N-Heterocyclic Carbenes as Chiral Brønsted Base Catalysts: A Highly Diastereo- and Enantioselective 1,6-Addition Reaction

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1. General Information:

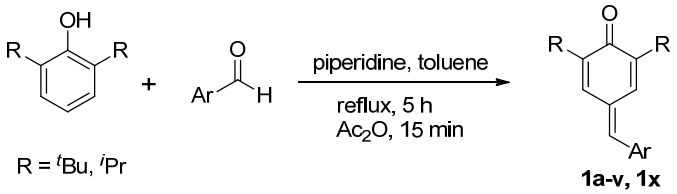
Unless otherwise stated, all reagents and solvents were purchased from commercial suppliers and used without further purification. Toluene was freshly dried prior to the reaction over Na. 4Å MS was activated by heating at elevated temperature (> 200 ºC) under vacuum for 12 h. All reactions were performed in flame-dried schlenk tubes (inner diameter = 18 mm, length = 105 mm) with glass stoppers/silicon septum and Teflon coated magnetic stirring bar. Reactions were monitored by thin layer chromatography (TLC) analysis on silica gel 60 F_{254} and visualization was accomplished with short wave UV light at 254 nm or $KMnO_4$ staining solutions followed by heating, crude product was purified by column chromatography on Merck silica gel (100-200 mesh). ^1H and ^{13}C NMR spectra were recorded on Bruker AVANCE III 500, 400 and 300 MHz spectrometers in deuterated solvents. Proton chemical shifts are reported in ppm (δ) relative to tetramethylsilane (TMS) with the solvent resonance employed as the internal standard ($CDCl_3$ δ 7.26 ppm, acetone-d_6 δ 2.05 and CD_3CN δ 1.94 ppm). ^1H NMR data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, dd = doublet of doublet, t = triplet, m = multiplet, br. = broad), coupling constants (Hz) and integration. ^{13}C chemical shifts are reported in ppm (δ) from tetramethylsilane (TMS) with the solvent resonance as the internal standard ($CDCl_3$ δ 77.0 ppm, acetone-d_6 δ 30.83 ppm). High resolution mass spectra were measured on Q-Tof micro MS system by electron spray ionization (ESI) technique. IR spectra were recorded on PerkinElmer FT-IR spectrometer (model: Spectrum Two) as Neat. The wave numbers (n) are reported in cm^{-1}. Optical rotations were measured on an Anton Paar automatic polarimeter and are reported as follows: concentration (c = g/dL), and solvent. The enantiomeric excesss were determined by HPLC (Shimadzu) analysis employing a chiral stationary phase column specified in the individual experiment, by comparing the samples with the appropriate racemic mixtures.

2. Literature Preparations: 4-Benzylidene-2,6-dimethylcyclohexa-2,5-dienone (**1w**),[1] 2,6-Di-*tert*-butyl-4-ethylidenecyclohexa-2,5-dienone (**1y**),[2] 3-Oxo-*N*-phenylbutanamide (**2a**),[3] *N*-([1,1'-Biphenyl]-2-yl)-3-oxobutanamide (**2d**),[3] 3-Oxo-*N*-(quinolin-8-yl)butanamide (**2i**),[3] 2-(Naphthalen-2-yl)aniline,[4] 2',4',6'-Trimethyl-[1,1'-biphenyl]-2-amine,[5] 2',6'-diphenyl biphenyl-2-amine,[4] Ethyl 3-oxo-3-phenylpropanoate,[6] Ethyl 3-oxo-3-(p-tolyl)propanoate,[6] Ethyl 3-(4-

fluorophenyl)-3-oxopropanoate,[6] Ethyl 3-(naphthalen-2-yl)-3-oxopropanoate,[6] *N*-Methyl-3-oxo-*N*-phenylbutanamide (**2n**),[3] catalyst **3a-g**.[7]

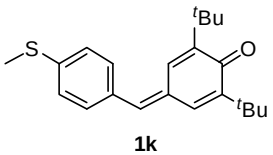
3. General Procedure I (GP-I): Synthesis of *p*-Quinone Methides (*p*-QMs)

The *p*-QMs **1a-v** and **1x** were prepared according to reported literature procedures.[2,8]



In a two neck flask equipped with a Dean-Stark apparatus, a solution of phenols (10.0 mmol) and the appropriate aldehydes (10.0 mmol) in toluene (40.0 mL) was heated under reflux. To the refluxing solution, piperidine (20.0 mmol) was added dropwise within 1 h. The reaction mixture was heated under reflux for 5 h. The reaction temperature was reduced to 100 °C, acetic anhydride (20.0 mmol) was added and stirring was continued for 15 min. The reaction mixture was then poured into ice-cold water and extracted with CH_2Cl_2 for three times. The combined organic layer was dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The crude product was purified by flash column chromatography on silica gel (*n*-Hexane or 1-3% EtOAc-Hexane as eluant) and further recrystallized from *n*-hexane to afford the desired *p*-QMs **1a-v** and **1x**; among them **1k** and **1q** are new compounds.

2,6-di-*tert*-Butyl-4-(4-(methylthio)benzylidene)cyclohexa-2,5-dienone (1k): Prepared according to GP-I, combining 4-(methylthio)benzaldehyde and 2,6-di-*tert*-butylphenol in presence of piperidine and acetic anhydride to afford **1k** as yellow solid in 70% yield.



1k

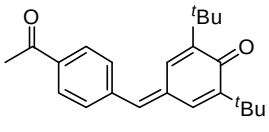
^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.53 (d, *J* = 2.0 Hz, 1H), 7.39 (d, *J* = 8.0 Hz, 2H), 7.30 (d, *J* = 8.0 Hz, 2H), 7.11 (s, 1H), 7.00 (d, *J* = 2.0 Hz, 1H), 2.54 (s, 3H), 1.33 (s, 9H), 1.31 (s, 9H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$) δ = 186.5, 149.3, 147.6, 141.9, 140.9, 135.1, 132.4, 131.5, 130.7, 127.5, 125.9, 35.4, 34.9, 29.5, 29.5, 15.1 ppm.

HRMS (ESI+) *m/z* calculated for $C_{22}H_{29}OS$ $[M+H]^+$ 341.1934, found 341.1935.

IR (Neat) ν_{max} = 3635, 3000, 2952, 2864, 1607, 1559, 1457, 1359, 917, 821 cm^{-1}.

4-(4-Acetylbenzylidene)-2,6-di-tert-butylcyclohexa-2,5-dienone (1q): Prepared according to GP-I, combining 4-acetylbenzaldehyde and 2,6-di-*tert*-butylphenol in presence of piperidine and acetic anhydride to afford **1q** as yellow solid in 52% yield.



1q

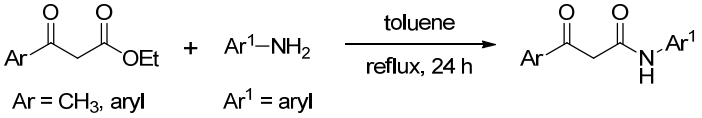
^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.03 (d, *J* = 8.4 Hz, 2H), 7.53 (d, *J* = 8.4 Hz, 2H), 7.45 (d, *J* = 2.4 Hz, 1H), 7.17 (s, 1H), 7.01 (d, *J* = 2.4 Hz, 1H), 2.64 (s, 3H), 1.33 (s, 9H), 1.29 (s, 9H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$) δ = 197.2, 186.5, 150.1, 148.6, 140.4, 140.1, 136.8, 134.6, 133.5, 130.3, 128.6, 127.1, 35.5, 35.0, 29.5, 29.5, 26.5 ppm.

HRMS (ESI+) *m/z* calculated for $C_{23}H_{29}O_2$ $[M+H]^+$ 337.2162, found 337.2164.

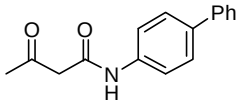
IR (Neat) ν_{max} = 2997, 2954, 2912, 2870, 1678, 1611, 1566, 1359, 1265, 918, 820 cm^{-1}.

4. General Procedure II (GP-II): Synthesis of *β*-Ketoamides



All the *β*-ketoamides were synthesized by following the standard reported literature procedure[3] by placing aniline (1.0 equiv), *β*-ketoester (1.0 equiv) and toluene (2 M) in an oven dried round-bottom flask equipped with a magnetic stir bar. The resulting mixture was heated under reflux for 24 h. The reaction mixture was allowed to cool to ambient temperature and toluene was removed under reduced pressure. The oily residue was purified by gradient column chromatography from 20% EtOAc-Hexane to 60% EtOAc-Hexane to afford the desired *β*-ketoamides **2a-n**; among them **2b**, **2c**, **2e-h** and **2j-m** are new compounds.

***N*-([1,1'-Biphenyl]-4-yl)-3-oxobutanamide (2b):** Prepared according to GP-II, combining ethyl 3-oxobutanoate and 4-aminobiphenyl in presence of toluene to afford **2b** as white solid in 46% yield.



2b

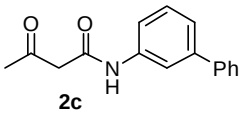
^{1}H NMR (400 MHz, $CDCl_3$) δ = 9.18 (s, br., 1H), 7.65-7.60 (m, 2H), 7.60-7.54 (m, 4H), 7.43 (t, *J* = 7.6 Hz, 2H), 7.33 (t, *J* = 7.2 Hz, 1H), 3.62 (s, 2H), 2.35 (s, 3H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$) δ = 205.3, 163.2, 140.5, 137.4, 136.7, 128.7, 127.6, 127.1, 126.8, 120.4, 49.5, 31.3 ppm.

HRMS (ESI+) *m/z* calculated for $C_{16}H_{16}NO_2$ $[M+H]^+$ 254.1176, found 254.1178.

IR (Neat) ν_{max} = 3294, 3056, 1711, 1656, 1598, 1537, 1362, 1166, 838, 752 cm^{-1}.

***N*-([1,1'-Biphenyl]-3-yl)-3-oxobutanamide (2c):** Prepared according to GP-II, combining ethyl 3-oxobutanoate and 3-aminobiphenyl in presence of toluene to afford **2c** as white solid in 42% yield.



2c

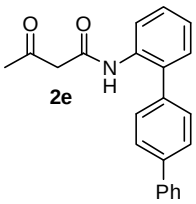
^{1}H NMR (400 MHz, $CDCl_3$) δ = 9.19 (s, br., 1H), 7.79-7.75 (m, 1H), 7.62-7.53 (m, 3H), 7.47-7.39 (m, 3H), 7.38-7.32 (m, 2H), 3.62 (s, 2H), 2.35 (s, 3H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$) δ = 205.2, 163.3, 142.1, 140.6, 137.9, 129.3, 128.7, 127.5, 127.1, 123.4, 119.0, 118.9, 49.6, 31.3 ppm.

HRMS (ESI+) *m/z* calculated for $C_{16}H_{16}NO_2$ $[M+H]^+$ 254.1176, found 254.1177.

IR (Neat) ν_{max} = 3300, 3059, 1715, 1657, 1594, 1550, 1478, 1420, 1326, 756, 697 cm^{-1}.

***N*-([1,1':4',1''-Terphenyl]-2-yl)-3-oxobutanamide (2e):** Prepared according to GP-II, combining ethyl 3-oxobutanoate and [1,1':4',1''-terphenyl]-2-amine[4] in presence of toluene to afford **2e** as white solid in 45% yield.



2e

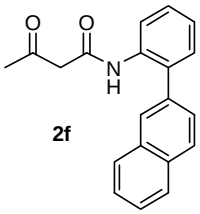
^{1}H NMR (400 MHz, $CDCl_3$) δ = 13.58 (s, br., $1H_{enol}$), 8.66 (s, br., $1H_{keto}$), 8.24 (d, *J* = 8.0 Hz, $1H_{keto}$), 7.77-7.62 (m, 8H, $4H_{keto}$, $4H_{enol}$), 7.52-7.42 (m, 8H, $4H_{keto}$, $4H_{enol}$), 7.42-7.34 (m, 4H, $2H_{keto}$, $2H_{enol}$), 7.34-7.28 (m, 2H, $1H_{keto}$, $1H_{enol}$), 7.25-7.18 (m, 2H, $1H_{keto}$, $1H_{enol}$), 6.79 (s, $1H_{enol}$), 4.79 (s, $1H_{enol}$), 3.46 (s, $2H_{keto}$), 2.21 (s, $3H_{keto}$), 1.92 (s, $3H_{enol}$) ppm.

^{13}C NMR (100 MHz, $CDCl_3$) δ = 203.5, 163.5, 140.7, 140.5, 137.0, 134.5, 132.9, 130.2, 129.7, 128.8, 128.3, 127.5, 127.5, 127.1, 124.8, 122.1, 50.5, 30.9 ppm.

HRMS (ESI+) *m/z* calculated for $C_{22}H_{20}NO_2$ $[M+H]^+$ 330.1489, found 330.1487.

