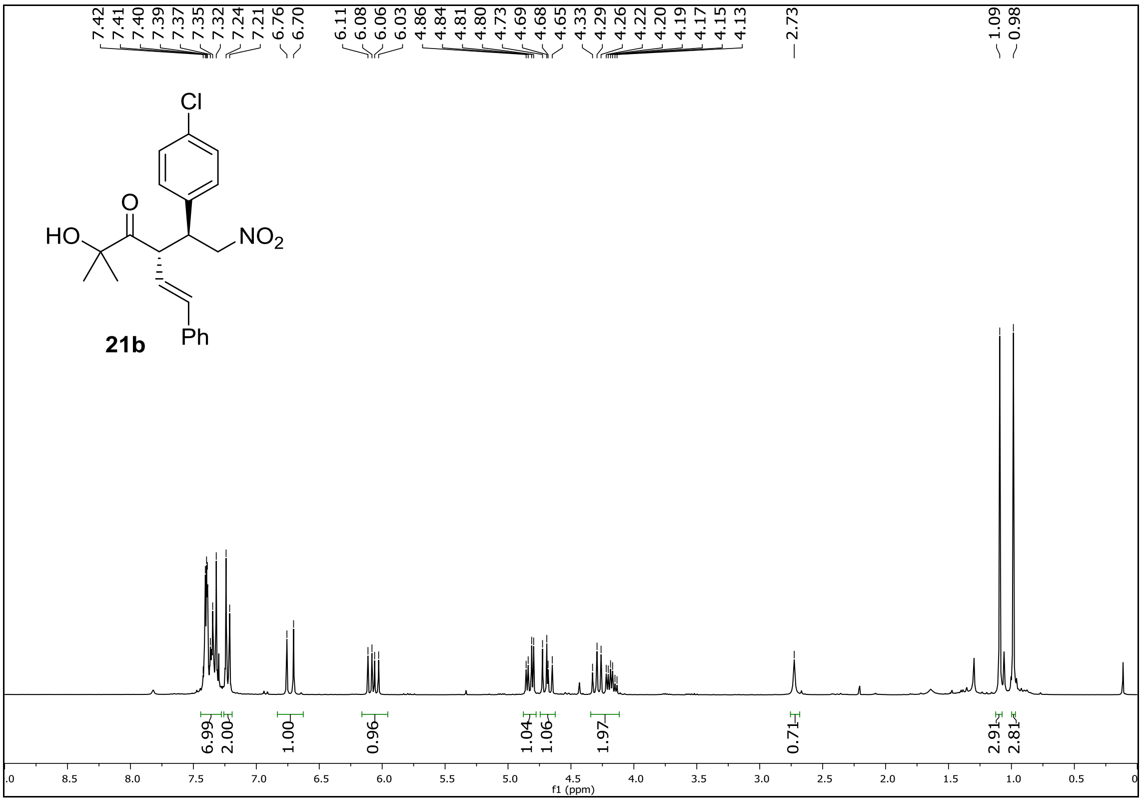
20

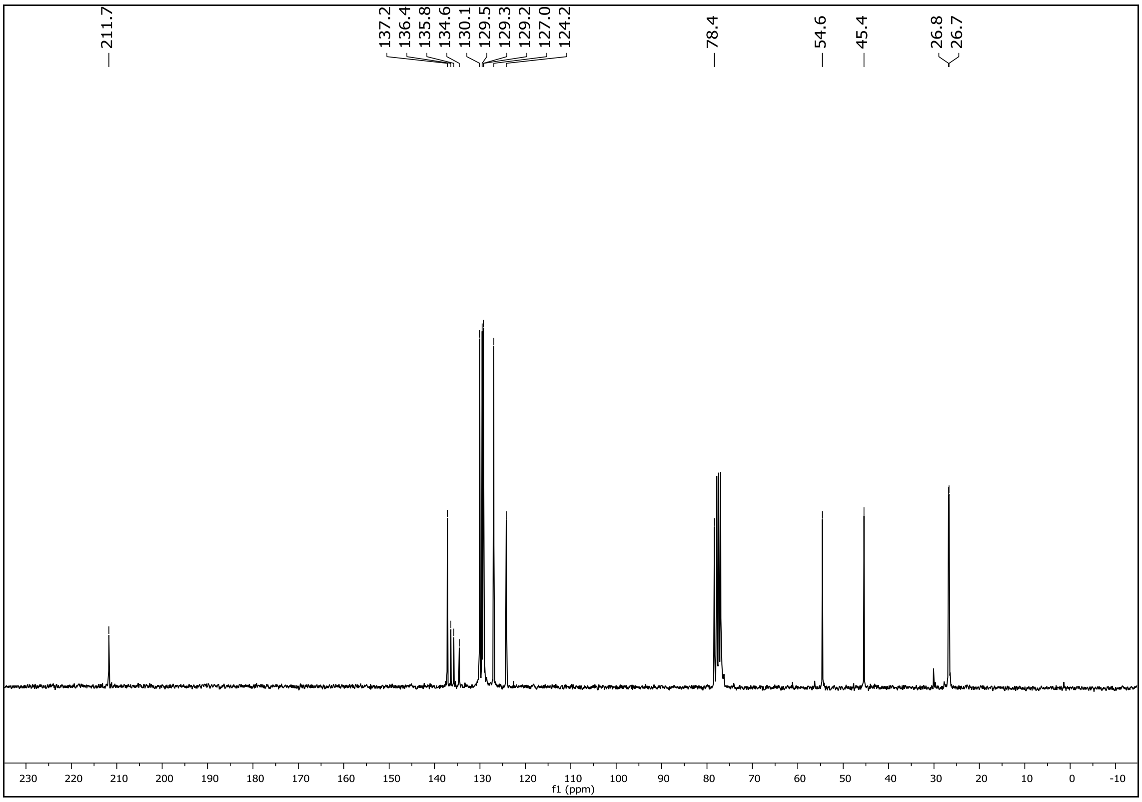


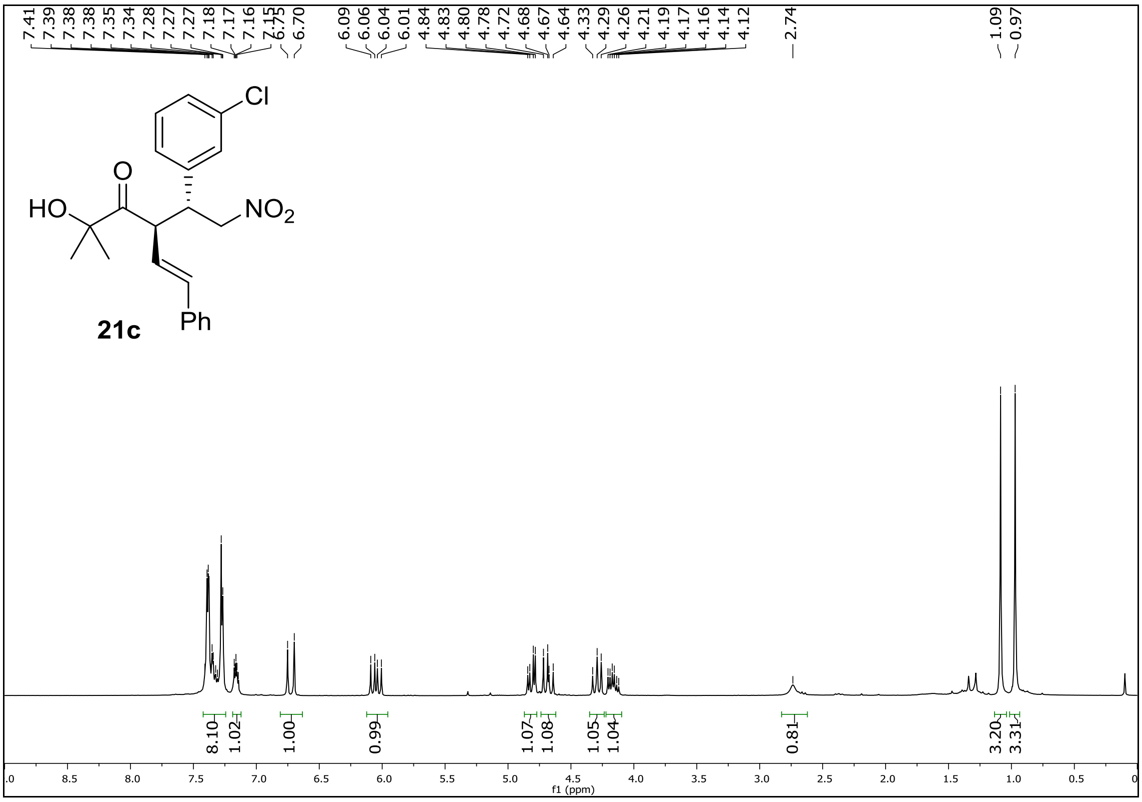


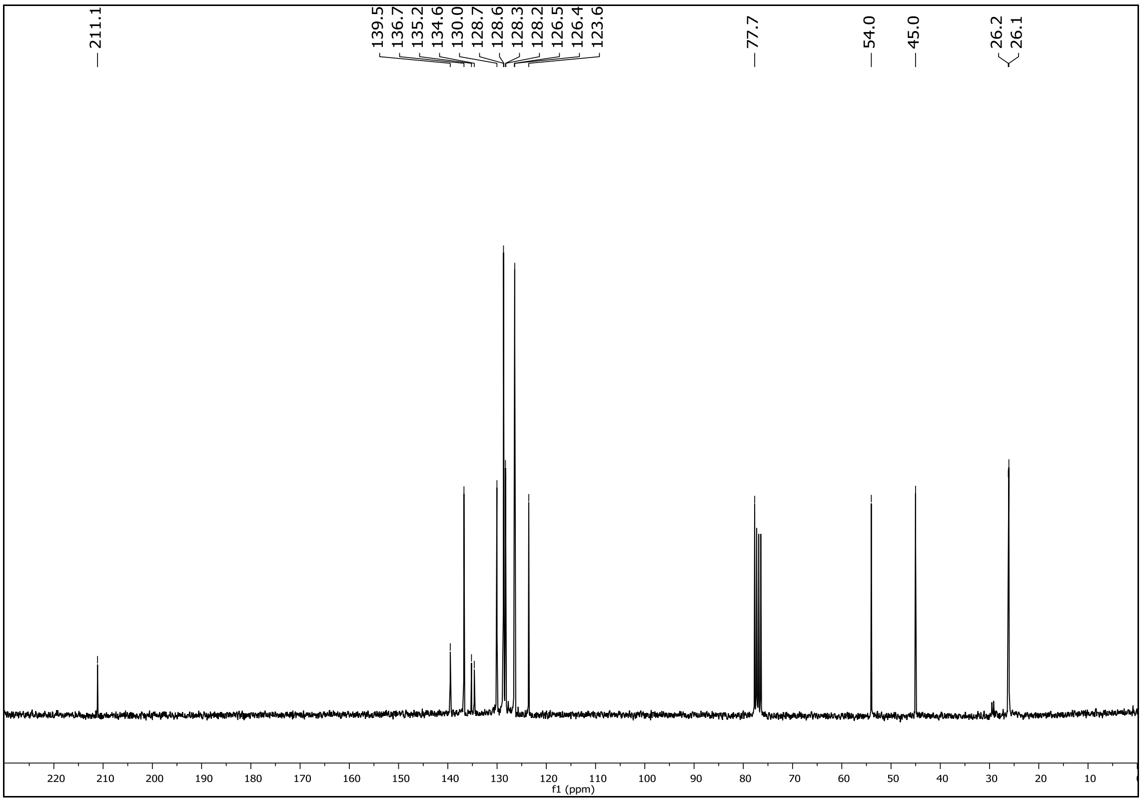

7.43
7.41
7.40
7.39
7.36
7.35
7.33
7.31
7.29
7.29
7.26
6.75
6.70
6.15
6.12
6.09
6.06
4.87
4.85
4.83
4.81
4.78
4.75
4.74
4.70
4.33
4.30
4.26
4.24
4.22
4.20
4.19
4.17
4.15
2.73
1.08
0.90
HO
O
Ph
NO2
Ph
21a
10.37
1.00
0.99
2.10
2.08
0.72
3.11
3.35
f1 (ppm)

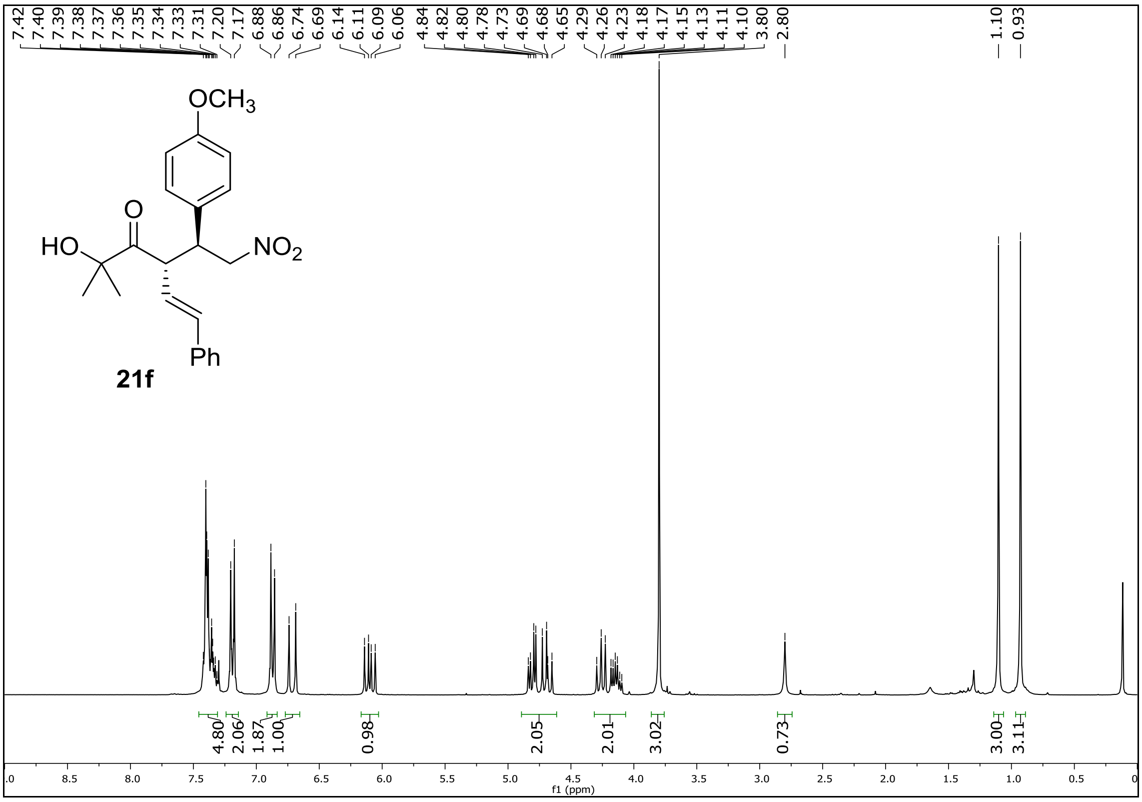

211.6
137.4
136.4
135.5
128.9
128.8
128.6
128.3
126.5
124.3
78.0
77.3
54.5
45.7
26.1
25.9
f1 (ppm)


7.42
7.41
7.40
7.39
7.37
7.35
7.32
7.24
7.21
6.76
6.70
6.11
6.08
6.06
6.03
4.86
4.84
4.81
4.80
4.73
4.69
4.68
4.65
4.33
4.29
4.26
4.22
4.20
4.19
4.17
4.15
4.13
2.73
1.09
0.98
Cl
HO
O
NO2
Ph
21b
6.99
2.00
1.00
0.96
1.04
1.06
1.97
0.71
2.91
2.81
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

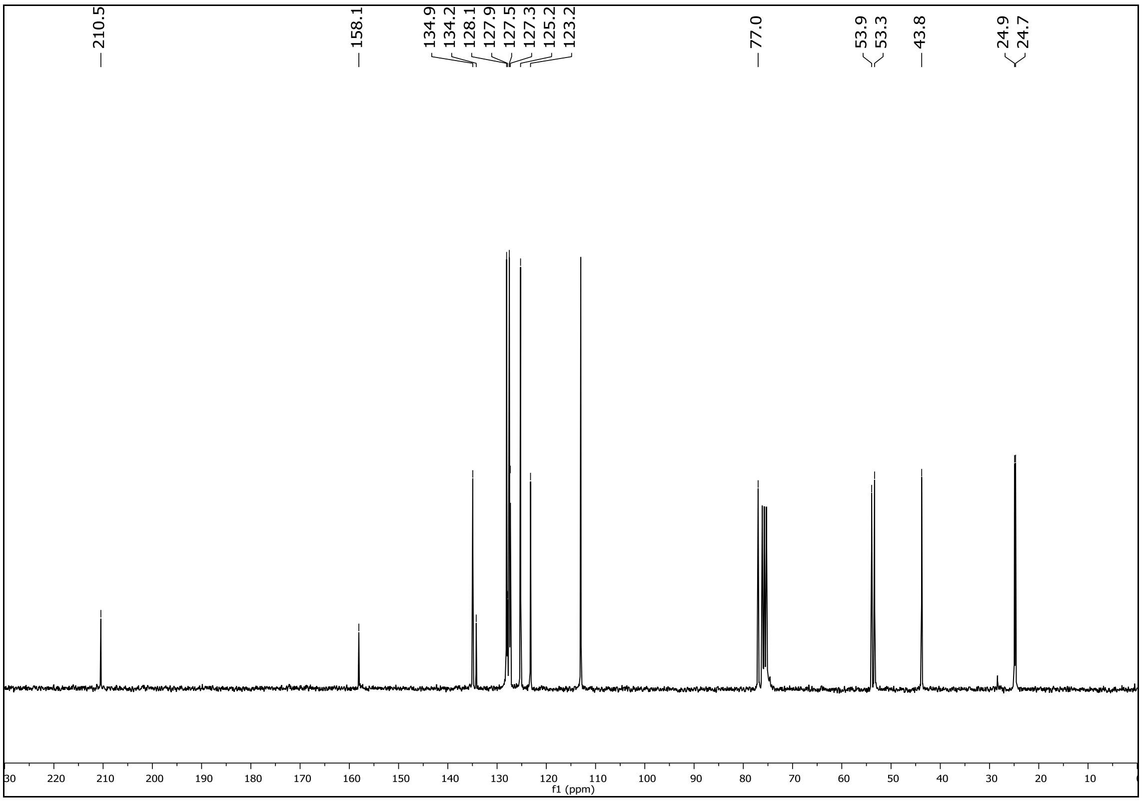

211.7
137.2
136.4
135.8
134.6
130.1
129.5
129.3
129.2
127.0
124.2
78.4
54.6
45.4
26.8
26.7
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

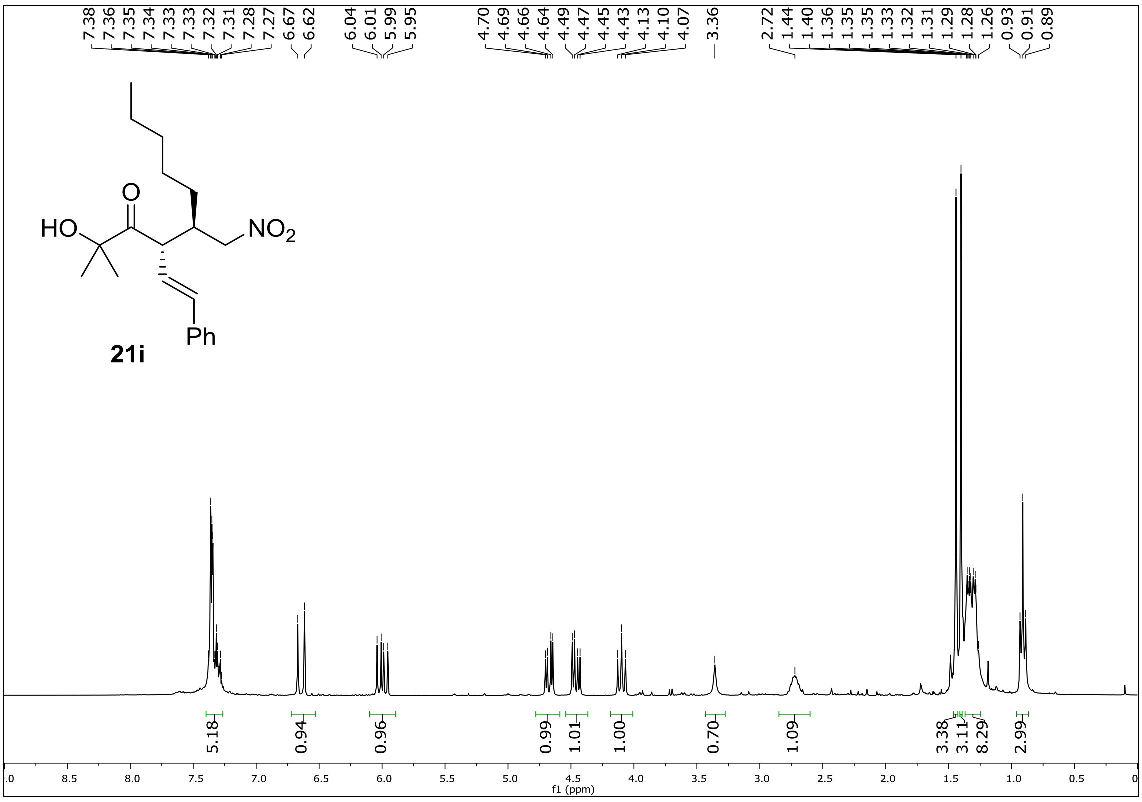

7.41
7.39
7.38
7.38
7.35
7.34
7.28
7.27
7.27
7.18
7.17
7.16
7.15
6.75
6.70
6.09
6.06
6.04
6.01
4.84
4.83
4.80
4.78
4.72
4.68
4.67
4.64
4.33
4.29
4.26
4.21
4.19
4.17
4.16
4.14
4.12
2.74
1.09
0.97
Cl
O
HO
NO2
Ph
21c
8.10
1.02
1.00
0.99
1.07
1.08
1.05
1.04
0.81
3.20
3.31
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

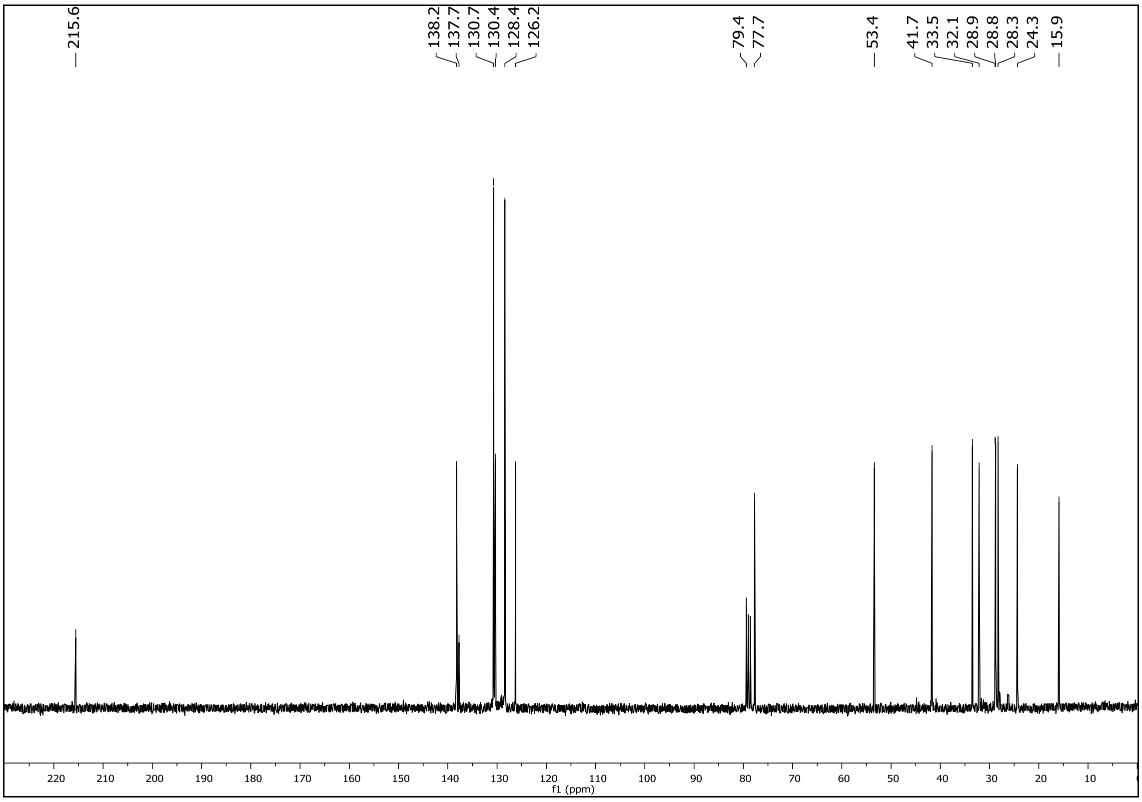

211.1
139.5
136.7
135.2
134.6
130.0
128.7
128.6
128.3
128.2
126.5
126.4
123.6
77.7
54.0
45.0
26.2
26.1
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

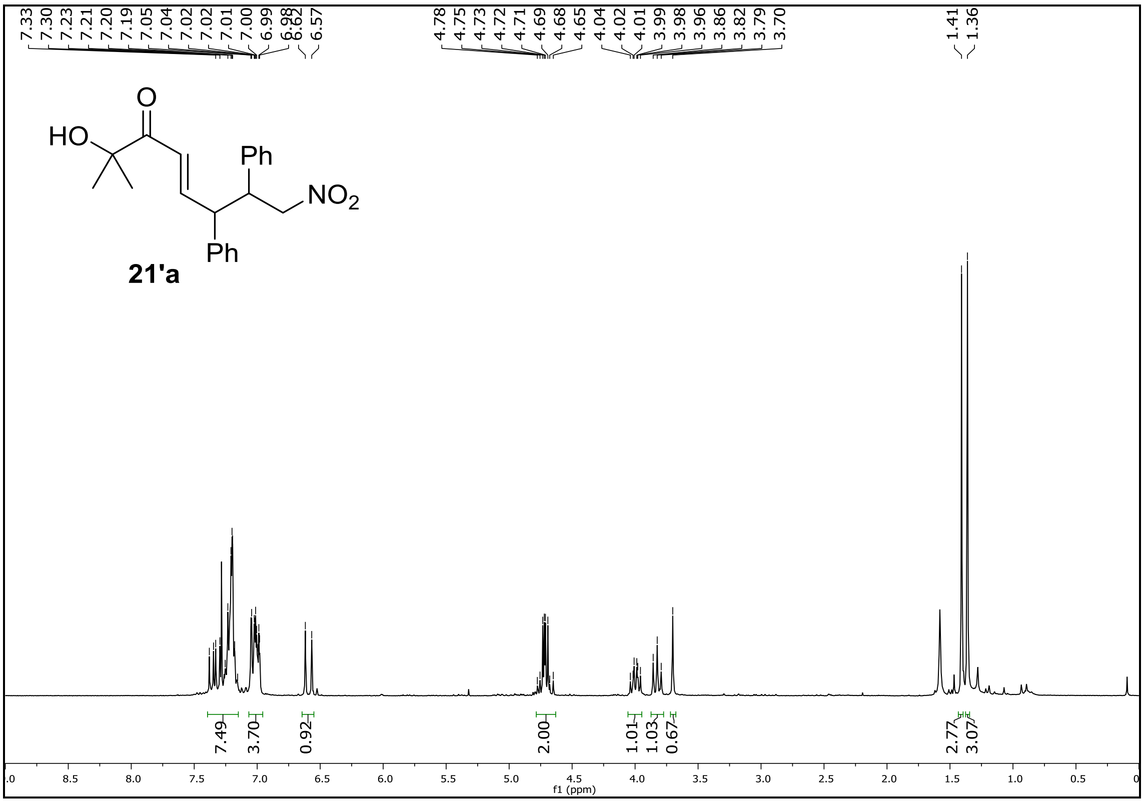

7.42
7.40
7.39
7.38
7.37
7.36
7.35
7.34
7.33
7.31
7.20
7.17
6.88
6.86
6.74
6.69
6.14
6.11
6.09
6.06
4.84
4.82
4.80
4.78
4.73
4.69
4.68
4.65
4.29
4.26
4.23
4.18
4.17
4.15
4.13
4.11
4.10
3.80
2.80
1.10
0.93
OCH3
O
HO
NO2
Ph
4.80
2.06
1.87
1.00
0.98
2.05
2.01
3.02
0.73
3.00
3.11
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

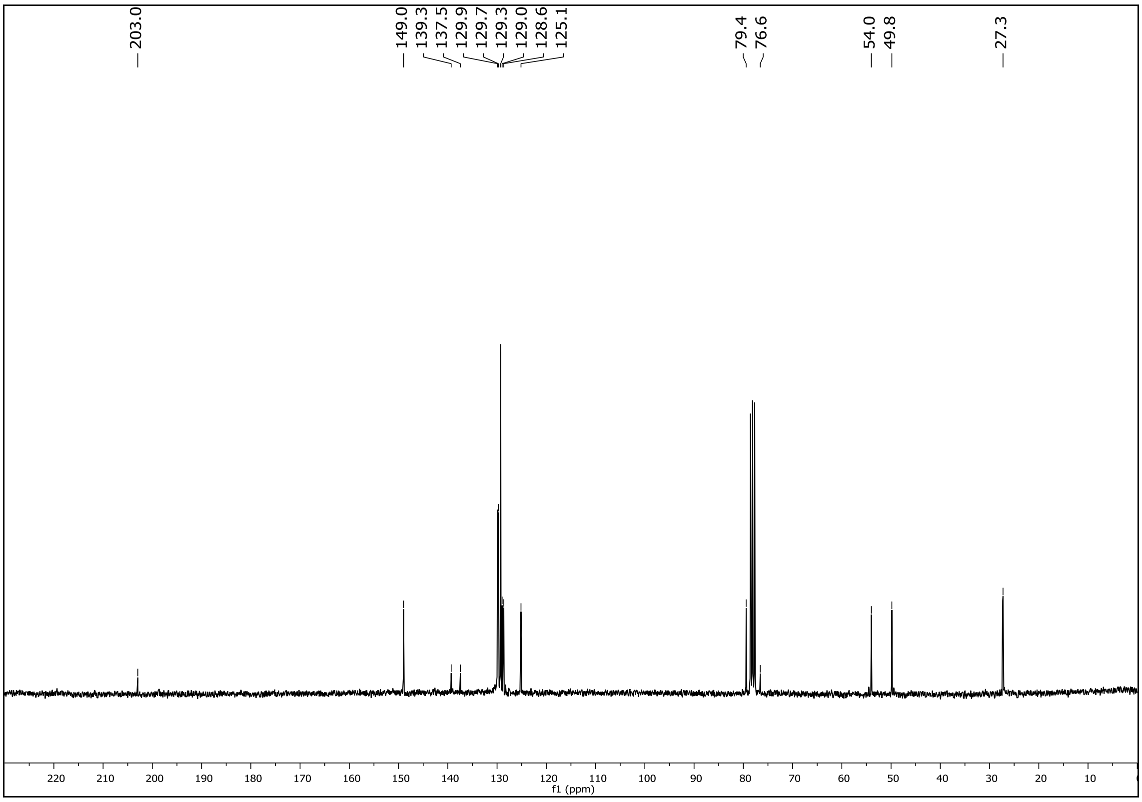
21f

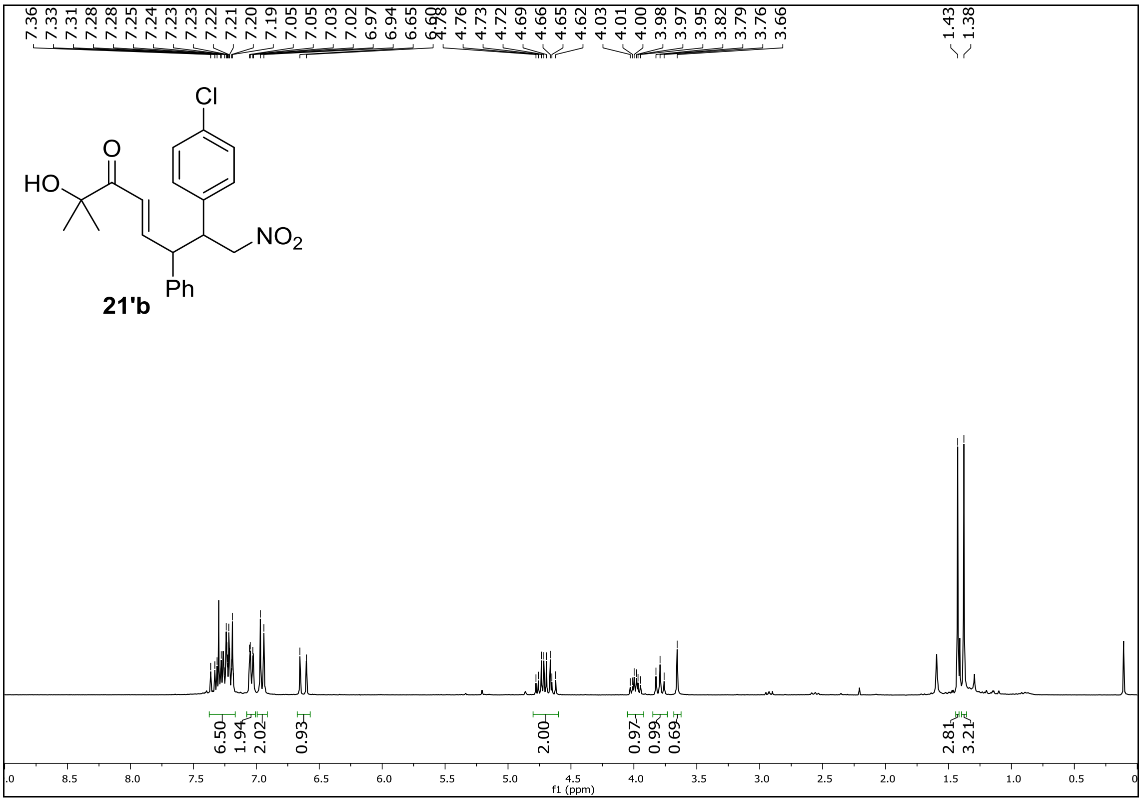

210.5
158.1
134.9
134.2
128.1
127.9
127.5
127.3
125.2
123.2
77.0
53.9
53.3
43.8
24.9
24.7
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

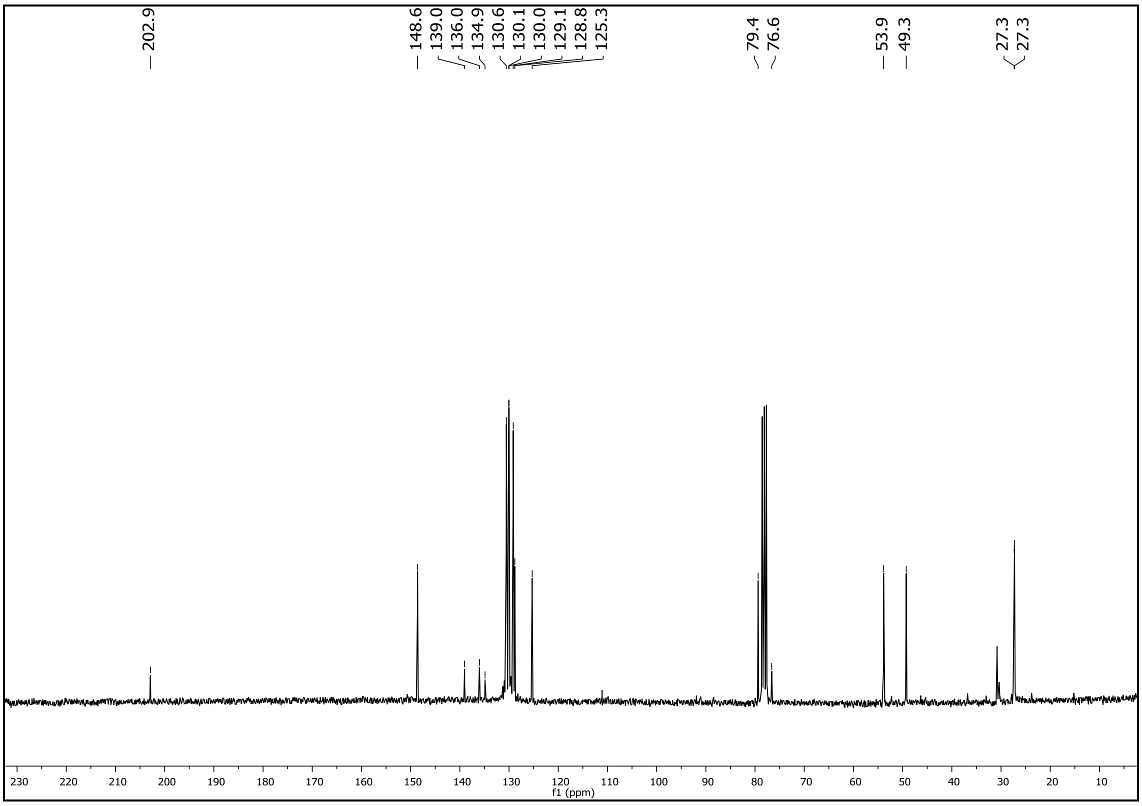

7.38
7.36
7.35
7.34
7.33
7.33
7.32
7.31
7.28
7.27
6.67
6.62
6.04
6.01
5.99
5.95
4.70
4.69
4.66
4.64
4.49
4.47
4.45
4.43
4.13
4.10
4.07
3.36
2.72
1.44
1.40
1.36
1.35
1.35
1.33
1.32
1.31
1.29
1.28
1.26
0.93
0.91
0.89
O
HO
NO2
Ph
21i
5.18
0.94
0.96
0.99
1.01
1.00
0.70
1.09
3.38
3.11
8.29
2.99
.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
f1 (ppm)