IR (Neat) ν_{max} = 3279, 3028, 1716, 1663, 1582, 1525, 1448, 756, 698 cm^{-1}.

***N*-(2-(Naphthalen-2-yl)phenyl)-3-oxobutanamide (2f):** Prepared according to GP-II, combining ethyl 3-oxobutanoate and 2-(naphthalen-2-yl)aniline[4] in presence of toluene to afford **2f** as white solid in 52% yield.



2f

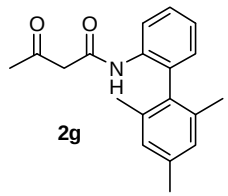
^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.55 (s, br., 1H), 8.17 (d, *J* = 8.1 Hz, 1H), 7.87 (d, *J* = 8.1 Hz, 1H), 7.85-7.74 (m, 3H), 7.51-7.37 (m, 3H), 7.36-7.23 (m, 2H), 7.20-7.11 (m, 1H), 3.30 (s, 2H), 2.06 (s, 3H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$) δ = 203.5, 163.6, 135.4, 134.6, 133.4, 133.1, 132.6, 130.5, 128.5, 128.4, 128.3, 128.1, 127.7, 127.1, 126.4, 126.3, 124.8, 122.2, 50.5, 30.8 ppm.

HRMS (ESI+) *m/z* calculated for $C_{20}H_{18}NO_2$ $[M+H]^+$ 304.1338, found 304.1369.

IR (Neat) ν_{max} = 3224, 3018, 1714, 1648, 1489, 1318, 1223, 831, 755 cm^{-1}.

3-Oxo-*N*-(2',4',6'-trimethyl-[1,1'-biphenyl]-2-yl)butanamide (2g): Prepared according to GP-II, combining ethyl 3-oxobutanoate and 2',4',6'-trimethyl-[1,1'-biphenyl]-2-amine[5] in presence of toluene to afford **2g** as white solid in 48% yield.



2g

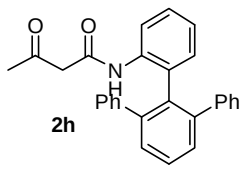
^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.39 (d, *J* = 8.1 Hz, 1H), 8.25 (s, br., 1H), 7.43-7.28 (m, 1H), 7.21-7.14 (m, 1H), 7.06 (dd, *J* = 7.5, 1.5 Hz, 1H), 7.03 (s, 2H), 3.37 (s, 2H), 2.37 (s, 3H), 2.17 (s, 3H), 1.95 (s, 6H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$) δ = 203.6, 163.3, 137.7, 136.8, 135.3, 133.2, 130.7, 129.7, 128.7, 128.5, 127.9, 124.4, 120.5, 50.4, 30.8, 21.1, 20.1 ppm.

HRMS (ESI+) *m/z* calculated for $C_{19}H_{22}NO_2$ $[M+H]^+$ 296.1651, found 296.1652.

IR (Neat) ν_{max} = 3270, 2916, 1717, 1658, 1525, 1446, 1314, 1204, 852, 755 cm^{-1}.

3-Oxo-*N*-(6'-phenyl-[1,1':2',1''-terphenyl]-2-yl)butanamide (2h): Prepared according to GP-II, combining ethyl 3-oxobutanoate and 2',6'-diphenyl biphenyl-2-amine[4] in presence of toluene to afford **2h** as white solid in 48% yield.



2h

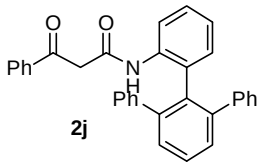
^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.43 (s, br., 1H), 7.88 (d, *J* = 8.0 Hz, 1H), 7.65-7.57 (m, 1H), 7.53 (d, *J* = 7.6 Hz, 2H), 7.19-7.11 (m, 6H), 7.10-7.02 (m, 5H), 6.90 (d, *J* = 6.4 Hz, 1H), 6.83 (t, *J* = 7.2 Hz, 1H), 3.32 (s, 2H), 2.18 (s, 3H) ppm.

^{13}C NMR (75 MHz, $CDCl_3$) δ = 204.28, 162.76, 142.59, 140.96, 135.57, 134.05, 132.36, 130.19, 129.89, 129.18, 128.62, 127.78, 127.73, 127.65, 126.75, 123.60, 120.88, 50.15, 30.89 ppm.

HRMS (ESI+) *m/z* calculated for $C_{28}H_{24}NO_2$ $[M+H]^+$ 406.1801, found 406.1802.

IR (Neat) ν_{max} = 3322, 3065, 1710, 1674, 1584, 1523, 756, 700 cm^{-1}.

3-Oxo-3-phenyl-N-(6'-phenyl-[1,1':2',1''-terphenyl]-2-yl)propanamide (2j): Prepared according to GP-II, combining ethyl 3-oxo-3-phenylpropanoate[6] and 2',6'-diphenyl biphenyl-2-amine in presence of toluene to afford **2j** as white solid in 58% yield.



2j

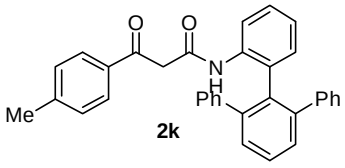
^{1}H NMR (300 MHz, $CDCl_3$) δ = 13.95 (s, br., $1H_{enol}$), 8.55 (s, br., $1H_{keto}$), 8.02-7.79 (m, $3H_{keto}$), 7.78-7.67 (m, $3H_{enol}$), 7.67-7.36 (m, 12H, $6H_{keto}$, $6H_{enol}$), 7.26-6.97 (m, 22H, $10H_{keto}$, $12H_{enol}$), 6.97-6.71 (m, $3H_{keto}$), 6.57 (s, br., $1H_{enol}$), 5.29 (s, br., $1H_{enol}$), 3.86 (s, $2H_{keto}$) ppm.

^{13}C NMR (75 MHz, $CDCl_3$) δ = 195.5, 162.9, 142.5, 140.9, 136.0, 135.5, 134.0, 134.0, 132.3, 130.8, 130.2, 129.8, 129.2, 128.8, 128.5, 128.4, 127.8, 127.6, 127.5, 126.9, 126.6, 125.8, 123.5, 120.8, 46.2 ppm.

HRMS (ESI+) *m/z* calculated for $C_{33}H_{26}NO_2$ $[M+H]^+$ 468.1958, found 468.1957.

IR (Neat) ν_{max} = 3259, 3056, 3022, 1688, 1620, 1580, 1520, 1446, 1298, 754, 698 cm^{-1}.

3-Oxo-*N*-(6'-phenyl-[1,1':2',1''-terphenyl]-2-yl)-3-(p-tolyl)propanamide (2k): Prepared according to GP-II, combining ethyl 3-oxo-3-(p-tolyl)propanoate[6] and 2',6'-diphenyl biphenyl-2-amine in presence of toluene to afford **2k** as white solid in 55% yield.



2k

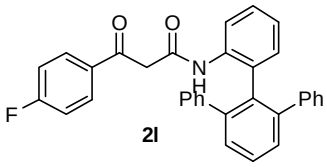
^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.59 (s, 1H), 7.88 (d, *J* = 8.0 Hz, 1H), 7.80 (d, *J* = 8.0 Hz, 2H), 7.61 (t, *J* = 7.5 Hz, 1H), 7.50 (d, *J* = 7.5 Hz, 2H), 7.25 (d, *J* = 5.5 Hz, 1H), 7.12-7.00 (m, 12H), 6.90 (d, *J* = 7.5 Hz, 1H), 6.82 (t, *J* = 7.5 Hz, 1H), 3.82 (s, 2H), 2.40 (s, 3H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$) δ = 195.0, 163.1, 145.1, 142.5, 140.9, 135.6, 134.0, 133.6, 132.3, 130.2, 129.8, 129.5, 129.2, 129.1, 128.6, 128.5, 127.8, 127.6, 127.5, 126.9, 126.6, 125.8, 123.4, 120.8, 46.1, 21.6 ppm.

HRMS (ESI+) *m/z* calculated for $C_{34}H_{28}NO_2$ $[M+H]^+$ 482.2115, found 482.2116.

IR (Neat) ν_{max} = 3262, 3057, 1685, 1669, 1605, 1527, 1440, 1184, 814, 756, 703 cm^{-1}.

3-(4-Fluorophenyl)-3-oxo-*N*-(6'-phenyl-[1,1':2',1''-terphenyl]-2-yl)propanamide (2l):



2l

Prepared according to GP-II, combining ethyl 3-(4-fluorophenyl)-3-oxopropanoate[6] (1.0 equiv) and 2',6'-diphenyl biphenyl-2-amine (1.0 equiv) in presence of toluene to afford **2l** as white solid in 58% yield.

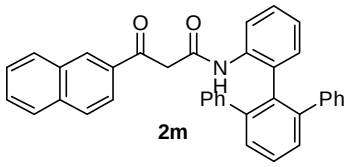
^{1}H NMR (300 MHz, $CDCl_3$) δ = 14.02 (s, br., $1H_{enol}$), 8.39 (s, br., $1H_{keto}$), 8.02-7.89 (m, $2H_{keto}$), 7.85 (d, *J* = 8.1 Hz, $1H_{keto}$), 7.71 (s, br., $3H_{enol}$), 7.65-7.56 (m, 2H, $1H_{keto}$, $1H_{enol}$), 7.55-7.46 (m, 4H, $2H_{keto}$, $2H_{enol}$), 7.23-6.96 (m, 25H, $13H_{keto}$, $12H_{enol}$), 6.95-6.78 (m, 4H, $2H_{keto}$, $2H_{enol}$), 6.56 (s, br., $1H_{enol}$), 5.20 (s, br., $1H_{enol}$), 3.82 (s, $2H_{keto}$) ppm.

^{13}C NMR (75 MHz, $CDCl_3$) δ = 193.7, 167.9, 164.5, 162.7, 142.8, 142.5, 140.8, 140.6, 135.3, 134.9, 134.0, 133.9, 132.4, 132.3, 132.3, 131.4, 131.3, 130.3, 129.8, 129.1, 128.7, 128.5, 128.0, 127.9, 127.8, 127.7, 127.6, 126.9, 126.7, 123.6, 120.9, 116.1, 115.8, 115.6, 115.3, 46.5 ppm.

HRMS (ESI+) *m/z* calculated for $C_{33}H_{25}FNO_2$ $[M+H]^+$ 486.1864, found 486.1866.

IR (Neat) ν_{max} = 3408, 3356, 3054, 1731, 1683, 1598, 1526, 1158, 832, 754, 699 cm^{-1}.

3-(Naphthalen-2-yl)-3-oxo-*N*-(6'-phenyl-[1,1':2',1''-terphenyl]-2-yl)propanamide (2m):



2m

Prepared according to GP-II, combining ethyl 3-(naphthalen-2-yl)-3-oxopropanoate[6] and 2',6'-diphenyl biphenyl-2-amine in presence of toluene to afford **2m** as white solid in 62% yield.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.56 (s, br., 1H), 8.47 (s, 1H), 8.00-7.92 (m, 2H), 7.92-7.85 (m, 3H), 7.66-7.45 (m, 6H), 7.19-6.98 (m, 10H), 6.92 (d, *J* = 7.6 Hz, 1H), 6.83 (t, *J* = 7.6 Hz, 1H), 3.99 (s, 2H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$) δ = 195.3, 163.0, 142.5, 140.9, 135.9, 135.5, 134.0, 133.3, 132.3, 132.3, 130.9, 130.4, 129.8, 129.2, 129.0, 128.7, 128.5, 127.8, 127.7, 127.6, 127.5, 127.0, 126.9, 126.6, 123.6, 123.5, 121.0, 46.5 ppm.

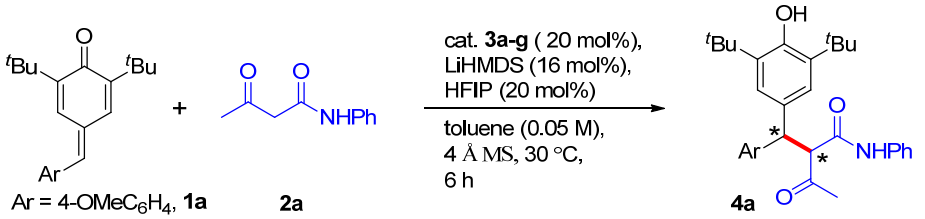
HRMS (ESI+) *m/z* calculated for $C_{37}H_{28}NO_2$ $[M+H]^+$ 518.2120, found 518.2147.

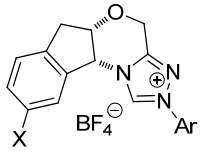
IR (Neat) ν_{max} = 3240, 3200, 3058, 1682, 1585, 1532, 1439, 1184, 755, 698 cm^{-1}.