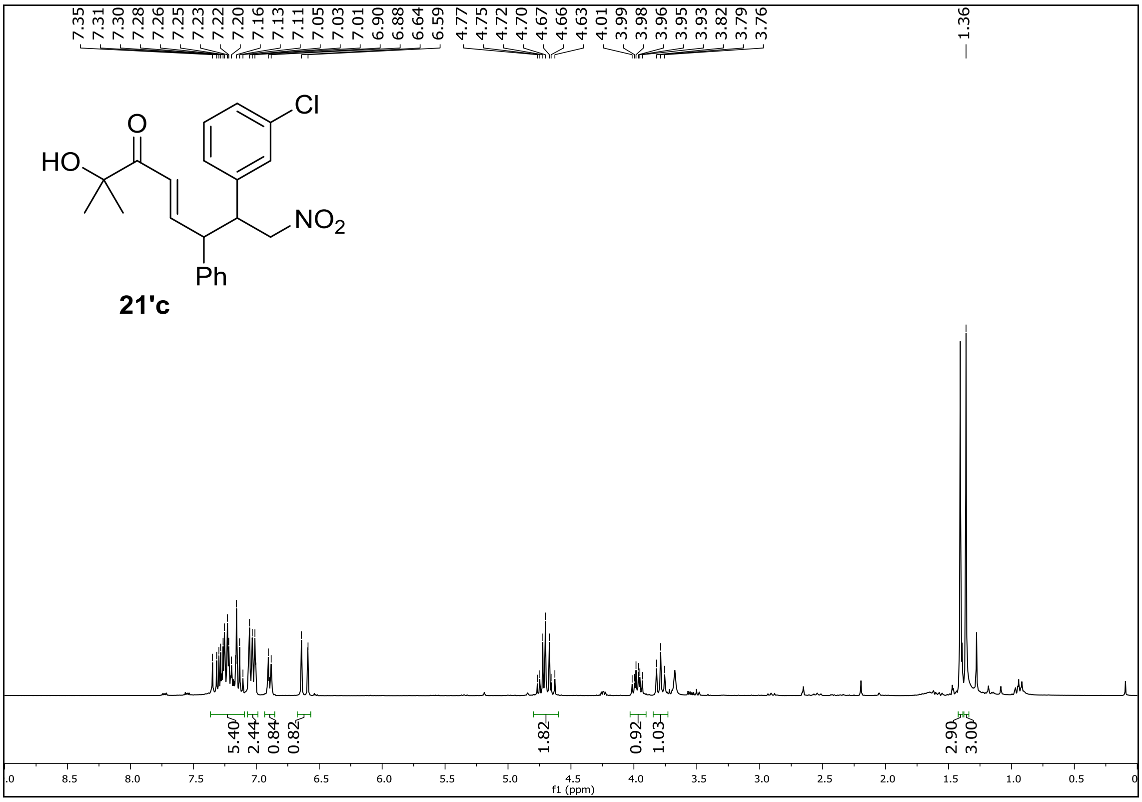

215.6
138.2
137.7
130.7
130.4
128.4
126.2
79.4
77.7
53.4
41.7
33.5
32.1
28.9
28.8
28.3
24.3
15.9
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)


7.33
7.30
7.23
7.21
7.20
7.19
7.05
7.04
7.02
7.02
7.01
7.00
6.99
6.98
6.62
6.57
4.78
4.75
4.73
4.72
4.71
4.69
4.68
4.65
4.04
4.02
4.01
3.99
3.98
3.96
3.86
3.82
3.79
3.70
1.41
1.36
O
HO
Ph
NO_2
Ph
21'a
7.49
3.70
0.92
2.00
1.01
1.03
0.67
2.77
3.07
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)


203.0
149.0
139.3
137.5
129.9
129.7
129.3
129.0
128.6
125.1
79.4
76.6
54.0
49.8
27.3
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

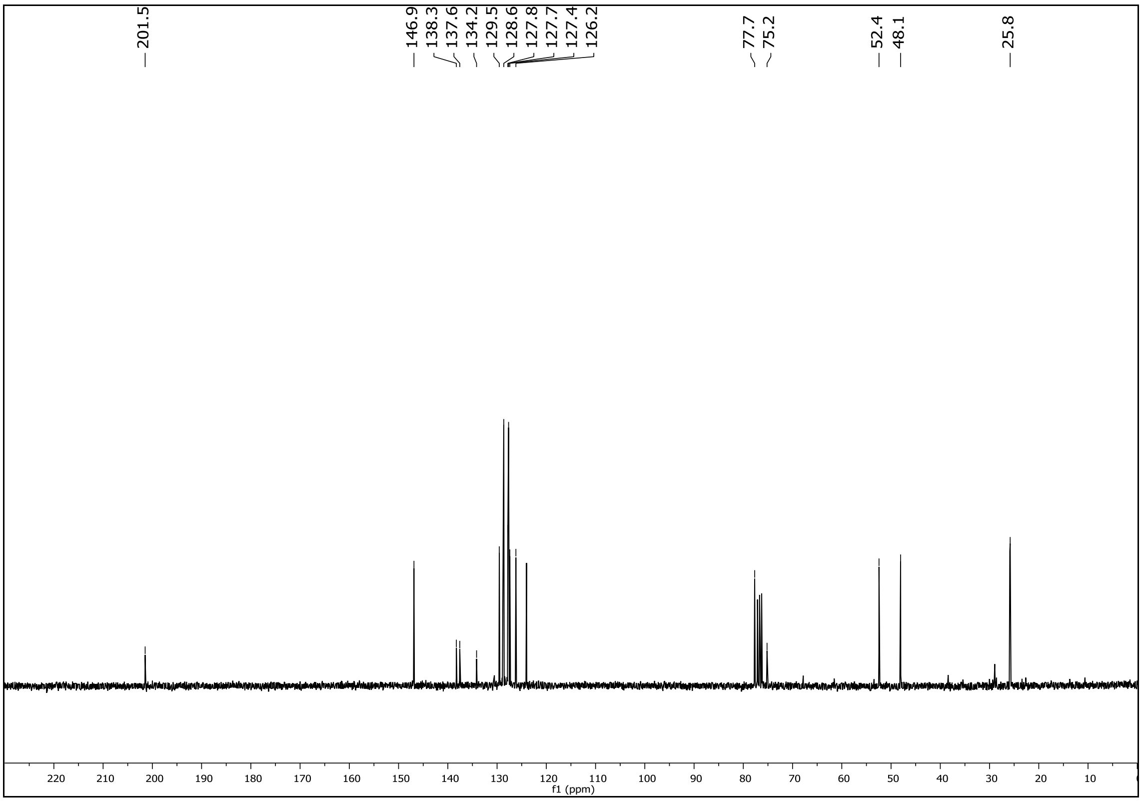

7.36
7.33
7.31
7.28
7.25
7.24
7.23
7.23
7.22
7.21
7.20
7.19
7.05
7.05
7.03
7.02
6.97
6.94
6.65
6.60
4.78
4.76
4.73
4.72
4.69
4.66
4.65
4.62
4.03
4.01
4.00
3.98
3.97
3.95
3.82
3.79
3.76
3.66
1.43
1.38
Cl
O
HO
NO2
Ph
21'b
6.50
1.94
2.02
0.93
2.00
0.97
0.99
0.69
2.81
3.21
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
f1 (ppm)


202.9
148.6
139.0
136.0
134.9
130.6
130.1
130.0
129.1
128.8
125.3
79.4
76.6
53.9
49.3
27.3
27.3
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

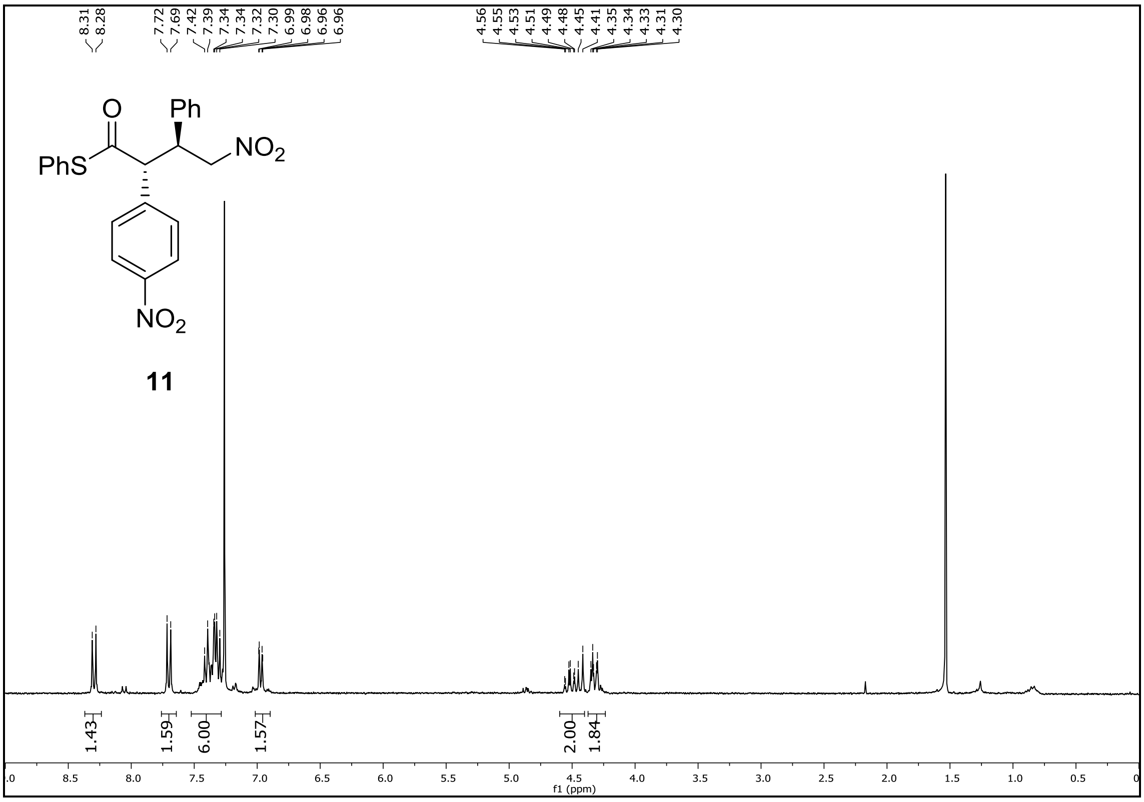


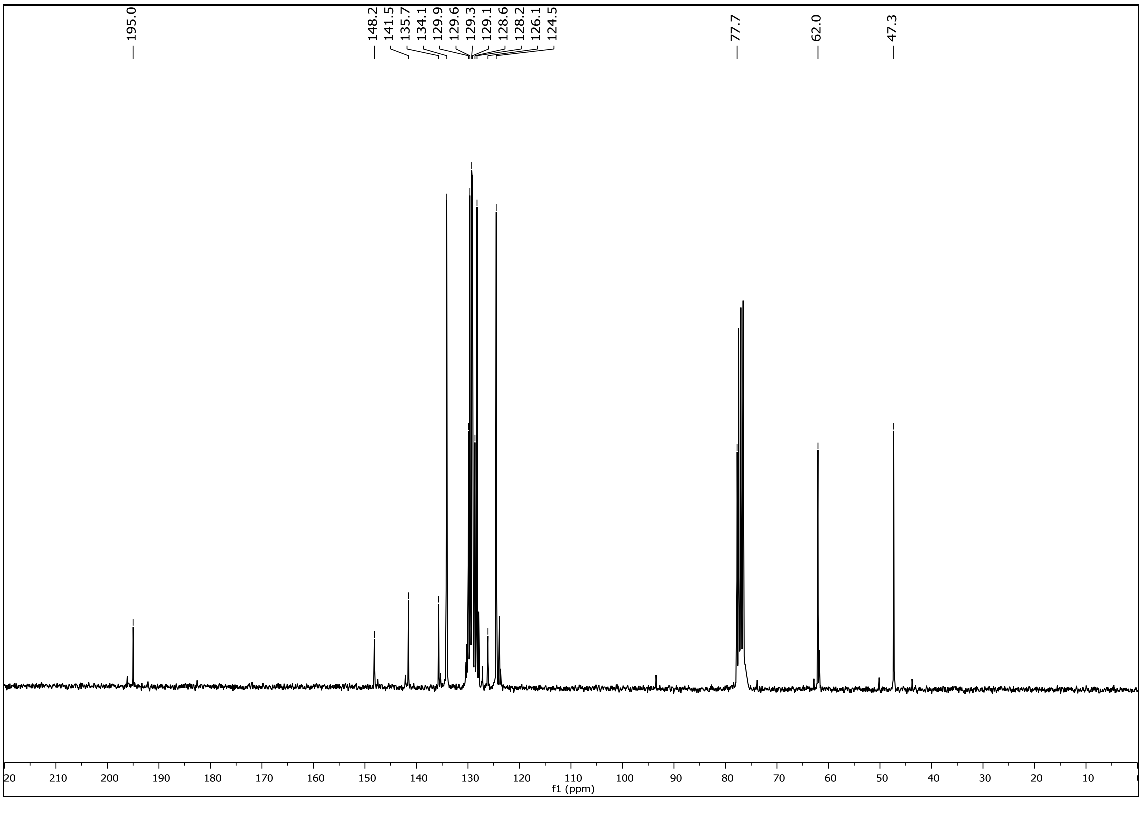
21'c

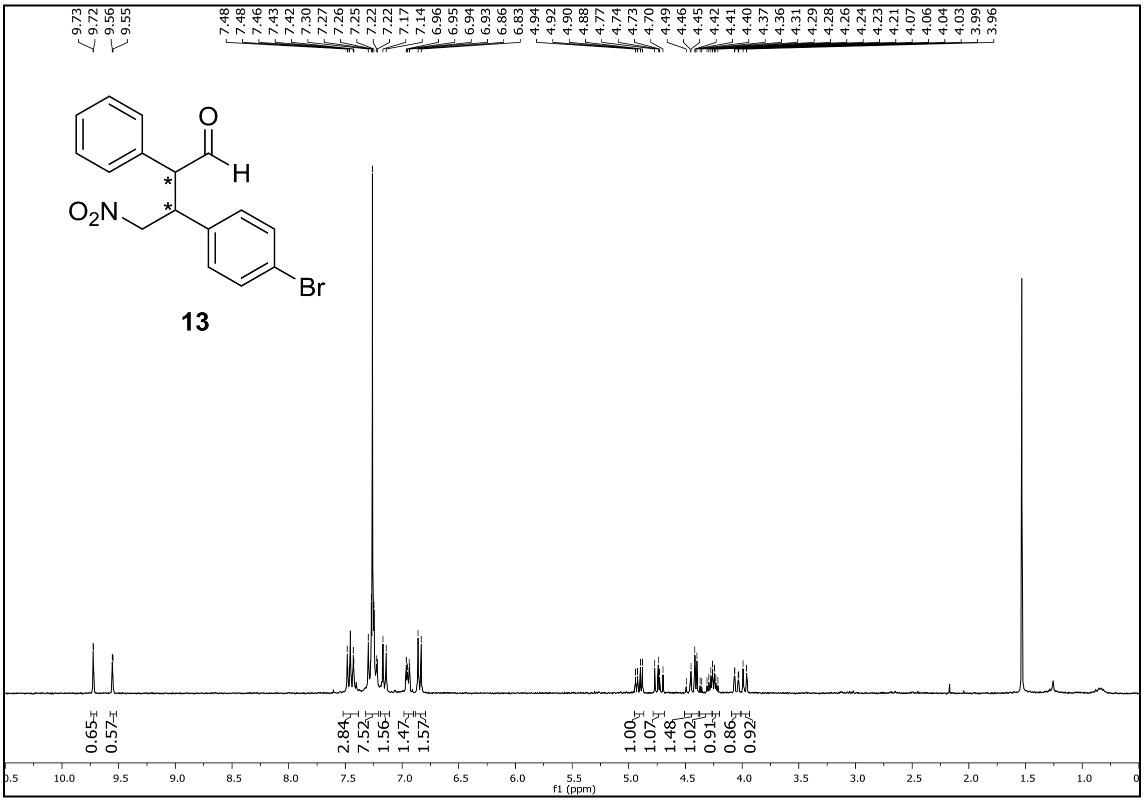
7.35 7.31 7.30 7.28 7.26 7.25 7.23 7.22 7.20 7.16 7.13 7.11 7.05 7.03 7.01 6.90 6.88 6.64 6.59
4.77 4.75 4.72 4.70 4.67 4.66 4.63
4.01 3.99 3.98 3.96 3.95 3.93 3.82 3.79 3.76
1.36
Cl
O
HO
NO2
Ph
5.40 2.44 0.84 0.82
1.82
0.92 1.03
2.90 3.00
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)

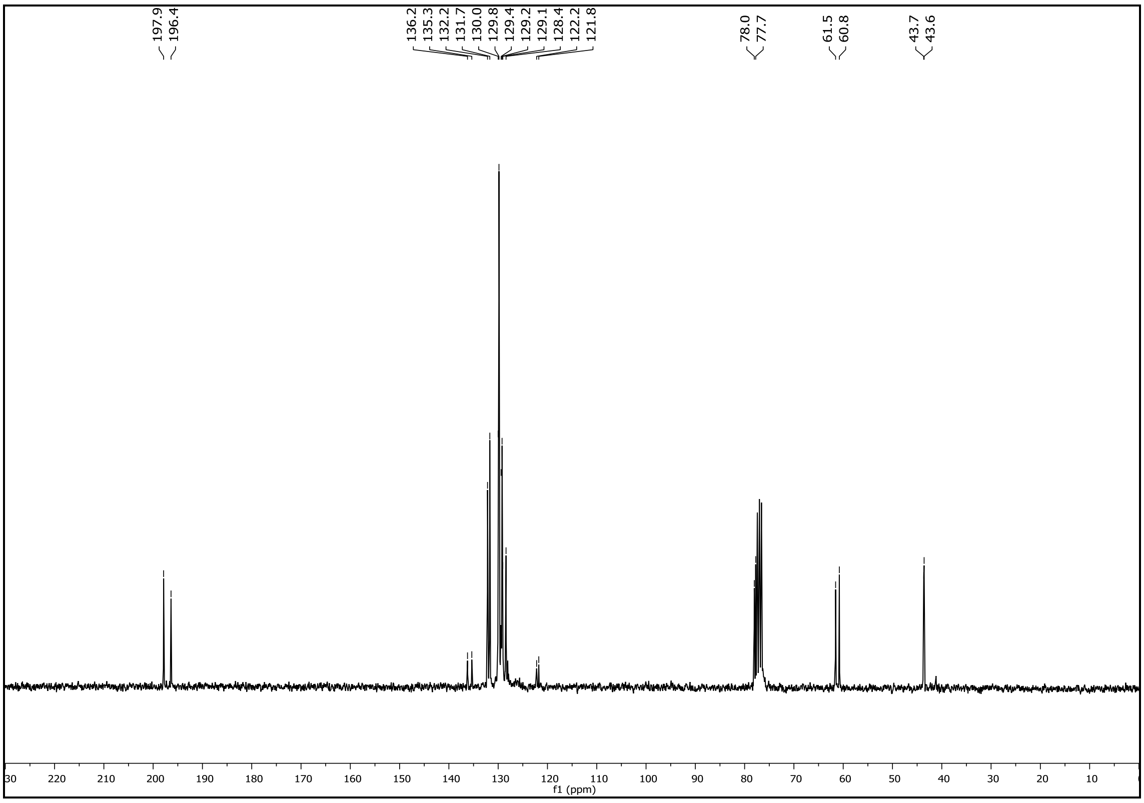


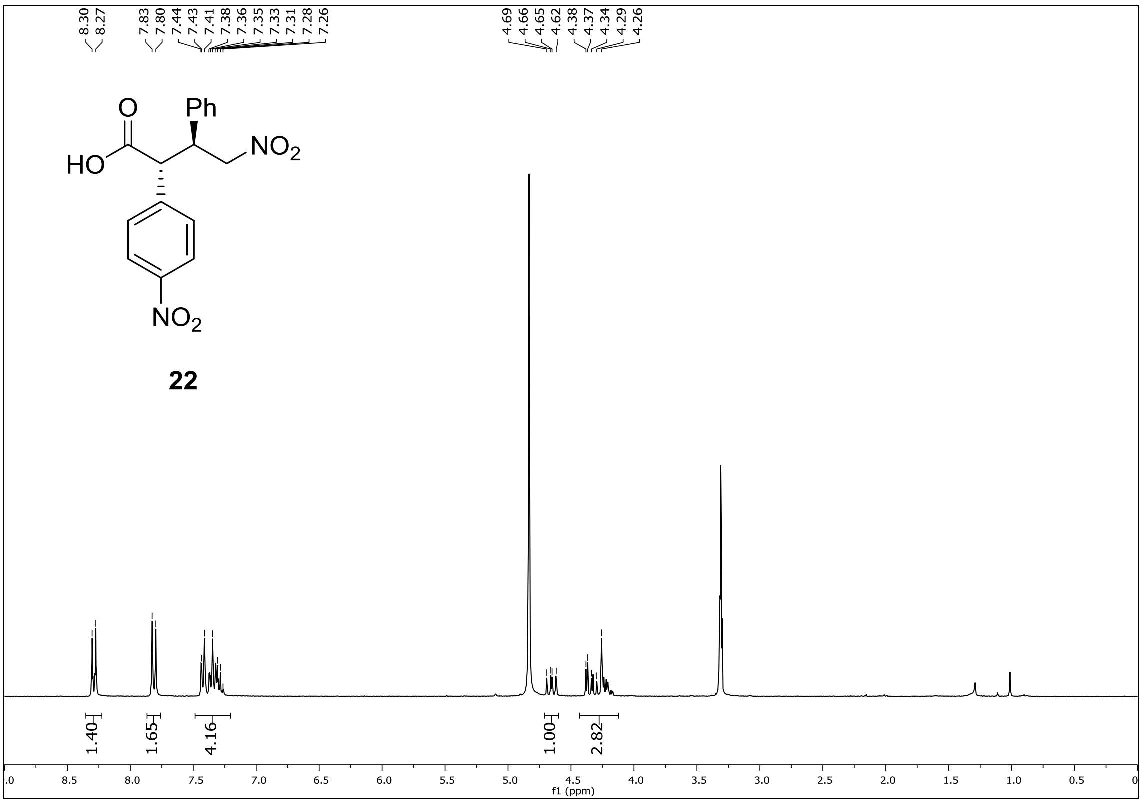
201.5
146.9 138.3 137.6 134.2 129.5 128.6 127.8 127.7 127.4 126.2
77.7 75.2
52.4 48.1
25.8
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)

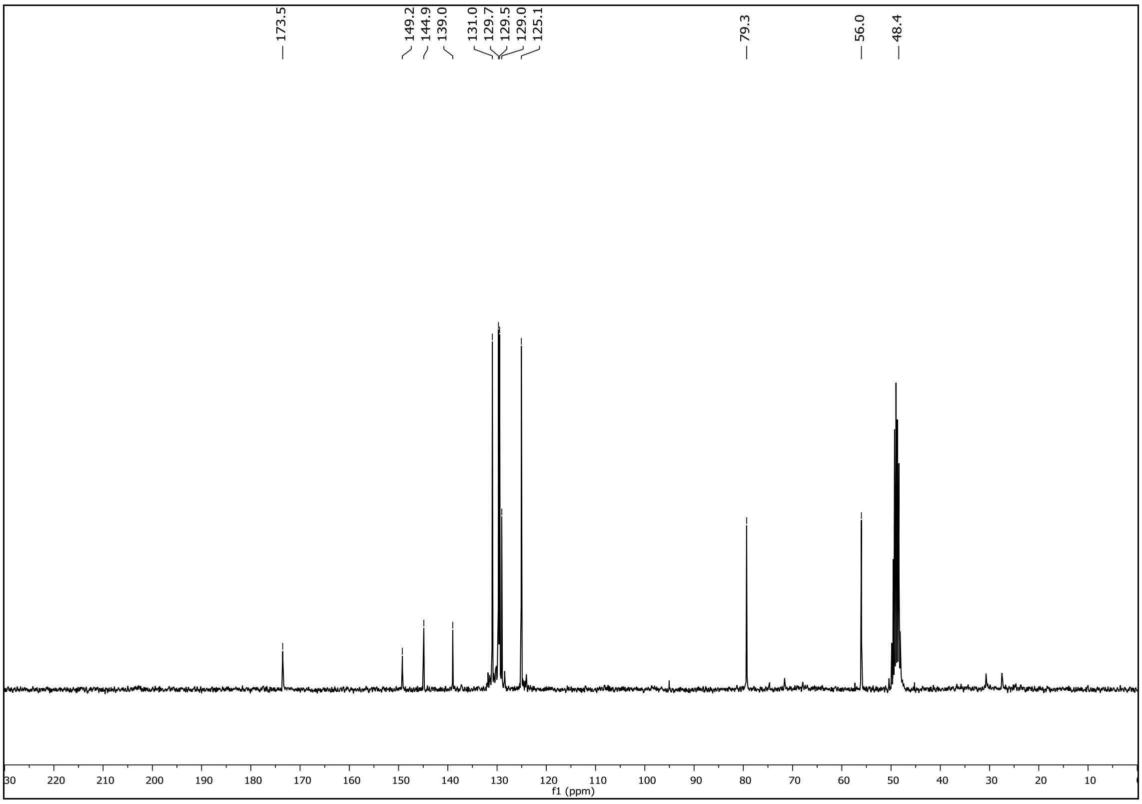

8.31
8.28
7.72
7.69
7.42
7.39
7.34
7.34
7.32
7.30
6.99
6.98
6.96
6.96
4.56
4.55
4.53
4.51
4.49
4.48
4.45
4.41
4.35
4.34
4.33
4.31
4.30
O
Ph
PhS
NO2
NO2
11
1.43
1.59
6.00
1.57
2.00
1.84
f1 (ppm)

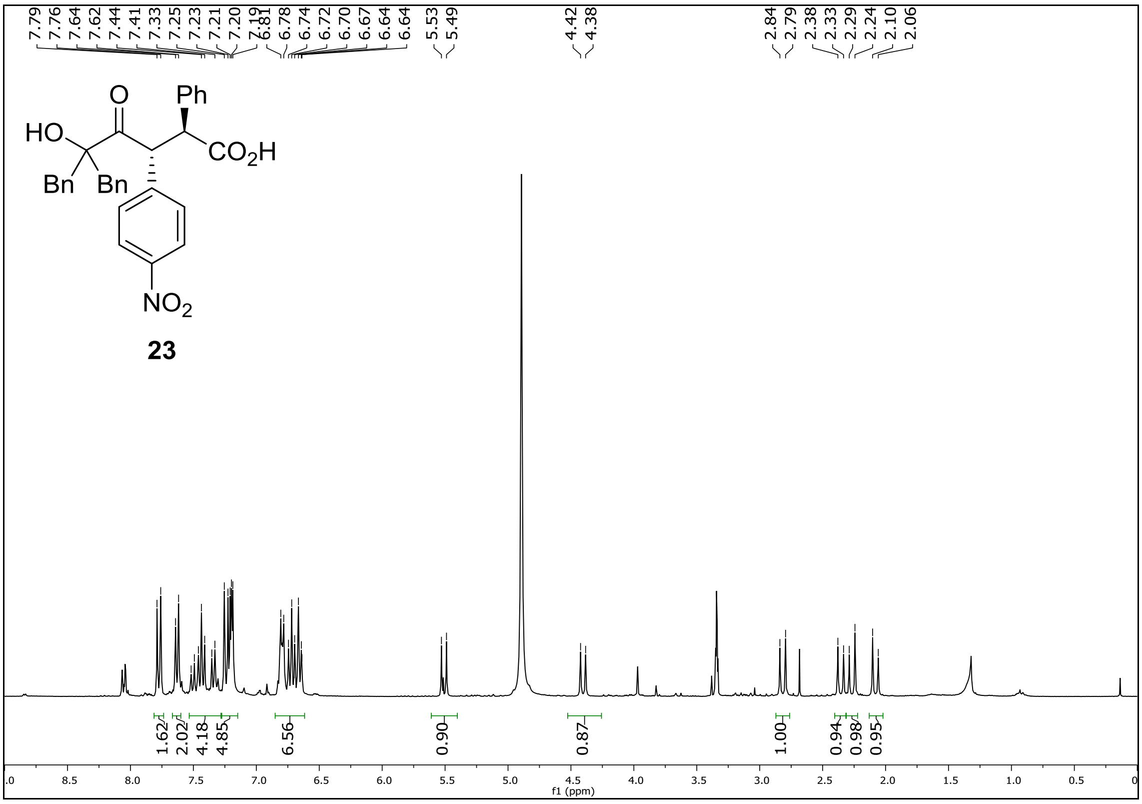

195.0
148.2
141.5
135.7
134.1
129.9
129.6
129.3
129.1
128.6
128.2
126.1
124.5
77.7
62.0
47.3
f1 (ppm)

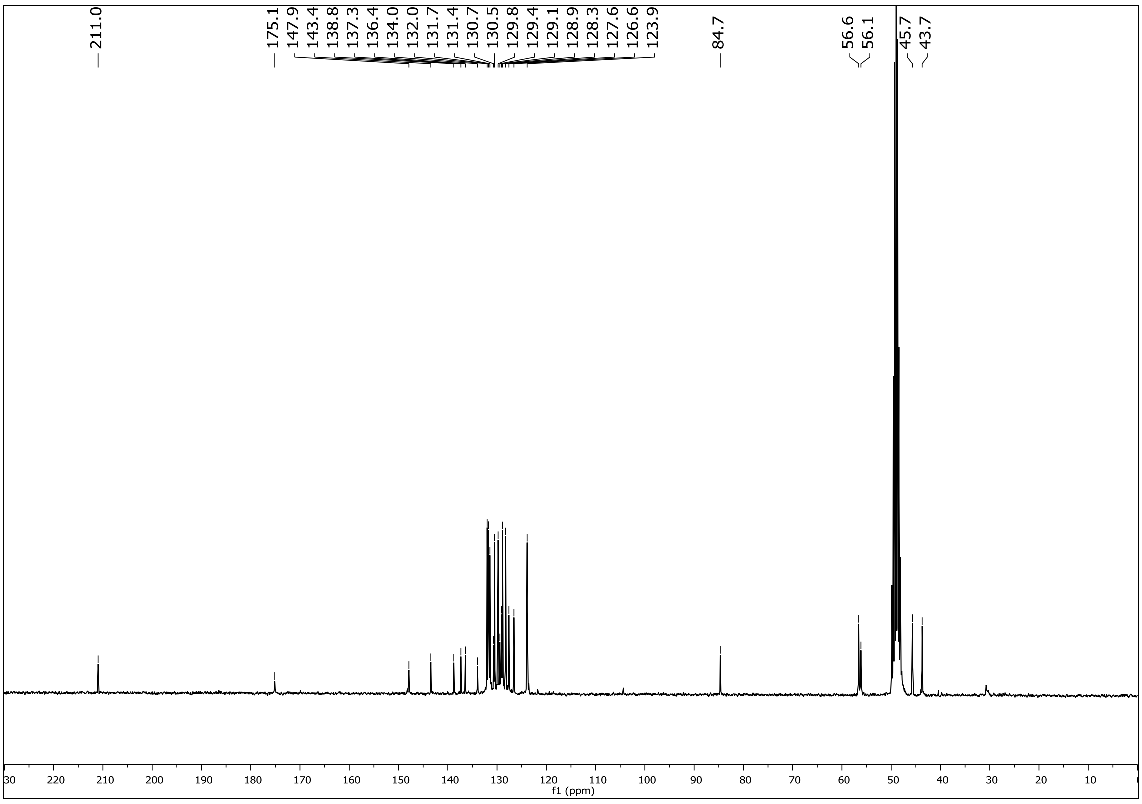

9.73
9.72
9.56
9.55
7.48
7.48
7.46
7.43
7.42
7.30
7.27
7.26
7.25
7.22
7.22
7.17
7.14
6.96
6.95
6.94
6.93
6.86
6.83
4.94
4.92
4.90
4.88
4.77
4.74
4.73
4.70
4.49
4.46
4.45
4.42
4.41
4.40
4.37
4.36
4.31
4.29
4.28
4.26
4.24
4.23
4.21
4.07
4.06
4.04
4.03
3.99
3.96
O
H
*
*
O2N
Br
13
0.65
0.57
2.84
7.52
1.56
1.47
1.57
1.00
1.07
1.48
1.02
0.91
0.86
0.92
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
f1 (ppm)

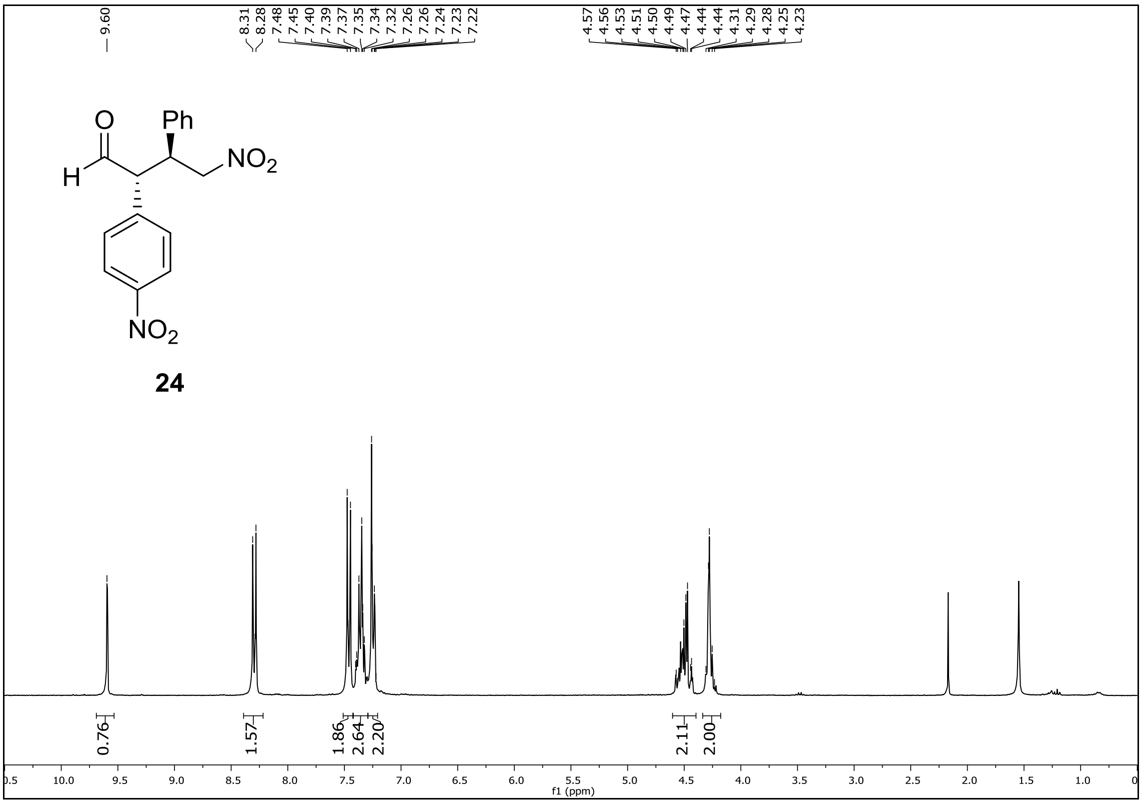

197.9
196.4
136.2
135.3
132.2
131.7
130.0
129.8
129.4
129.2
129.1
128.4
122.2
121.8
78.0
77.7
61.5
60.8
43.7
43.6
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

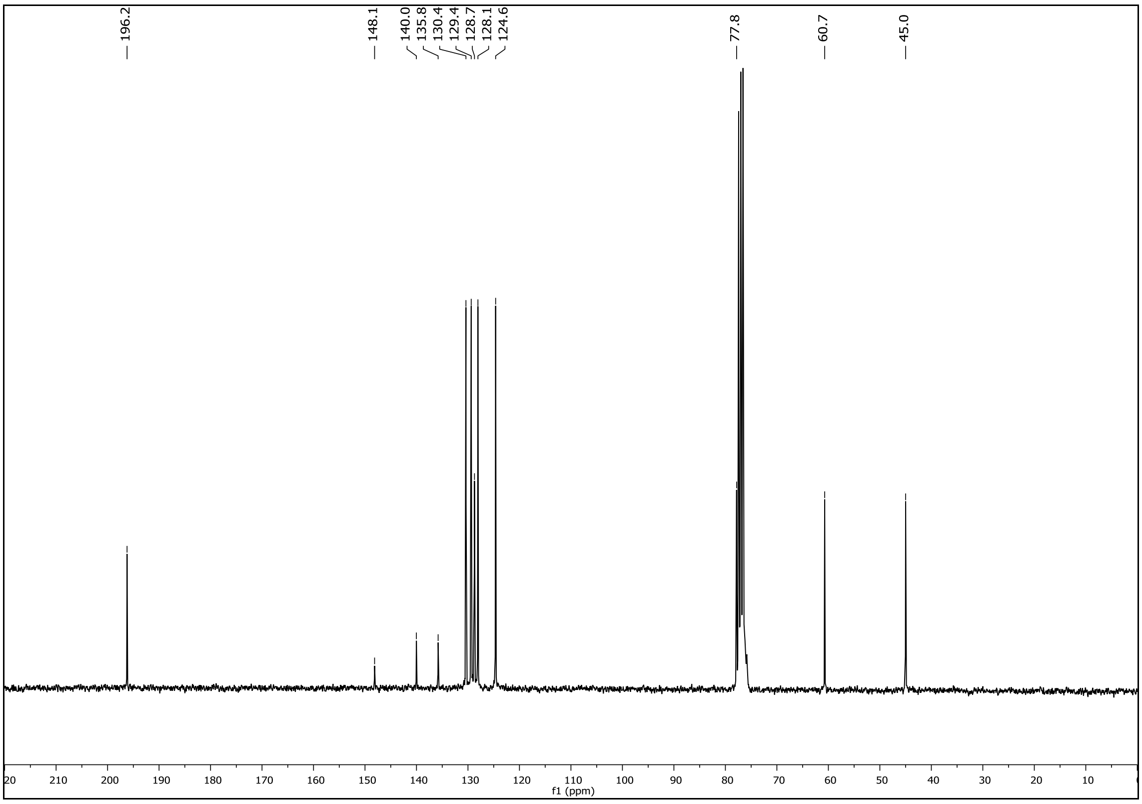

8.30
8.27
7.83
7.80
7.44
7.43
7.41
7.38
7.36
7.35
7.33
7.31
7.28
7.26
4.69
4.66
4.65
4.62
4.38
4.37
4.34
4.29
4.26
O
Ph
HO
NO_2
NO_2
22
1.40
1.65
4.16
1.00
2.82
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
f1 (ppm)

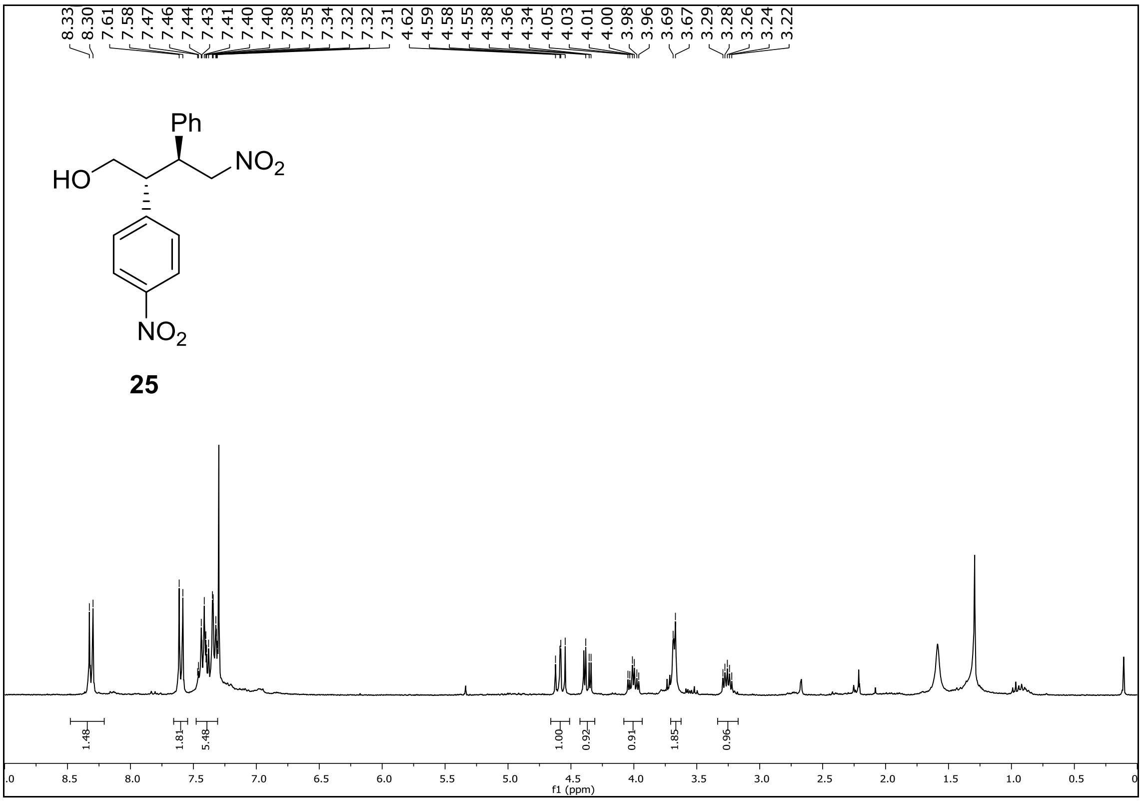

173.5
149.2
144.9
139.0
131.0
129.7
129.5
129.0
125.1
79.3
56.0
48.4
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


7.79
7.76
7.64
7.62
7.44
7.41
7.33
7.25
7.23
7.21
7.20
7.19
6.81
6.78
6.74
6.72
6.70
6.67
6.64
6.64
5.53
5.49
4.42
4.38
2.84
2.79
2.38
2.33
2.29
2.24
2.10
2.06
HO
O
Ph
CO2H
Bn
Bn
NO2
23
1.62
2.02
4.18
4.85
6.56
0.90
0.87
1.00
0.94
0.98
0.95
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

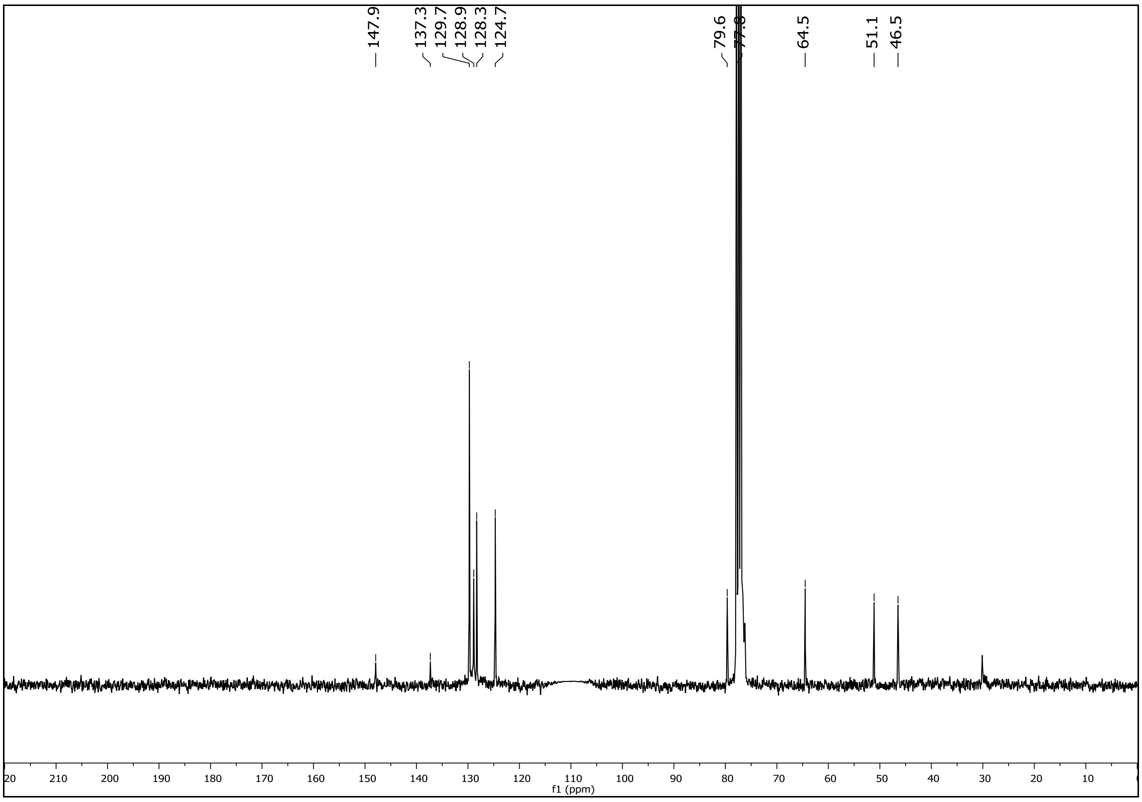

211.0
175.1
147.9
143.4
138.8
137.3
136.4
134.0
132.0
131.7
131.4
130.7
130.5
129.8
129.4
129.1
128.9
128.3
127.6
126.6
123.9
84.7
56.6
56.1
45.7
43.7
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

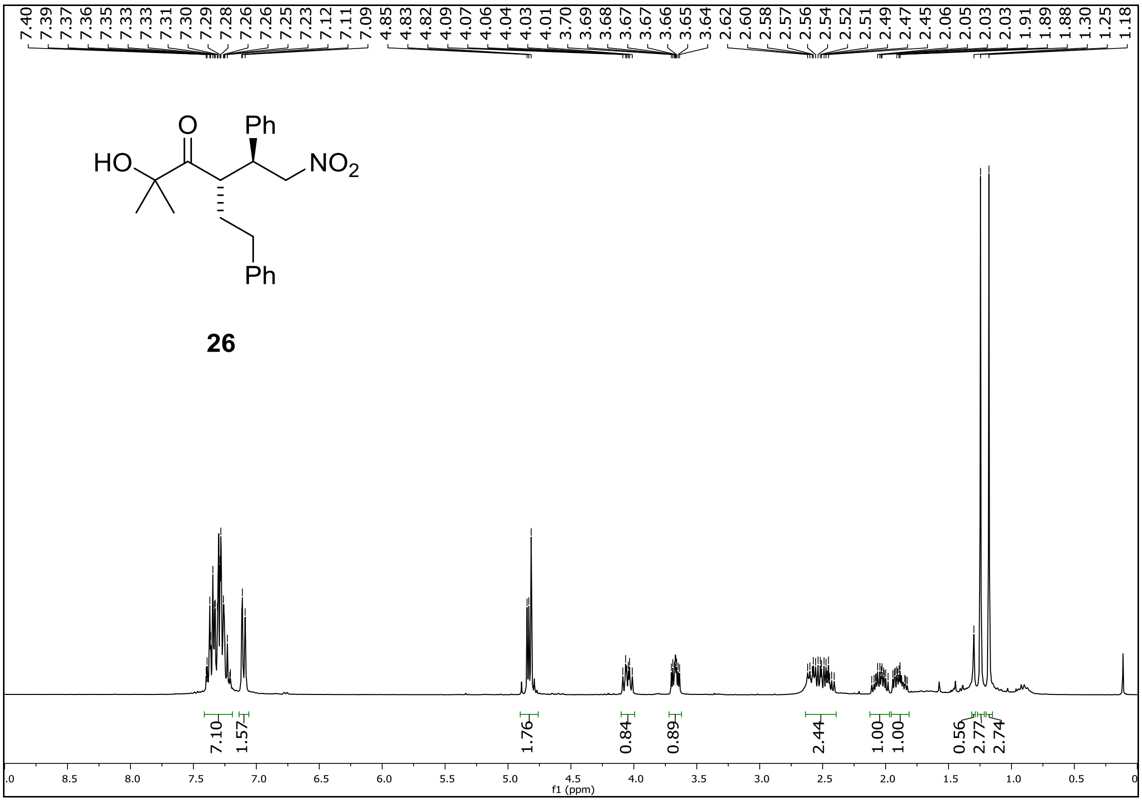

9.60
8.31
8.28
7.48
7.45
7.40
7.39
7.37
7.35
7.34
7.32
7.26
7.26
7.24
7.23
7.22
4.57
4.56
4.53
4.51
4.50
4.49
4.47
4.44
4.44
4.31
4.29
4.28
4.25
4.23
O
Ph
H
NO2
NO2
24
0.76
1.57
1.86
2.64
2.20
2.11
2.00
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
f1 (ppm)


196.2
148.1
140.0
135.8
130.4
129.4
128.7
128.1
124.6
77.8
60.7
45.0
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

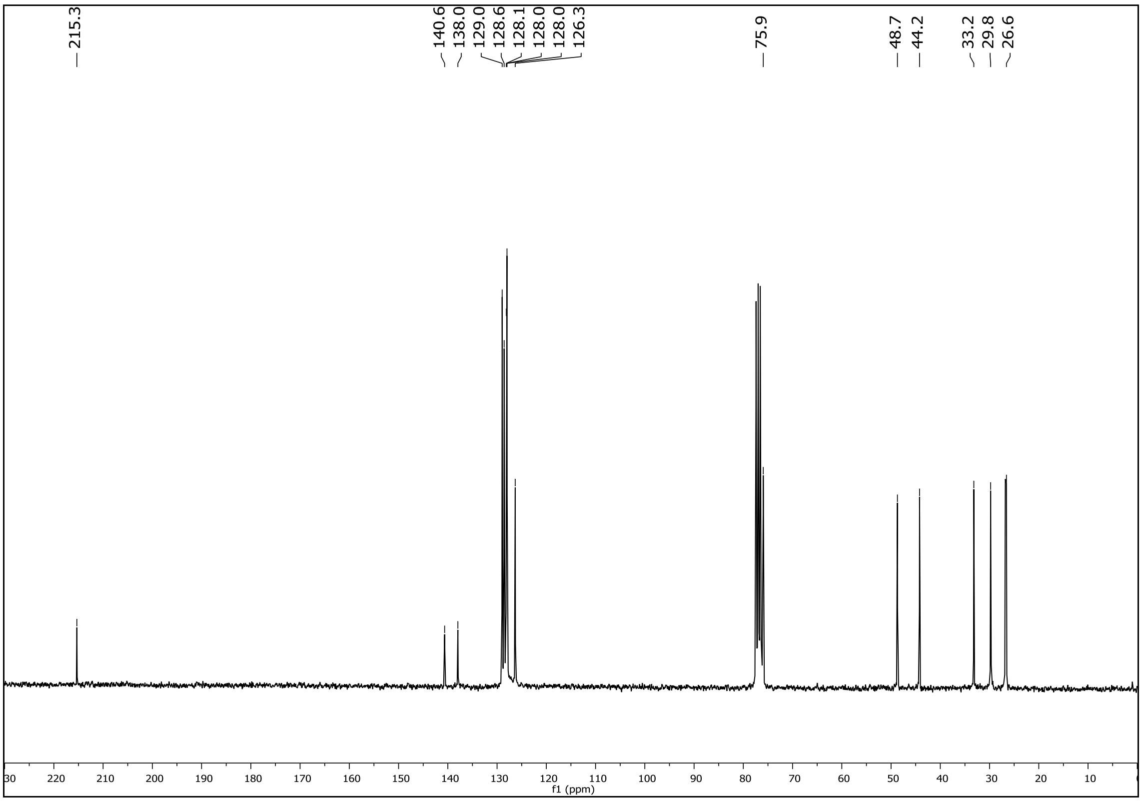

8.33
8.30
7.61
7.58
7.47
7.46
7.44
7.43
7.41
7.40
7.38
7.35
7.34
7.32
7.32
7.31
4.62
4.59
4.58
4.55
4.38
4.36
4.34
4.05
4.03
4.01
4.00
3.98
3.96
3.69
3.67
3.29
3.28
3.26
3.24
3.22
Ph
HO
NO2
NO2
1.48
1.81
5.48
1.00
0.92
0.91
1.85
0.96
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

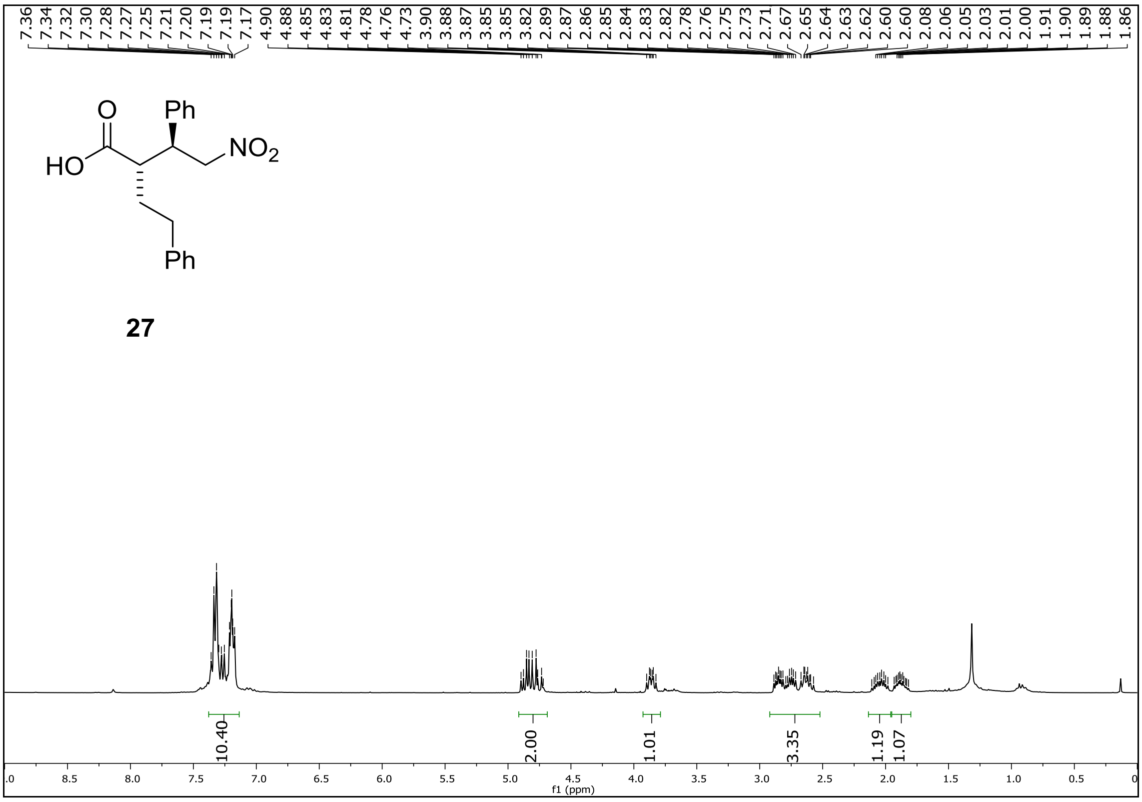
25

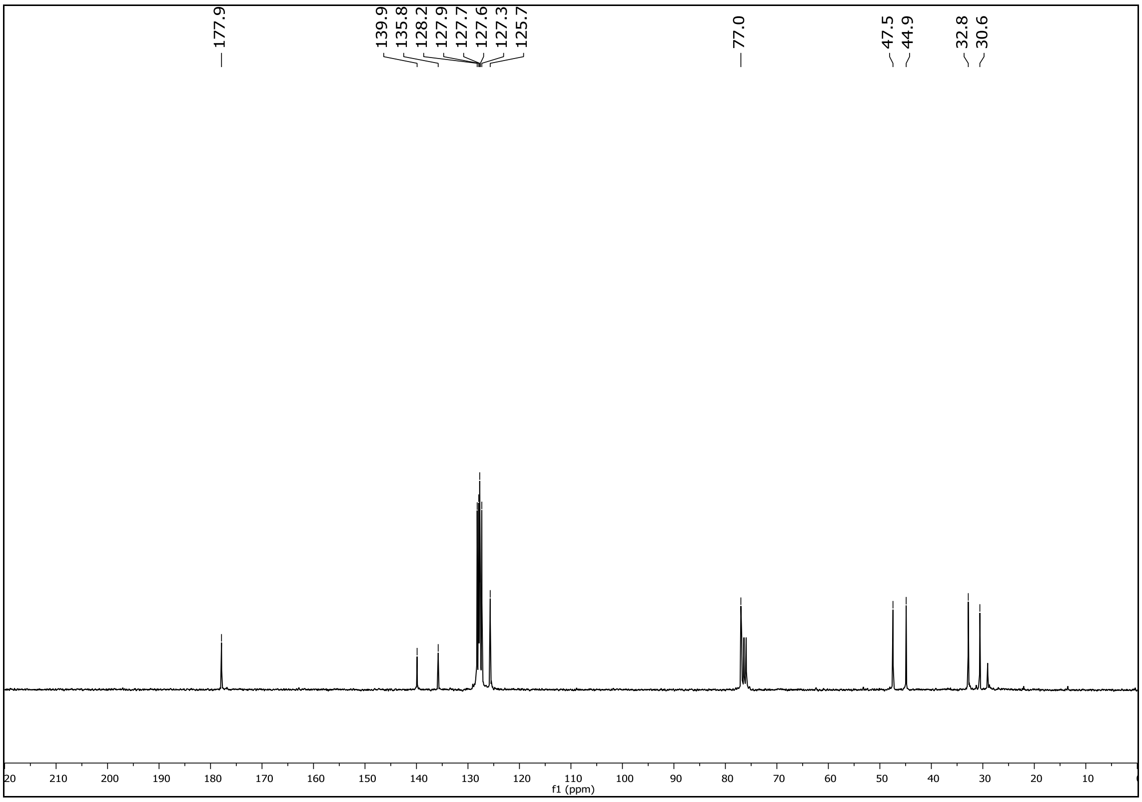

147.9
137.3
129.7
128.9
128.3
124.7
79.6
77.0
64.5
51.1
46.5
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

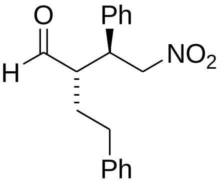

7.40
7.39
7.37
7.36
7.35
7.33
7.33
7.31
7.30
7.29
7.28
7.26
7.26
7.25
7.23
7.12
7.11
7.09
4.85
4.83
4.82
4.09
4.07
4.06
4.04
4.03
4.01
3.70
3.69
3.68
3.67
3.67
3.66
3.65
3.64
2.62
2.60
2.58
2.57
2.56
2.54
2.52
2.51
2.49
2.47
2.45
2.06
2.05
2.03
2.03
1.91
1.89
1.88
1.30
1.25
1.18
O
Ph
HO
NO_2
Ph
7.10
1.57
1.76
0.84
0.89
2.44
1.00
1.00
0.56
2.77
2.74
.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
f1 (ppm)

26

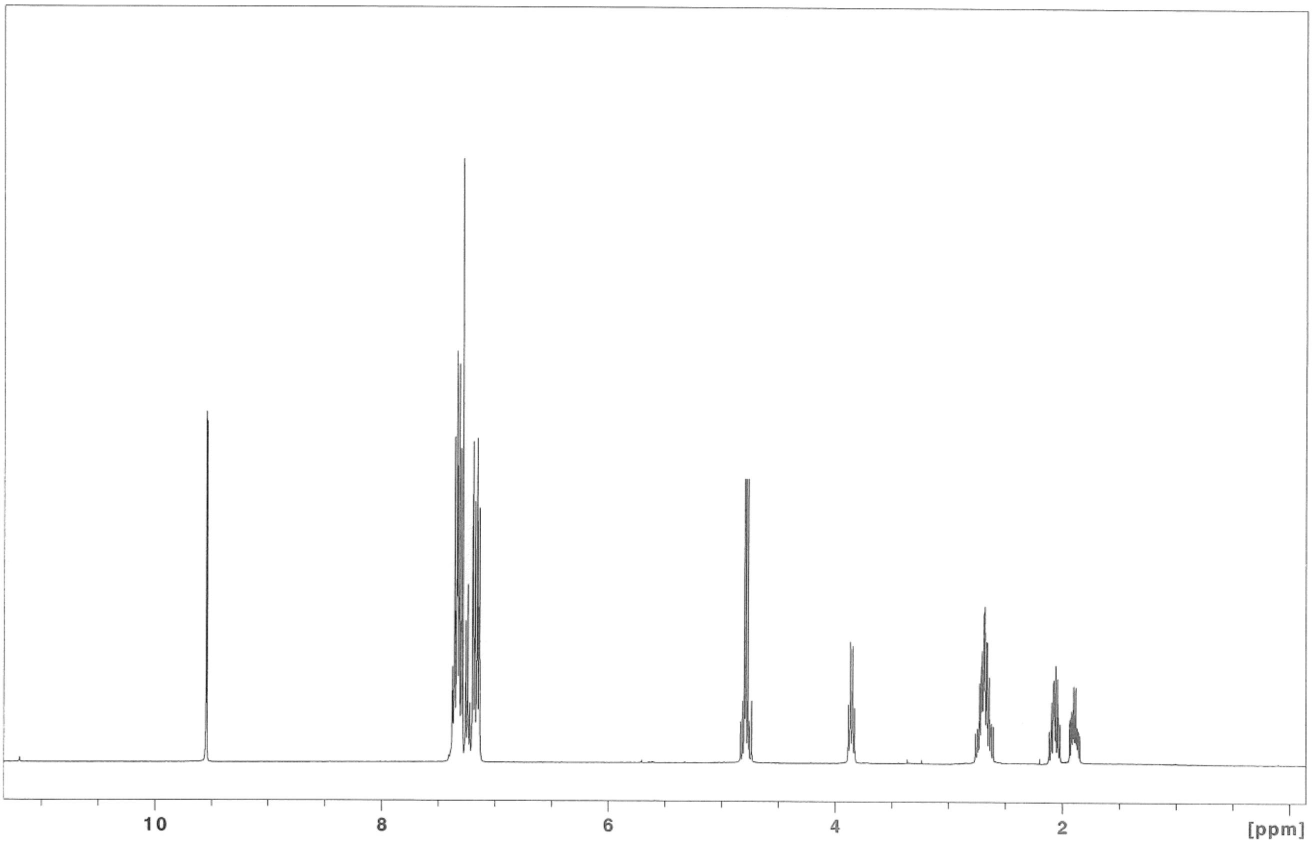

215.3
140.6
138.0
129.0
128.6
128.1
128.0
128.0
126.3
75.9
48.7
44.2
33.2
29.8
26.6
30
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

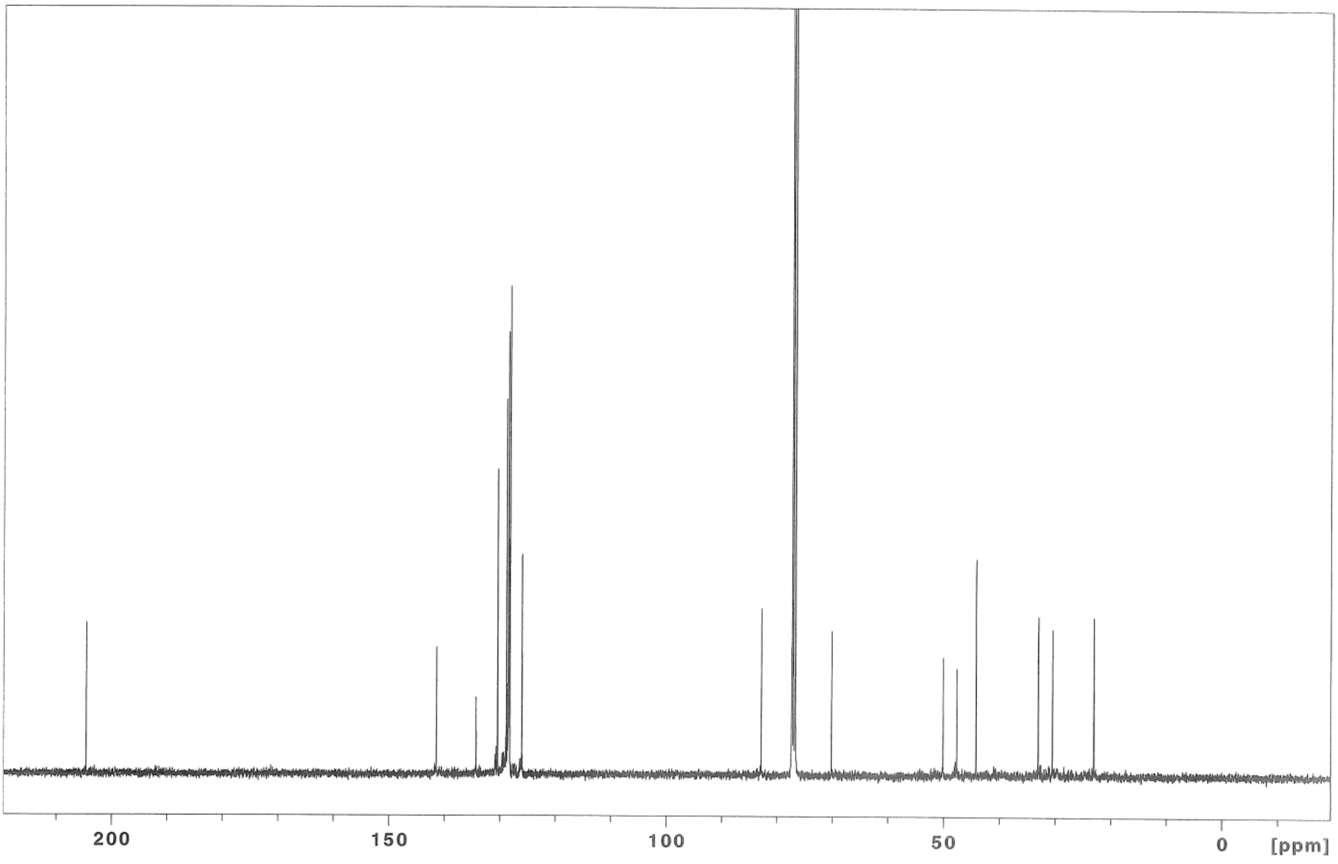

7.36
7.34
7.32
7.30
7.28
7.27
7.25
7.21
7.20
7.19
7.19
7.17
4.90
4.88
4.85
4.83
4.81
4.78
4.76
4.73
3.90
3.88
3.87
3.85
3.85
3.82
2.89
2.87
2.86
2.85
2.84
2.83
2.82
2.78
2.76
2.75
2.73
2.71
2.67
2.65
2.64
2.63
2.62
2.60
2.60
2.08
2.06
2.05
2.03
2.01
2.00
1.91
1.90
1.89
1.88
1.86
O
Ph
HO
NO2
Ph
27
10.40
2.00
1.01
3.35
1.19
1.07
f1 (ppm)

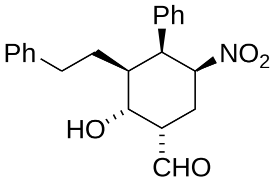

177.9
139.9
135.8
128.2
127.9
127.7
127.6
127.3
125.7
77.0
47.5
44.9
32.8
30.6
f1 (ppm)