5. Initial Reaction Optimization:

Our studies towards developing the 1,6-conjugate addition were commenced using *p*-QM **1a** and *N*-phenylacetoacetamide **2a** as model substrates under various reaction conditions in the presence of a series of chiral NHCs and HFIP as proton shuttle (Table 1). The reaction found ineffective with catalyst **3a**. This may be due to unfavorable basicity of the corresponding NHC, as it contains a strong electron deficient aryl moiety at *N*-centre of the catalyst. Apart from **3a**, all others triazolium salts **3b-g** promoted the reaction in good efficacy upon treatment with LiHMDS. However, only poor stereoselectivity of the final product was obtained with NHC-precursor **3b-e** (Table 1, entries 2-5). A slightly improved enantioselectivity was observed; when mesityl substituted catalysts **3f** and **3g** were tested (Table 1, entry 6 and 7). Importantly, the catalyst **3g** shows better reactivity and similar stereoselectivity compare to the catalyst **3f**.

Table 1. Catalyst Identification[a]



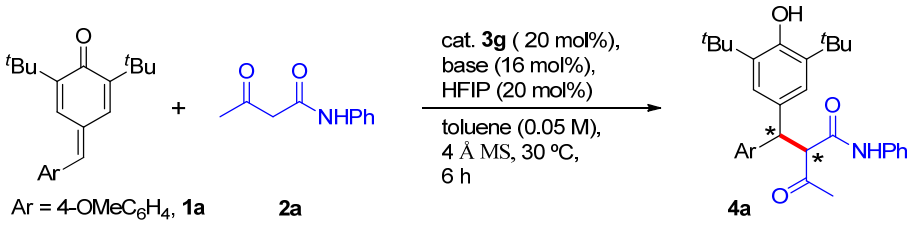


3a[b], X = H, Ar = C_6F_5
3b, X = H, Ar = C_6H_5
3c[b], X = H, Ar = 2,4,6-$^{i}Pr_3C_6H_2$
3d, X = H, Ar = 2,6-$Et_2C_6H_3$
3e[b], X = NO_2, Ar = C_6H_5
3f, X = Br, Ar = 2,4,6-$Me_3C_6H_2$
3g, X = H, Ar = 2,4,6-$Me_3C_6H_2$

Entry	Catalyst	Conv. (%)	ee (%)	dr
1	**3a**	no reaction	-	-
2	**3b**	100	6,8	61:39
3	**3c**	100	0	76:24
4	**3d**	100	10,10	62:38
5	**3e**	50	0	63:37
6	**3f**	90	19,19	64:36
7	**3g**	100	20,23	58:42

[a]Reaction conditions: **1a** (0.05 mmol), **2a** (0.05 mmol) and 4Å MS (35 mg) in 1.0 mL toluene at 30 ºC; reaction conversion was determined by ^{1}H NMR analysis. [b]Catalyst with opposite enantiomer.

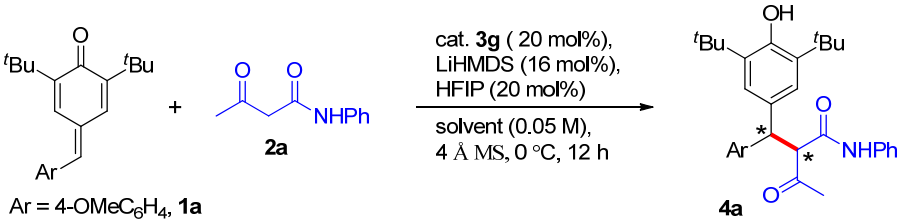
Table 2. Base Screening[a]



Entry	Base	Conv. (%)	ee (%)	dr
1	Et_3N	trace	-	-
2	Hunig base	trace	-	-
3	K_2CO_3	no reaction	-	-
4	NaOAc	no reaction	-	-
5	DBU	100	0	59:41
6	Cs_2CO_3	100	4, 2	67:33

[a]Reaction conditions: **1a** (0.05 mmol), **2a** (0.05 mmol) and 4Å MS (35 mg) in 1.0 mL toluene at 30 ºC; reaction conversion was determined by ^{1}H NMR analysis.

Table 3. Solvent Screening[a]

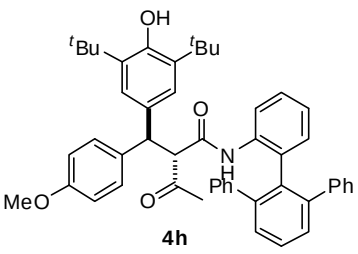


Entry	Solvent	Conv. (%)	ee (%)	dr.
1	MTBE	100	22, 15	73:27
2	Et_2O	100	17, 6	71:29
3	$CHCl_3$	60	6, 0	81: 19
4	$PhCH_3$	100	44, 48	64:36

[a]Reaction conditions: **1a** (0.05 mmol), **2a** (0.05 mmol) and 4Å MS (35 mg) in 1.0 mL solvent at 0 ºC; reaction conversion was determined by ^{1}H NMR analysis..

6. General Procedure III (GP-III): NHC-Catalyzed 1,6-Conjugate Addition Reaction: To a flame dried schlenk tube equipped with a magnetic stir bar, carbene precursor **3g** (6.3 mg, 0.015 mmol, 0.15 equiv), activated 4Å MS (70.0 mg) and toluene (0.8 mL) were placed under argon. To the resulting heterogeneous mixture, LiHMDS (12.0 µL, 0.012 mmol, 0.12 equiv, 1(M) in THF) was added and stirred at 25 °C for 1h under argon. The reaction mixture was cooled to -40 °C or -78 °C prior to the addition of a solution of *β*-ketoamide (0.1 mmol, 1.0 equiv) in 0.8 mL of toluene. The mixture was stirred for 10 min. To the cold reaction mixture, a solution of *p*-QM (0.1 mmol, 1.0 equiv) in 0.4 mL of toluene was added dropwise. The reaction was continued for 12-24 h, while maintaining the appropriate reaction temperature (reaction temparature is specified in the individual experiment). The progress of the reaction was monitored by TLC analysis. After running the reaction to an appropriate time (reaction time is specified in the individual experiment), the reaction was quenched with 1.0 mL of water and extracted with EtOAc (twice), the combined organic layer was dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The crude material was purified by column chromatography (SiO_2, eluant: 10-20% EtOAc-Hexane) to afford the desired compound.

Compound 4h: Prepared according to GP-III, combining *p*-QM **1a** (32.4 mg, 0.1 mmol, 1.0 equiv), amide **2h** (40.5 mg, 0.1 mmol, 1.0 equiv), **3g** (6.3 mg, 0.015 mmol, 15.0 mol%), LiHMDS (12.0 µL, 0.012 mmol, 12.0 mol%) and 4Å MS (70.0 mg) in toluene (0.05 M, 2.0 mL) at -40°C for 24 h. The crude product was purified by column chromatography (SiO_2, 10% EtOAc-Hexane, R_f = 0.4 for the product) to afford the title compound **4h** (68.0 mg, 93%) as white solid.



4h

^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.64-7.54 (m, 2H), 7.49 (d, *J* = 7.2 Hz, 1H), 7.24-7.16 (m, 8H), 7.14-7.07 (m, 3H), 7.02-6.93 (m, 4H), 6.91 (s, 2H), 6.88-6.77 (m, 4H), 5.04 (s, 1H), 4.30 (d, *J* = 12.0 Hz, 1H), 4.10 (d, *J* = 12.0 Hz, 1H), 3.76 (s, 3H), 1.89 (s, 3H), 1.31 (s, 18H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$) δ = 205.6, 164.6, 158.2, 152.4, 142.4, 142.0, 140.9, 140.7, 135.6, 134.8, 134.1, 133.8, 132.0, 132.0, 131.4, 129.8, 129.7, 129.6, 129.2, 128.7, 128.4, 127.7, 127.6, 127.4, 126.9, 126.5, 124.3, 124.1, 122.9, 114.0, 69.1, 55.1, 52.5, 34.2, 30.2, 30.0 ppm.

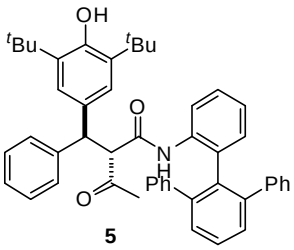
HRMS (ESI+) *m/z* calculated for $C_{50}H_{51}NO_4Na$ $[M+Na]^+$ 752.3716, found 752.3713.

IR (Neat) ν_{max} = 3629, 3382, 2955, 1688, 1583, 1511, 1439, 1178, 756, 701 cm^{-1}.

$[\alpha]_D^{25}$ = -87.05 (c = 0.34, $CHCl_3$).

HPLC: The enantiomeric excess (% of ee = 98) and diastereomeric ratio (dr = 98:2) were determined by HPLC analysis using Daicel Chiralpak IA-3 column: *n*-hexane:*i*-PrOH = 98:2, flow rate 1.0 mL/min, λ = 254 nm: τ_{minor} = 13.27 min, τ_{major} = 27.49 min.

Compound 5: Prepared according to GP-III, combining *p*-QM **1b** (29.4 mg, 0.1 mmol, 1.0 equiv), amide **2h** (40.5 mg, 0.1 mmol, 1.0 equiv), **3g** (6.3 mg, 0.015 mmol, 15.0 mol%), LiHMDS (12.0 µL, 0.012 mmol, 12.0 mol%) and 4Å MS (70.0 mg) in toluene (0.05 M, 2.0 mL) at -40°C for 24 h. The crude product was purified by column chromatography (SiO_2**,** 10% EtOAc-Hexane, R_f = 0.4 for the product) to afford the title compound **5** (63.0 mg, 90%) as white solid.



5

^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.71-7.64 (m, 2H), 7.56 (d, *J* = 6.4 Hz, 1H), 7.39-7.36 (m, 5H), 7.31-7.29 (m, 5H), 7.19-7.18 (m, 3H), 7.08-7.01 (m, 4H), 7.00 (s, 2H), 6.95 (d, *J* = 7.2 Hz, 1H), 6.92-6.86 (m, 1H), 5.12 (s, 1H), 4.42(d, *J* = 12.0 Hz, 1H), 4.24 (d, *J* = 12.0 Hz, 1H), 1.96 (s, 3H), 1.39 (s, 18H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$) δ = 205.4, 164.5, 152.5, 142.4, 141.9, 141.7, 140.9, 140.7, 135.6, 134.7, 134.1, 132.1, 131.1, 129.8, 129.7, 129.2, 128.7, 128.4, 127.7, 127.7, 127.6, 127.4, 127.0, 126.7, 126.5, 124.4, 124.2, 123.0, 68.9, 53.2, 34.2, 30.2, 30.0 ppm.

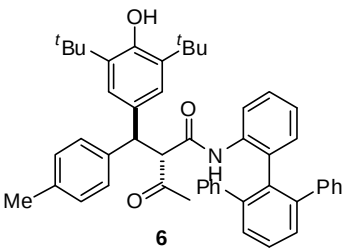
HRMS (ESI+) *m/z* calculated for $C_{49}H_{50}NO_3$ $[M+H]^+$ 700.3791, found 700.3787.

IR (Neat) ν_{max} = 3632, 3389, 2958, 1688, 1584, 1520, 1439, 1158, 757, 701 cm^{-1}.

$[\alpha]_D^{25}$ = -263.41 (c = 0.65, $CHCl_3$).

HPLC: The enantiomeric excess (% of ee = 99) and diastereomeric ratio (dr = 99:1) were determined by HPLC analysis using Daicel Chiralpak IA-3 column: *n*-hexane:*i*-PrOH = 98:2, flow rate 1.0 mL/min, λ = 254 nm: τ_{minor} = 9.46 min, τ_{major} = 18.78 min.

Compound 6: Prepared according to GP-III, combining *p*-QM **1c** (30.8 mg, 0.1 mmol, 1.0 equiv), amide **2h** (40.5 mg, 0.1 mmol, 1.0 equiv), **3g** (6.3 mg, 0.015 mmol, 15.0 mol%), LiHMDS (12.0 µL, 0.012 mmol, 12.0 mol%) and 4Å MS (70.0 mg) in toluene (0.05 M, 2.0 mL) at -40°C for 24 h. The crude product was purified by column chromatography



6

(SiO_2**,** 10% EtOAc-Hexane, R_f = 0.4 for the product) to afford the title compound **6** (66.0 mg, 93%) as white solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.61-7.55 (m, 2H), 7.47 (d, *J* = 7.0 Hz, 1H), 7.21 (s, 4H), 7.16-7.13 (m, 3H), 7.09-7.07(m, 5H), 6.96-6.94 (m, 4H), 6.90 (s, 2H), 6.84 (d, *J* = 7.5 Hz, 1H), 6.81-6.78 (m, 1H), 5.00 (s, 1H), 4.29 (d, *J* = 12.0 Hz, 1H), 4.12 (d, *J* = 12.0 Hz, 1H), 2.28 (s, 3H), 1.87(s, 3H), 1.30 (s, 18H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$) δ = 205.4, 164.6, 152.5, 142.4, 142.0, 140.9, 140.7, 138.8, 136.2, 135.6, 134.8, 134.2, 132.1, 131.4, 129.8, 129.7, 129.7, 129.3, 129.2, 128.4, 127.7, 127.6, 127.6, 127.4, 126.9, 126.5, 124.4, 124.2, 123.0, 69.0, 52.9, 34.2, 30.2, 30.0, 20.9 ppm.