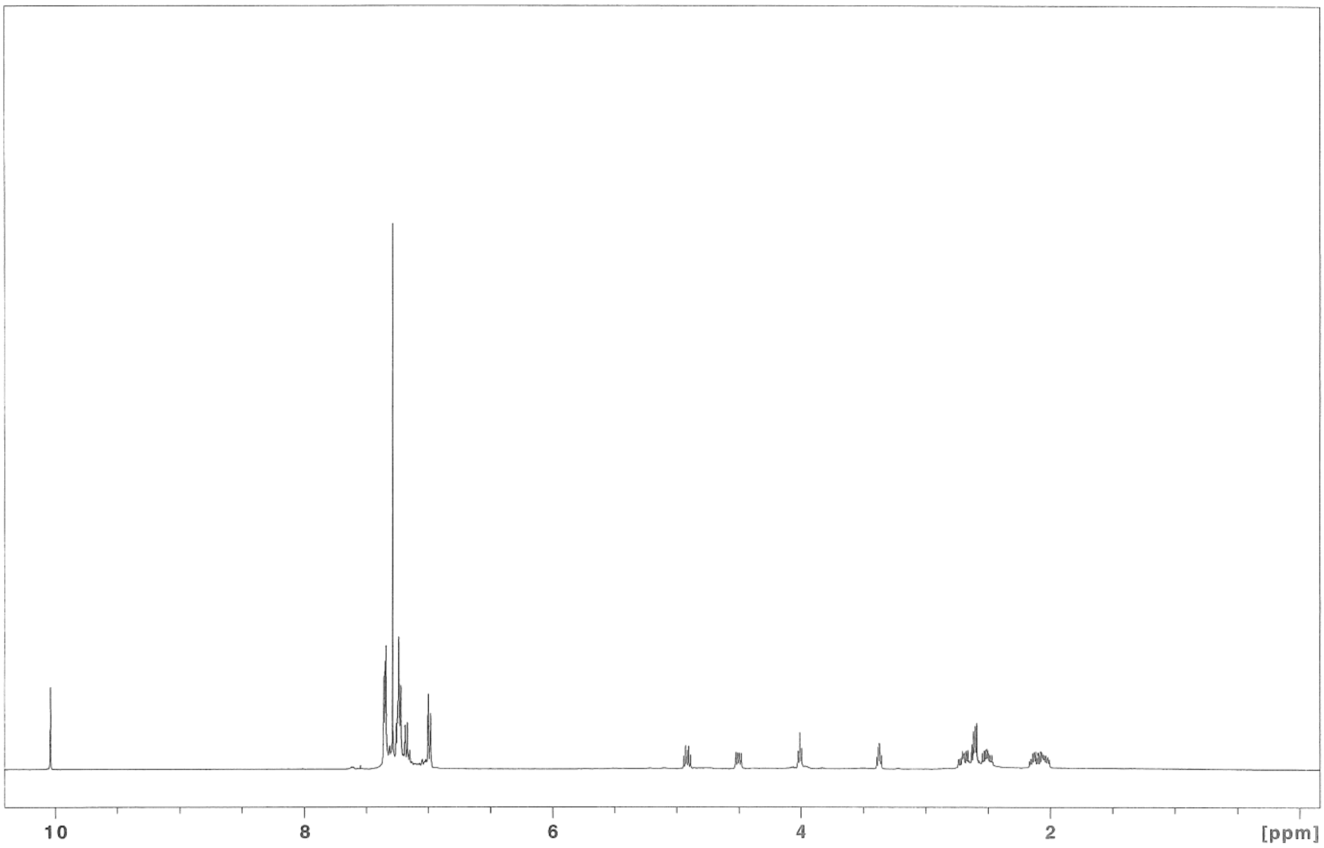
28

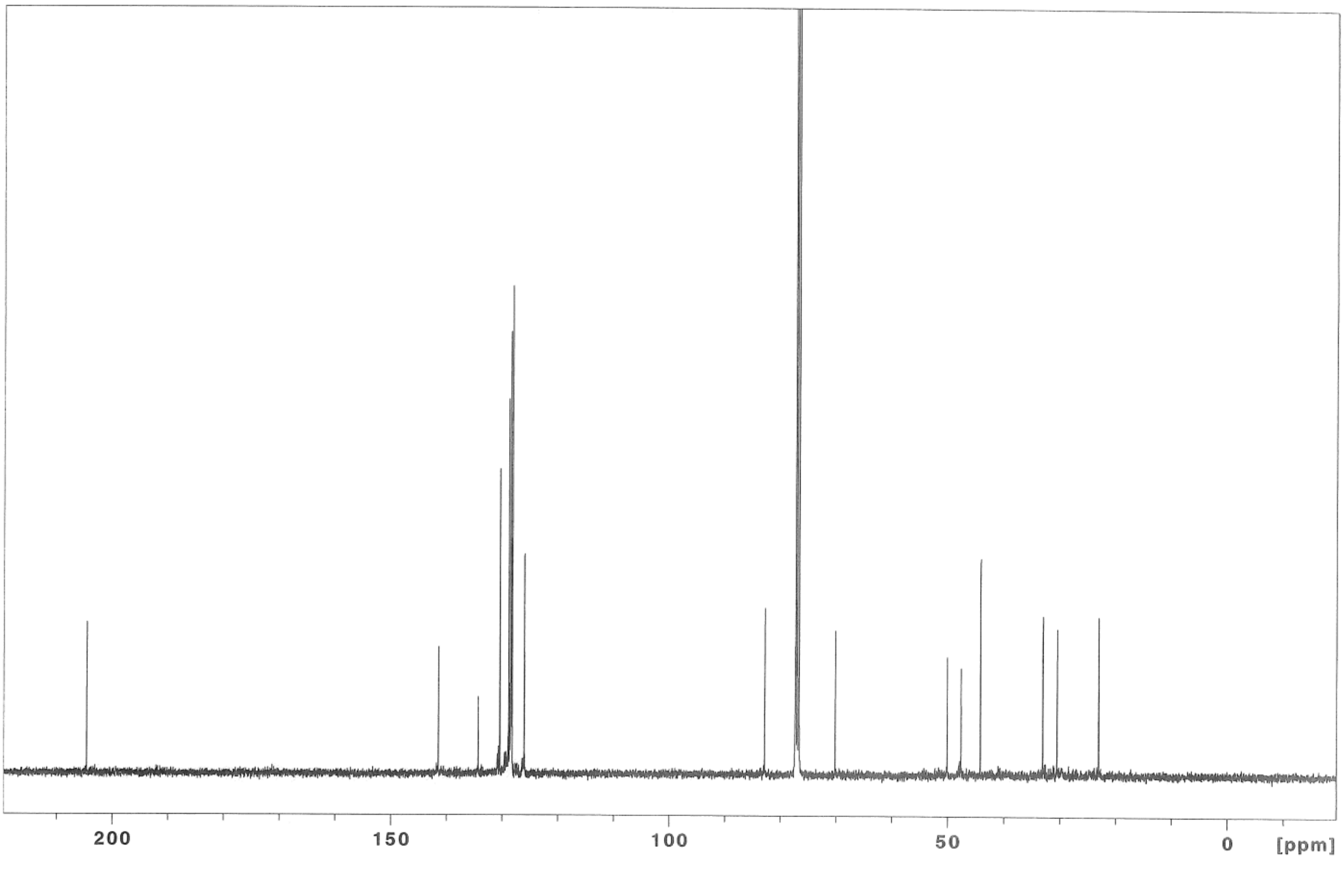


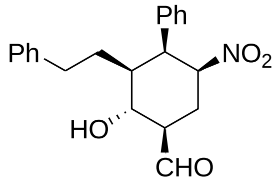




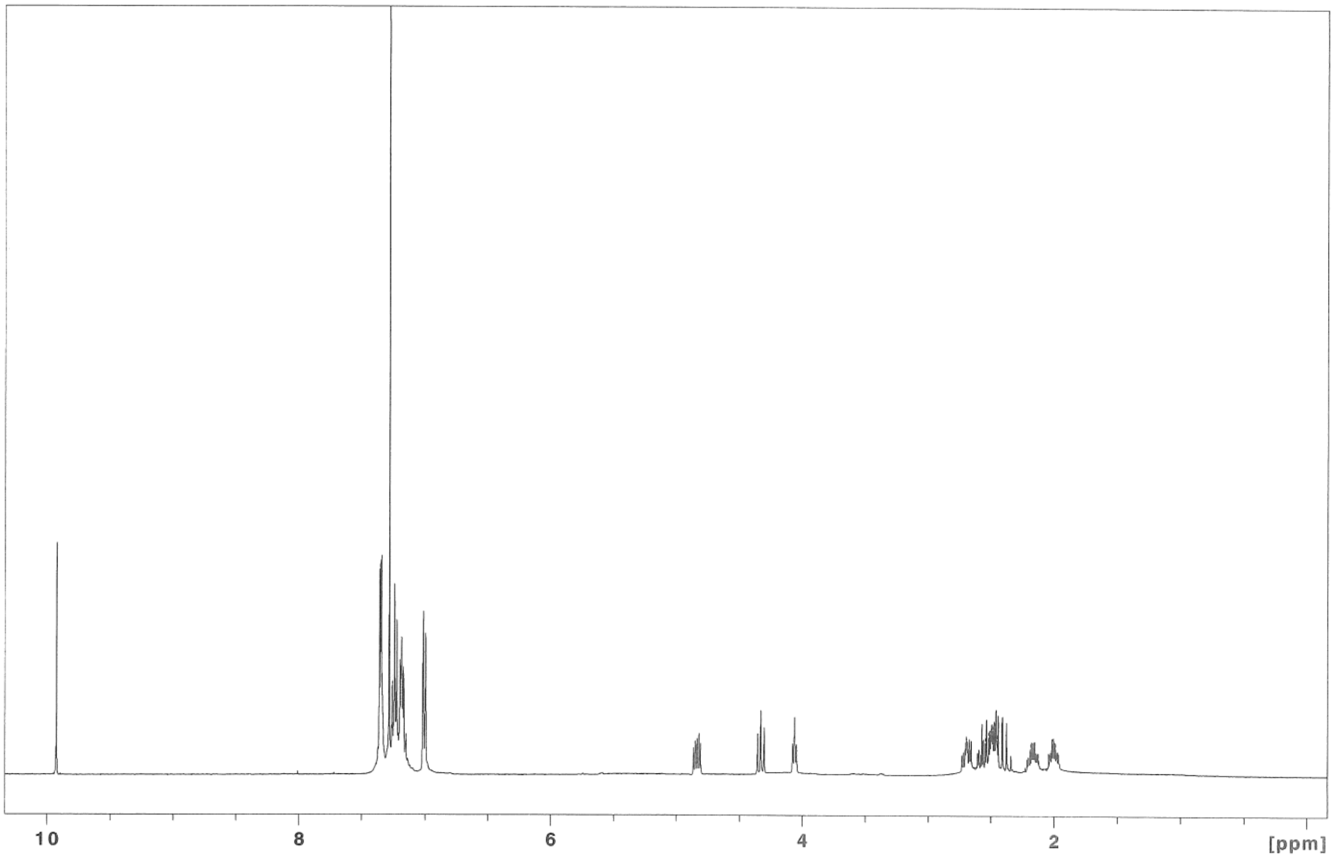
29

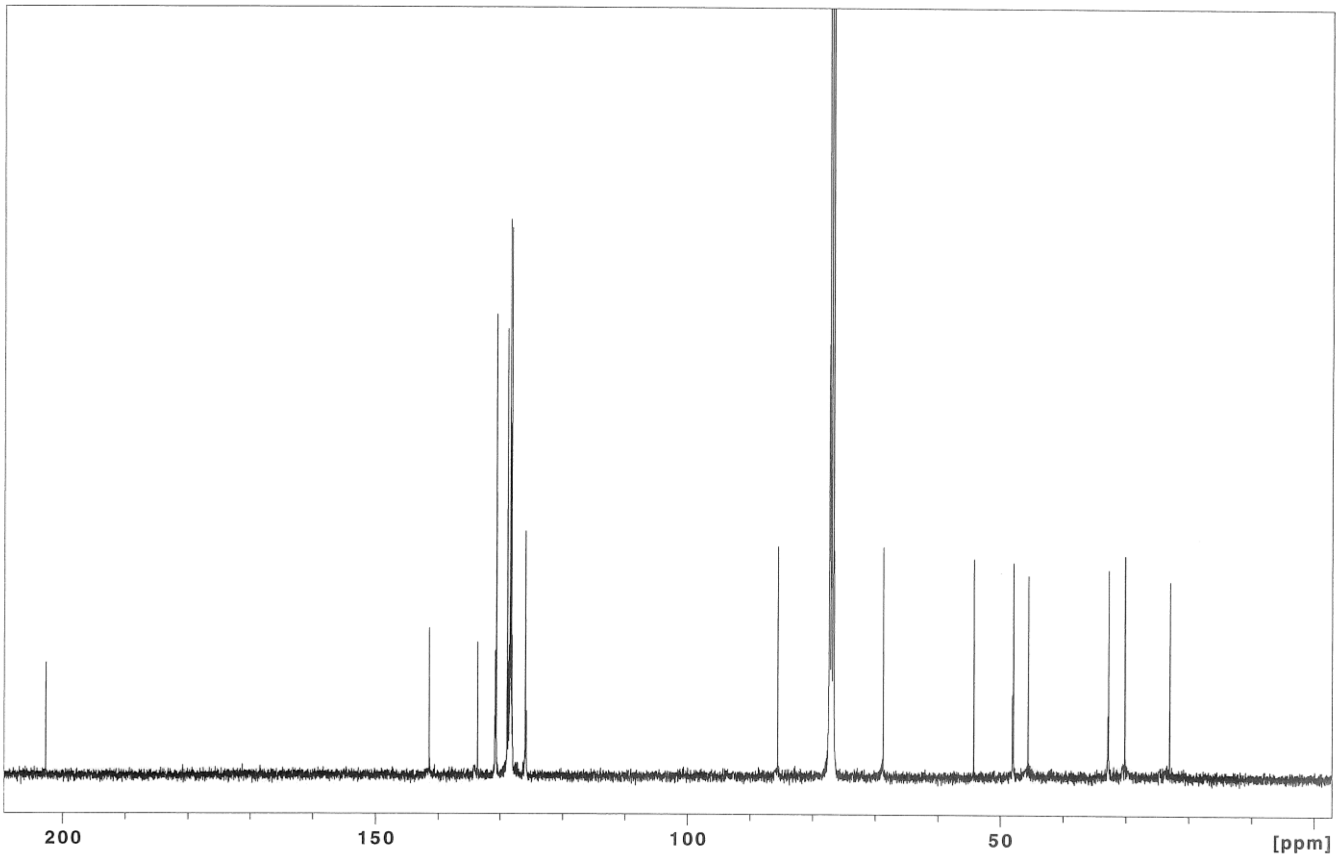


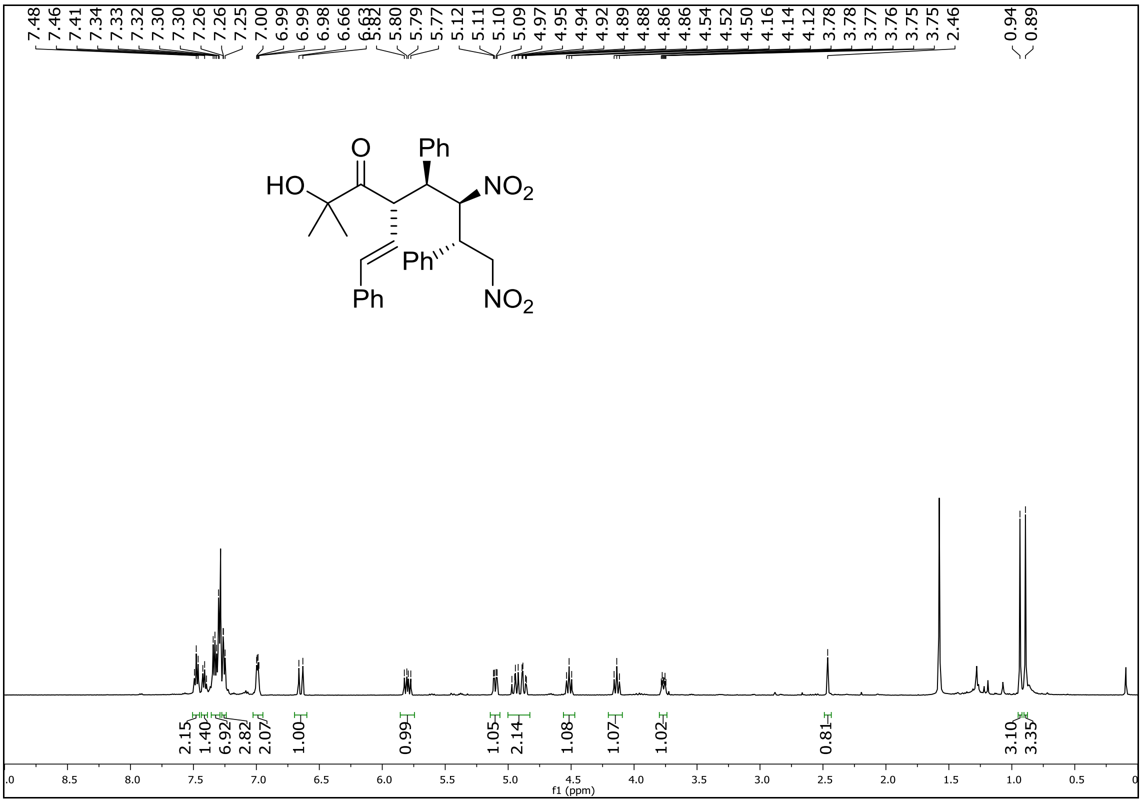


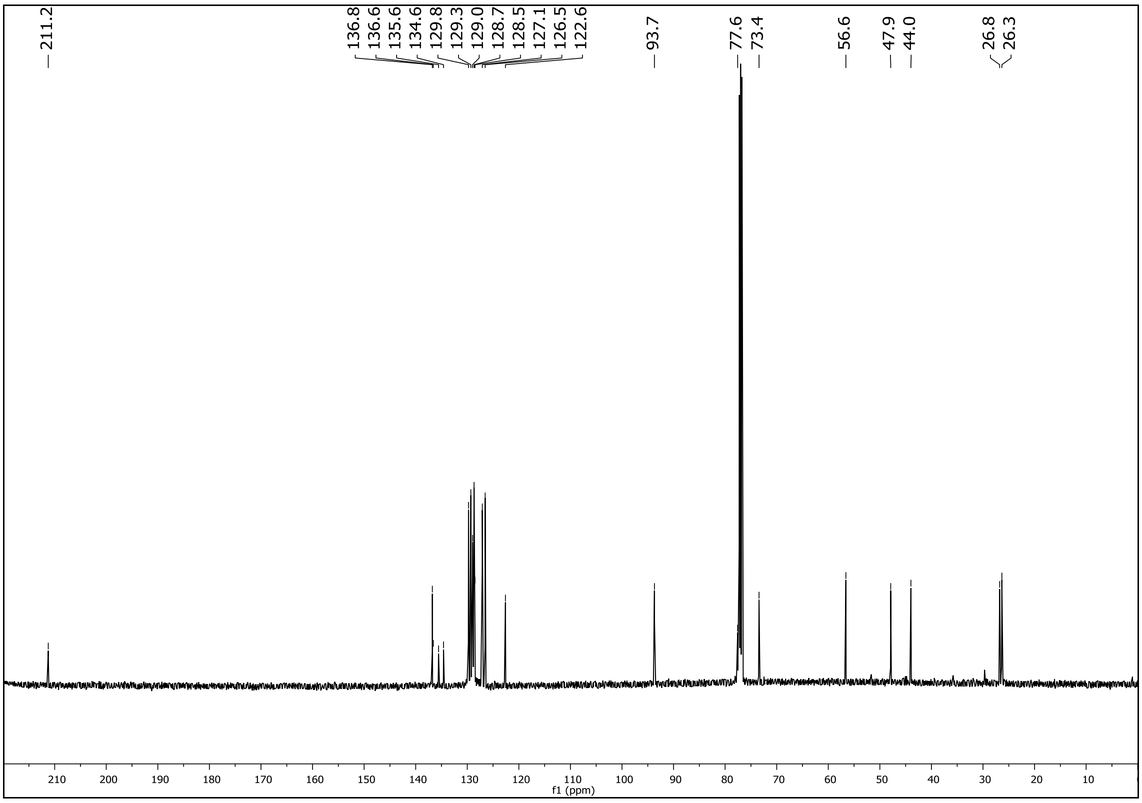


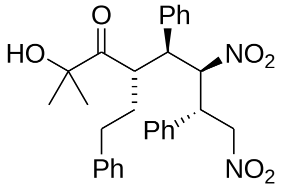
30



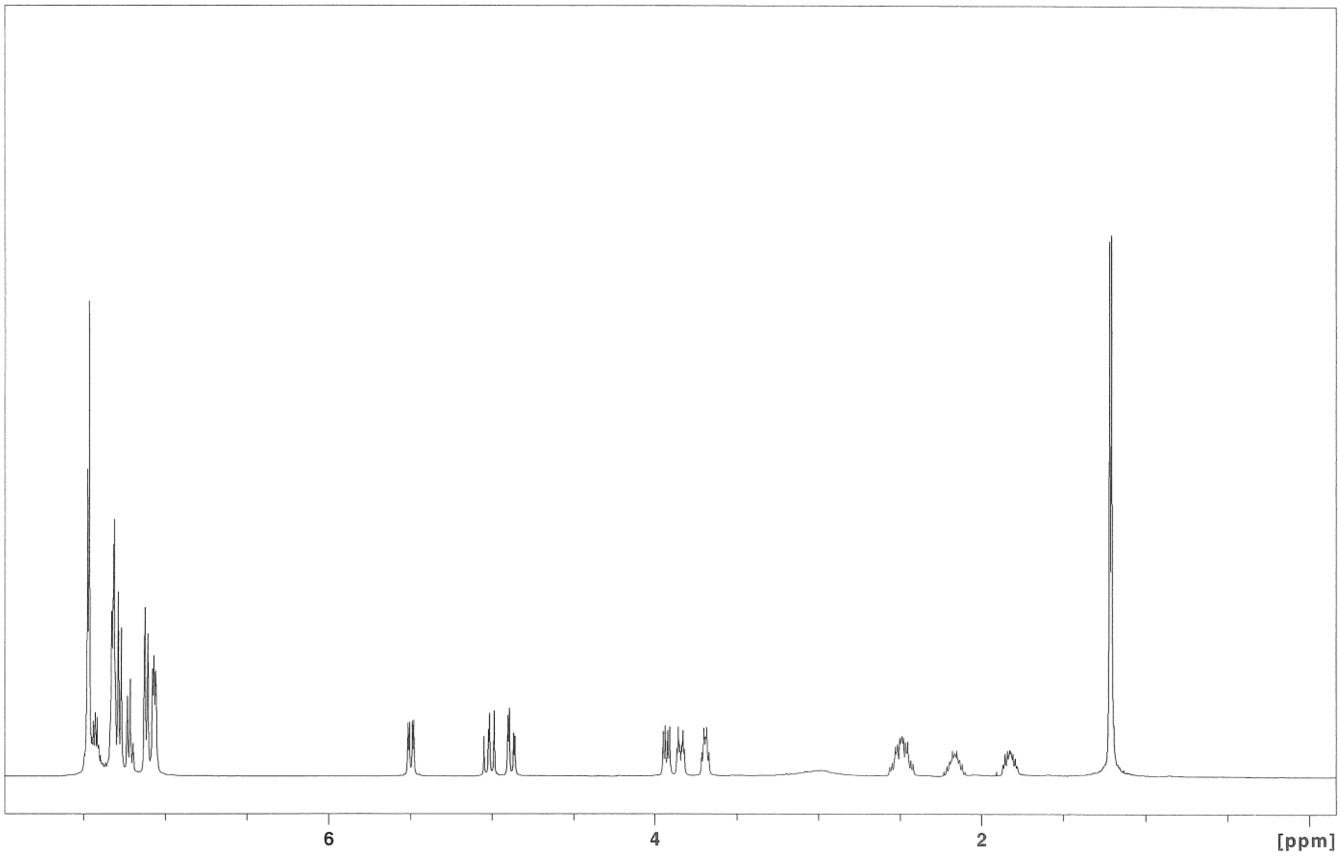


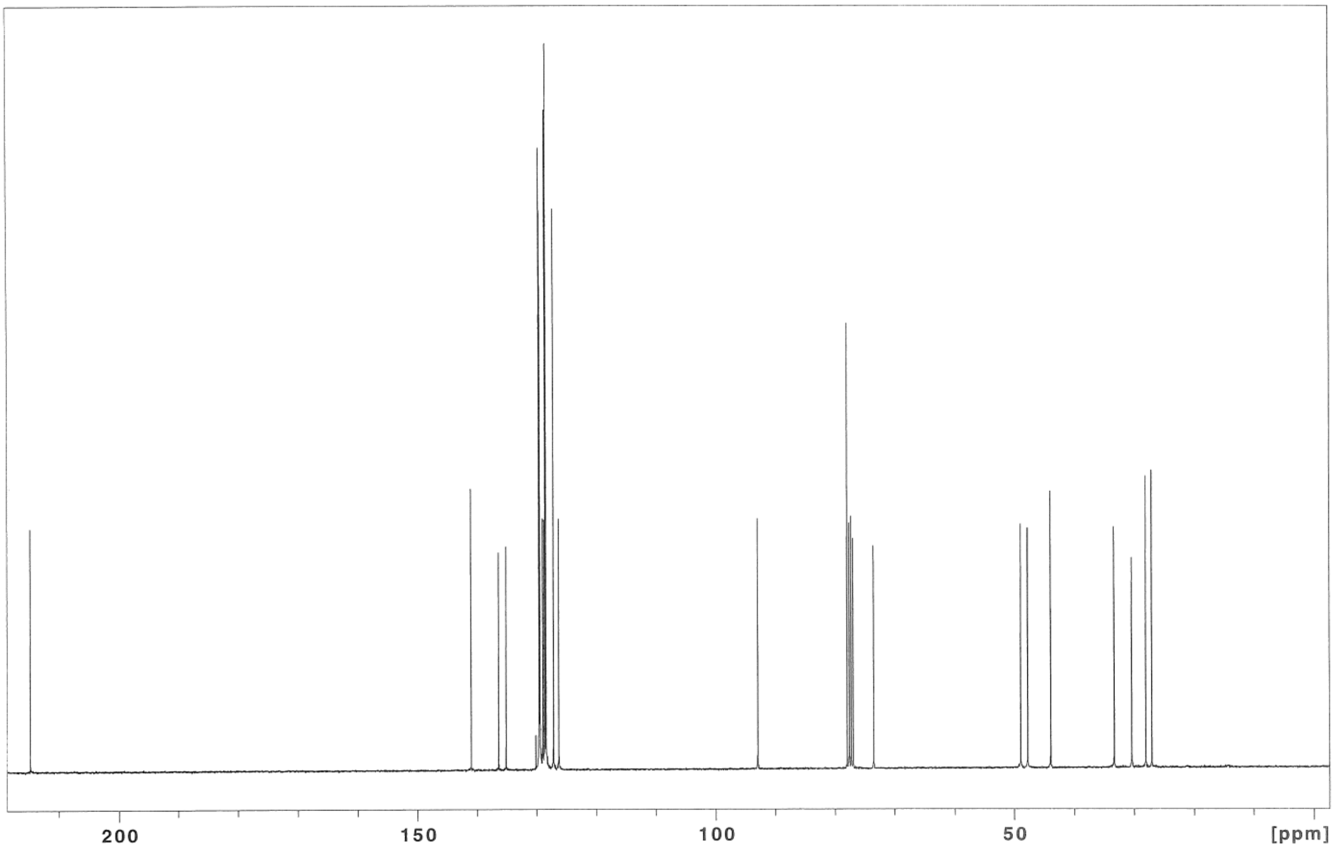

7.48
7.46
7.41
7.34
7.33
7.32
7.30
7.30
7.26
7.26
7.25
7.00
6.99
6.99
6.98
6.66
6.63
5.82
5.80
5.79
5.77
5.12
5.11
5.10
5.09
4.97
4.95
4.94
4.92
4.89
4.88
4.86
4.86
4.54
4.52
4.50
4.16
4.14
4.12
3.78
3.78
3.77
3.76
3.75
3.75
2.46
0.94
0.89
O
Ph
HO
NO2
Ph
Ph
NO2
2.15
1.40
6.92
2.82
2.07
1.00
0.99
1.05
2.14
1.08
1.07
1.02
0.81
3.10
3.35
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

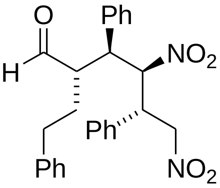

211.2
136.8
136.6
135.6
134.6
129.8
129.3
129.0
128.7
128.5
127.1
126.5
122.6
93.7
77.6
73.4
56.6
47.9
44.0
26.8
26.3
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)