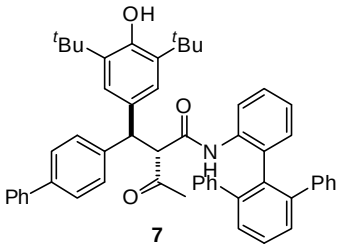
HRMS (ESI+) *m/z* calculated for $C_{50}H_{51}NO_3Na$ $[M+Na]^+$ 736.3767, found 736.3741.

IR (Neat) ν_{max} = 3635, 3379, 2957, 1689, 1515, 1439, 1157, 758, 702 cm^{-1}.

$[\alpha]_D^{25}$ = -209.62 (c = 0.29, $CHCl_3$).

HPLC: The enantiomeric excess (% of ee = 99) and diastereomeric ratio (dr = 99:1) were determined by HPLC analysis using Daicel Chiralpak IE-3 column: *n*-hexane:*i*-PrOH = 98:2, flow rate 1.0 mL/min, λ = 254 nm: τ_{minor} = 8.26 min, τ_{major} = 9.74 min.

Compound 7: Prepared according to GP-III, combining *p*-QM **1d** (37.0 mg, 0.1 mmol, 1.0 equiv), amide **2h** (40.5 mg, 0.1 mmol, 1.0 equiv), **3g** (6.3 mg, 0.015 mmol, 15.0 mol%), LiHMDS (12.0 µL, 0.012 mmol, 12.0 mol%) and 4Å MS (70.0 mg) in toluene (0.05 M, 2.0 mL) at -40°C for 24 h. The crude product was purified by column chromatography (SiO_2**,** 10% EtOAc-Hexane, R_f = 0.5 for the product) to afford the title compound **7** (65.0 mg, 84%) as white solid.



7

^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.63-7.57 (m, 2H), 7.56-7.50 (m, 4H), 7.48 (d, *J* = 7.5 Hz, 1H), 7.42 (t, *J* = 7.5 Hz, 2H), 7.37-7.30 (m, 3H), 7.23 (s, 5H), 7.16 (s, 1H), 7.13-7.09 (m, 3H), 6.95 (d, *J* = 7.5 Hz, 6H), 6.86 (d, *J* = 7.5 Hz, 1H), 6.84-6.78 (m, 1H), 5.05 (s, 1H), 4.39 (d, *J* = 12.0 Hz, 1H), 4.19 (d, *J* = 12.0 Hz, 1H), 1.92 (s, 3H), 1.31 (s, 18H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$) δ = 205.4, 164.4, 152.6, 142.4, 141.9, 140.9, 140.8, 140.7, 140.5, 139.5, 135.7, 134.7, 134.1, 132.2, 132.1, 131.0, 129.8, 129.7, 129.2, 128.7, 128.5, 128.1, 127.7, 127.7, 127.4, 127.2, 127.0, 126.9, 126.5, 124.5, 124.3, 123.0, 68.9, 52.8, 34.2, 30.2, 30.0 ppm.

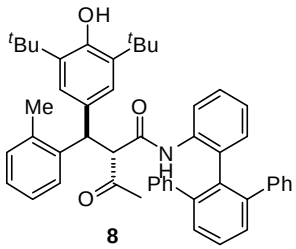
HRMS (ESI+) *m/z* calculated for $C_{55}H_{53}NO_3Na$ $[M+Na]^+$ 798.3923, found 798.3920.

IR (Neat) ν_{max} = 3642, 3389, 2957, 1689, 1519, 1439, 1157, 758, 701 cm^{-1}.

$[\alpha]_D^{25}$ = -151.09 (c = 0.36, $CHCl_3$).

HPLC: The enantiomeric excess (% of ee = 99) and diastereomeric ratio (dr = 99:1) were determined by HPLC analysis using Daicel Chiralpak IE-3 column: *n*-hexane:*i*-PrOH = 98:2, flow rate 1.0 mL/min, λ = 254 nm: τ_{minor} = 11.14 min, τ_{major} = 12.13 min.

Compound 8: Prepared according to GP-III, combining *p*-QM **1e** (30.8 mg, 0.1 mmol, 1.0 equiv), amide **2h** (40.5 mg, 0.1 mmol, 1.0 equiv), **3g** (6.3 mg, 0.015 mmol, 15.0 mol%), LiHMDS (12.0 μL, 0.012 mmol, 12.0 mol%) and 4Å MS (70.0 mg) in toluene (0.05 M, 2.0 mL) at -40°C for 24 h. The crude product was purified by column chromatography (SiO_2**,** 10% EtOAc-Hexane, R_f = 0.5 for the product) to afford the title compound **8** (56.4 mg, 79%) as white solid.



8

^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.55-7.43 (m, 2H), 7.38 (dd, *J* = 7.2, 1.8 Hz, 1H), 7.22-7.17 (m, 1H), 7.15-7.06 (m, 6H), 7.05-6.97 (m, 6H), 6.96-6.81 (m, 6H), 6.80-6.69 (m, 2H), 4.93 (s, 1H), 4.53 (d, *J* = 12.0 Hz, 1H), 4.12 (d, *J* = 12.0 Hz, 1H), 2.34 (s, 3H), 1.79 (s, 3H), 1.19 (s, 18H) ppm.

^{13}C NMR (75 MHz, $CDCl_3$) δ = 205.3, 164.5, 152.4, 142.3, 142.0, 140.8, 140.6, 139.9, 136.0, 135.5, 134.6, 134.1, 132.2, 132.0, 130.9, 130.2, 129.7, 129.7, 129.6, 129.2, 128.4, 127.7, 127.6, 127.4, 126.9, 126.5, 126.5, 126.1, 125.6, 124.9, 124.3, 123.1, 69.1, 47.9, 34.2, 30.2, 29.6, 20.1 ppm.

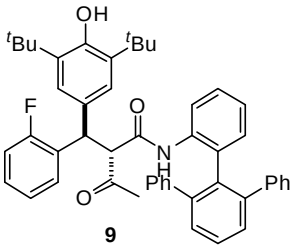
HRMS (ESI+) *m/z* calculated for $C_{50}H_{51}NO_3Na$ $[M+Na]^+$ 736.3767, found 736.3741.

IR (Neat) ν_{max} = 3622, 2956, 1694, 1586, 1513, 1435, 1150, 751, 703 cm^{-1}.

$[\alpha]_D^{25}$ = -140.99 (c = 0.40, $CHCl_3$).

HPLC: The enantiomeric excess (% of ee = 99) and diastereomeric ratio (dr = 97:3) were determined by HPLC analysis using Daicel Chiralpak IA-3 column: *n*-hexane:*i*-PrOH = 97:3, flow rate 1.0 mL/min, λ = 254 nm: τ_{minor} = 4.88 min, τ_{major} = 13.16 min.

Compound 9: Prepared according to GP-III, combining *p*-QM **1f** (31.2 mg, 0.1 mmol, 1.0 equiv), amide **2h** (40.5 mg, 0.1 mmol, 1.0 equiv), **3g** (6.3 mg, 0.015 mmol, 15.0 mol%), LiHMDS (12.0 µL, 0.012 mmol, 12.0 mol%) and 4Å MS (70.0 mg) in toluene (0.05 M, 2.0 mL) at -40°C for 16 h. The crude product was purified by column chromatography (SiO_2**,** 10% EtOAc-Hexane, R_f = 0.45 for the product) to afford the title compound **9** (70.0 mg, 98%, combined yield) as white solid.



9

^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.54-7.43 (m, 2H), 7.40-7.35 (m, 1H), 7.24-7.11 (m, 6H), 7.09-6.96 (m, 6H), 6.94-6.69 (m, 9H), 4.97 (s, 1H), 4.62 (d, *J* = 12.0 Hz, 1H), 4.19 (d, *J* = 12.0 Hz, 1H), 1.81 (s, 3H), 1.21 (s, 18H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$) δ = 204.6, 164.3, 161.2, 159.2, 152.6, 142.3, 141.9, 141.0, 140.6, 135.6, 134.4, 134.2, 132.6, 132.1, 130.0, 129.8, 129.7, 129.7, 129.2, 129.0, 128.9, 128.4, 128.3, 128.2, 127.9, 127.7, 127.4, 127.1, 126.5, 124.6, 124.5, 124.2, 124.2, 123.4, 116.2, 116.0, 67.8, 45.4, 34.2, 30.2, 29.4 ppm.

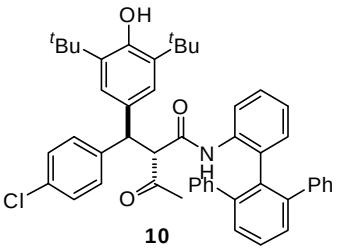
HRMS (ESI+) *m/z* calculated for $C_{49}H_{49}FNO_3$ $[M+H]^+$ 718.3696, found 718.3723.

IR (Neat) ν_{max} = 3631, 3381, 2957, 1689, 1584, 1518, 1438, 1157, 757, 702 cm^{-1}.

$[\alpha]_D^{25}$ = -108.95 (c = 0.25, $CHCl_3$).

HPLC: The enantiomeric excess (% of ee = 98, major diastereoisomer) and diastereomeric ratio (dr = 95:5) were determined by HPLC analysis using Daicel Chiralpak IE-3 column: *n*-hexane:*i*-PrOH = 98:2, flow rate 1.0 mL/min, λ = 254 nm: τ_{minor} = 8.31 min, τ_{major} = 9.95 min.

Compound 10: Prepared according to GP-III, combining *p*-QM **1g** (32.8 mg, 0.1 mmol, 1.0 equiv), amide **2h** (40.5 mg, 0.1 mmol, 1.0 equiv), **3g** (6.3 mg, 0.015 mmol, 15.0 mol%), LiHMDS (12.0 µL, 0.012 mmol, 12.0 mol%) and 4Å MS (70.0 mg) in toluene (0.05 M, 2.0 mL) at -40°C for 12 h. The crude product was purified by column chromatography (SiO_2**,** 10% EtOAc-Hexane, R_f = 0.45 for the product) to afford the title compound **10** (70.0 mg, 95%) as white solid.



10

^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.60 (t, *J* = 7.5 Hz, 1H), 7.55 (d, *J* = 7.5 Hz, 1H), 7.48 (d, *J* = 7.5 Hz, 1H), 7.24 (s, 1H), 7.21-7.16 (m, 7H), 7.12-7.08 (m, 3H), 7.04 (s, 1H), 6.98-6.92 (m, 4H),

6.88-6.83 (m, 3H), 6.83-6.78 (m, 1H), 5.05 (s, 1H), 4.32 (d, *J* = 12.0 Hz, 1H), 4.08 (d, *J* = 12.0 Hz, 1H), 1.88 (s, 3H), 1.29 (s, 18H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$) δ = 204.8, 164.2, 152.7, 142.4, 141.9, 140.8, 140.6, 140.4, 135.8, 134.6, 134.0, 132.5, 132.2, 132.1, 130.6, 129.8, 129.6, 129.2, 129.1, 128.8, 128.5, 127.7, 127.7, 127.4, 127.0, 126.6, 124.4, 124.3, 123.0, 68.9, 52.1, 34.2, 30.2, 29.8 ppm.

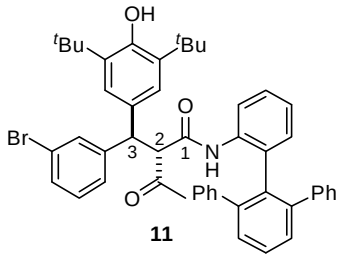
HRMS (ESI+) *m/z* calculated for $C_{49}H_{48}ClNO_3Na$ $[M+Na]^+$ 756.3220, found 756.3222.

IR (Neat) ν_{max} = 3632, 3392, 2957, 1689, 1583, 1520, 1439, 1157, 757, 702 cm^{-1}.

$[\alpha]_D^{25}$ = -104.43 (c = 0.36, $CHCl_3$).

HPLC: The enantiomeric excess (% of ee = 99) and diastereomeric ratio (dr = 97:3) were determined by HPLC analysis using Daicel Chiralpak IA-3 column: *n*-hexane:*i*-PrOH = 98:2, flow rate 1.0 mL/min, λ = 254 nm: τ_{minor} = 22.35 min, τ_{major} = 34.32 min.