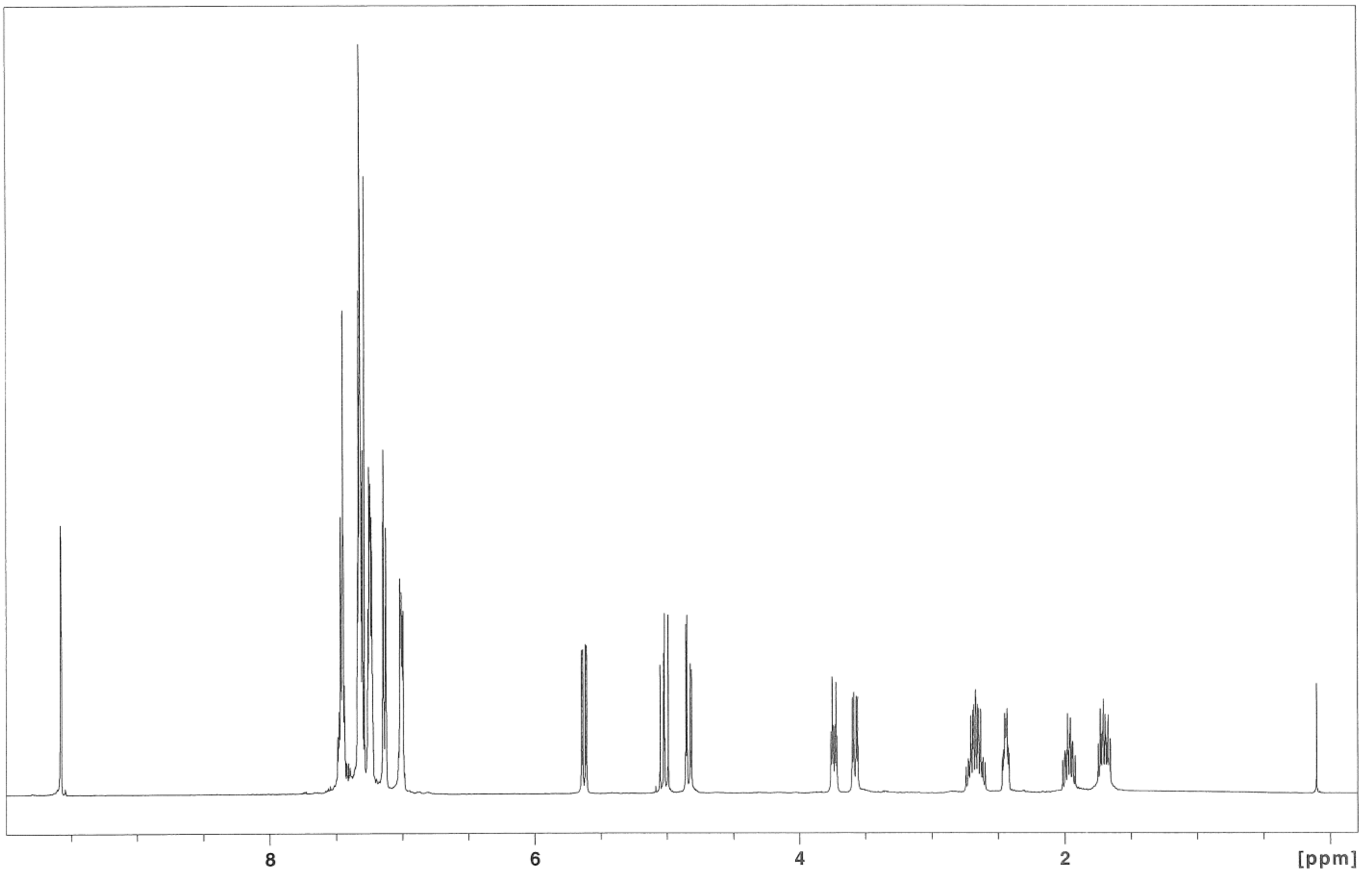
31

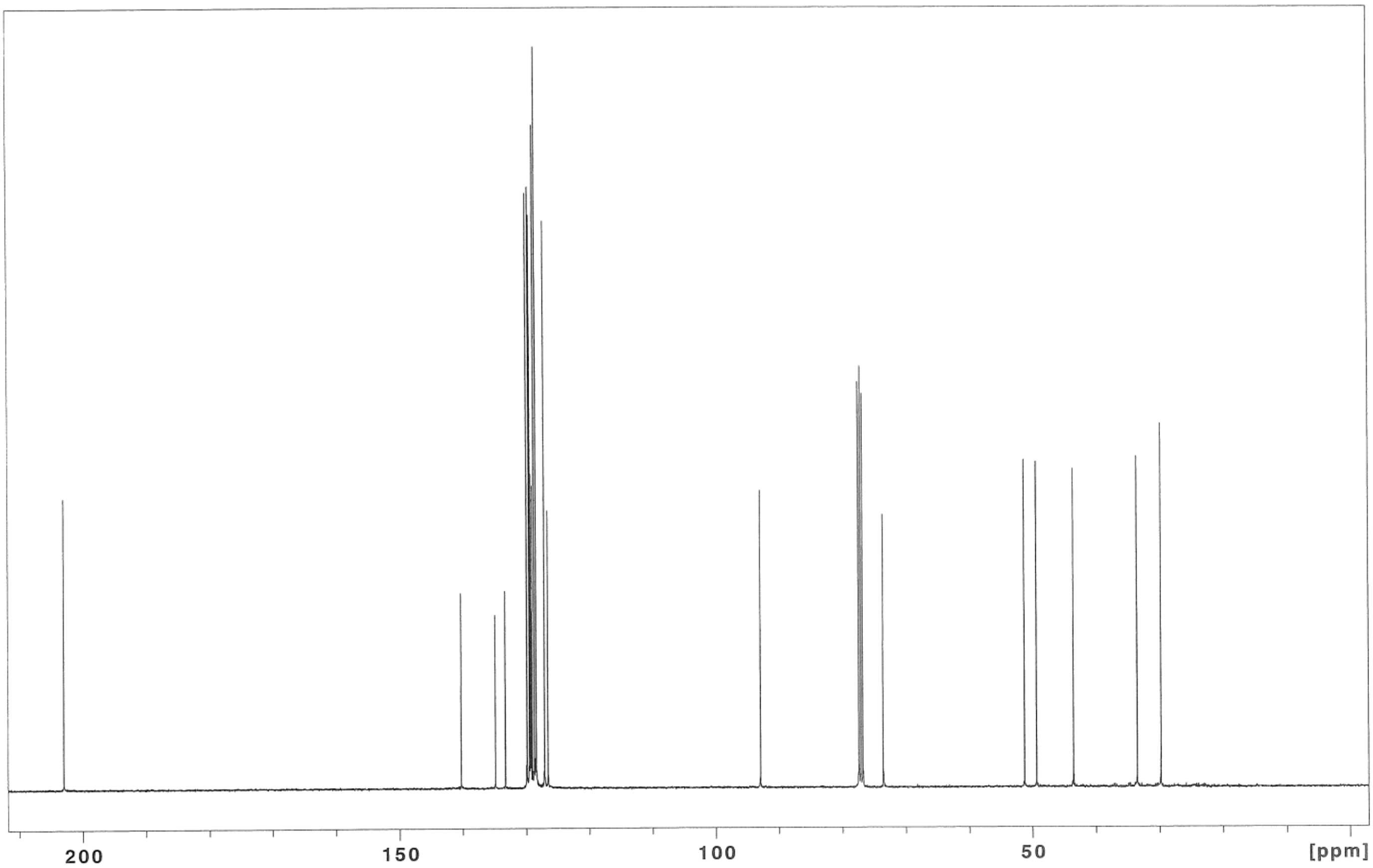


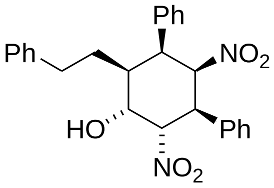




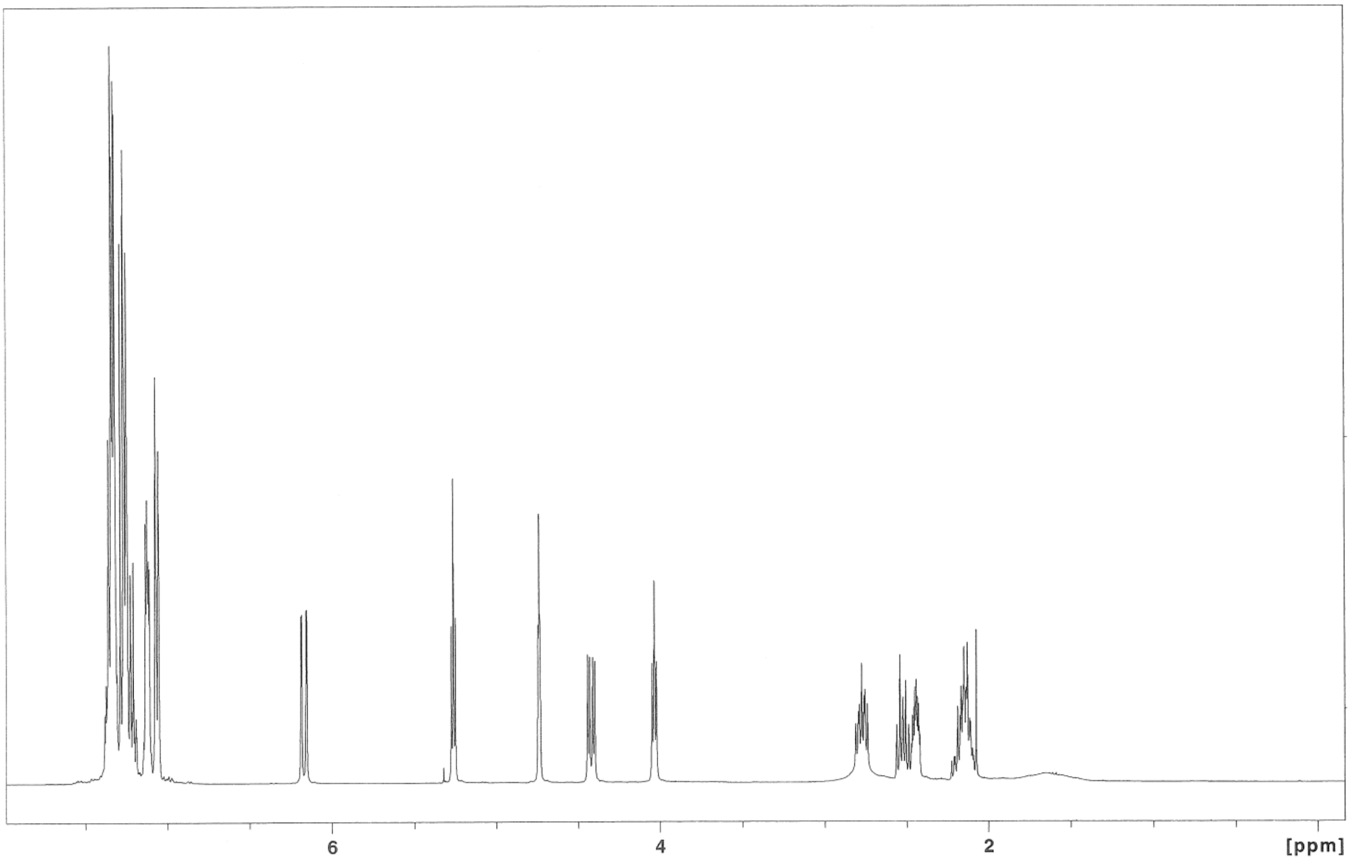
32

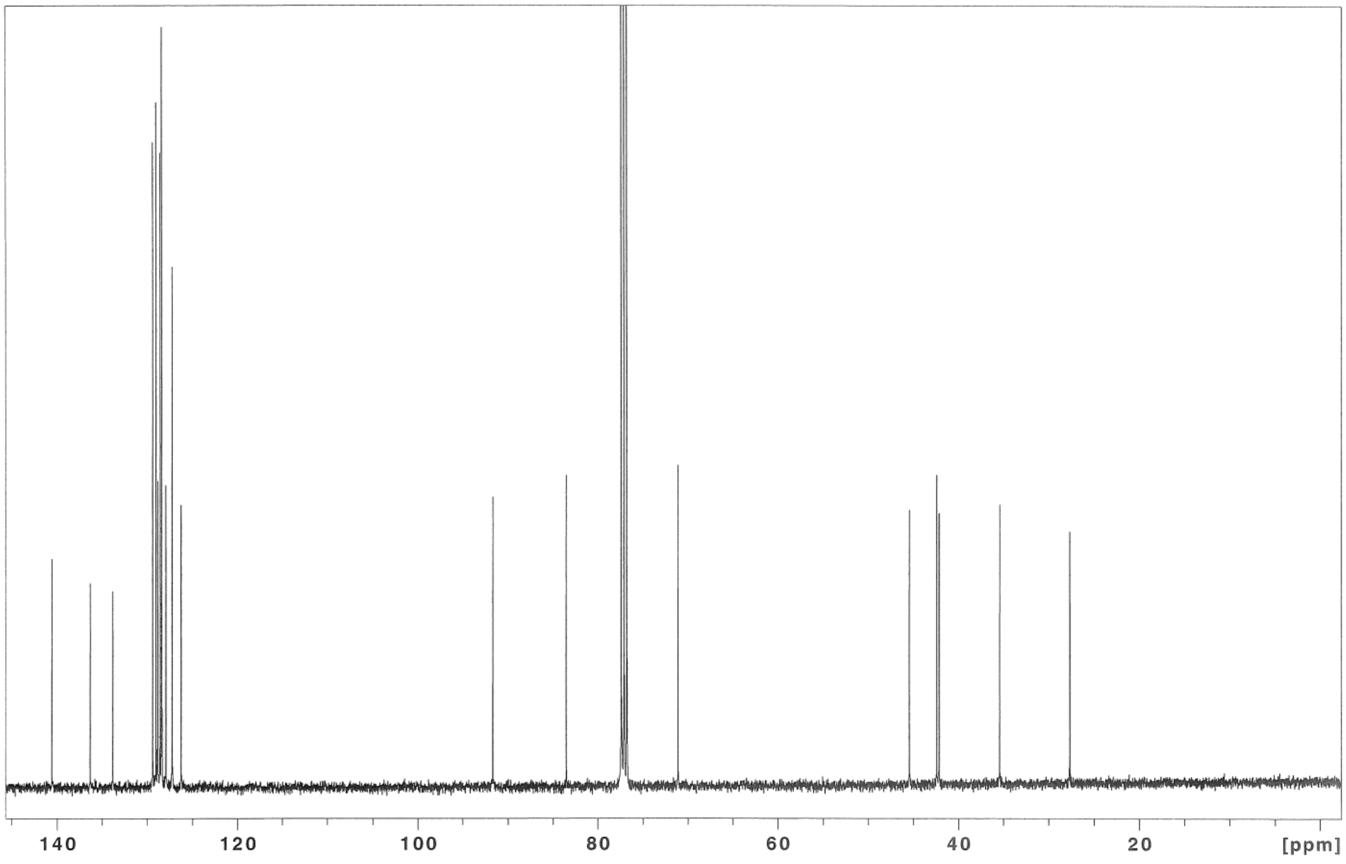


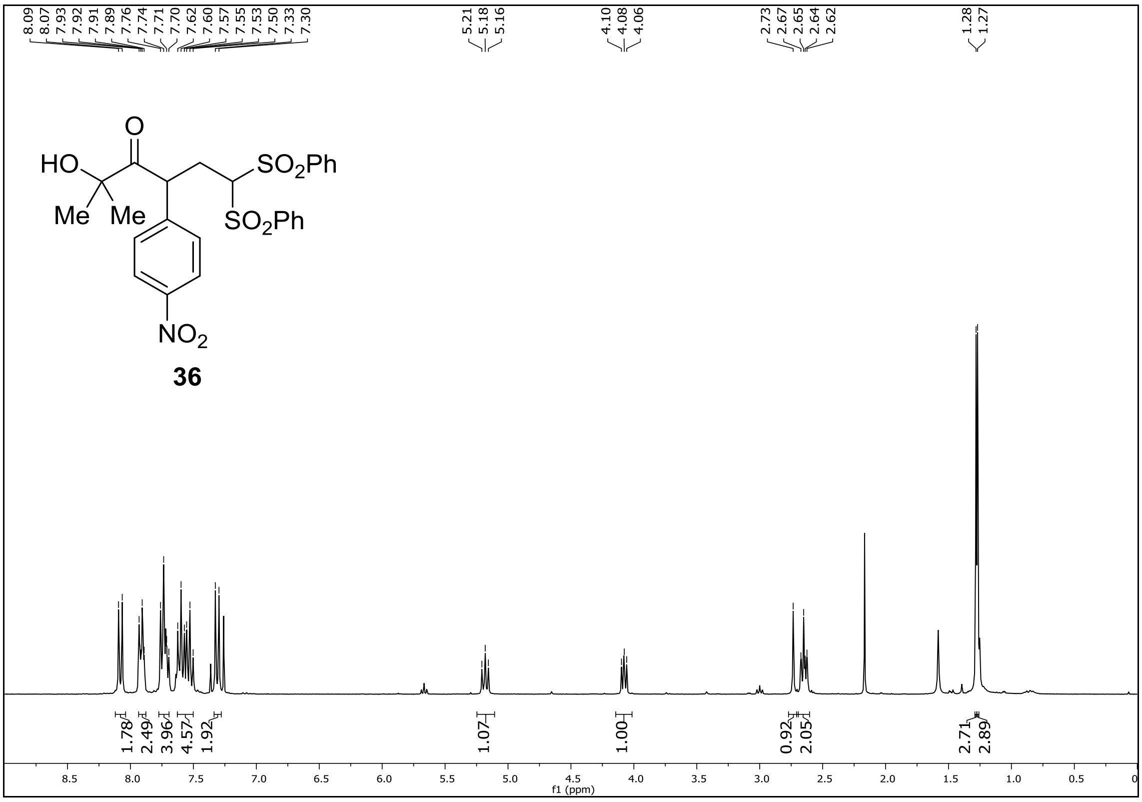


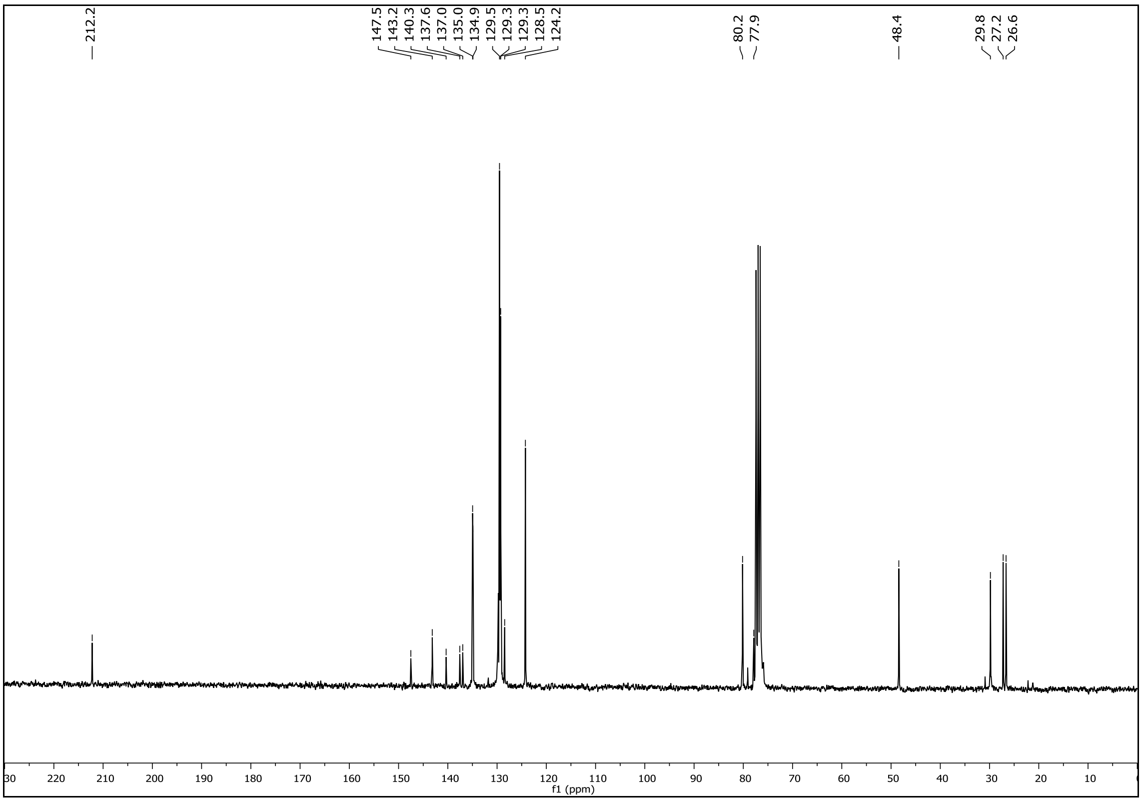


33

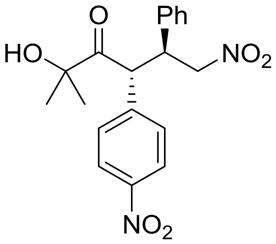





8.09
8.07
7.93
7.92
7.91
7.89
7.76
7.74
7.71
7.70
7.62
7.60
7.57
7.55
7.53
7.50
7.33
7.30
5.21
5.18
5.16
4.10
4.08
4.06
2.73
2.67
2.65
2.64
2.62
1.28
1.27
O
HO
SO2Ph
Me
Me
SO2Ph
NO2
36
1.78
2.49
3.96
4.57
1.92
1.07
1.00
0.92
2.05
2.71
2.89
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
f1 (ppm)


212.2
147.5
143.2
140.3
137.6
137.0
135.0
134.9
129.5
129.3
129.3
128.5
124.2
80.2
77.9
48.4
29.8
27.2
26.6
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

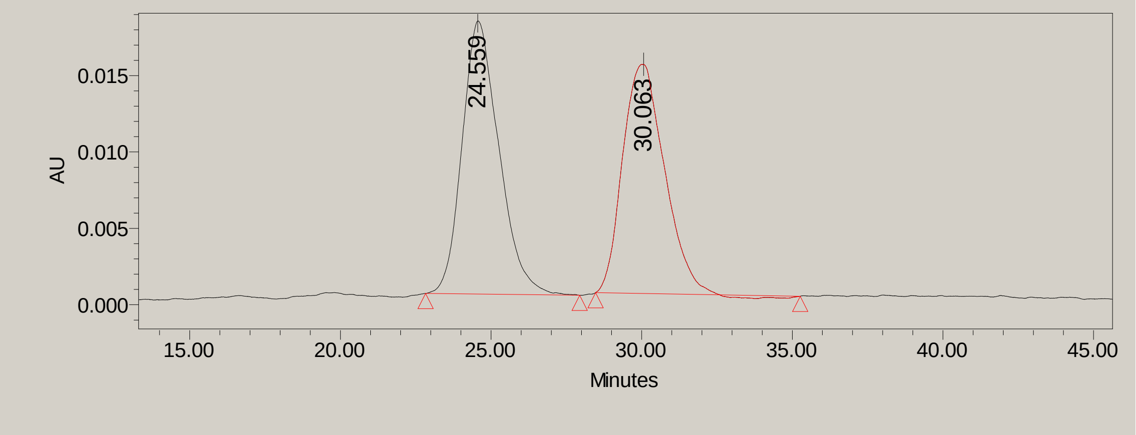
12. HPLC Chromatograms



6Aa

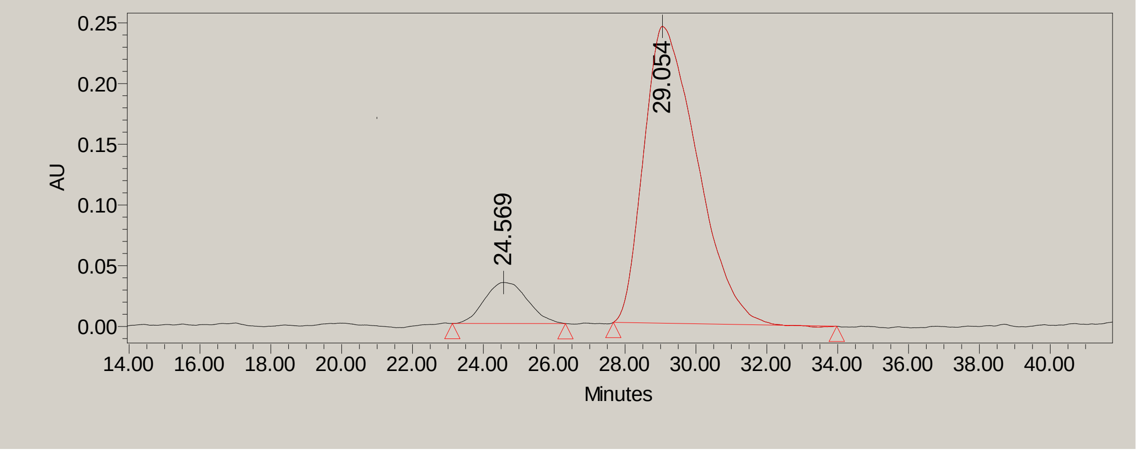
Daicel Chiralpak OD-H, hexane/isopropanol 90/10 flow rate = 1.0 mL/min, λ: 210.0 nm.

Rac-**6Aa**

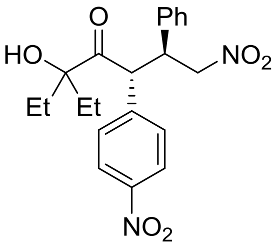


	Retention Time	% Area
1	24.559	50.77
2	30.063	49.23

6Aa



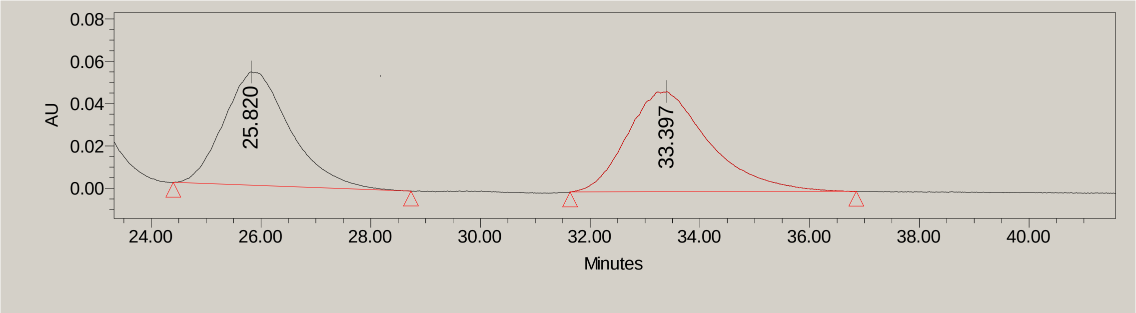
	Retention Time	% Area
1	24.569	9.96
2	29.054	90.04



7Aa

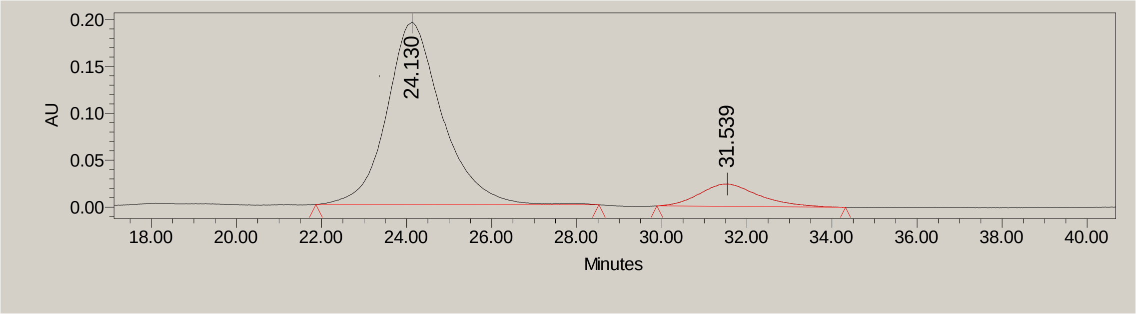
Daicel Chiralpak AD-H, hexane/isopropanol 90/10 flow rate = 1.0 mL/min, λ: 210.0 nm.

Rac-**7Aa**

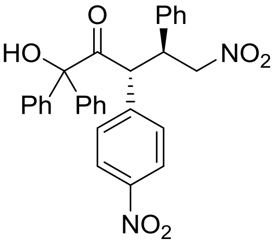


	Retention Time	% Area
1	25.820	47.81
2	33.397	52.19

7Aa



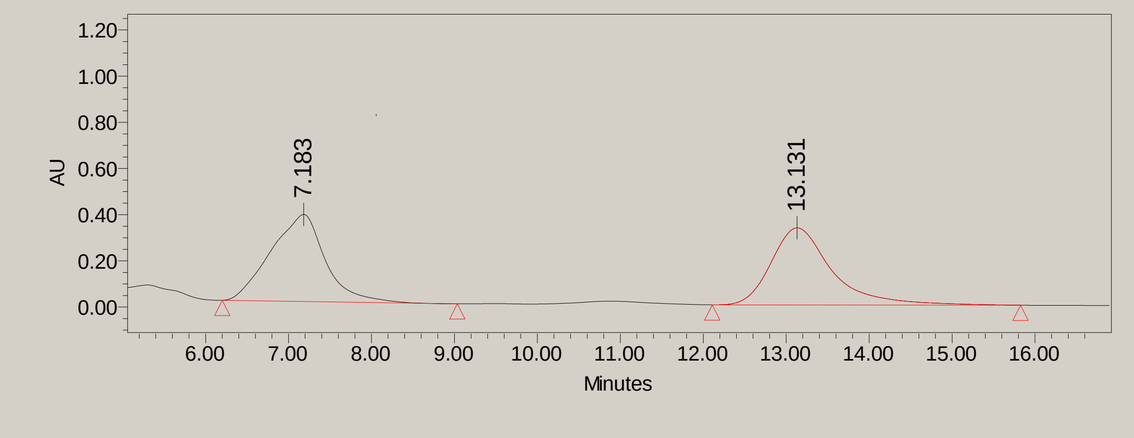
	Retention Time	% Area
1	24.130	89.89
2	31.539	10.11



8Aa

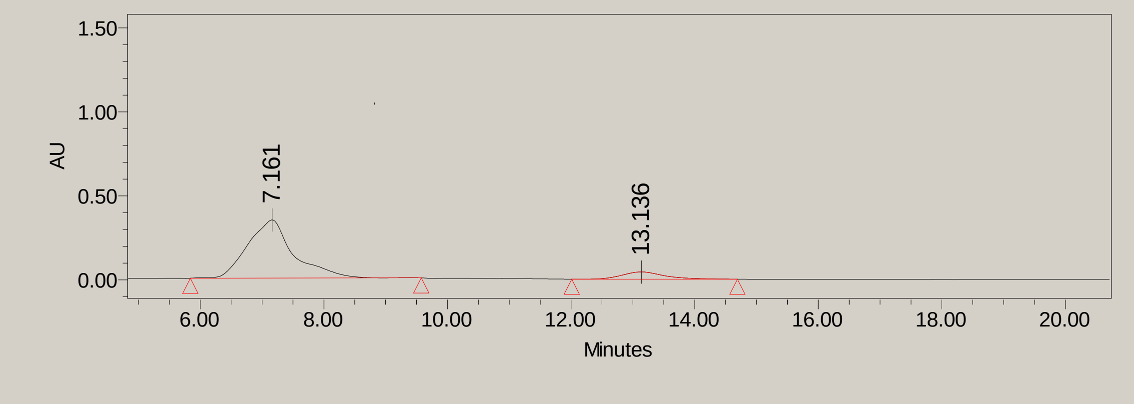
Daicel Chiralpak IA, hexane/isopropanol 70/30 flow rate = 1.0 mL/min, λ: 210.0 nm.

Rac-**8Aa**

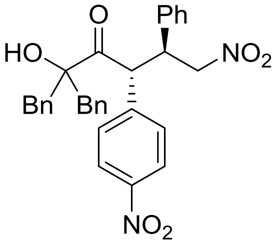


	Retention Time	% Area
1	7.183	50.38
2	13.131	49.62

8Aa



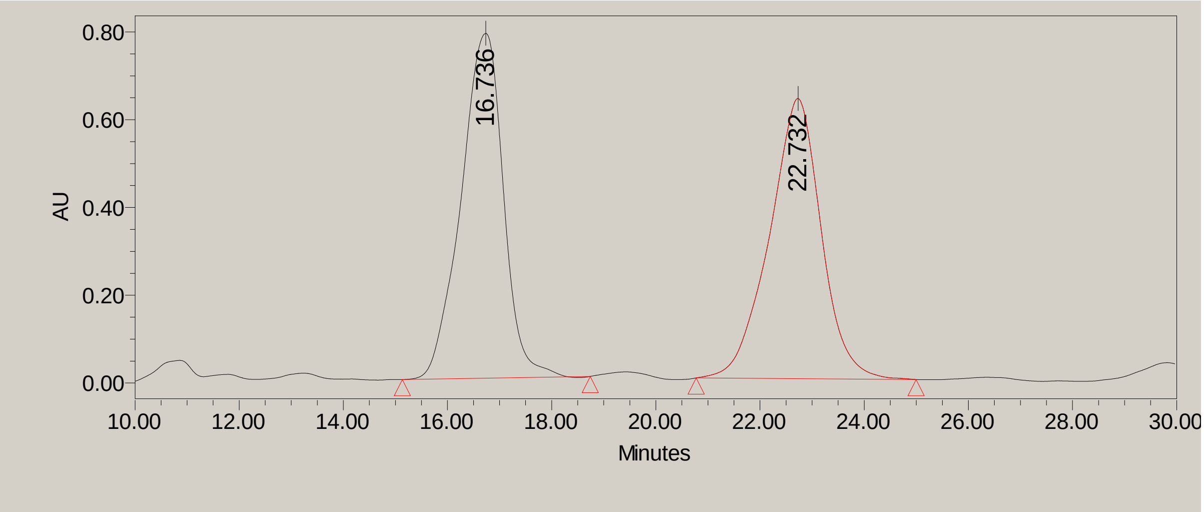
	Retention Time	% Area
1	7.161	89.71
2	13.136	10.29



9Aa

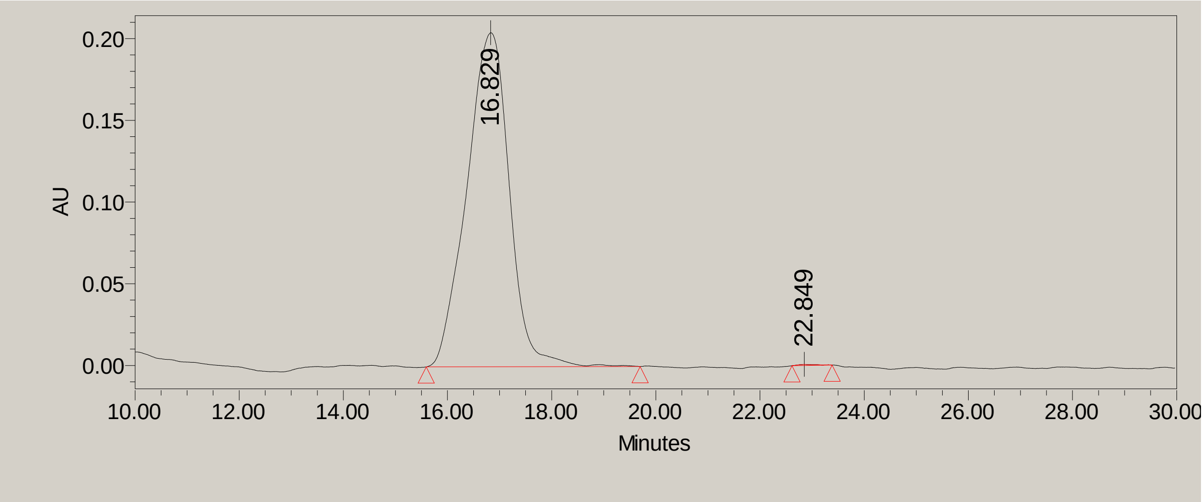
Daicel Chiralpak IA, hexane/isopropanol 90/10 flow rate = 1.0 mL/min, λ: 210.0 nm.

Rac-**9Aa**

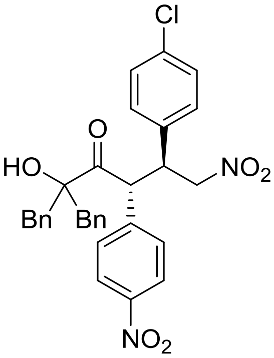


	Retention Time	% Area
1	16.736	50.24
2	22.732	49.76

9Aa

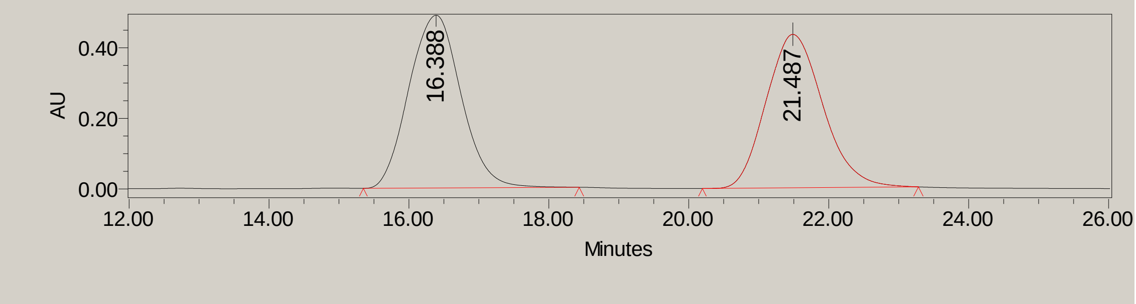


	Retention Time	% Area
1	16.829	99.86
2	22.849	0.14



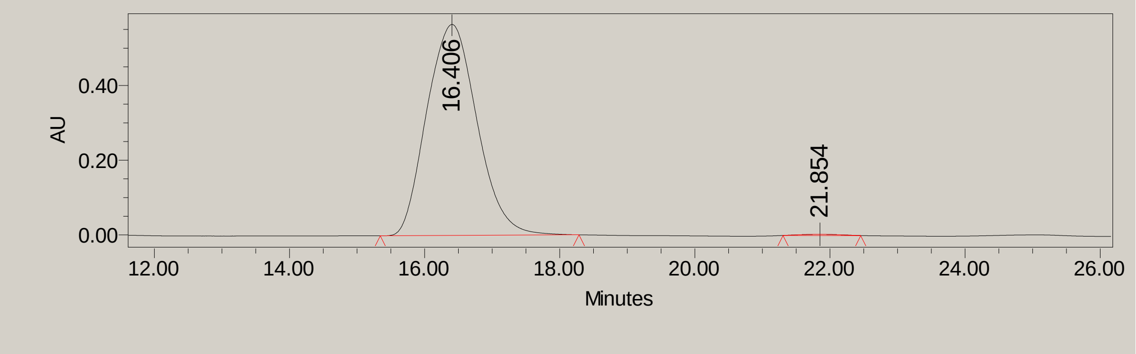
Daicel Chiralpak IA, hexane/isopropanol 90/10 flow rate = 1.0 mL/min, λ: 256.0 nm.

Rac-**9Ab**

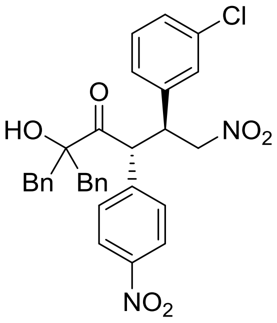


	Retention Time	% Area
	16.388	50.84
	21.487	49.16

Scalemic **9Ab**



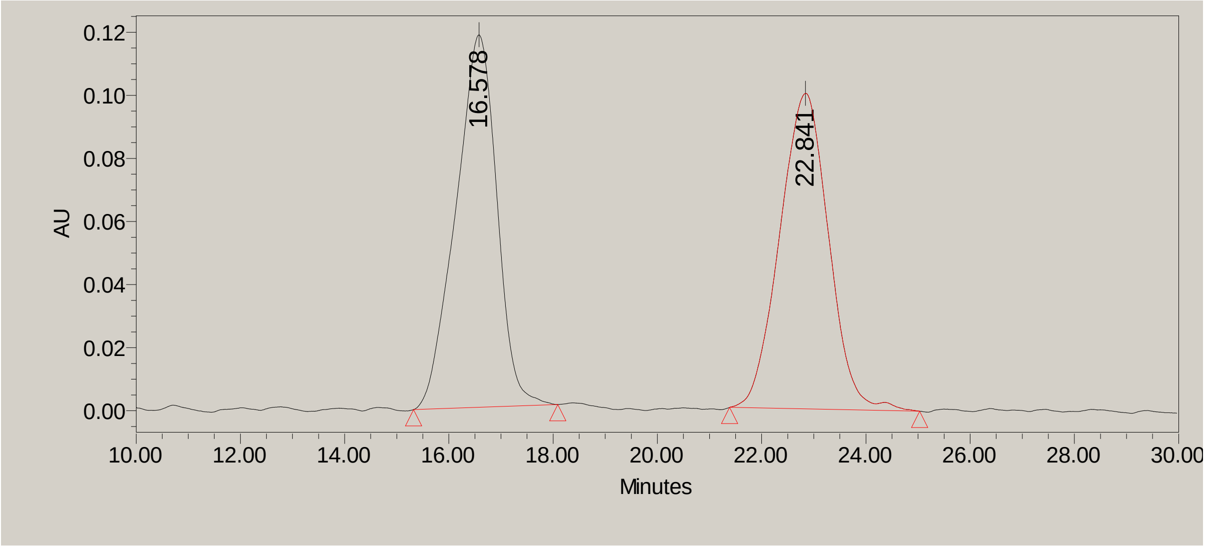
	Retention Time	% Area
	16.406	99.53
	21.854	0.47



9Ac

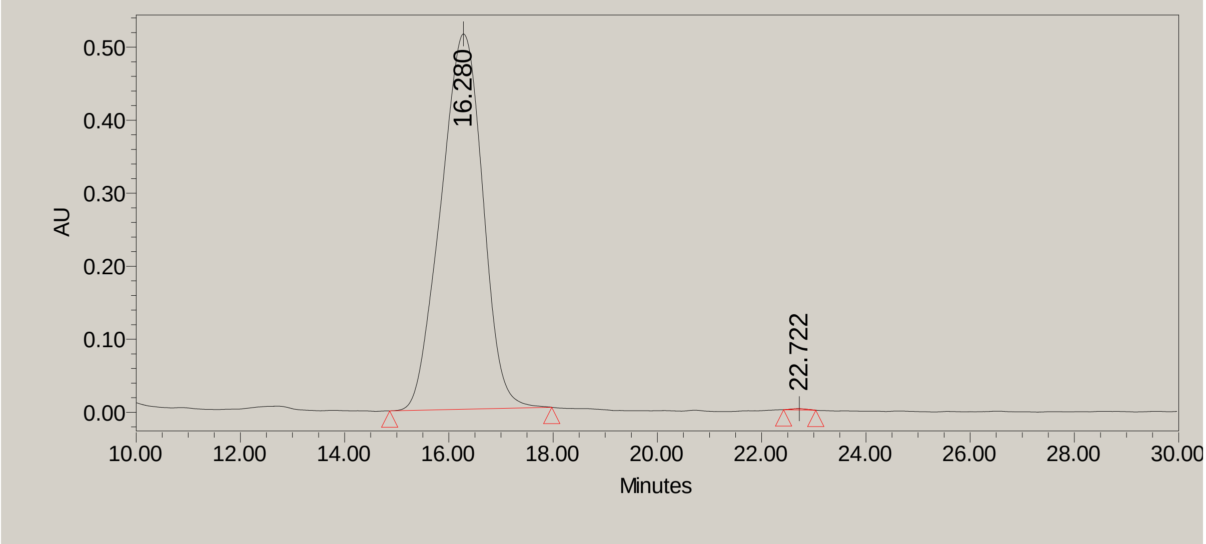
Daicel Chiralpak IA, hexane/isopropanol 90/10 flow rate = 1.0 mL/min, λ: 210.0 nm.

Rac-**9Ac**



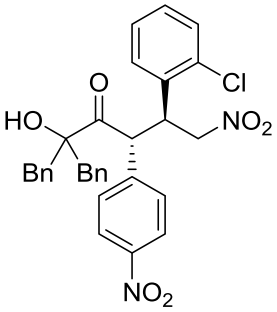
	Retention Time	% Area
1	16.578	49.81
2	22.841	50.19

9Ac



	Retention Time	% Area

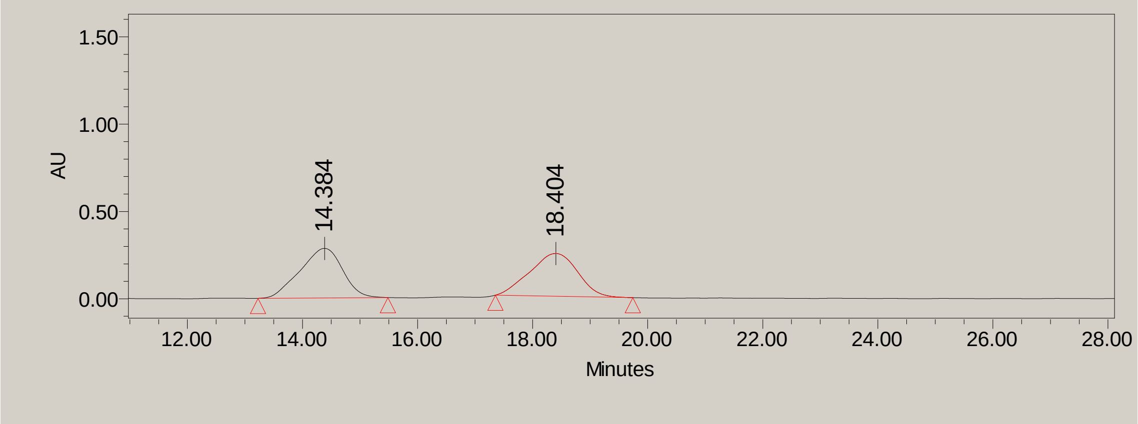
1	16.280	99.87
2	22.722	0.13



9Ad

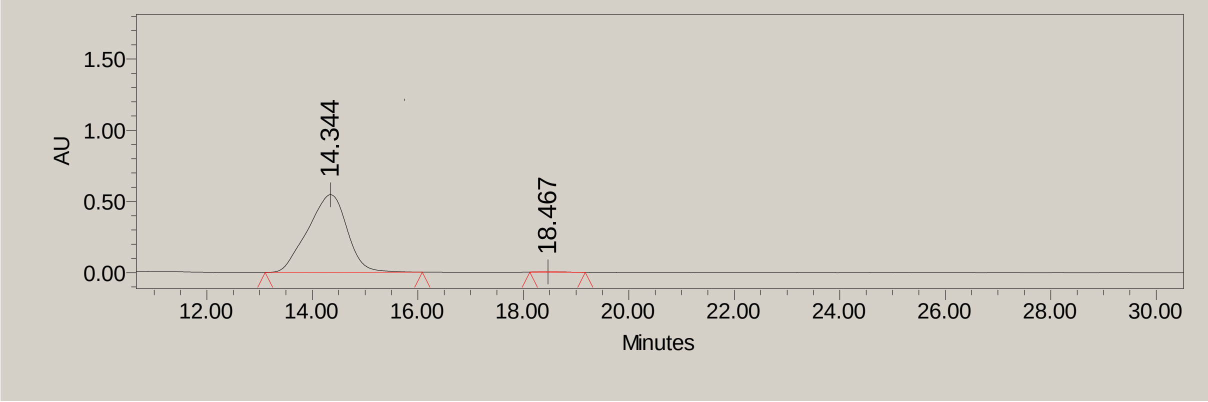
Daicel Chiralpak IA, hexane/isopropanol 90/10 flow rate = 1.0 mL/min, λ: 210.0 nm.

Rac-**9Ad**

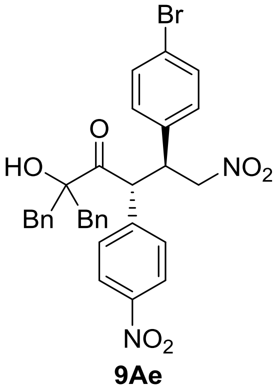


	Retention Time	% Area
1	14.384	50.77
2	18.404	49.23

Scalemic **9Ad**



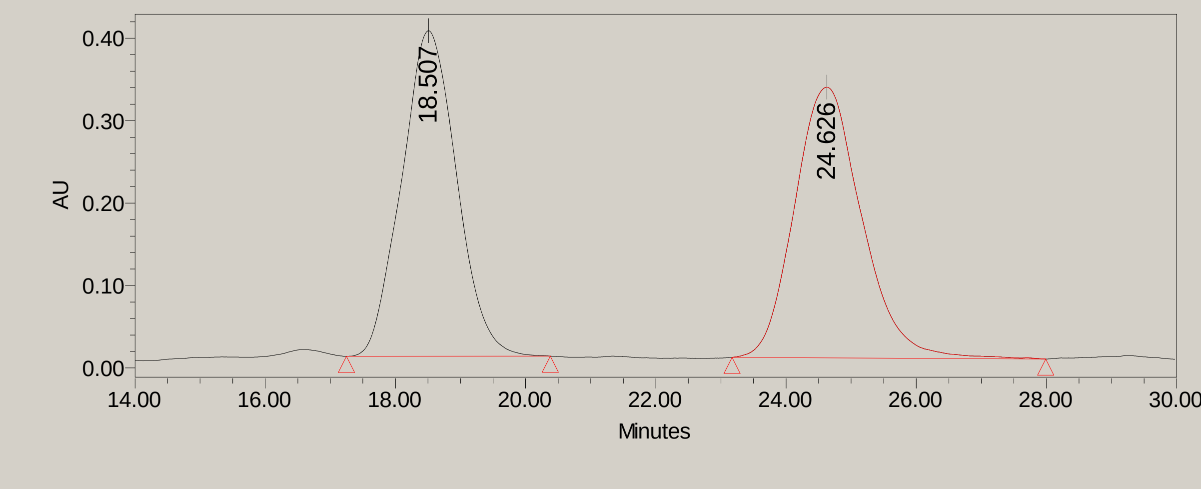
	Retention Time	% Area
1	14.344	99.66
2	18.467	0.34



9Ae

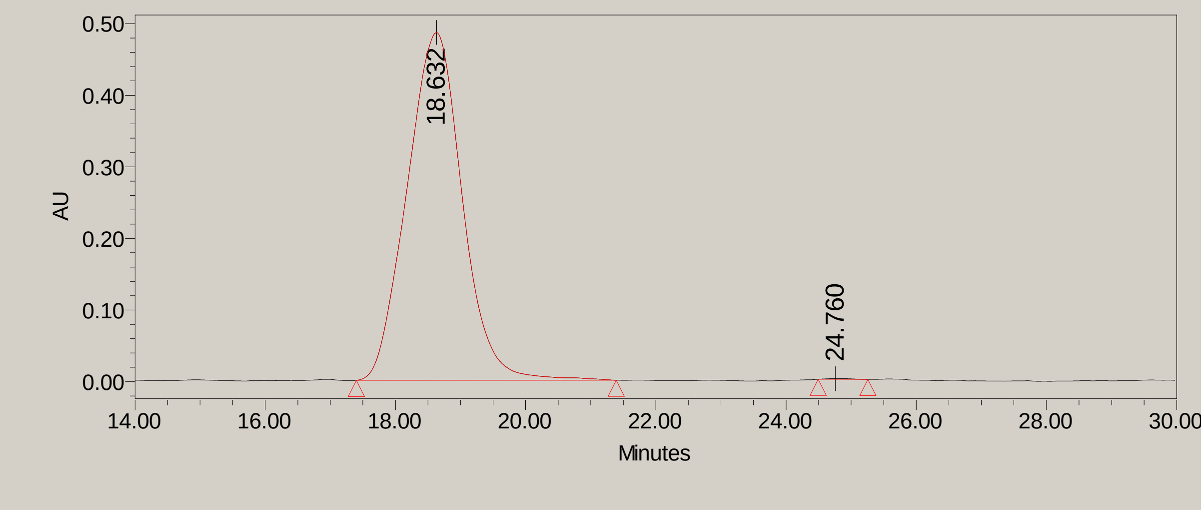
Daicel Chiralpak IA, hexane/isopropanol 90/10 flow rate = 1.0 mL/min, λ: 210.0 nm.