Compound 11: Prepared according to GP-III, combining *p*-QM **1h** (37.3 mg, 0.1 mmol, 1.0 equiv), amide **2h** (40.5 mg, 0.1 mmol, 1.0 equiv), **3g** (6.3 mg, 0.015 mmol, 15.0 mol%), LiHMDS (12.0 μL, 0.012 mmol, 12.0 mol%) and 4Å MS (70.0 mg) in toluene (0.05 M, 2.0 mL) at -40°C for 18 h. The crude product was purified by column chromatography (SiO_2**,** 10% EtOAc-Hexane, R_f = 0.5 for the product) to afford the title compound **11** (71.0 mg, 91%) as white solid. Compound **11** was crystallized by slow evaporation from a mixture of MeOH:$CHCl_3$ (10:1) and its absolute configuration assigned by X-ray crystallography as 2S, 3R.



11

^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.64-7.53 (m, 2H), 7.47 (dd, *J* = 7.2, 1.2 Hz, 1H), 7.40 (s, 1H), 7.31 (d, *J* = 7.6 Hz, 1H), 7.24-7.18 (m, 5H), 7.16 (d, *J* = 7.6 Hz, 1H), 7.13-7.08 (m, 3H), 7.06 (s, 1H), 6.99-6.89 (m, 4H), 6.89-6.78 (m, 4H), 5.07 (s, 1H), 4.29 (d, *J* = 12.0 Hz, 1H), 4.10 (d, *J* = 12.0 Hz, 1H), 1.89 (s, 3H), 1.30 (s, 18H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$) δ = 204.8, 164.1, 152.7, 144.1, 142.4, 141.9, 140.9, 140.6, 135.8, 134.5, 134.1, 132.3, 132.1, 131.1, 130.3, 130.2, 129.9, 129.8, 129.6, 129.2, 128.5, 127.7, 127.7, 127.4, 127.0, 126.6, 126.1, 124.4, 123.1, 122.7, 68.7, 52.4, 34.2, 30.2, 29.9 ppm.

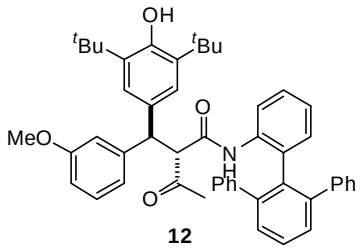
HRMS (ESI+) *m/z* calculated for $C_{49}H_{49}BrNO_3$ $[M+H]^+$ 778.2896, found 778.2914.

IR (Neat) ν_{max} = 3634, 3382, 2957, 1688, 1584, 1519, 1439, 1156, 757, 702 cm^{-1}.

$[\alpha]_D^{25}$ = -69.77 (c = 0.90, $CHCl_3$).

HPLC: The enantiomeric excess (% of ee = 99) and diastereomeric ratio (dr = 99:1) were determined by HPLC analysis using Daicel Chiralpak IA-3 column: *n*-hexane:*i*-PrOH = 98:2, flow rate 1.0 mL/min, λ = 254 nm: τ_{minor} = 10.71 min, τ_{major} = 28.92 min.

Compound 12: Prepared according to GP-III, combining *p*-QM **1i** (32.4 mg, 0.1 mmol, 1.0 equiv), amide **2h** (40.5 mg, 0.1 mmol, 1.0 equiv), **3g** (6.3 mg, 0.015 mmol, 15.0 mol%), LiHMDS (12.0 µL, 0.012 mmol, 12.0 mol%) and 4Å MS (70.0 mg) in toluene (0.05 M, 2.0 mL) at -40°C for 24 h. The crude product was purified by column chromatography (SiO_2**,** 10% EtOAc-Hexane, R_f = 0.5 for the product) to afford the title compound **12** (60.5 mg, 83%) as white solid.



12

^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.62-7.53 (m, 2H), 7.49-7.44 (m, 1H), 7.24-7.14 (m, 7H), 7.12-7.07 (m, 3H), 6.96-6.91 (m, 3H), 6.90 (s, 2H), 6.88-6.83 (m, 2H), 6.82-6.77 (m, 2H), 6.71 (dd, *J* = 8.0, 2.0 Hz, 1H), 5.03 (s, 1H), 4.28 (d, *J* = 12.0 Hz, 1H), 4.13 (d, *J* = 12.0 Hz, 1H), 3.78 (s, 3H), 1.89 (s, 3H), 1.29 (s, 18H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$) δ = 205.3, 164.5, 159.7, 152.6, 143.3, 142.4, 141.9, 140.9, 140.7, 135.6, 134.7, 134.1, 132.1, 132.1, 130.9, 129.8, 129.8, 129.7, 129.6, 129.2, 128.4, 127.7, 127.6, 127.4, 127.0, 126.5, 124.4, 124.3, 123.0, 119.9, 114.2, 111.7, 68.7, 55.1, 53.3, 34.2, 30.2, 30.1 ppm.

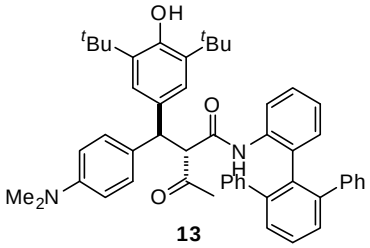
HRMS (ESI+) *m/z* calculated for $C_{50}H_{51}NO_4Na$ $[M+Na]^+$ 752.3716, found 752.3713.

IR (Neat) ν_{max} = 3634, 3379, 2958, 1688, 1584, 1519, 1437, 1264, 1155, 757, 702 cm^{-1}.

$[\alpha]_D^{25}$ = -94.10 (c = 0.34, $CHCl_3$).

HPLC: The enantiomeric excess (% of ee = 99) and diastereomeric ratio (dr = 99:1) were determined by HPLC analysis using Daicel Chiralpak IA-3 column: *n*-hexane:*i*-PrOH = 96:4, flow rate 1.0 mL/min, λ = 254 nm: τ_{minor} = 6.13 min, τ_{major} = 11.85 min.

Compound 13: Prepared according to GP-III, combining *p*-QM **1j** (33.7 mg, 0.1 mmol, 1.0 equiv), amide **2h** (40.5 mg, 0.1 mmol, 1.0 equiv), **3g** (6.3 mg, 0.015 mmol, 15.0 mol%), LiHMDS (12.0 μL, 0.012 mmol, 12.0 mol%) and 4Å MS (70.0 mg) in toluene (0.05 M, 2.0 mL) at -40°C for 24 h. The crude product was purified by column chromatography (SiO_2**,** 10% EtOAc-Hexane, R_f = 0.5 for the product) to afford the title compound **13** (35.6 mg, 48%) as white solid.



13

^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.61-7.55 (m, 2H), 7.46 (dd, *J* = 7.5, 1.5 Hz, 1H), 7.22-7.19 (m, 6H), 7.13 (d, *J* = 8.5 Hz, 2H), 7.09-7.08 (m, 3H), 6.95-6.94 (m, 3H), 6.91 (s, 2H), 6.84 (d, *J* = 7.5 Hz, 1H), 6.80-6.76 (m, 1H), 6.64 (d, *J* = 8.5 Hz, 2H), 4.98 (s, 1H), 4.22 (d, *J* = 12.0 Hz, 1H), 4.08 (d, *J* = 12.0 Hz, 1H), 2.89 (s, 6H), 1.87 (s, 3H), 1.30 (s, 18H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$) δ = 205.9, 164.8, 152.3, 149.4, 142.4, 142.0, 141.0, 140.8, 135.5, 135.0, 134.2, 132.0, 132.0, 131.9, 129.8, 129.7, 129.7, 129.6, 129.2, 128.4, 128.4, 127.7, 127.6, 127.4, 126.9, 126.5, 124.3, 124.0, 122.9, 112.8, 69.2, 52.9, 40.5, 34.2, 30.3 ppm.

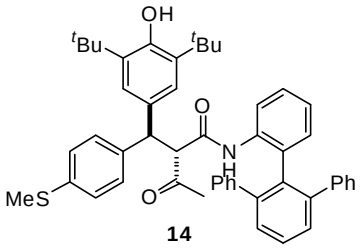
HRMS (ESI+) *m/z* calculated for $C_{51}H_{54}N_2O_3Na$ $[M+Na]^+$ 765.4032, found 765.4031.

$[\alpha]_D^{25}$ = -29.54 (c = 0.71, $CHCl_3$).

IR (Neat) ν_{max} = 3642, 2954, 2877, 1683, 1613, 1586, 1519, 1436, 1354, 1155, 757, 700 cm^{-1}.

HPLC: The enantiomeric excess (% of ee = 88) and diastereomeric ratio (dr = 98:2) were determined by HPLC analysis using Daicel Chiralpak IA-3 column: *n*-hexane:*i*-PrOH = 97:3, flow rate 1.0 mL/min, λ = 254 nm: τ_{minor} = 7.10 min, τ_{major} = 10.68 min.

Compound 14: Prepared according to GP-II, combining *p*-QM **1k** (34.0 mg, 0.1 mmol, 1.0 equiv), amide **2h** (40.5 mg, 0.1 mmol, 1.0 equiv), **3g** (6.3 mg, 0.015 mmol, 15.0 mol%), LiHMDS (12.0 μL, 0.012 mmol, 12.0 mol%) and 4Å MS (70.0 mg) in toluene (0.05 M, 2.0 mL) at -40°C for 24 h. The crude product was purified by column chromatography (SiO_2**,** 10% EtOAc-Hexane, R_f = 0.5 for the product) to afford the title compound **14** (68.0 mg, 91%) as white solid.



14

^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.55-7.44 (m, 2H), 7.39 (d, *J* = 7.2 Hz, 1H), 7.16-7.06 (m, 9H), 7.06-6.97 (m, 4H), 6.91-6.82 (m, 4H), 6.80 (s, 2H), 6.78-6.67 (m, 2H), 4.95 (s, 1H), 4.21 (d, *J* = 12.0 Hz, 1H), 4.02 (d, *J* = 12.0 Hz, 1H), 2.35 (s, 3H), 1.80 (s, 3H), 1.21 (s, 18H) ppm.

^{13}C NMR (75 MHz, $CDCl_3$) δ = 205.1, 164.4, 152.6, 142.4, 142.0, 140.9, 140.7, 138.8, 136.7, 135.8, 134.7, 134.1, 132.2, 132.1, 131.1, 129.8, 129.6, 129.2, 128.4, 128.2, 127.7, 127.4, 127.0, 126.9, 126.5, 124.4, 124.2, 123.0, 68.9, 52.5, 34.2, 30.2, 29.8, 15.8 ppm.

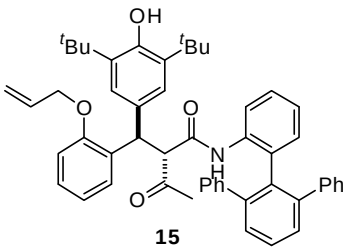
HRMS (ESI+) *m/z* calculated for $C_{50}H_{51}NO_3SNa$ $[M+Na]^+$ 768.3487, found 768.3461.

IR (Neat) ν_{max} = 3623, 3376, 2955, 1693, 1584, 1517, 1434, 1152, 755, 702 cm^{-1}.

$[\alpha]_D^{25}$ = -81.47 (c = 0.54, $CHCl_3$).

HPLC: The enantiomeric excess (% of ee = 98) and diastereomeric ratio (dr = 99:1) were determined by HPLC analysis using Daicel Chiralpak IE-3 column: *n*-hexane:*i*-PrOH = 97:3, flow rate 1.0 mL/min, λ = 254 nm: τ_{minor} = 8.54 min, τ_{major} = 9.86 min.

Compound 15: Prepared according to GP-III, combining *p*-QM **1l** (35.0 mg, 0.1 mmol, 1.0 equiv), amide **2h** (40.5 mg, 0.1 mmol, 1.0 equiv), **3g** (6.3 mg, 0.015 mmol, 15.0 mol%), LiHMDS (12.0 µL, 0.012 mmol, 12.0 mol%) and 4Å MS (70.0 mg) in toluene (0.05 M, 2.0 mL) at -40°C for 24 h. The crude product was purified by column chromatography (SiO_2**,** 10% EtOAc-Hexane, R_f = 0.5 for the product) to afford the title compound **15** (39.0 mg, 52%) as white solid.



15

^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.50 (t, *J* = 7.5 Hz, 1H), 7.44 (d, *J* = 7.5 Hz, 1H), 7.38 (d, *J* = 7.5 Hz, 1H), 7.16 (d, *J* = 7.5 Hz, 1H), 7.09 (s, 5H), 7.04-7.01 (m, 4H), 6.97 (d, *J* = 8.0 Hz, 1H), 6.94 (s, 1H), 6.92 (s, 2H), 6.90-6.83 (m, 3H), 6.81 (t, *J* = 7.5 Hz, 1H), 6.76 (d, *J* = 7.0 Hz, 1H), 6.73-6.68 (m, 2H), 6.00-5.90 (m, 1H), 5.33 (d, *J* = 18.0 Hz, 1H), 5.20 (d, *J* = 11.0 Hz, 1H), 4.89 (s, 1H), 4.87 (d, *J* = 12.0 Hz, 1H), 4.50 (dd, *J* = 13.0, 5.0 Hz, 1H), 4.44 (dd, *J* = 13.0, 5.0 Hz, 1H), 4.17 (d, *J* = 12.0 Hz, 1H), 1.83 (s, 3H), 1.20 (s, 18H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$) δ = 205.1, 164.8, 155.5, 152.2, 142.3, 142.2, 140.9, 140.7, 135.2, 134.8, 134.1, 133.3, 132.1, 132.0, 131.2, 130.4, 129.7, 129.7, 129.5, 129.2, 128.4, 127.8, 127.7, 127.7, 127.6, 127.4, 126.8, 126.5, 124.8, 124.2, 123.0, 120.7, 117.3, 112.3, 68.8, 68.2, 45.6, 34.2, 30.2, 28.9 ppm.

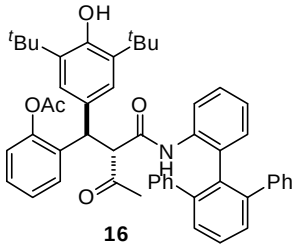
HRMS (ESI+) *m/z* calculated for $C_{52}H_{53}NO_4Na$ $[M+Na]^+$ 778.3872, found 778.3843.

IR (Neat) ν_{max} = 3636, 3395, 2956, 1688, 1584, 1519, 1491, 1439, 1237, 1157, 756, 702 cm^{-1}.

$[\alpha]_D^{25}$ = -93.78 (c = 0.25, $CHCl_3$).

HPLC: The enantiomeric excess (% of ee = 97) and diastereomeric ratio (dr = 96:4) were determined by HPLC analysis using Daicel Chiralpak IE-3 column: *n*-hexane:*i*-PrOH = 98:2, flow rate 1.0 mL/min, λ = 254 nm: τ_{major} = 11.98 min, τ_{minor} = 20.21 min.

Compound 16: Prepared according to GP-III, combining *p*-QM **1m** (35.2 mg, 0.1 mmol, 1.0 equiv), amide **2h** (40.5 mg, 0.1 mmol, 1.0 equiv), **3g** (6.3 mg, 0.015 mmol, 15.0 mol%), LiHMDS (12.0 µL, 0.012 mmol, 12.0 mol%) and 4Å MS (70.0 mg) in toluene (0.05 M, 2.0 mL) at -40°C for 24 h. The crude product was purified by column chromatography (SiO_2**,** 10% EtOAc-Hexane, R_f = 0.5 for the product) to afford the title compound **16** (70.0 mg, 93%) as white solid.



16

^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.59 (t, *J* = 7.5 Hz, 1H), 7.51 (d, *J* = 7.5 Hz, 1H), 7.47 (d, *J* = 7.5 Hz, 1H), 7.29-7.26 (m, 1H), 7.23-7.16 (m, 3H), 7.16-7.11 (m, 3H), 7.11-7.06 (m, 5H), 7.03-6.99 (m, 1H), 6.97 (t, *J* = 7.5 Hz, 1H), 6.94-6.89 (m, 2H), 6.87 (s, 3H), 6.84-6.77 (m, 2H), 5.00 (s, 1H), 4.75 (d, *J* = 12.0 Hz, 1H), 4.02 (d, *J* = 12.0 Hz, 1H), 2.24 (s, 3H), 1.91 (s, 3H), 1.27 (s, 18H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$) δ = 204.4, 168.4, 164.3, 152.5, 148.3, 142.4, 142.4, 140.8, 140.6, 135.6, 134.8, 133.9, 133.5, 132.1, 131.8, 130.4, 129.8, 129.7, 129.5, 129.2, 128.6, 127.7, 127.7, 127.6, 127.5, 126.7, 126.6, 125.9, 124.6, 124.3, 123.3, 122.6, 68.9, 45.1, 34.2, 30.2, 28.3, 21.0, ppm.

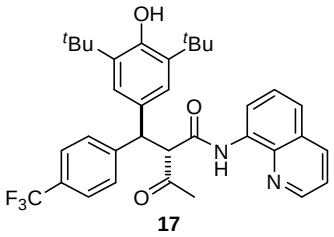
HRMS (ESI+) *m/z* calculated for $C_{51}H_{51}NO_5Na$ $[M+Na]^+$ 780.3665, found 780.3663.

$[\alpha]_D^{25}$ = -62.85 (c = 0.42, $CHCl_3$).

IR (Neat) ν_{max} = 3632, 2961, 2922, 1768, 1688, 1586, 1518, 1437, 1363, 1194, 756, 701 cm^{-1}.

HPLC: The enantiomeric excess (% of ee = 99, major diastereoisomer) and diastereomeric ratio (dr = 93:7) were determined by HPLC analysis using Daicel Chiralpak IE-3 column: *n*-hexane:*i*-PrOH = 97:3, flow rate 0.6 mL/min, λ = 254 nm: τ_{minor} = 11.71 min, τ_{major} = 12.67 min.

Compound 17: Prepared according to GP-III, combining *p*-QM **1n** (36.2 mg, 0.1 mmol, 1.0 equiv), amide **2i** (22.8 mg, 0.1 mmol, 1.0 equiv), **3g** (6.3 mg, 0.015 mmol, 15.0 mol%), LiHMDS (12.0 µL, 0.012 mmol, 12.0 mol%) and 4Å MS (70.0 mg) in toluene (0.05 M, 2.0 mL) at -78°C for 18 h. The crude product was purified by column chromatography (SiO_2**,** 15% EtOAc-Hexane, R_f = 0.4 for the product) to afford the title compound **17** (40.0 mg, 68%, combined yield) as white solid.



17

^{1}H NMR (500 MHz, $CDCl_3$) δ = 9.88 (s, 1H), 8.79 (d, *J* = 4.0 Hz, 1H), 8.56 (dd, *J* = 6.5, 2.5 Hz, 1H), 8.11 (d, *J* = 7.5 Hz, 1H), 7.59 (d, *J* = 8.0 Hz, 2H), 7.52 (d, *J* = 8.0 Hz, 2H), 7.48-7.40 (m, 3H), 7.07 (s, 2H), 4.95 (d, *J* = 12.0 Hz, 1H), 4.86 (s, 1H), 4.51 (d, *J* = 12.0 Hz, 1H), 2.24 (s, 3H), 1.17 (s, 18H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$) δ = 203.8, 165.0, 152.6, 148.3, 145.9, 138.2, 136.1, 136.0, 133.8, 130.6, 129.2, 128.9, 128.2, 127.7, 127.0, 125.8, 125.7, 125.7, 125.6, 125.4, 124.3, 122.7, 121.9, 121.6, 116.3, 69.7, 51.7, 34.1, 29.9, 29.4 ppm.

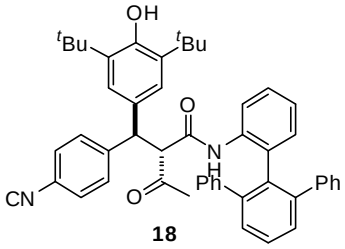
HRMS (ESI+) *m/z* calculated for $C_{35}H_{37}F_3N_2O_3Na$ $[M+Na]^+$ 613.2654, found 613.2656.

IR (Neat) ν_{max} = 3622, 3334, 2955, 1712, 1689, 1530, 1327, 1157, 1116, 1071, 831, 701 cm^{-1}.

$[\alpha]_D^{25}$ = -105.25 (c = 0.38, $CHCl_3$).

HPLC: The enantiomeric excess (% of ee = 98, major diastereoisomer) and diastereomeric ratio (dr = 95:5) were determined by HPLC analysis using Daicel Chiralpak IE-3 column: *n*-hexane:*i*-PrOH = 92:8, flow rate 1.0 mL/min, λ = 254 nm: τ_{minor} = 10.35 min, τ_{major} = 11.71 min.

Compound 18: Prepared according to GP-III, combining *p*-QM **1o** (31.9 mg, 0.1 mmol, 1.0 equiv), amide **2h** (40.5 mg, 0.1 mmol, 1.0 equiv), **3g** (6.3 mg, 0.015 mmol, 15.0 mol%), LiHMDS (12.0 µL, 0.012 mmol, 12.0 mol%) and 4Å MS (70.0 mg) in toluene (0.05 M, 2.0 mL) at -40°C for 24 h. The crude product was purified by column chromatography (SiO_2**,** 10% EtOAc-Hexane, R_f = 0.5 for the product) to afford the title compound **18** (64.0 mg, 89%) as white solid.



18

^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.56-7.43 (m, 4H), 7.40 (dd, *J* = 7.5, 1.5 Hz, 1H), 7.27 (d, *J* = 8.4 Hz, 2H), 7.15-6.99 (m, 8H), 6.91-6.80 (m, 5H), 6.78-6.71 (m, 3H), 5.01 (s, 1H), 4.32 (d, *J* = 12.0 Hz, 1H), 4.04 (d, *J* = 12.0 Hz, 1H), 1.78 (s, 3H), 1.21 (s, 18H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$) δ = 204.0, 163.8, 152.9, 147.5, 142.3, 141.9, 140.8, 140.6, 136.1, 134.3, 134.0, 132.5, 132.2, 129.8, 129.8, 129.7, 129.6, 129.2, 128.5, 128.5, 127.8, 127.7, 127.5, 127.0, 126.6, 124.7, 124.4, 123.2, 118.5, 110.6, 68.5, 52.1, 34.2, 30.1, 29.4 ppm.

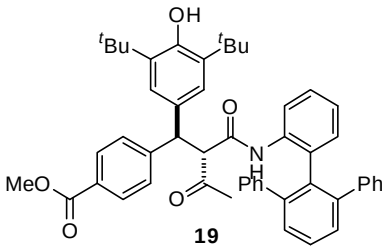
HRMS (ESI+) *m/z* calculated for $C_{50}H_{48}N_2O_3Na$ $[M+Na]^+$ 747.3563, found 747.3561.

IR (Neat) ν_{max} = 3632, 3386, 3058, 2959, 2231, 1689, 1583, 1519, 1439, 1162, 757, 702 cm^{-1}.

$[\alpha]_D^{25}$ = -129.50 (c = 0.21, $CHCl_3$).

HPLC: The enantiomeric excess (% of ee = 99) and diastereomeric ratio (dr = 98:2) were determined by HPLC analysis using Daicel Chiralpak IA-3 column: *n*-hexane:*i*-PrOH = 96:4, flow rate 1.0 mL/min, λ = 254 nm: τ_{minor} = 18.84 min, τ_{major} = 35.34 min.

Compound 19: Prepared according to GP-III, combining *p*-QM **1p** (35.2 mg, 0.1 mmol, 1.0 equiv), amide **2h** (40.5 mg, 0.1 mmol, 1.0 equiv), **3g** (6.3 mg, 0.015 mmol, 15.0 mol%), LiHMDS (12.0 µL, 0.012 mmol, 12.0 mol%) and 4Å MS (70.0 mg) in toluene (0.05 M, 2.0 mL) at -40°C for 14 h. The crude product was purified by column chromatography (SiO_2**,** 10% EtOAc-Hexane, R_f = 0.4 for the product) to afford the title compound **19** (73.0 mg, 96%) as white solid.



19

^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.97 (d, *J* = 8.0 Hz, 2H), 7.61 (t, *J* = 7.5 Hz, 1H), 7.56 (d, *J* = 7.5 Hz, 1H), 7.49 (dd, *J* = 7.5, 1.0 Hz, 1H), 7.35 (d, *J* = 8.0 Hz, 2H), 7.25-7.17 (m, 5H), 7.14-7.09 (m, 3H), 7.08 (s, 1H), 7.00-6.94 (m, 4H), 6.89 (s, 2H), 6.87 (d, *J* = 7.5 Hz, 1H), 6.84-6.80 (m, 1H), 5.08 (s, 1H), 4.42 (d, *J* = 12.0 Hz, 1H), 4.17 (d, *J* = 12.0 Hz, 1H), 3.89 (s, 3H), 1.88 (s, 3H), 1.30 (s, 18H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$) δ = 204.6, 166.7, 164.1, 152.7, 147.0, 142.3, 141.9, 140.8, 140.6, 135.8, 134.5, 134.0, 132.2, 132.1, 130.2, 130.0, 129.7, 129.6, 129.2, 128.6, 128.5, 127.7, 127.7, 127.4, 127.0, 126.6, 124.4, 123.0, 68.6, 52.6, 52.0, 34.2, 30.1, 29.7 ppm.