Rac-**9Ae**

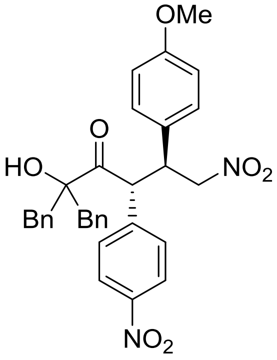


	Retention Time	% Area
1	18.507	49.60
2	24.626	50.40

Scalemic **9Ae**



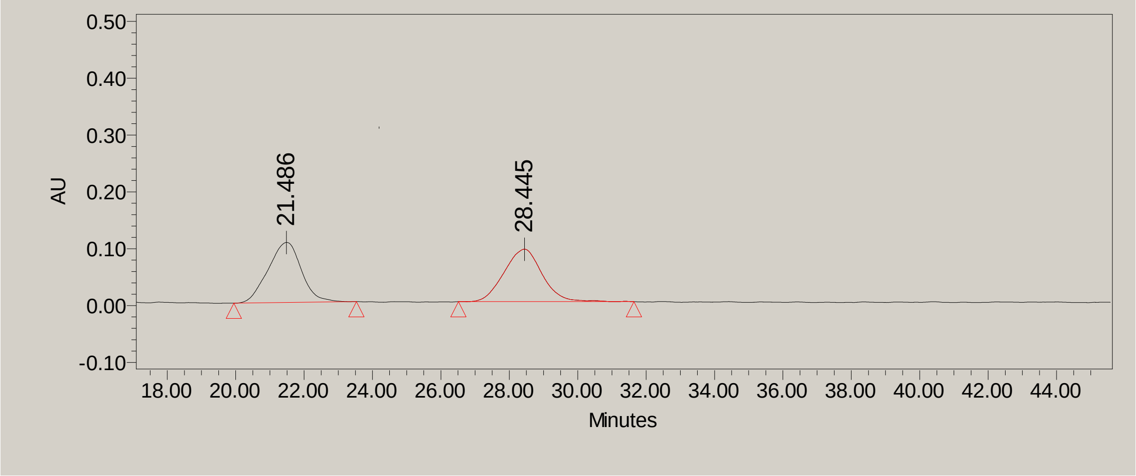
	Retention Time	% Area
1	18.632	99.90
2	24.760	0.10



9Af

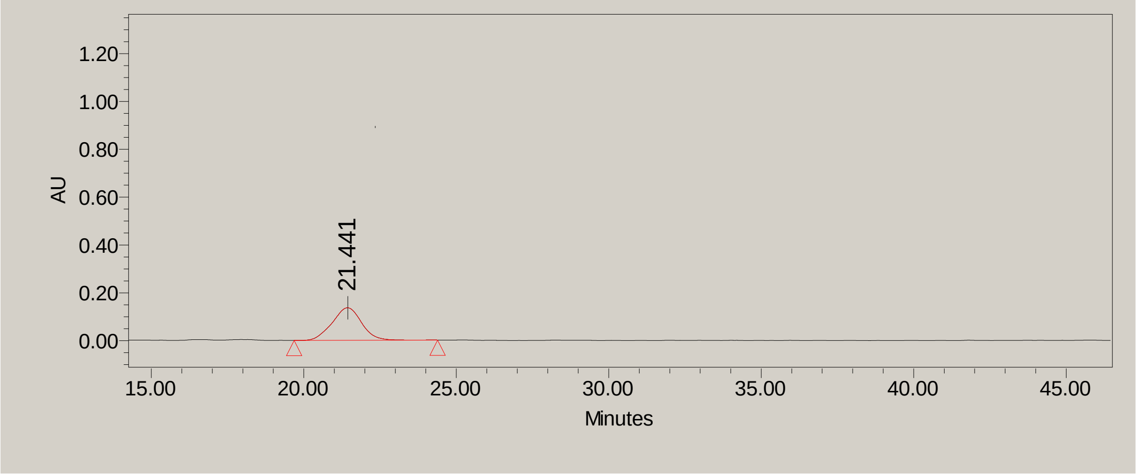
Daicel Chiralpak IA, hexane/isopropanol 90/10 flow rate = 1.0 mL/min, λ: 210.0 nm.

Rac-**9Af**

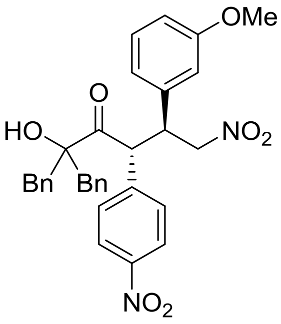


	Retention Time	% Area
1	21.486	50.10
2	28.445	49.90

Scalemic **9Af**



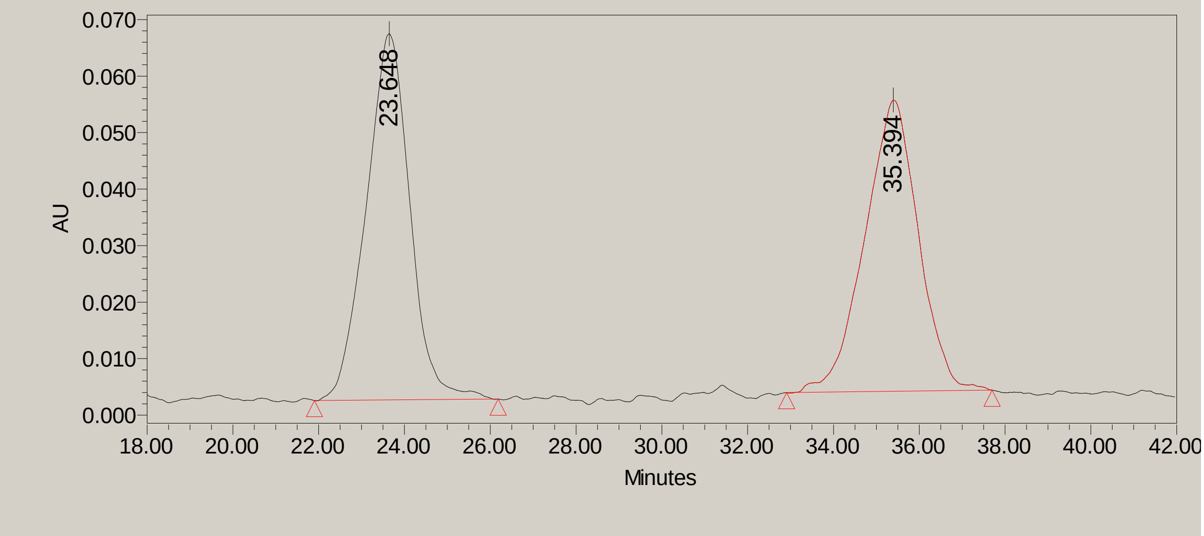
	Retention Time	% Area
1	21.441	100.00



9Ag

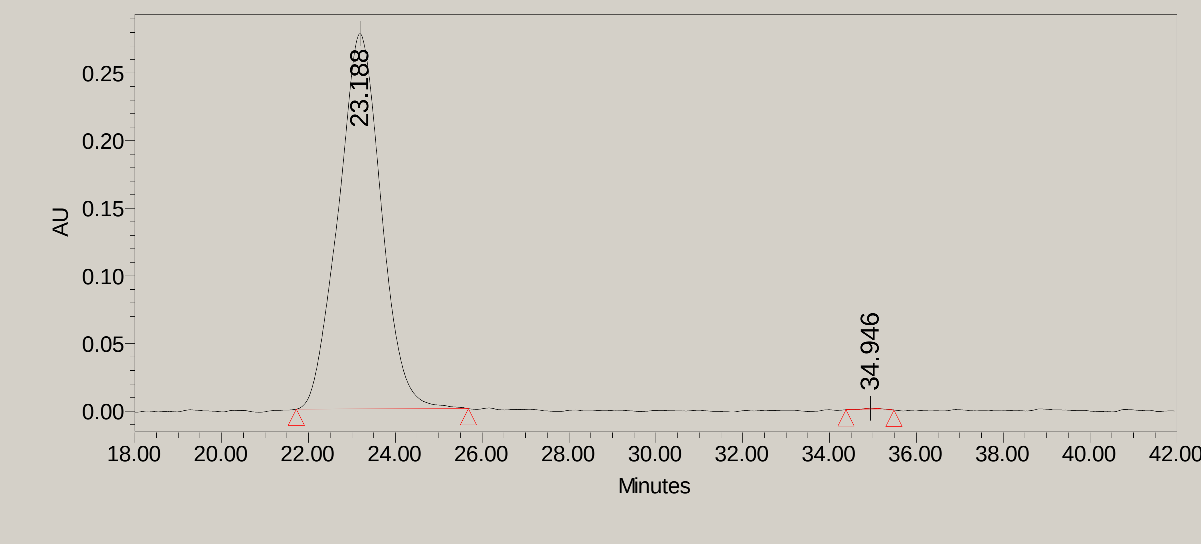
Daicel Chiralpak IA, hexane/isopropanol 90/10 flow rate = 1.0 mL/min, λ: 210.0 nm.

Rac-**9Ag**

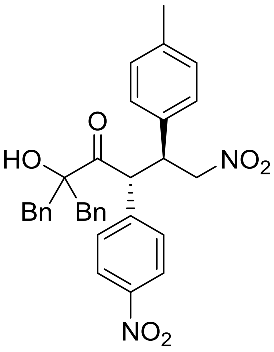


	Retention Time	% Area
1	23.648	50.67
2	35.394	49.33

Scalemic **9Ag**



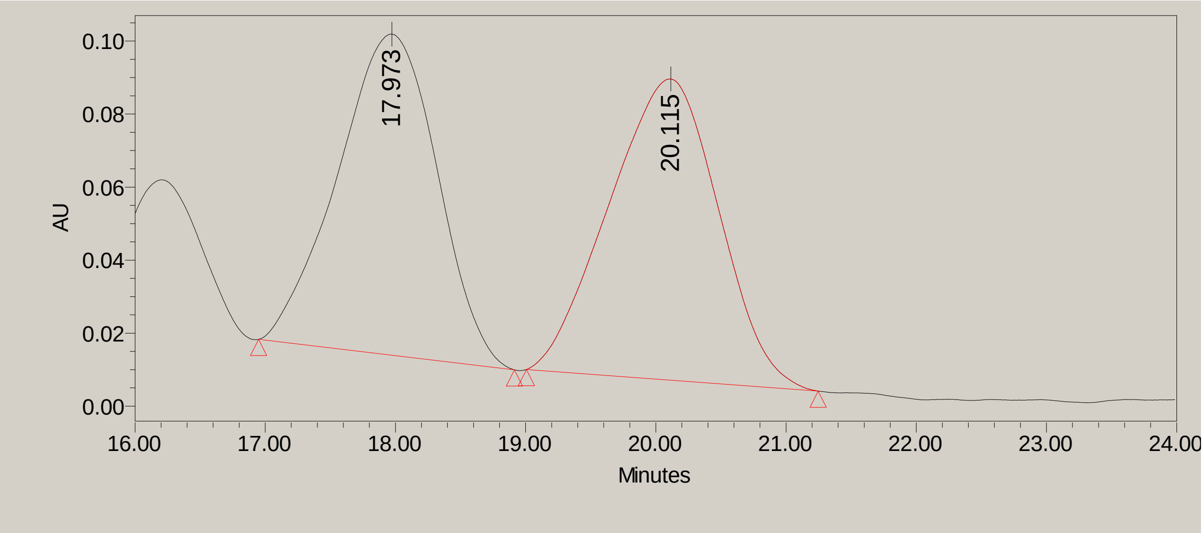
	Retention Time	% Area
1	23.188	99.77
2	34.946	0.23



9Ah

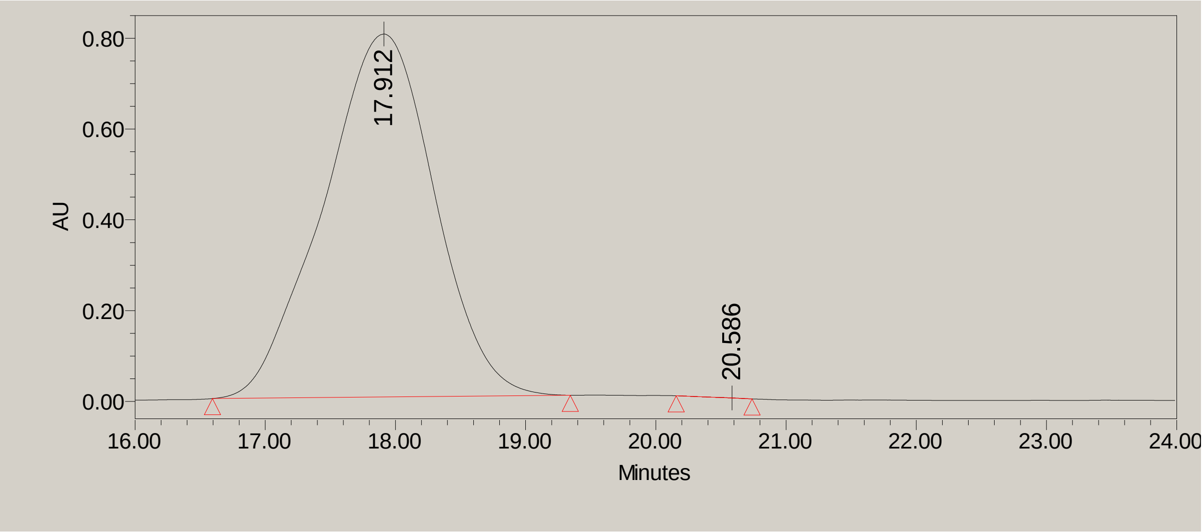
Daicel Chiralpak IA, hexane/isopropanol 90/10 flow rate = 1.0 mL/min, λ: 210.0 nm.

Rac-**9Ah**

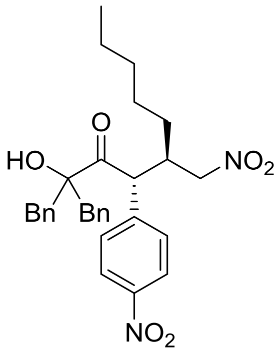


	Retention Time	% Area
1	17.973	49.22
2	20.115	50.78

Scalemic **9Ah**



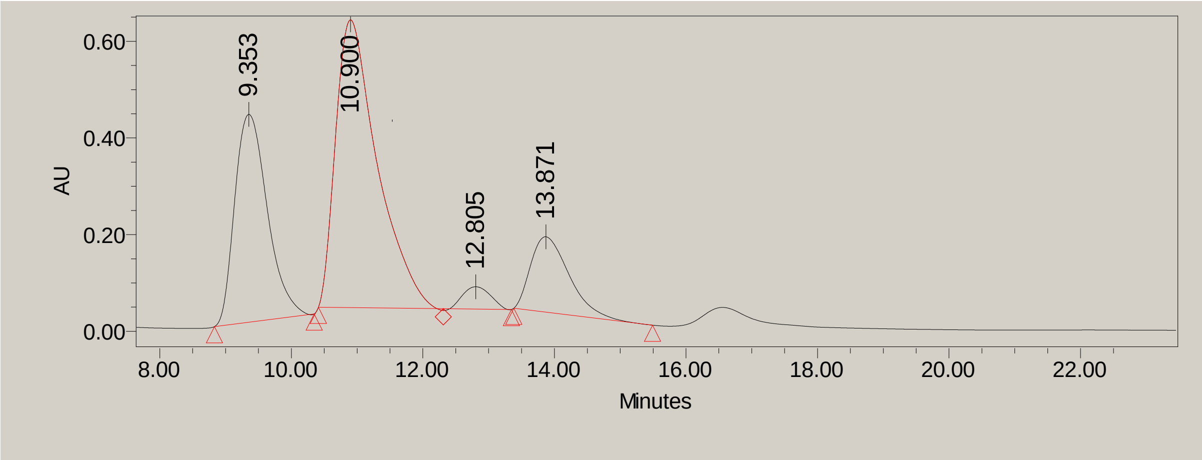
	Retention Time	% Area
1	17.912	99.99
2	20.586	0.01



9Ai

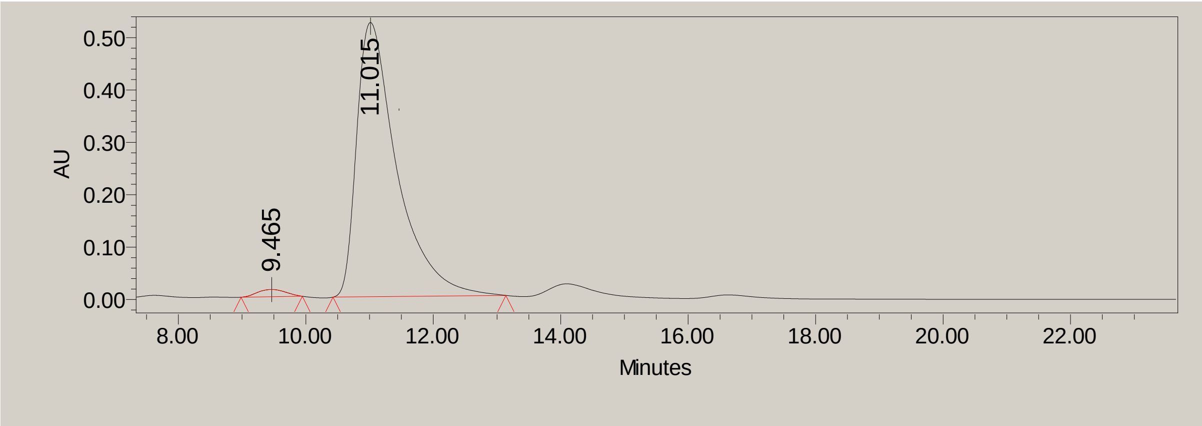
Daicel Chiralpak IA, hexane/isopropanol 90/10 flow rate = 1.0 mL/min, λ: 256.0 nm.

Rac-**9Ai**

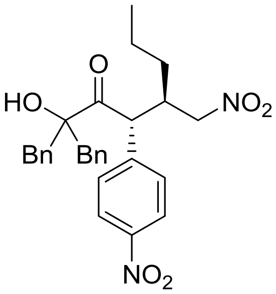


	Retention Time	% Area
1	9.353	30.42
2	10.900	53.70
3	12.805	2.84
4	13.871	13.04

Scalemic **9Ai**



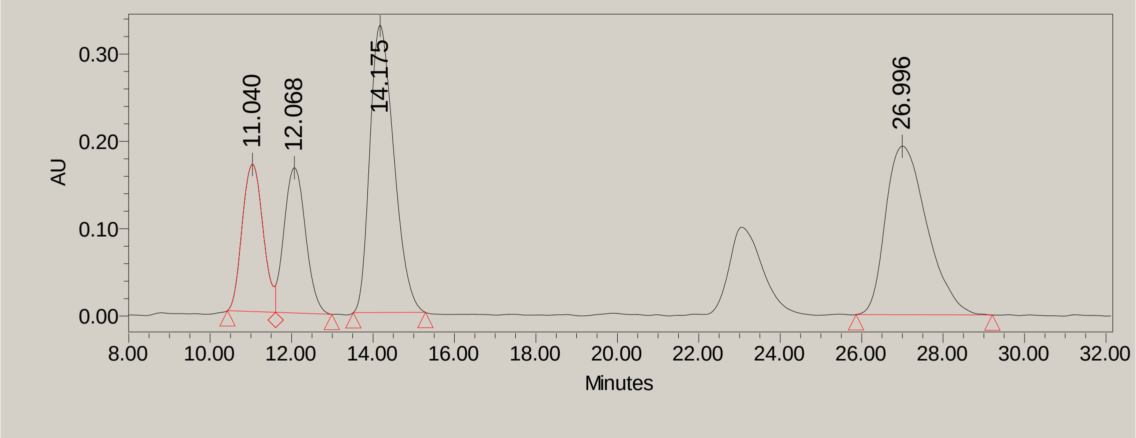
	Retention Time	% Area
1	9.465	1.83
2	11.015	98.17



9Aj

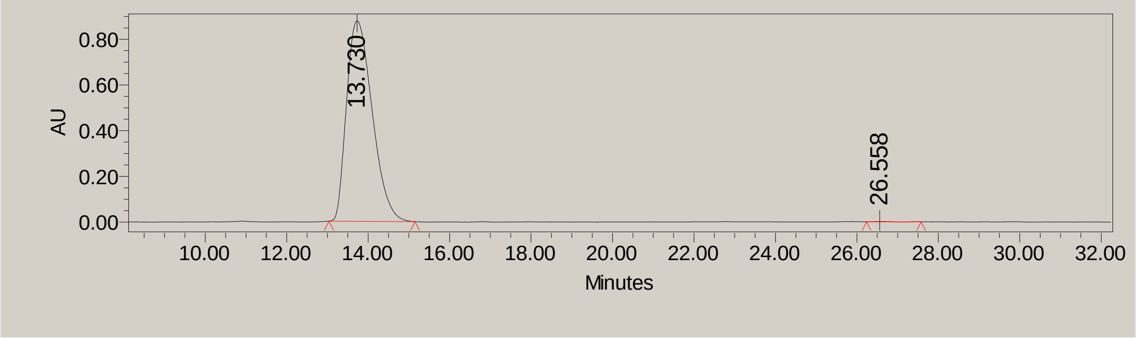
Daicel Chiralpak ADH, hexane/isopropanol 90/10 flow rate = 1.0 mL/min, λ: 210 nm.

Rac-**9Aj**



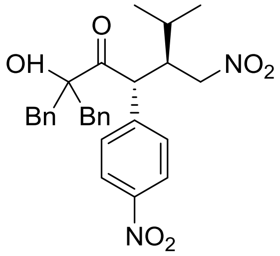
	Retention Time	% Area
1	11.040	15.36
2	12.068	15.55
3	14.175	34.38
4	26.996	34.72

Scalemic **9Aj**



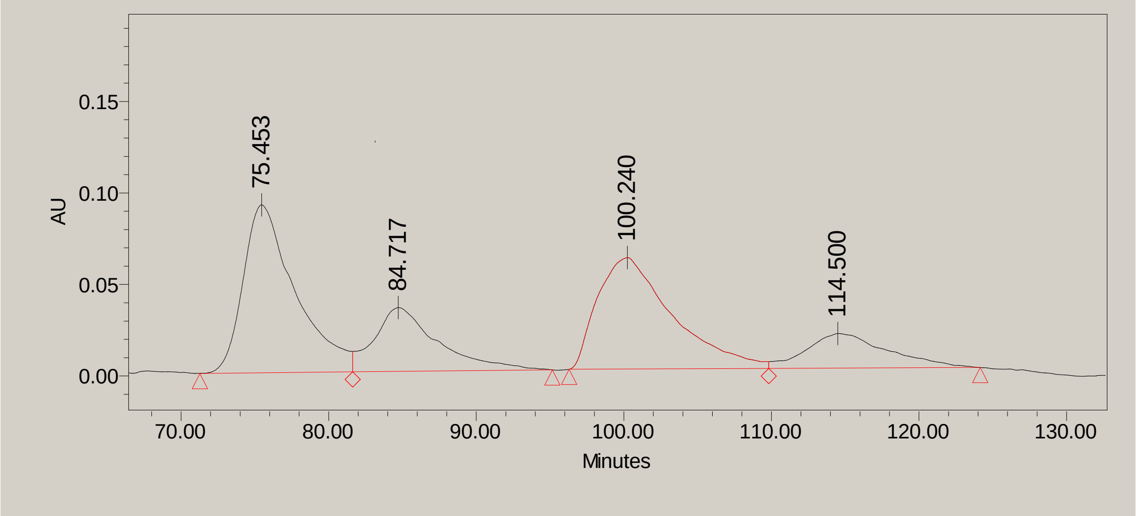
	Retention Time	% Area
1	13.730	99.95
2	26.558	0.05

Daicel Chiralpak IA, hexane/isopropanol 99/1 flow rate = 1.0 mL/min, λ: 210.0 nm.



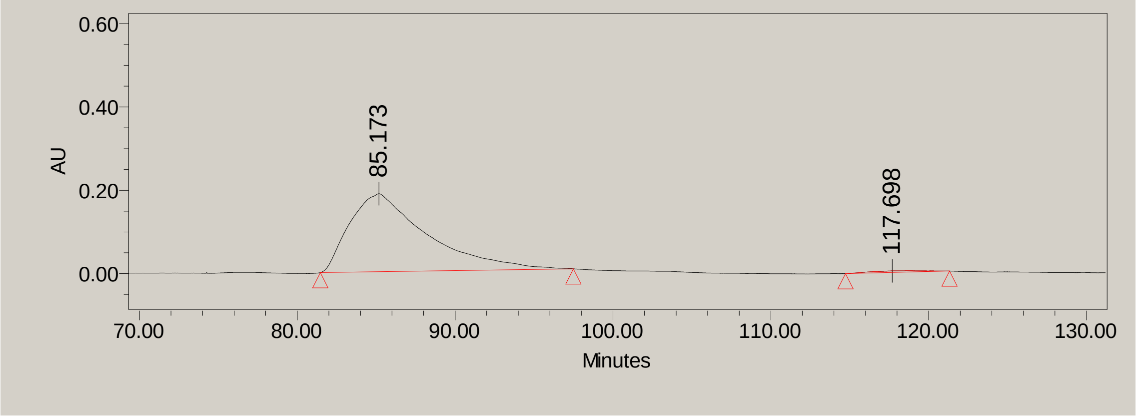
9Ak

Rac-**9Ak**

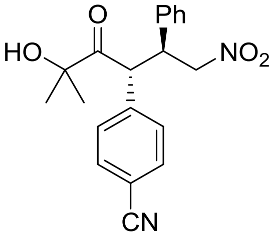


	Retention Time	% Area
1	75.453	36.51
2	84.717	16.91
3	100.240	34.85
4	114.500	11.73

Scalemic **9Ak**



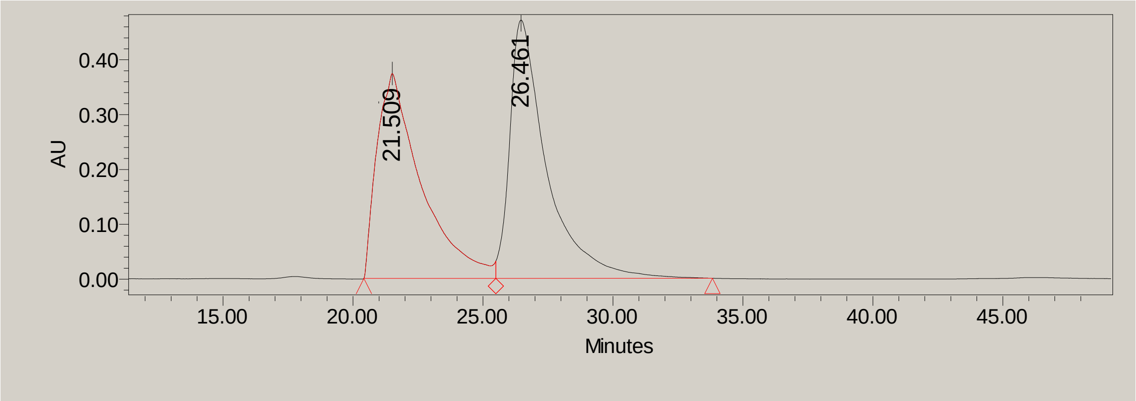
	Retention Time	% Area
1	85.173	98.65
2	117.698	1.35



6Ba

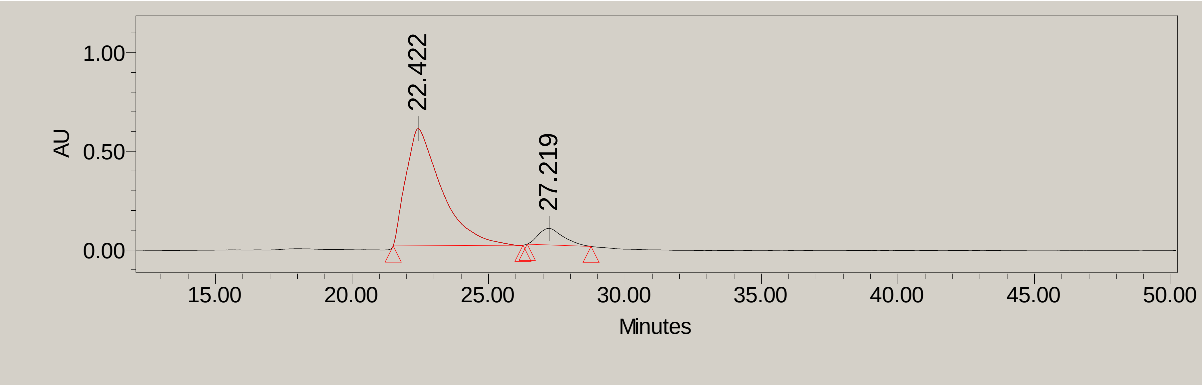
Daicel Chiralpak IA, hexane/isopropanol 90/10 flow rate = 1.0 mL/min, λ: 210.0 nm.

Rac-**6Ba**

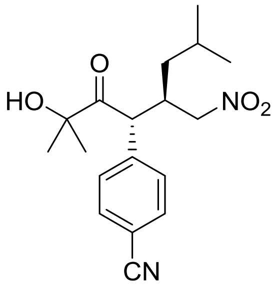


	Retention Time	% Area
1	21.509	48.85
2	26.461	51.15

Scalemic **6Ba**



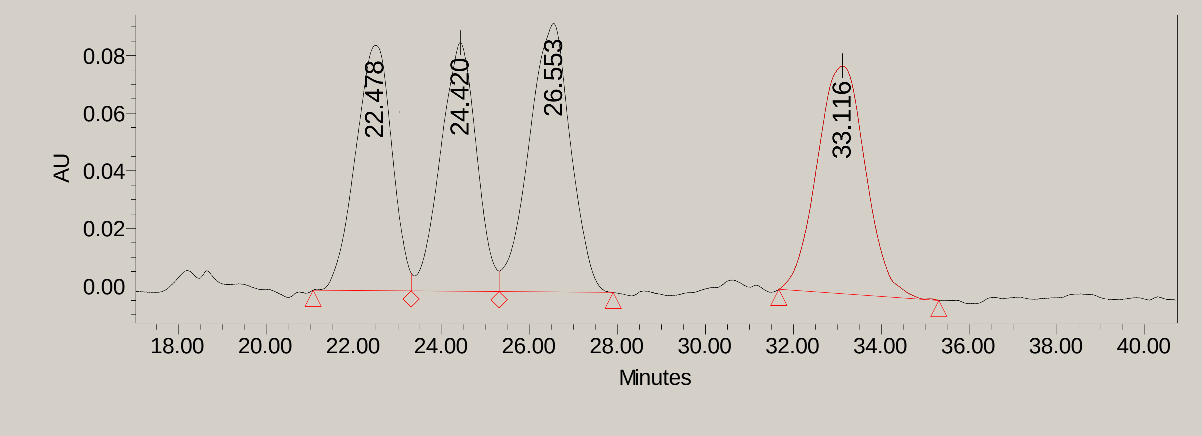
	Retention Time	% Area
1	22.422	91.11
2	27.219	8.89



6Bk

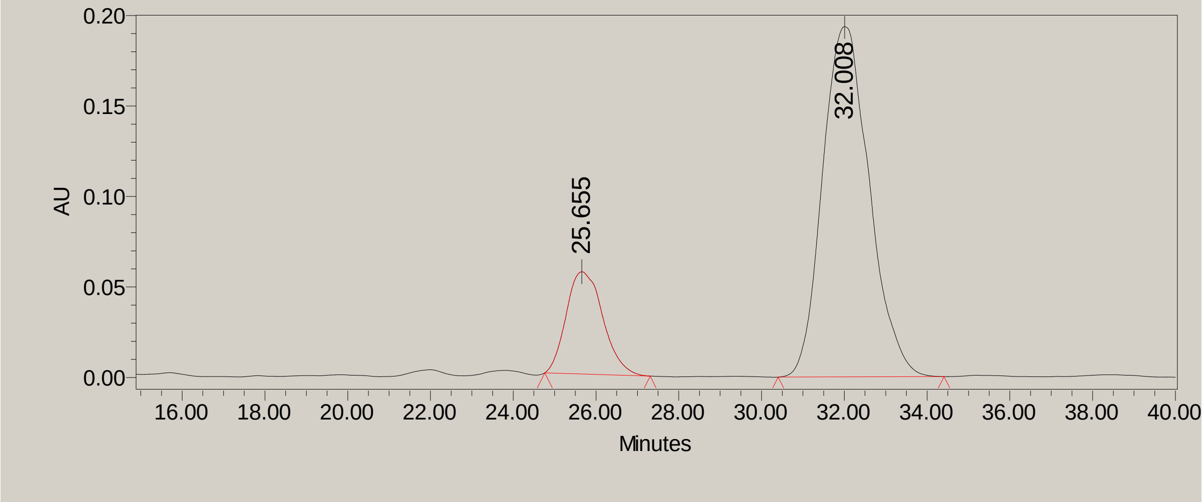
Daicel Chiralpak IC, hexane/isopropanol 95/5 flow rate = 1.0 mL/min, λ: 210.0 nm.

Rac-**6Bk**

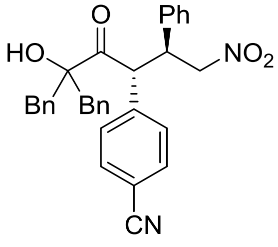


	Retention Time	% Area
1	22.478	22.35
2	24.420	22.34
3	26.553	27.74
4	33.116	27.57

Scalemic **6Bk**



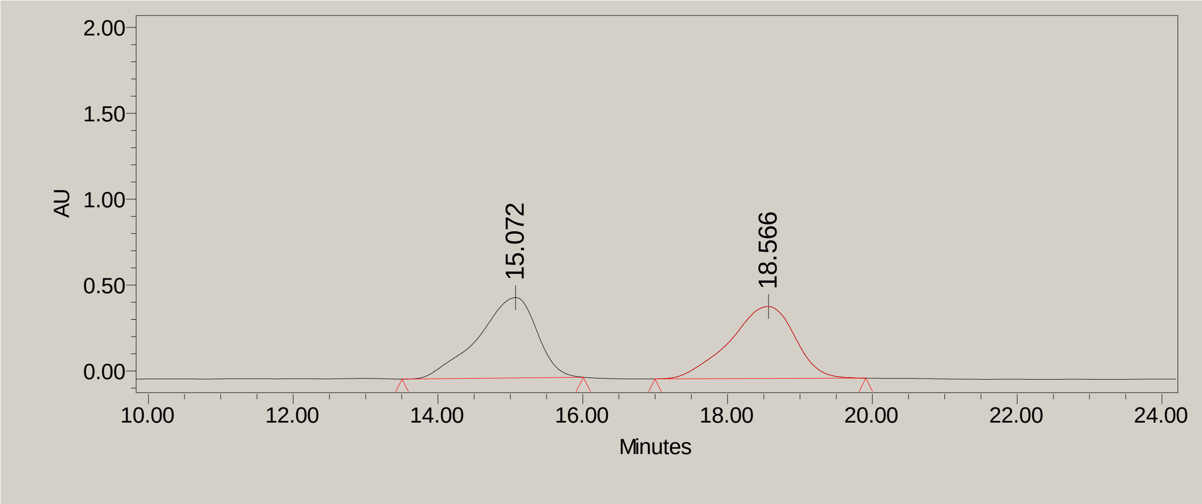
	Retention Time	% Area
1	25.655	18.60
2	32.008	81.40



9Ba

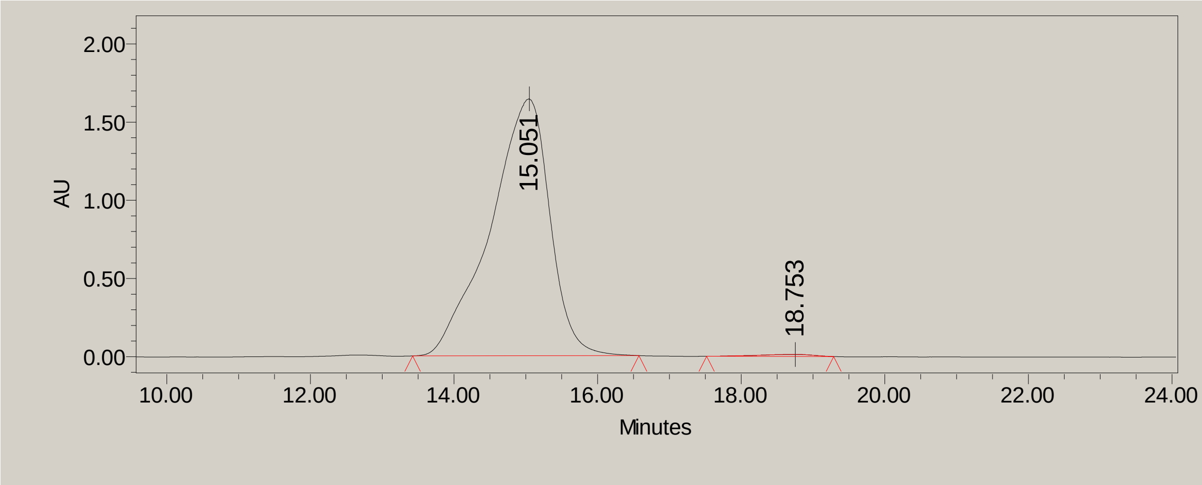
Daicel Chiralpak IA, hexane/isopropanol 90/10 flow rate = 1.0 mL/min, λ: 210.0 nm.

Rac-**9Ba**

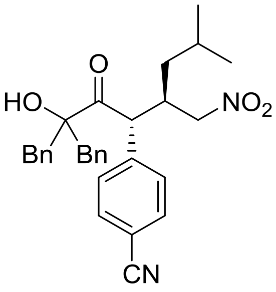


	Retention Time	% Area
1	15.072	50.33
2	18.566	49.67

Scalemic **9Ba**



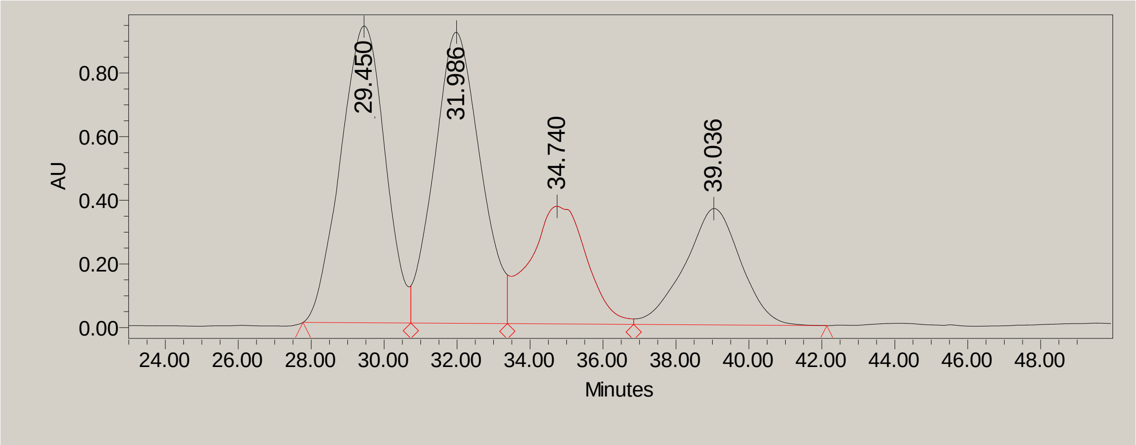
	Retention Time	% Area
1	15.051	99.29
2	18.753	0.71



9Bk

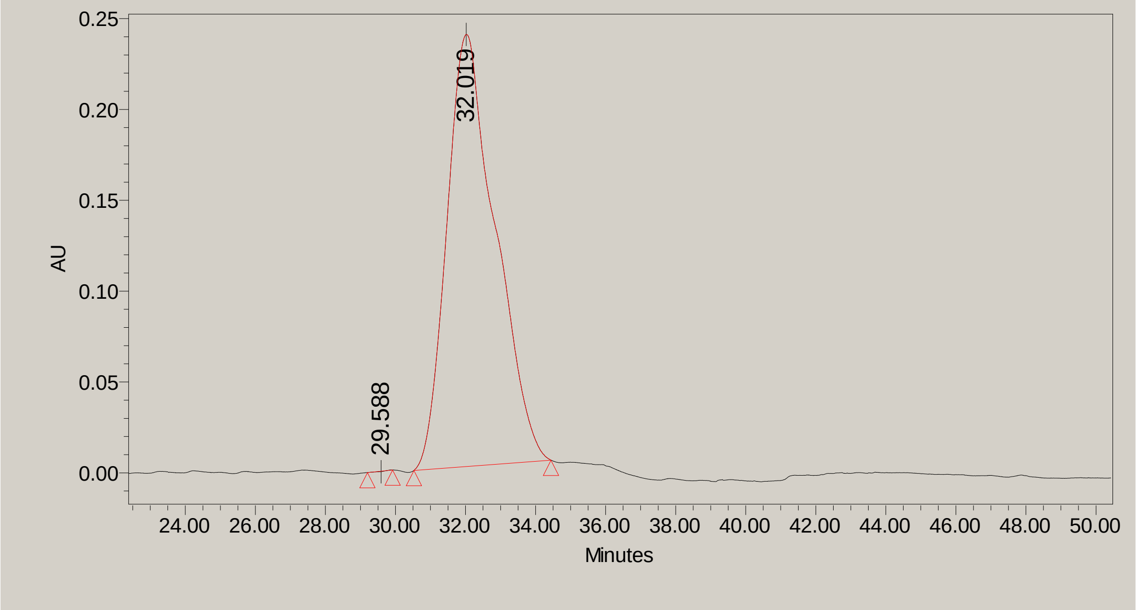
Daicel Chiralpak IA, hexane/isopropanol 90/10 flow rate = 1.0 mL/min, λ: 210.0 nm.

Rac-**9Bk**

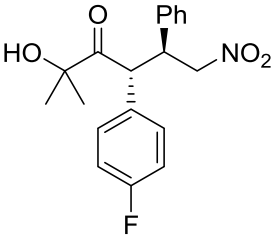


	Retention Time	% Area
1	29.450	34.05
2	31.986	34.56
3	34.740	15.84
4	39.036	15.55

Scalemic **9Bk**



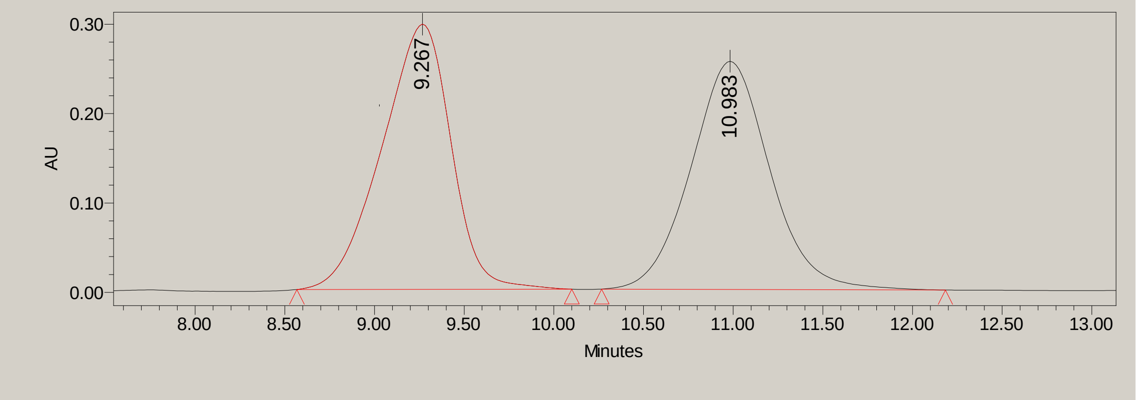
	Retention Time	% Area
1	29.588	0.02
2	32.019	99.98



6Ca

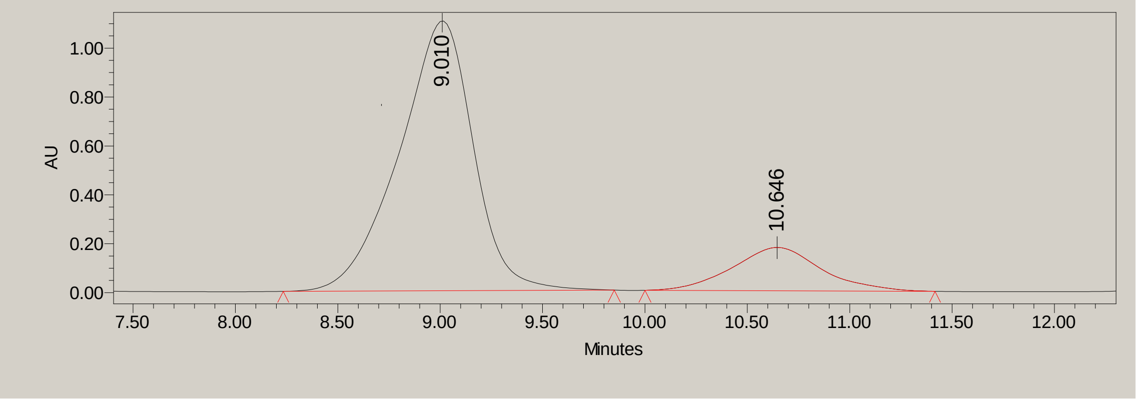
Daicel Chiralpak IA, hexane/isopropanol 90/10 flow rate = 1.0 mL/min, λ: 210.0 nm.

Rac-**6Ca**

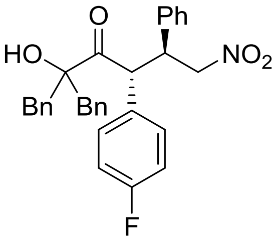


	Retention Time	% Area
	9.267	50.50
	10.983	49.50

Scalemic **6Ca**



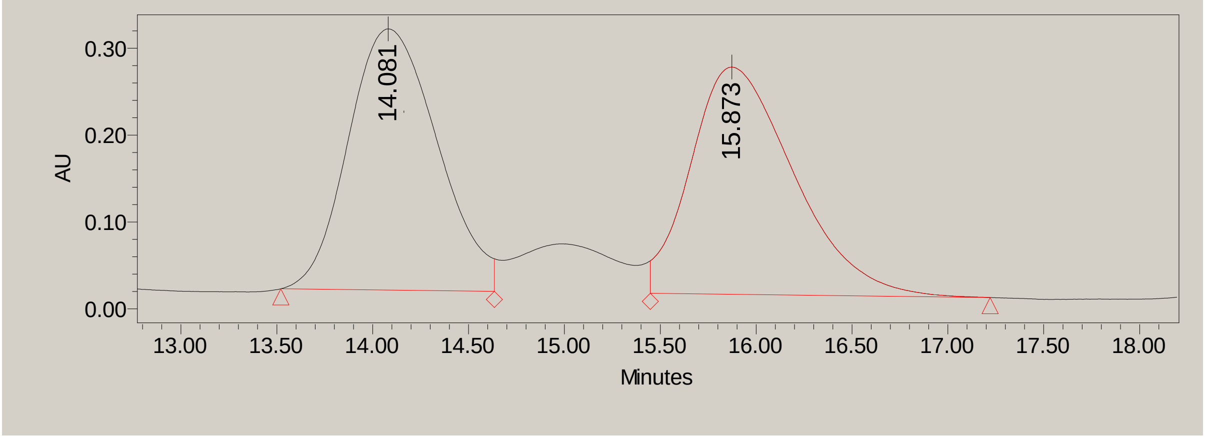
	Retention Time	% Area
	9.010	83.85
	10.646	16.15



Daicel Chiralpak IB, hexane/isopropanol 95/5 flow rate = 1.0 mL/min, λ: 210.0 nm.

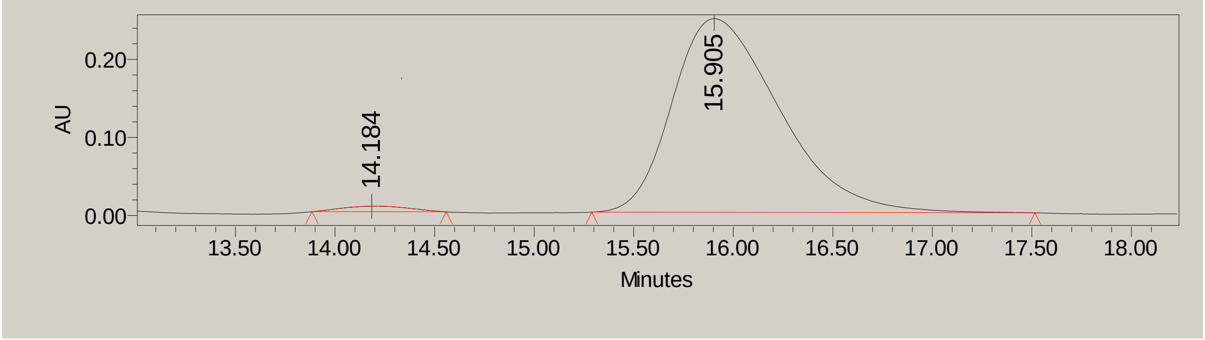
9Ca

Rac-**9Ca**

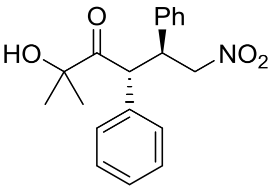


	Retention Time	% Area
1	14.081	49.74
2	15.873	50.26

Scalemic **9Ca**



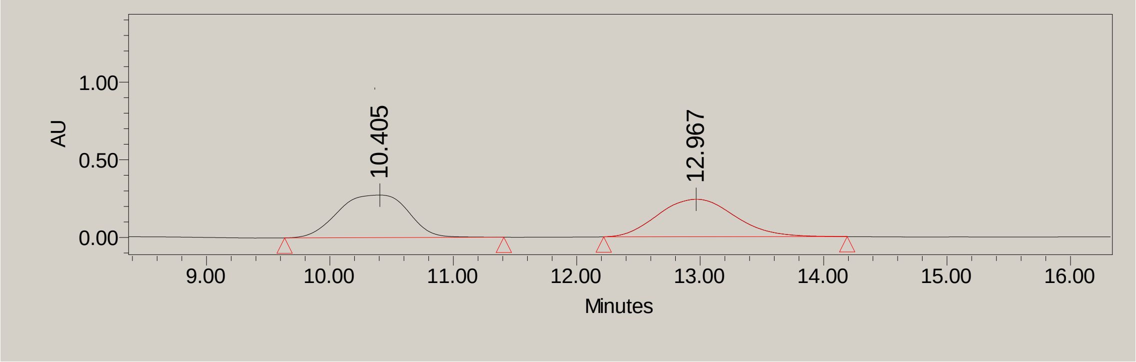
	Retention Time	% Area
1	14.184	1.80
2	15.905	98.20



6Da

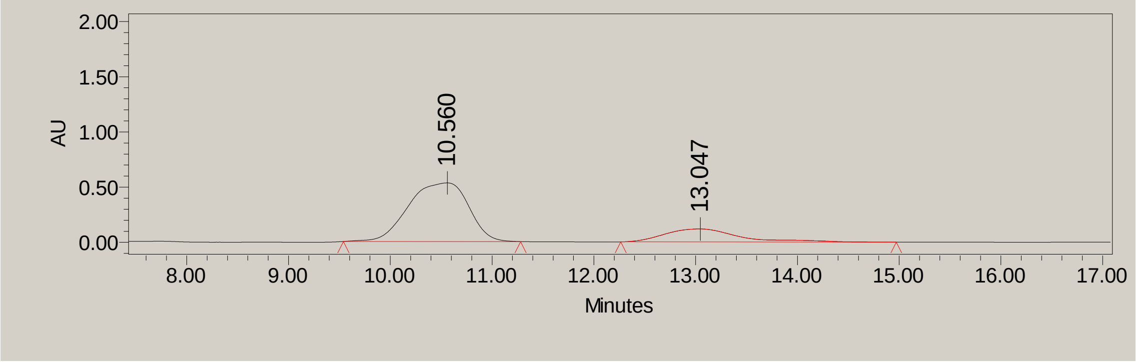
Daicel Chiralpak IA, hexane/isopropanol 90/10 flow rate = 1.0 mL/min, λ: 210.0 nm.

Rac-**6Da**

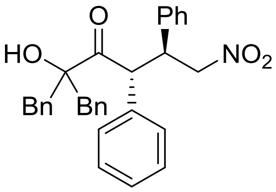


	Retention Time	% Area
1	10.405	50.79
2	12.967	49.21

Scalemic **6Da**



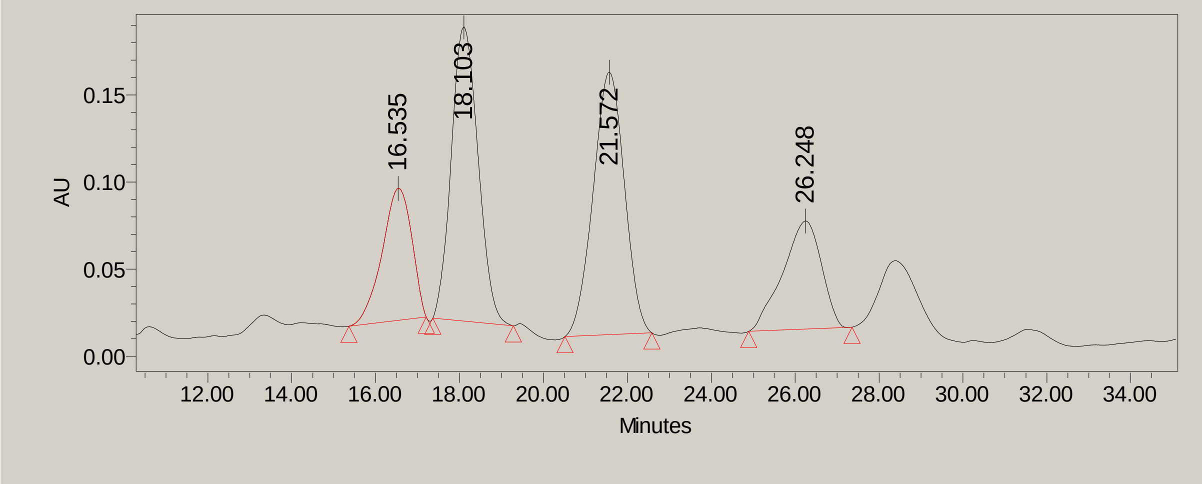
	Retention Time	% Area
1	10.560	78.53
2	13.047	21.47



9Da

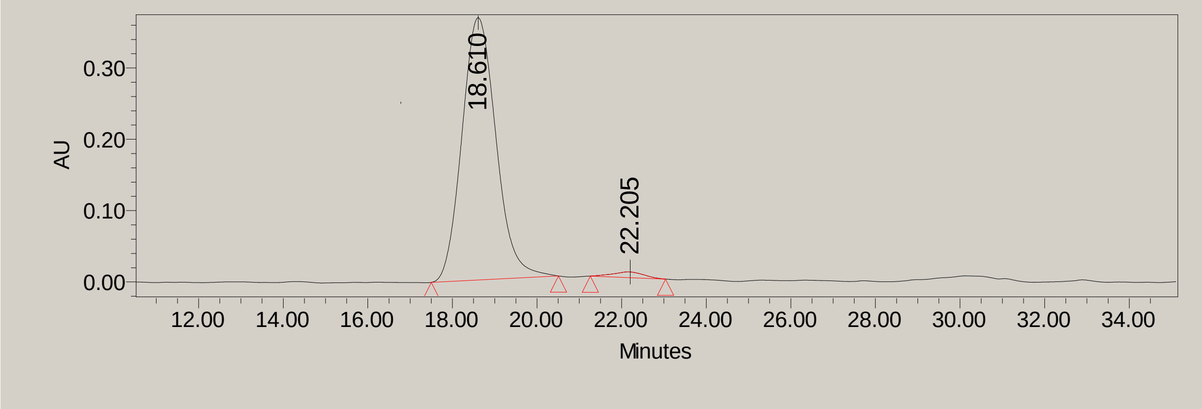
Daicel Chiralpak IC, hexane/isopropanol 98/2 flow rate = 1.0 mL/min, λ: 210.0 nm.

Rac-**9Da**

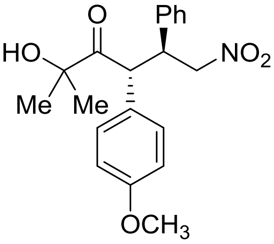


	Retention Time	% Area
1	16.535	16.17
2	18.103	32.59
3	21.572	33.97
4	26.248	17.27

Scalemic **9Da**



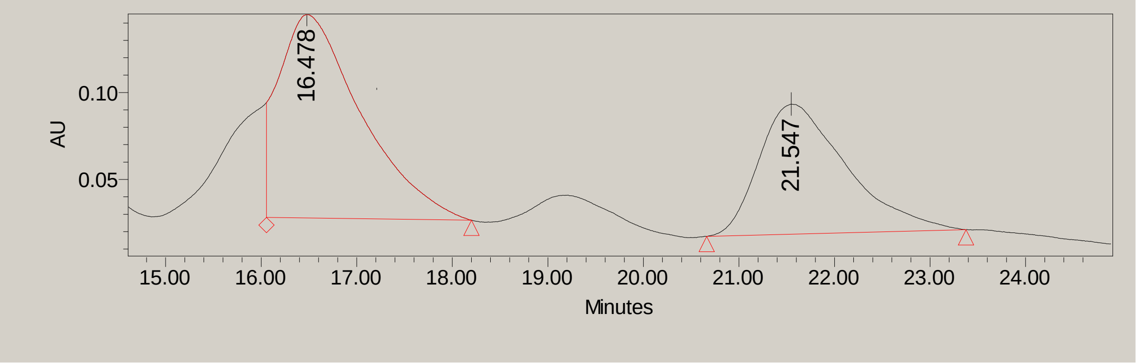
	Retention Time	% Area
1	18.610	98.07
2	22.205	1.93



6Ea

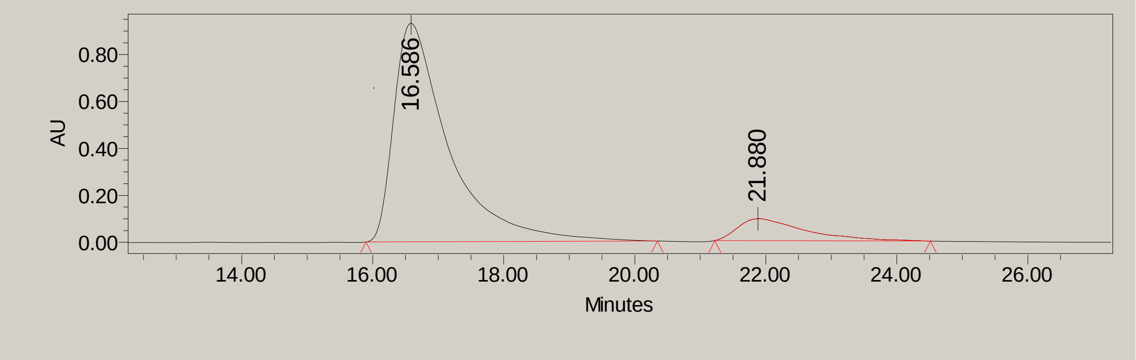
Daicel Chiralpak IA, hexane/isopropanol 90/10 flow rate = 1.0 mL/min, λ: 210.0 nm.

Rac-**6Ea**

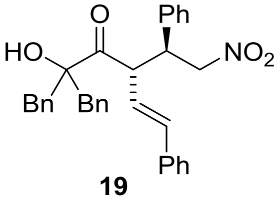


	Retention Time	% Area
	16.478	59.67
	21.547	40.33

Scalemic **6Ea**



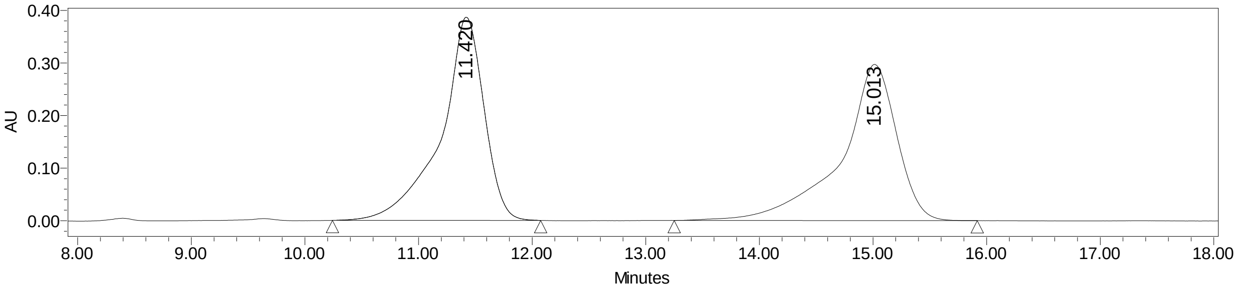
	Retention Time	% Area
	16.586	88.92
	21.880	11.08



19

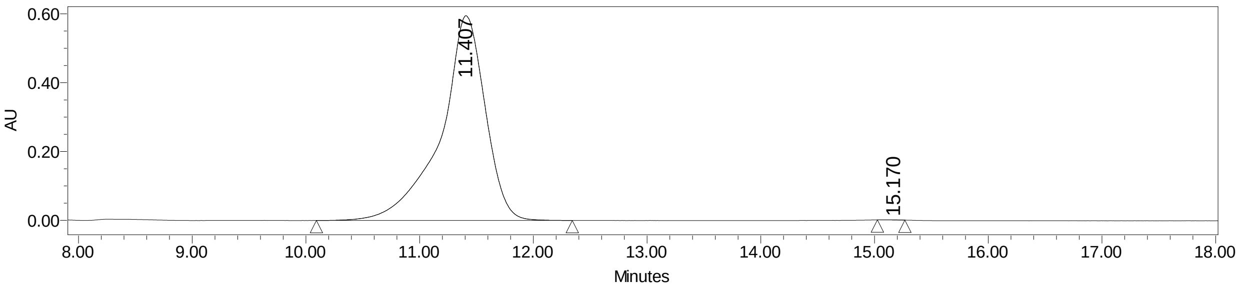
Daicel Chiralpak IA, hexane /isopropanol 90:10; flow rate = 1.0 mL/min, λ: 259 nm.

Rac-**19**

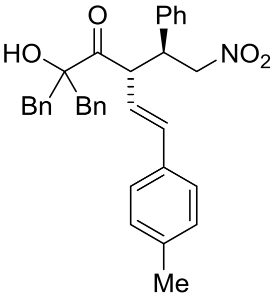


	Retention Time	Area	% Area	Height
	11.420	10214040	50.17	386590
	15.013	10143400	49.83	297062

Scalemic **19**



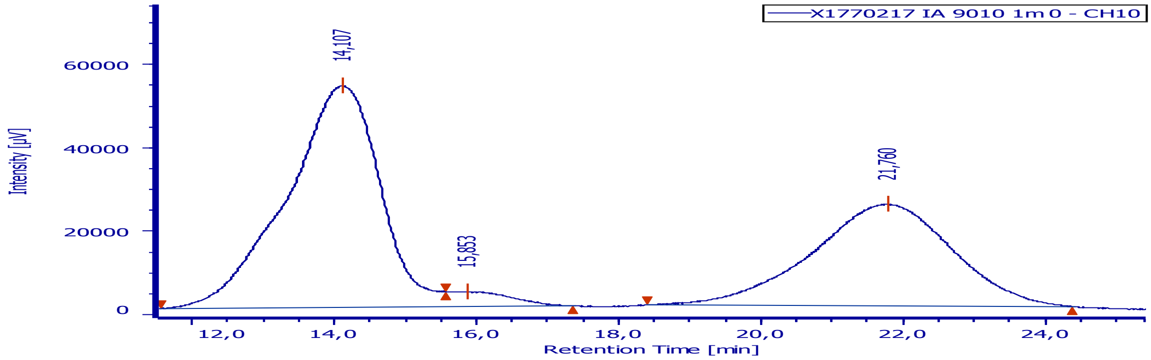
	Retention Time	Area	% Area	Height
	11.407	16158557	99.97	594836
	15.170	5301	0.03	559



20

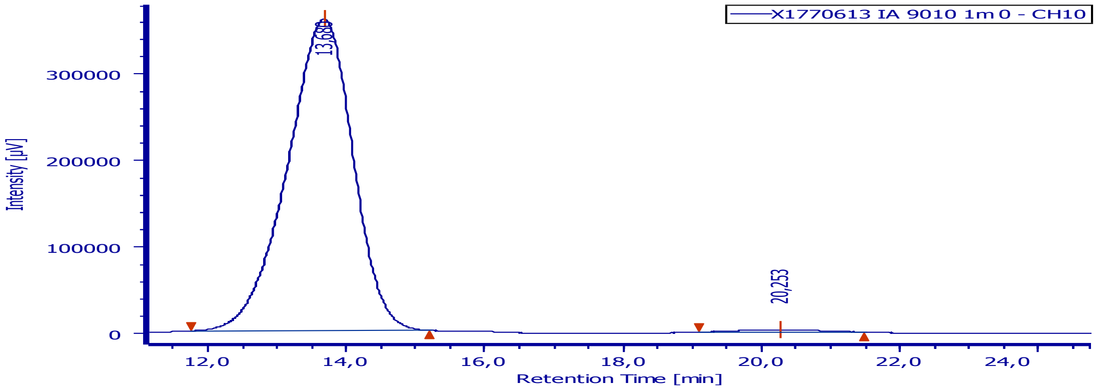
Daicel Chiralpak IA, hexane /isopropanol 90:10; flow rate = 1.0 mL/min, λ: 259 nm

Rac-**20**

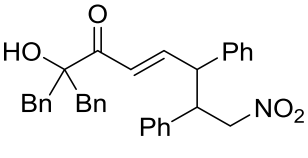


Peak Name	CH	tR	Area	Height	Area%	Height%
Unknown	10	14,107	4794381	52923	57,595	65,444
Unknown	10	15,853	226057	3644	2,716	4,506
Unknown	10	21,760	3303864	24301	39,689	30,050

Scalemic **20**



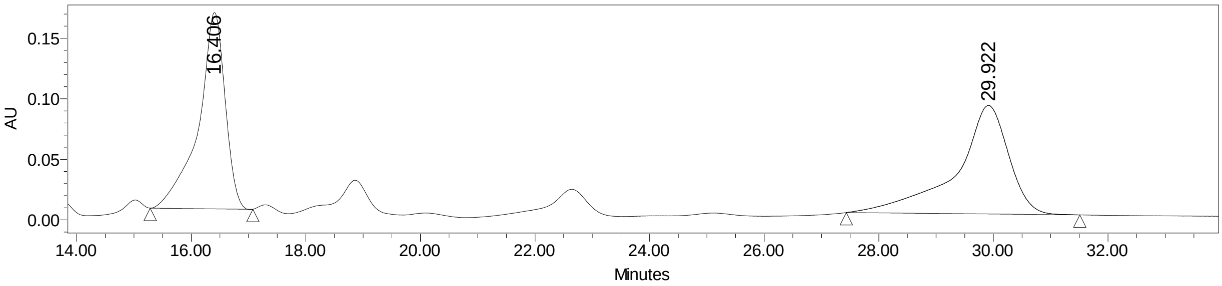
Peak Name	CH	tR	Area	Height	Area%	Height%
Unknown	10	13,680	23651655	358669	99,061	99,262
Unknown	10	20,253	224228	2668	0,939	0,738



19'

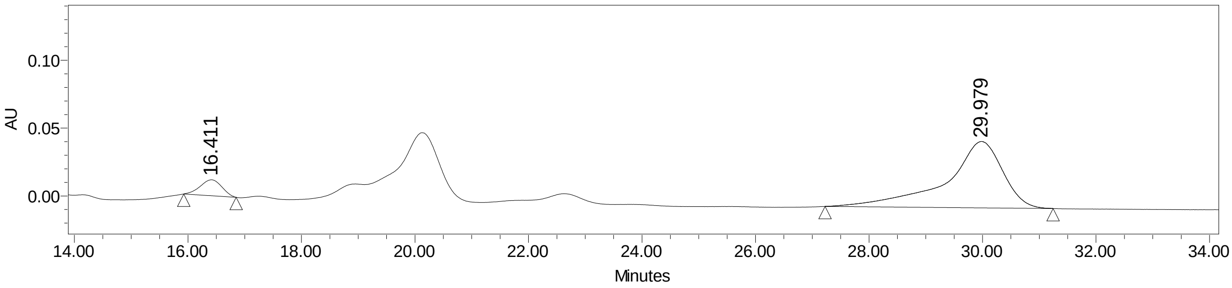
Daicel Chiralpak IA, hexane /isopropanol 90:10; flow rate = 1.0 mL/min, λ: 235.3 nm

Rac-**19'**

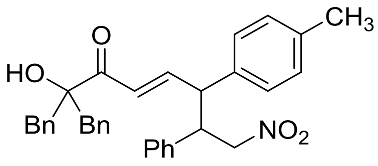


	Retention Time	Area	% Area	Height
	16.406	5258530	48.04	162057
	29.922	5687078	51.96	89779

Scalemic **19'**



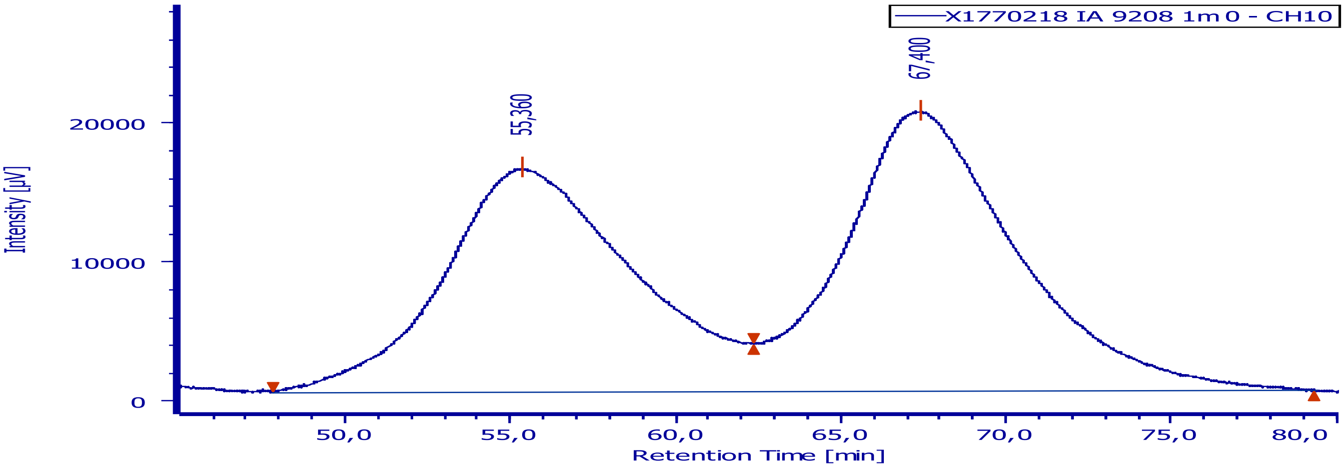
	Retention Time	Area	% Area	Height
	16.411	311087	8.42	11793
	29.979	3382553	91.58	48925



20'

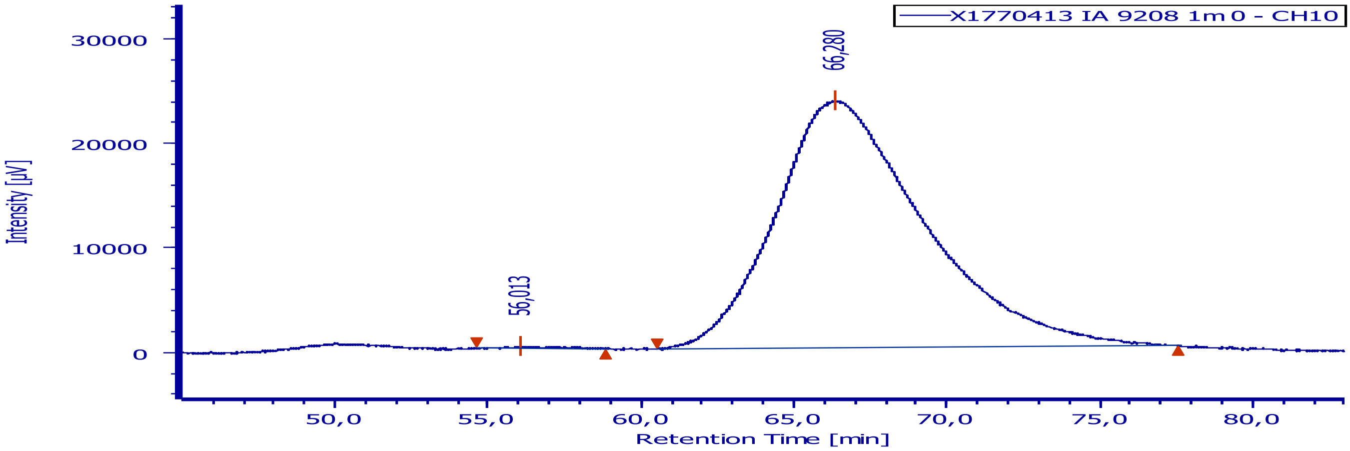
Daicel Chiralpak IA, hexane /isopropanol 92:08; flow rate = 1.0 mL/min, λ: 235.3 nm.