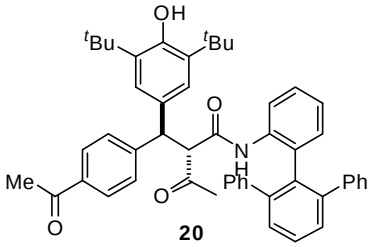
HRMS (ESI+) *m/z* calculated for $C_{51}H_{52}NO_5$ $[M+H]^+$ 758.3845, found 758.3851.

IR (Neat) ν_{max} = 3635, 3386, 2955, 1721, 1688, 1610, 1584, 1519, 1436, 1281, 757, 702 cm^{-1}.

$[\alpha]_D^{25}$ = -116.26 (c = 0.43, $CHCl_3$).

HPLC: The enantiomeric excess (% of ee = 98) and diastereomeric ratio (dr = 98:2) were determined by HPLC analysis using Daicel Chiralpak IC-3 column: *n*-hexane:*i*-PrOH = 97:3, flow rate 1.0 mL/min, λ = 254 nm: τ_{major} = 10.68 min, τ_{minor} = 11.86 min.

Compound 20: Prepared according to GP-III, combining *p*-QM **1q** (33.6 mg, 0.1 mmol, 1.0 equiv), amide **2h** (40.5 mg, 0.1 mmol, 1.0 equiv), **3g** (6.3 mg, 0.015 mmol, 15.0 mol%), LiHMDS (12.0 μL, 0.012 mmol, 12.0 mol%) and 4Å MS (70.0 mg) in toluene (0.05 M, 2.0 mL) at -40°C for 12 h. The crude product was purified by column chromatography (SiO_2**,** 10% EtOAc-Hexane, R_f = 0.5 for the product) to afford the title compound **20** (70.8 mg, 96%) as white solid.



20

^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.88 (d, *J* = 8.0 Hz, 2H), 7.60 (t, *J* = 7.5 Hz, 1H), 7.54 (dd, *J* = 7.5, 1.5 Hz, 1H), 7.47 (d, *J* = 7.5 Hz, 1H), 7.35 (d, *J* = 8.0 Hz, 2H), 7.20-7.17 (m, 5H), 7.10-7.09 (m, 3H), 7.02 (s, 1H), 6.98-6.95 (m, 4H), 6.87 (s, 2H), 6.86-6.79 (m, 2H), 5.06 (s, 1H), 4.41 (d, *J* = 12.0 Hz, 1H), 4.16 (d, *J* = 12.0 Hz, 1H), 2.55 (s, 3H), 1.87 (s, 3H), 1.29 (s, 18H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$) δ = 204.6, 197.5, 164.1, 152.8, 147.4, 142.4, 141.9, 140.8, 140.6, 135.9, 135.6, 134.5, 134.0, 132.3, 132.1, 130.2, 129.8, 129.6, 129.2, 128.8, 128.5, 127.9, 127.7, 127.7, 127.5, 127.0, 126.6, 124.5, 124.4, 123.1, 68.6, 52.5, 34.2, 30.2, 29.6, 26.5 ppm.

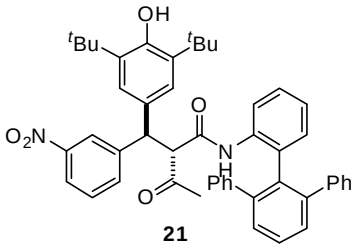
HRMS (ESI+) *m/z* calculated for $C_{51}H_{51}NO_4Na$ $[M+Na]^+$ 764.3716, found 764.3714.

IR (Neat) ν_{max} = 3635, 3392, 2958, 1685, 1607, 1520, 1439, 1269, 758, 702 cm^{-1}.

$[\alpha]_D^{25}$ = -98.87(c = 0.36, $CHCl_3$).

HPLC: The enantiomeric excess (% of ee = 99) and diastereomeric ratio (dr = 99:1) were determined by HPLC analysis using Daicel Chiralpak IA-3 column: *n*-hexane:*i*-PrOH = 92:8, flow rate 1.0 mL/min, λ = 254 nm: τ_{major} = 10.41 min, τ_{minor} = 14.19 min.

Compound 21: Prepared according to GP-III, combining *p*-QM **1r** (33.9 mg, 0.1 mmol, 1.0 equiv), amide **2h** (40.5 mg, 0.1 mmol, 1.0 equiv), **3g** (6.3 mg, 0.015 mmol, 15.0 mol%), LiHMDS (12.0 μL, 0.012 mmol, 12.0 mol%) and 4Å MS (70.0 mg) in toluene (0.05 M, 2.0 mL) at -40°C for 12 h. The crude product was purified by column chromatography (SiO_2**,** 10% EtOAc-Hexane, R_f = 0.4 for the product) to afford the



21

title compound **21** (66.4 mg, 89%, combined yield) as white solid.

^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.07 (t, *J* = 1.8 Hz, 1H), 7.97 (dd, *J* = 8.4, 1.2 Hz, 1H), 7.57-7.45 (m, 3H), 7.43-7.35 (m, 2H), 7.18-7.08 (m, 5H), 7.07-7.01 (m, 3H), 6.94-6.84 (m, 4H), 6.82-6.73 (m, 5H), 5.03 (s, 1H), 4.37 (d, *J* = 12.0 Hz, 1H), 4.10 (d, *J* = 12.0 Hz, 1H), 1.80 (s, 3H), 1.22 (s, 18H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$) δ = 203.9, 163.8, 153.0, 148.4, 144.4, 142.4, 141.8, 140.9, 140.6, 136.2, 134.3, 134.1, 133.8, 132.7, 132.2, 129.8, 129.8, 129.7, 129.6, 129.2, 128.5, 127.8, 127.8, 127.5, 127.1, 126.7, 124.8, 124.5, 123.5, 122.6, 121.8, 68.6, 51.8, 34.3, 30.2, 29.5 ppm.

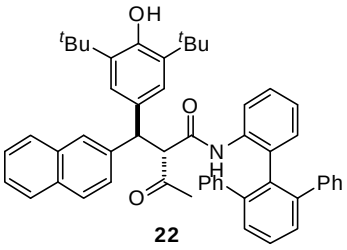
HRMS (ESI+) *m/z* calculated for $C_{49}H_{49}N_2O_5$ $[M+H]^+$ 745.3641, found 745.3639.

IR (Neat) ν_{max} = 3632, 3389, 3058, 2958, 1689, 1586, 1530, 1439, 1350, 758, 702 cm^{-1}.

$[\alpha]_D^{25}$ = -68.99 (c = 0.40, $CHCl_3$).

HPLC: The enantiomeric excess (% of ee = 98, major diastereoisomer) and diastereomeric ratio (dr = 95:5) were determined by HPLC analysis using Daicel Chiralpak IA-3 column: *n*-hexane:*i*-PrOH = 95:5, flow rate 1.0 mL/min, λ = 254 nm: τ_{minor} = 8.53 min, τ_{major} = 24.75 min.

Compound 22: Prepared according to GP-III, combining *p*-QM **1s** (34.4 mg, 0.1 mmol, 1.0 equiv), amide **2h** (40.5 mg, 0.1 mmol, 1.0 equiv), **3g** (6.3 mg, 0.015 mmol, 15.0 mol%), LiHMDS (12.0 μL, 0.012 mmol, 12.0 mol%) and 4Å MS (70.0 mg) in toluene (0.05 M, 2.0 mL) at -40°C for 24 h. The crude product was purified by column chromatography (SiO_2**,** 10% EtOAc-Hexane, R_f = 0.5 for the product) to afford the title compound **22** (72.0 mg, 96%) as white solid.



22

^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.72 (d, *J* = 8.0 Hz, 1H), 7.68 (d, *J* = 8.0 Hz, 2H), 7.60 (s, 1H), 7.55-7.46 (m, 2H), 7.43-7.30 (m, 4H), 7.16-7.07 (m, 6H), 7.04-7.00 (m, 3H), 6.94-6.84 (m, 6H), 6.77 (d, *J* = 7.0 Hz, 1H), 6.72 (t, *J* = 7.0 Hz, 1H), 4.95 (s, 1H), 4.44 (d, *J* = 12.0 Hz, 1H), 4.18 (d, *J* = 12.0 Hz, 1H), 1.79 (s, 3H), 1.21 (s, 18H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$) δ = 205.2, 164.5, 152.6, 142.4, 142.0, 140.9, 140.7, 139.2, 135.7, 134.7, 134.1, 133.4, 132.3, 132.1, 132.1, 131.0, 129.8, 129.6, 129.2, 128.5, 127.8, 127.7, 127.7, 127.5, 127.4, 127.0, 126.5, 126.1, 126.1, 125.7, 124.5, 124.3, 122.9, 68.9, 53.2, 34.2, 30.2, 29.9 ppm.

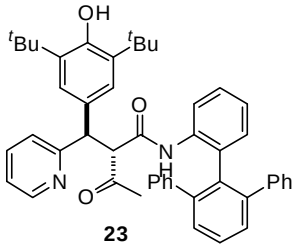
HRMS (ESI+) *m/z* calculated for $C_{53}H_{52}NO_3$ $[M+H]^+$ 750.3947, found 750.3943.

IR (Neat) ν_{max} = 3634, 3386, 3058, 2958, 1688, 1584, 1519, 1439, 1236, 1155, 757, 702 cm^{-1}.

$[\alpha]_D^{25}$ = -81.91 (c = 0.83, $CHCl_3$).

HPLC: The enantiomeric excess (% of ee = 99) and diastereomeric ratio (dr = 98:2) were determined by HPLC analysis using Daicel Chiralpak IA-3 column: *n*-hexane:*i*-PrOH = 98:2, flow rate 0.6 mL/min, λ = 254 nm: τ_{minor} = 19.28 min, τ_{major} = 39.27 min.

Compound 23: Prepared according to GP-III, combining *p*-QM **1t** (29.4 mg, 0.1 mmol, 1.0 equiv), amide **2h** (40.5 mg, 0.1 mmol, 1.0 equiv), **3g** (6.3 mg, 0.015 mmol, 15.0 mol%), LiHMDS (12.0 μL, 0.012 mmol, 12.0 mol%) and 4Å MS (70.0 mg) in toluene (0.05 M, 2.0 mL) at -40°C for 13 h. The crude product was purified by column chromatography (SiO_2**,** 10% EtOAc-Hexane, R_f = 0.4 for the product) to afford the title compound **23** (63.0 mg, 90%, combined yield) as white solid.



23

^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.33 (d, *J* = 4.4 Hz, $1H_{major}$), 8.14 (d, *J* = 4.4 Hz, $1H_{minor}$), 7.69-7.50 (m, 8H, $4H_{major}$, $4H_{minor}$), 7.50-7.41 (m, 2H, $1H_{major}$, $1H_{minor}$), 7.38-7.29 (m, 4H, $2H_{major}$, $2H_{minor}$), 7.25-7.22 (m, 4H, $2H_{major}$, $2H_{minor}$), 7.19 (s, 2H, $1H_{major}$, $1H_{minor}$), 7.16-7.07 (m, 8H, $4H_{major}$, $4H_{minor}$), 7.07-6.89 (m, 10H, $5H_{major}$, $5H_{minor}$), 6.89-6.72 (m, 8H, $4H_{major}$, $4H_{minor}$), 5.07 (s, $1H_{minor}$), 5.06 (s, $1H_{major}$), 4.61 (d, *J* = 10.4 Hz, $1H_{major}$), 4.54 (s, 2H, $1H_{major}$, $1H_{minor}$), 4.44 (d, *J* = 10.4 Hz, $1H_{major}$), 2.07 (s, $3H_{major}$), 1.83 (s, $3H_{minor}$), 1.40 (s, $18H_{minor}$), 1.27 (s, $18H_{major}$) ppm.

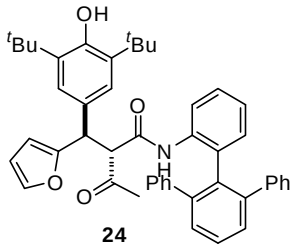
^{13}C NMR (125 MHz, $CDCl_3$) δ = 205.7, 204.1, 165.5, 165.0, 161.2, 160.3, 152.7, 148.8, 148.0, 142.9, 142.6, 142.1, 141.7, 141.1, 140.9, 140.8, 140.7, 136.3, 135.8, 135.6, 135.1, 134.9, 134.5, 134.3, 132.3, 132.1, 131.9, 130.8, 130.6, 130.5, 129.9, 129.8, 129.8, 129.5, 129.3, 129.1, 128.5, 128.4, 127.8, 127.8, 127.7, 127.6, 127.4, 127.0, 126.9, 126.6, 126.5, 125.2, 125.0, 124.1, 124.1, 123.8, 123.6, 123.1, 121.6, 121.4, 121.3, 67.1, 66.9, 53.7, 53.3, 34.3, 34.2, 30.2, 30.2, 29.7 ppm.

HRMS (ESI+) *m/z* calculated for $C_{48}H_{49}N_2O_3$ $[M+H]^+$ 701.3743, found 701.3742.