Rac-**20’**

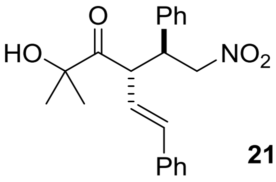


Peak Name	CH	tR	Area	Height	Area%	Height%
Unknown	10	55,360	6403699	16078	46,622	44,457
Unknown	10	67,400	7331740	20086	53,378	55,543

Scalemic **20’**



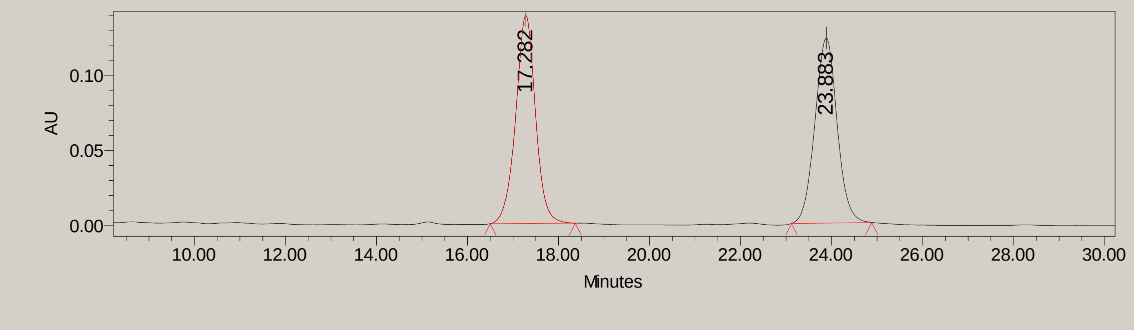
Peak Name	CH	tR	Area	Height	Area%	Height%
Unknown	10	56,013	16743	176	0,210	0,740
Unknown	10	66,280	7949616	23556	99,790	99,260



21a

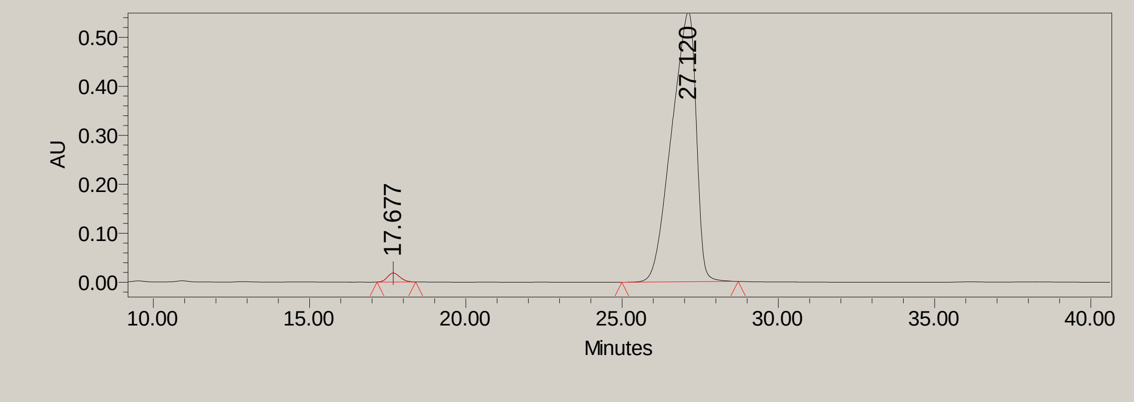
The enantiomeric purity was determined by HPLC analysis (Daicel Chiralpak IB hexane/isopropanol 90/10, flow rate= 1.0 mL/min.

rac-**21a**

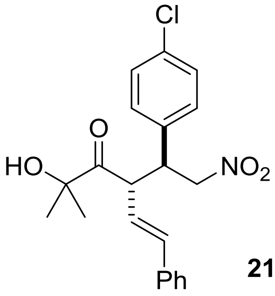


	Retention Time	% Area
	17.282	50.01
	23.883	49.99

scalemic-**21a**



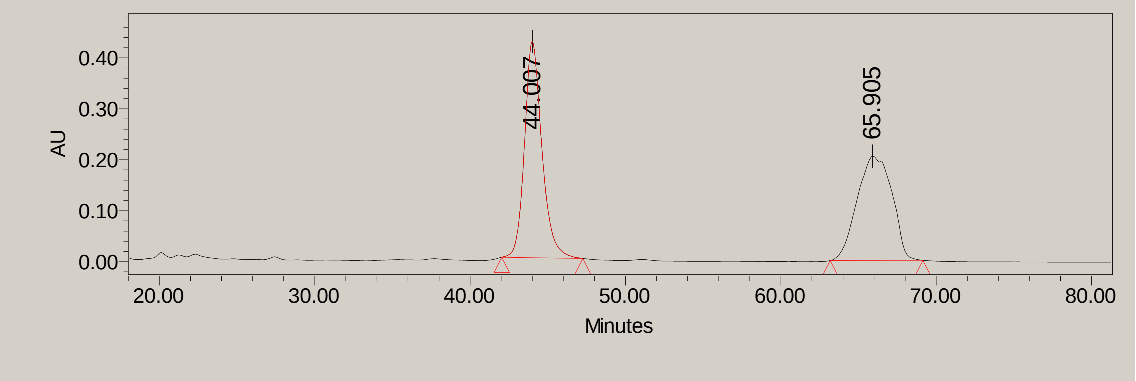
	Retention Time	% Area
	17.677	1.67
	27.120	98.33



21b

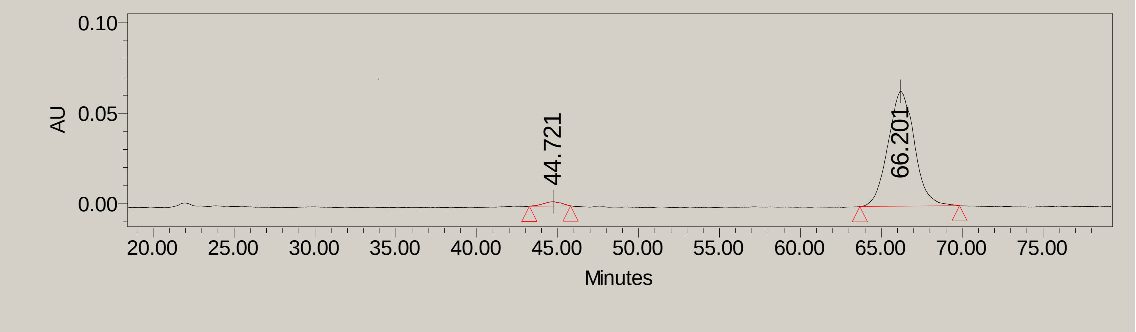
The enantiomeric purity was determined by HPLC analysis (Daicel Chiralpak IB hexane/isopropanol 95/5, flow rate= 1.0 mL/min.

rac-**21b**

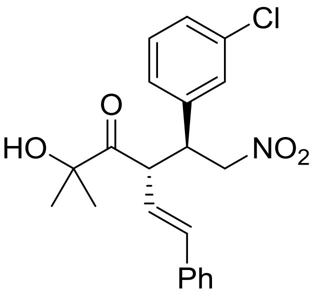


Retention Time	% Area
44.007	50.81
65.905	49.19

scalemic-**21b**



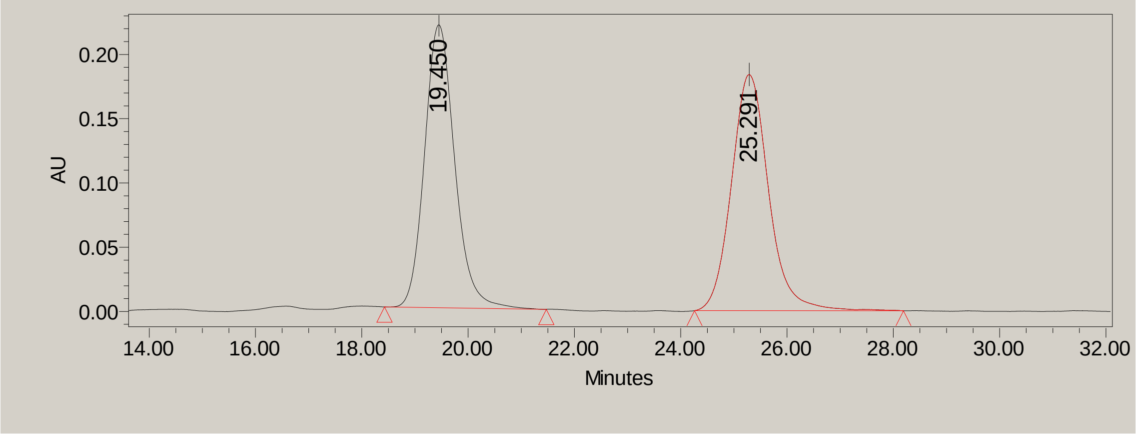
Retention Time	% Area
44.721	2.47
66.201	97.53



21c

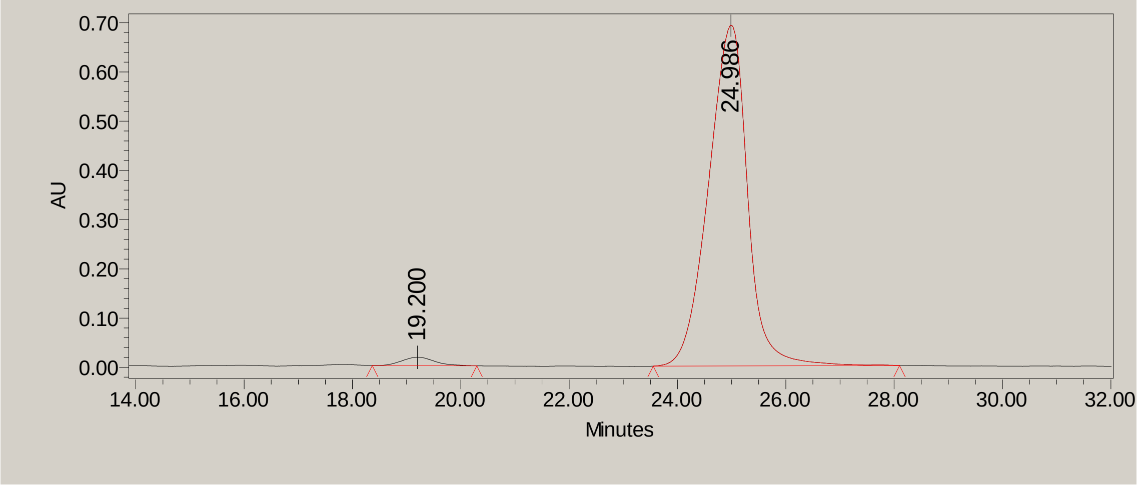
Daicel Chiralpak IB, hexane/isopropanol 90/10 flow rate = 1.0 mL/min, λ: 210.0 nm.

Rac-**21c**

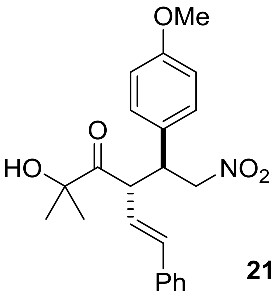


	Retention Time	% Area
1	19.450	49.24
2	25.291	50.76

Scalemic **21c**



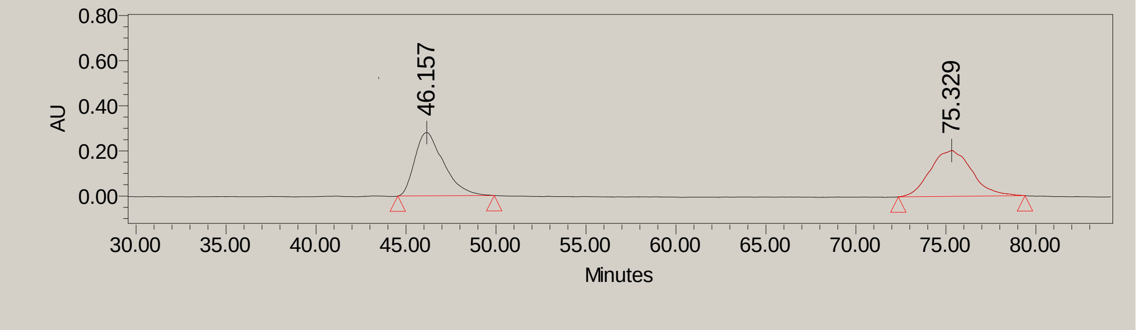
	Retention Time	% Area
1	19.200	2.03
2	24.986	97.97



21f

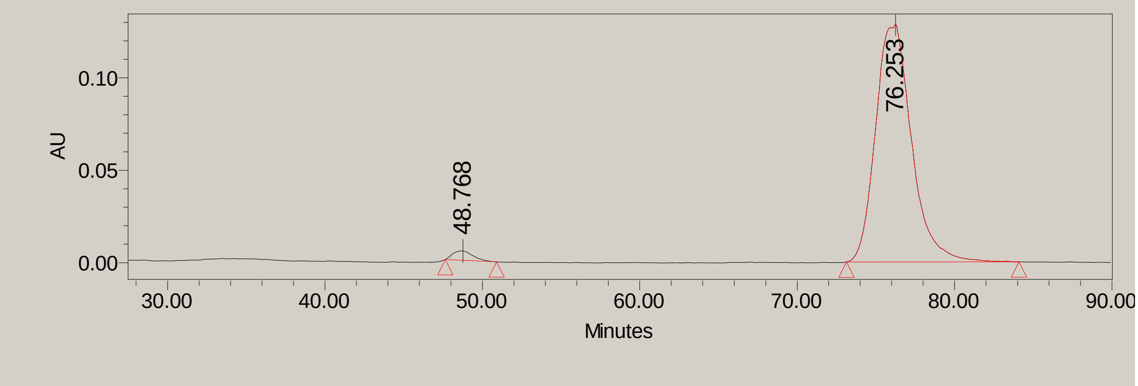
The enantiomeric purity was determined by HPLC analysis (Daicel Chiralpak IB hexane/isopropanol 95/5, flow rate= 1.0 mL/min.

rac-**21f**

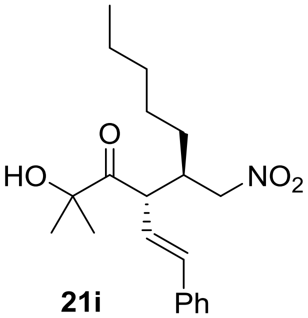


	Retention Time	% Area
	75.329	51.11
	46.157	48.89

scalemic-**21f**



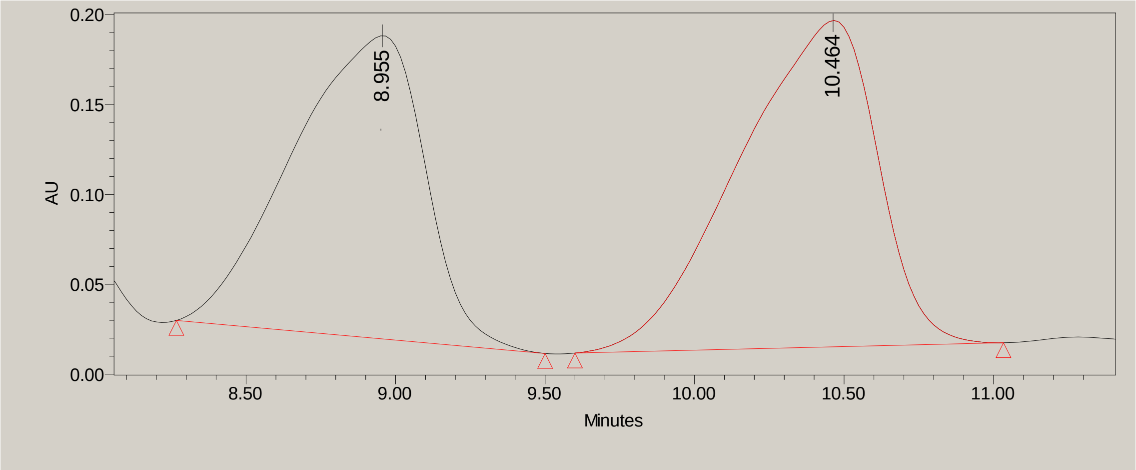
	Retention Time	% Area
	76.253	97.85
	48.768	2.15



21i

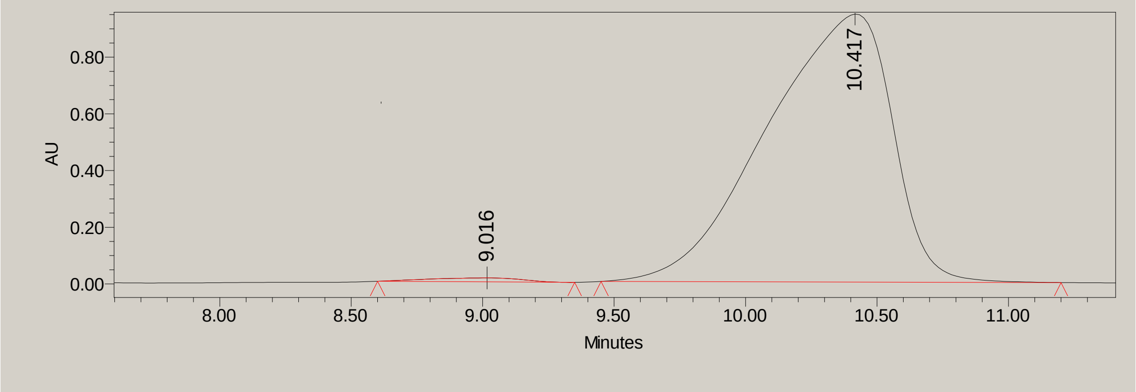
Daicel Chiralpak IB, hexane/isopropanol 90/10 flow rate = 1.0 mL/min, λ: 256.0 nm.

Rac-**21i**

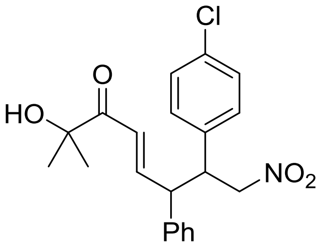


	Retention Time	% Area
1	8.955	46.92
2	10.464	53.08

Scalemic **21i**



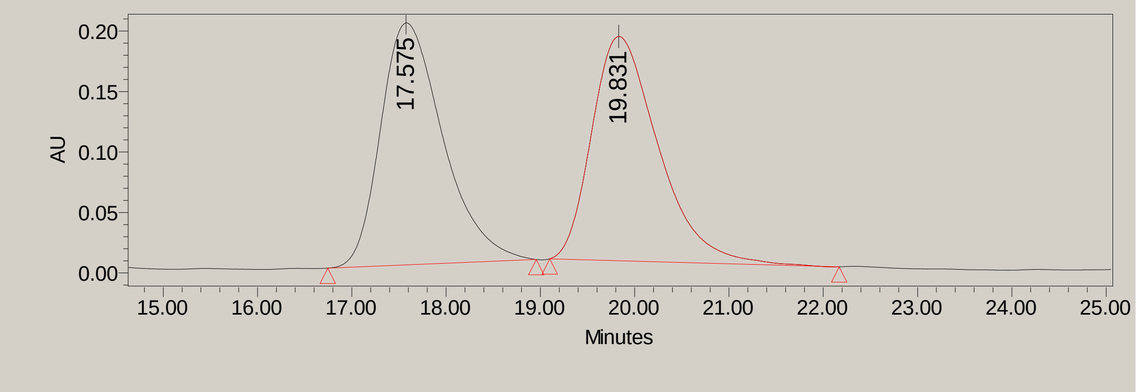
	Retention Time	% Area
1	9.016	1.06
2	10.417	98.94



21'b

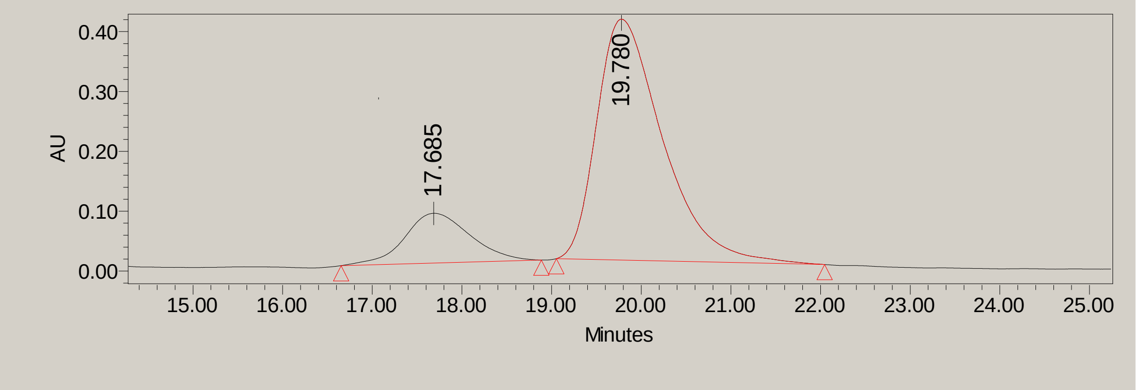
Daicel Chiralpak IB, hexane/isopropanol 90/10 flow rate = 1.0 mL/min, λ: 210.0 nm.

Rac-**21'b**

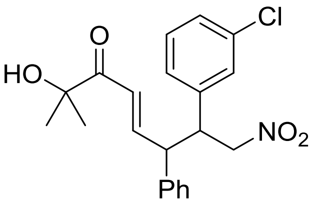


	Retention Time	% Area
	17.575	50.26
	19.831	49.74

Scalemic **21'b**



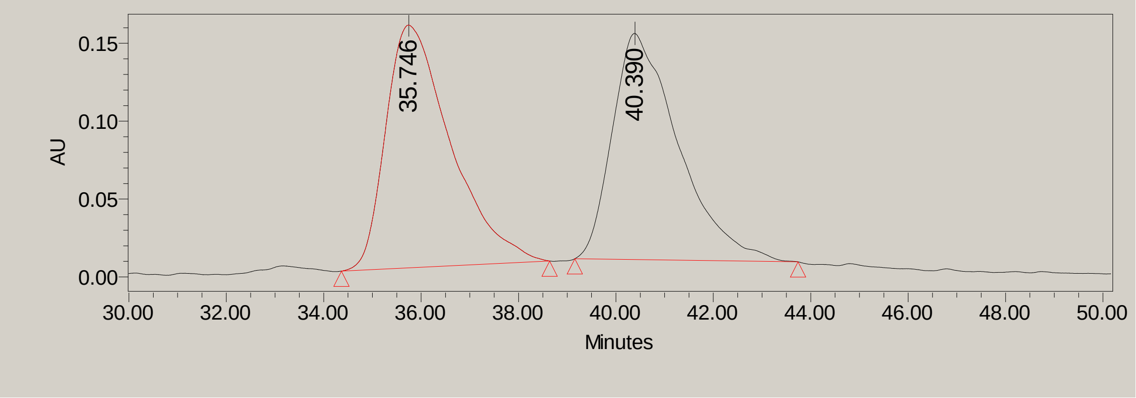
	Retention Time	% Area
	17.685	17.01
	19.780	82.99



21'c

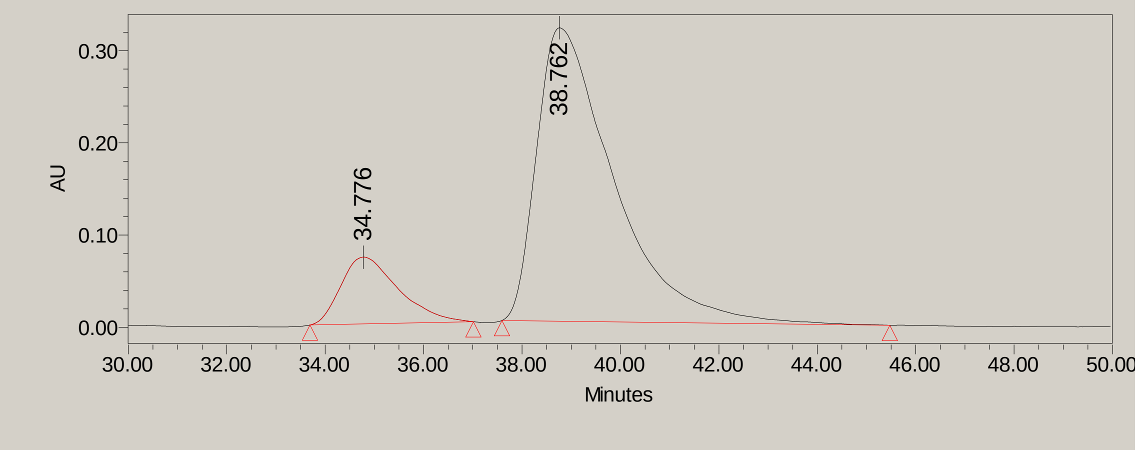
Daicel Chiralpak IB, hexane/isopropanol 95/05 flow rate = 1.0 mL/min, λ: 210.0 nm.

Rac-**21'c**

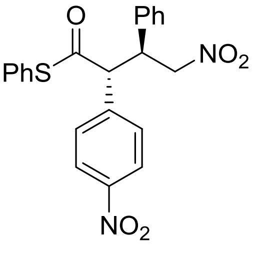


	Retention Time	% Area
	35.746	51.34
	40.390	48.66

Scalemic **21'c**



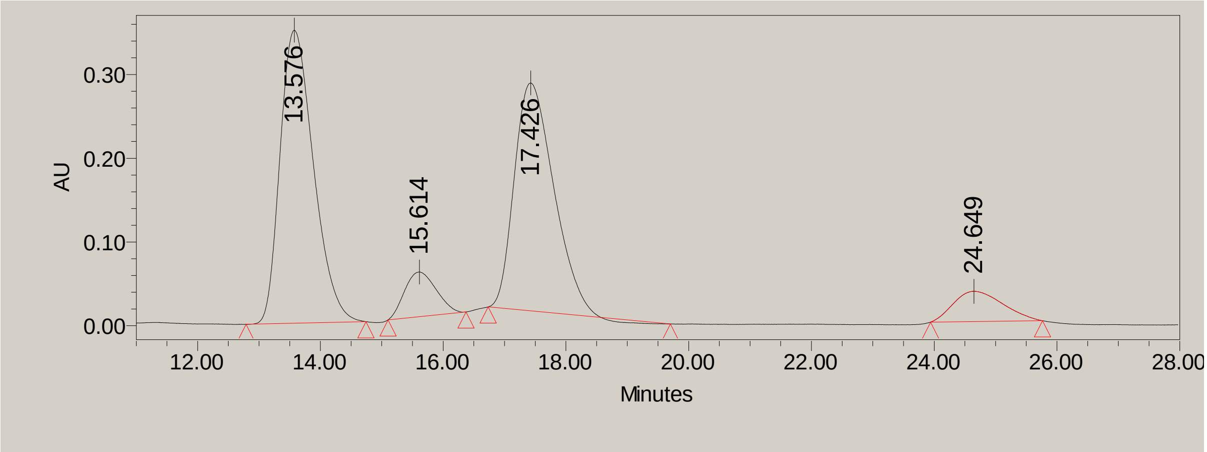
	Retention Time	% Area
	34.776	14.48
	38.762	85.52



11

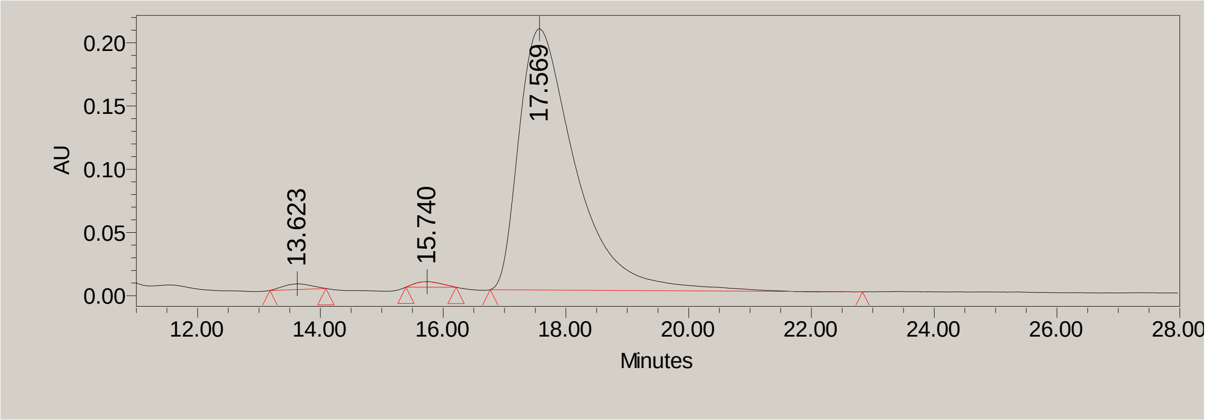
Daicel Chiralpak AD-H, hexane/isopropanol 80/20 flow rate = 1.0 mL/min, λ: 210.0 nm.

Rac-**11**

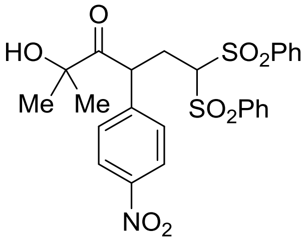


	Retention Time	% Area
1	13.576	44.86
2	15.614	6.44
3	17.426	41.88
4	24.649	6.81

Scalemic **11** (from derivatization of carboxylic acid **22**)



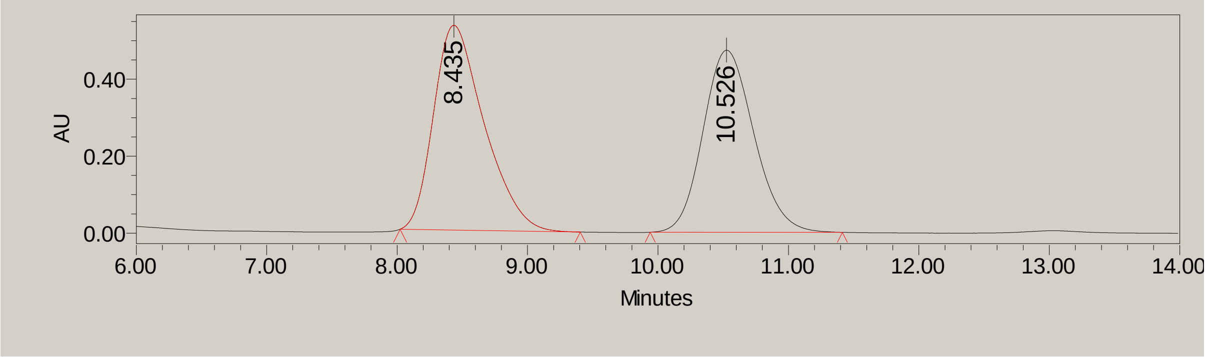
	Retention Time	% Area
1	13.623	1.05
2	15.740	0.94
3	17.569	98.01



36

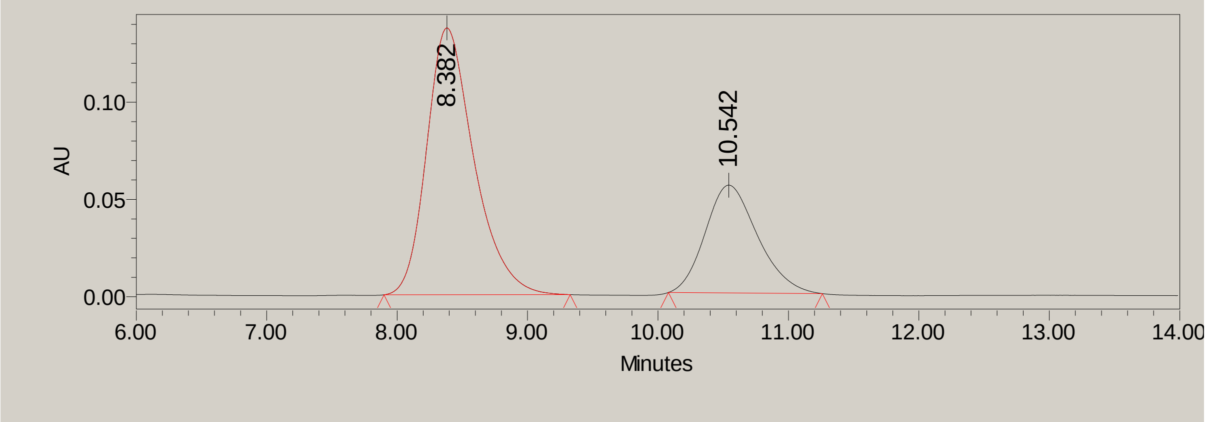
Daicel Chiralpak IA, hexane/isopropanol 50/50 flow rate = 1.0 mL/min, λ: 210.0 nm.

Rac-**36**



	Retention Time	% Area
1	8.435	52.80
2	10.526	47.20

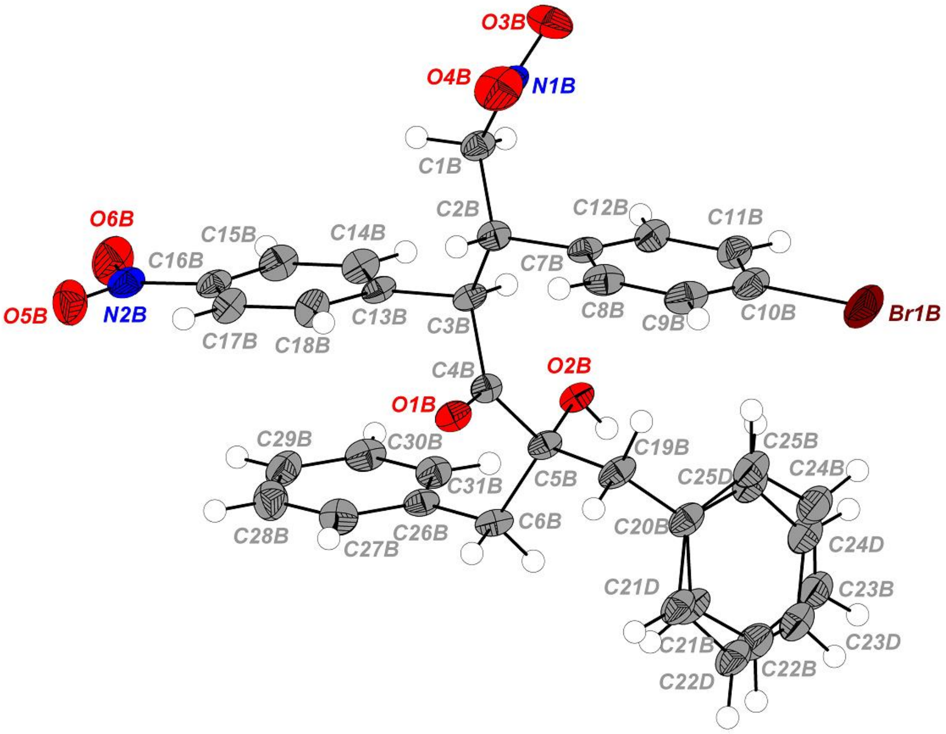
Scalemic **36**

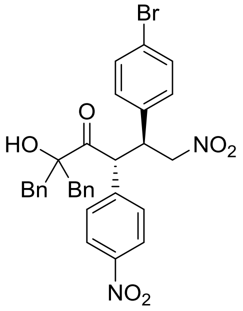


	Retention Time	% Area
1	8.382	69.09
2	10.542	30.91

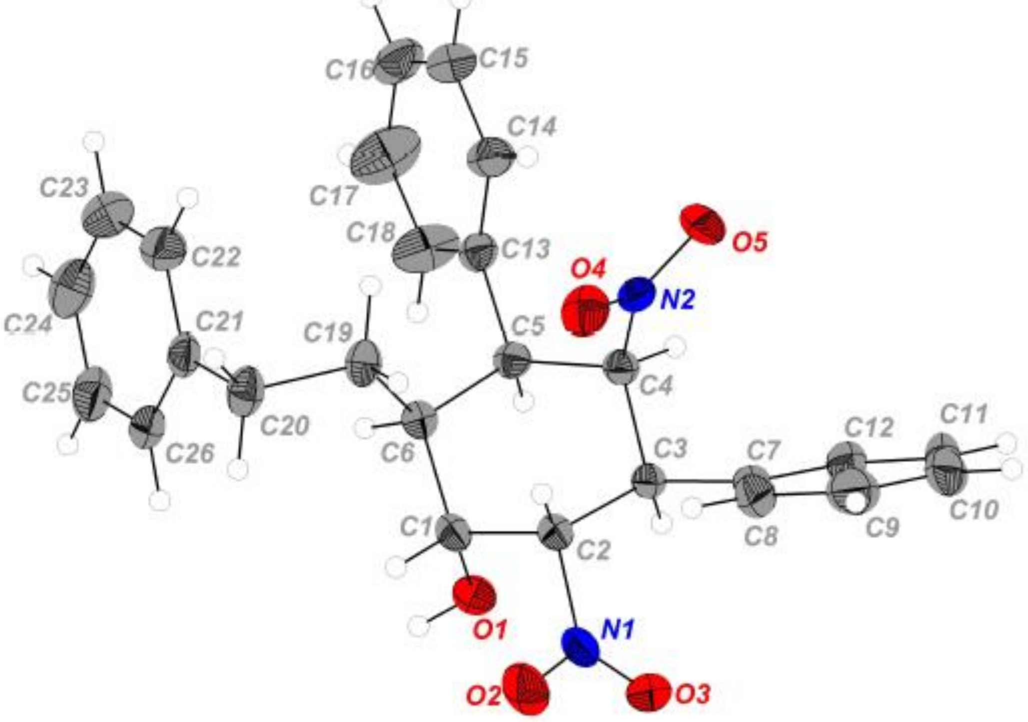
13. X-Ray analysis: ORTEP diagram of compound 9Ab and 33

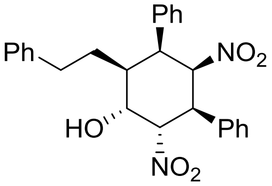
CCDC-1514777 (compound **9Ab**) and CCDC-1588229 (compound **33**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.





9Ab


C16
C15
C14
C23
C22
C17
C18
C13
O5
O4
N2
C24
C21
C19
C5
C4
C25
C20
C6
C3
C7
C12
C11
C26
C8
C9
C10
C1
C2
O1
N1
O2
O3


Ph
Ph
NO2
HO
Ph
NO2

33