IR (Neat) ν_{max} = 3632, 3389, 2957, 1687, 1585, 1520, 1433, 1159, 757, 702 cm^{-1}.

HPLC: The enantiomeric excess (% of ee = 98, major diastereoisomer) and diastereomeric ratio (dr = 78:22) were determined by HPLC analysis using Daicel Chiralpak IE-3 column: *n*-hexane:*i*-PrOH = 96:4, flow rate 1.0 mL/min, λ = 254 nm: τ_{minor} = 16.68 min, τ_{major} = 21.30 min.

Compound 24: Prepared according to GP-III, combining *p*-QM **1u** (28.4 mg, 0.1 mmol, 1.0 equiv), amide **2h** (40.5 mg, 0.1 mmol, 1.0 equiv), **3g** (6.3 mg, 0.015 mmol, 15.0 mol%), LiHMDS (12.0 µL, 0.012 mmol, 12.0 mol%) and 4Å MS (70.0 mg) in toluene (0.05 M, 2.0 mL) at -40°C for 24 h. The crude product was purified by column chromatography (SiO_2**,** 10% EtOAc-Hexane, R_f = 0.5 for the product) to afford the title compound **24** (61.0 mg, 88%, combined yield) as white solid.



24

^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.58-7.45 (m, 4H, $2H_{major}$, $2H_{minor}$), 7.41-7.36 (m, 2H, $1H_{major}$, $1H_{minor}$), 7.25-7.18 (m, 6H, $3H_{major}$, $3H_{minor}$), 7.17-7.05 (m, 8H, $4H_{major}$, $4H_{minor}$), 7.03-6.92 (m, 6H, $3H_{major}$, $3H_{minor}$), 6.90-6.84 (m, 4H, $2H_{major}$, $2H_{minor}$), 6.83-6.75 (m, 8H, $4H_{major}$, $4H_{minor}$), 6.75-6.69 (m, 2H, $1H_{major}$, $1H_{minor}$), 6.18 (dd, *J* = 3.0, 1.5 Hz, $1H_{major}$), 6.02 (dd, *J* = 3.0, 1.5 Hz, $1H_{minor}$), 5.98 (d, *J* = 3.0 Hz, $1H_{major}$), 5.70 (d, *J* = 3.0 Hz, $1H_{minor}$), 5.05 (s, $1H_{minor}$), 5.02 (s, $1H_{major}$), 4.33 (d, *J* = 12.0 Hz, $1H_{major}$), 4.22 (d, *J* = 12.0 Hz, $1H_{minor}$), 4.01 (d, *J* = 12.0 Hz, $1H_{minor}$), 3.88 (d, *J* = 12.0 Hz, $1H_{major}$), 1.89 (s, $3H_{major}$), 1.66 (s, $3H_{minor}$), 1.34 (s, $18H_{minor}$), 1.23 (s, $18H_{major}$) ppm.

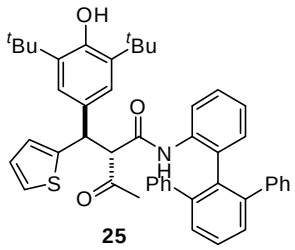
^{13}C NMR (125 MHz, $CDCl_3$) δ = 205.6, 163.9, 154.4, 152.9, 142.7, 142.4, 141.9, 141.8, 141.7, 141.0, 140.9, 140.7, 136.0, 135.7, 134.7, 134.1, 132.1, 131.8, 129.9, 129.8, 129.7, 129.5, 129.3, 129.1, 128.7, 128.5, 127.8, 127.7, 127.6, 127.4, 127.0, 126.5, 124.8, 124.7, 124.2, 122.8, 110.3, 106.7, 67.8, 47.1, 34.3, 34.2, 30.2, 29.5 ppm.

HRMS (ESI+) *m/z* calculated for $C_{47}H_{47}NO_4Na$ $[M+Na]^+$ 712.3403, found 712.3401.

IR (Neat) ν_{max} = 3632, 3382, 2957, 1690, 1585, 1520, 1437, 1156, 757, 702 cm^{-1}.

HPLC: The enantiomeric excess (% of ee = 97, major diastereoisomer) and diastereomeric ratio (dr = 6:1) were determined by HPLC analysis using Daicel Chiralpak IE-3 column: *n*-hexane:*i*-PrOH = 97:3, flow rate 1.0 mL/min, λ = 254 nm: τ_{minor} = 8.11 min, τ_{major} = 9.89 min.

Compound 25: Prepared according to GP-III, combining *p*-QM **1v** (30.0 mg, 0.1 mmol, 1.0 equiv), amide **2h** (40.5 mg, 0.1 mmol, 1.0 equiv), **3g** (6.3 mg, 0.015 mmol, 15.0 mol%), LiHMDS (12.0 µL, 0.012 mmol, 12.0 mol%) and 4Å MS (70.0 mg) in toluene (0.05 M, 2.0 mL) at -40°C for 24 h. The crude product was purified by column chromatography (SiO_2**,** 10% EtOAc-Hexane, R_f = 0.5 for the product) to afford the title compound **25**



25

(38.0 mg, 54%) as white solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.54-7.51 (m, 2H), 7.39-7.38 (m, 1H), 7.23 (d, *J* = 7.5 Hz, 2H), 7.19-7.13 (m, 5H), 7.07-7.04 (m, 1H), 7.01-7.00 (m, 3H), 6.88-6.78 (m, 7H), 6.74-6.69 (m, 2H), 5.01 (s, 1H), 4.49 (d, *J* = 11.5 Hz, 1H), 3.97 (d, *J* = 11.5 Hz, 1H), 1.85 (s, 3H), 1.24 (s, 18H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$) δ = 205.4, 163.9, 152.9, 145.3, 145.2, 144.7, 142.4, 141.8, 141.0, 140.8, 135.8, 134.6, 134.2, 132.3, 132.1, 130.4, 129.8, 129.8, 129.2, 128.4, 127.8, 127.6, 127.4, 127.1, 126.6, 126.5, 124.9, 124.6, 124.3, 124.2, 123.3, 70.2, 48.9, 34.2, 30.2 ppm.

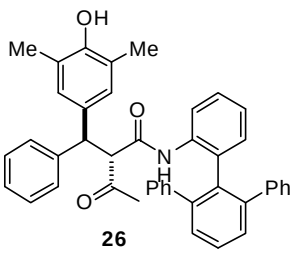
HRMS (ESI+) *m/z* calculated for $C_{47}H_{47}NO_3SNa$ $[M+Na]^+$ 728.3174, found 728.3162.

IR (Neat) ν_{max} = 3634, 3379, 2957, 1687, 1584, 1519, 1438, 1156, 757, 701 cm^{-1}.

$[\alpha]_D^{25}$ = -60.62 (c = 0.64, $CHCl_3$).

HPLC: The enantiomeric excess (% of ee = 98) and diastereomeric ratio (dr = 97:3) were determined by HPLC analysis using Daicel Chiralpak IE-3 column: *n*-hexane:*i*-PrOH = 97:3, flow rate 0.7 mL/min, λ = 254 nm: τ_{minor} = 10.91 min, τ_{major} = 13.23 min.

Compound 26: Prepared according to GP-III, combining *p*-QM **1w** (21.0 mg, 0.1 mmol, 1.0 equiv), amide **2h** (40.5 mg, 0.1 mmol, 1.0 equiv), **3g** (6.3 mg, 0.015 mmol, 15.0 mol%), LiHMDS (12.0 μL, 0.012 mmol, 12.0 mol%) and 4Å MS (70.0 mg) in toluene (0.05 M, 2.0 mL) at -40°C for 24 h. The crude product was purified by column chromatography (SiO_2**,** 15% EtOAc-Hexane, R_f = 0.5 for the product) to afford the title compound **26** (59.0 mg, 96%) as white solid.



26

^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.56 (t, *J* = 7.5 Hz, 1H), 7.49 (d, *J* = 7.5 Hz, 1H), 7.44 (d, *J* = 7.5 Hz, 1H), 7.26 (d, *J* = 8.5 Hz, 1H), 7.19-7.16 (m, 3H), 7.14-7.08 (m, 6H), 7.06-7.01 (m, 5H), 6.92-6.88 (m, 3H), 6.76 (dd, *J* = 7.5, 1.5 Hz, 1H), 6.71 (t, *J* = 7.5 Hz, 1H), 6.50 (s, 2H), 4.34 (s, 1H), 4.179 (d, *J* = 12.5 Hz, 1H), 4.07 (d, *J* = 12.5 Hz, 1H), 1.89 (s, 6H), 1.84 (s, 3H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$) δ = 205.0, 164.3, 151.0, 142.5, 142.0, 141.6, 140.7, 140.5, 134.8, 134.0, 132.0, 132.0, 131.1, 129.8, 129.8, 129.5, 129.2, 128.7, 128.5, 127.8, 127.6, 127.6, 127.5, 126.8, 126.8, 126.6, 123.9, 123.0, 121.6, 68.4, 52.0, 30.1, 15.8 ppm.

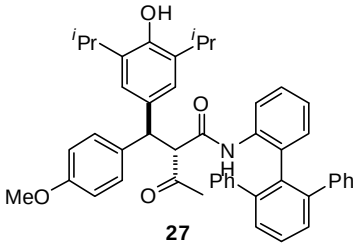
HRMS (ESI+) *m/z* calculated for $C_{43}H_{37}NO_3Na$ $[M+Na]^+$ 638.2671, found 638.2673.

IR (Neat) ν_{max} = 3379, 3068, 3022, 1682, 1584, 1521, 1490, 1447, 1200, 757, 701 cm^{-1}.

[α]$_D^{25}$ = -79.01 (c = 0.41, $CHCl_3$).

HPLC: The enantiomeric excess (% of ee = 92) and diastereomeric ratio (dr = 99:1) were determined by HPLC analysis using Daicel Chiralpak IA-3 column: *n*-hexane:*i*-PrOH = 92:8, flow rate 1.0 mL/min, λ = 254 nm: τ_{minor} = 14.26 min, τ_{major} = 20.00 min.

Compound 27: Prepared according to GP-III, combining *p*-QM **1x** (29.6 mg, 0.1 mmol, 1.0 equiv), amide **2h** (40.5 mg, 0.1 mmol, 1.0 equiv), **3g** (6.3 mg, 0.015 mmol, 15.0 mol%), LiHMDS (12.0 μL, 0.012 mmol, 12.0 mol%) and 4Å MS (70.0 mg) in toluene (0.05 M, 2.0 mL) at -78°C for 17 h. The crude product was purified by column chromatography (SiO_2**,** 10% EtOAc-Hexane, R_f = 0.45 for the product) to afford the title compound **27** (66.0 mg, 94%) as white solid.



27

^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.57-7.45 (m, 2H), 7.39 (d, *J* = 7.2 Hz, 1H), 7.15-7.05 (m, 8H), 7.05-6.98 (m, 4H), 6.89-6.78 (m, 3H), 6.77-6.65 (m, 6H), 4.57 (s, 1H), 4.23 (d, *J* = 12.0 Hz, 1H), 3.99 (d, *J* = 12.0 Hz, 1H), 3.67 (s, 3H), 2.96-2.84 (m, 2H), 1.81 (s, 3H), 1.05 (d, *J* = 6.8 Hz, 6H), 0.98 (d, *J* = 6.8 Hz, 6H) ppm.

^{13}C NMR (75 MHz, $CDCl_3$) δ = 205.5, 164.5, 158.3, 148.7, 142.5, 141.9, 140.9, 140.6, 134.8, 134.0, 133.8, 133.5, 132.8, 132.0, 131.3, 129.8, 129.8, 129.6, 129.2, 128.7, 128.5, 127.7, 127.6, 127.4, 126.9, 126.5, 123.9, 123.0, 122.2, 114.1, 69.3, 55.1, 52.3, 30.0, 27.2, 22.6, 22.6 ppm.

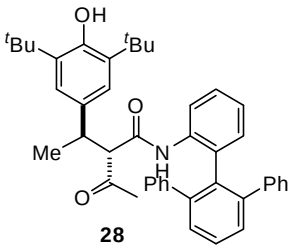
HRMS (ESI+) *m/z* calculated for $C_{48}H_{48}NO_4$ $[M+H]^+$ 702.3583, found 702.3590.

IR (Neat) ν_{max} = 3374, 2960, 1681, 1583, 1510, 1441, 1177, 756, 701 cm^{-1}.

[α]$_D^{25}$ = -64.63 (c = 0.63, $CHCl_3$).

HPLC: The enantiomeric excess (% of ee = 89) and diastereomeric ratio (dr = 98:2) were determined by HPLC analysis using Daicel Chiralpak IA-3 column: *n*-hexane:*i*-PrOH = 94:6, flow rate 1.0 mL/min, λ = 254 nm: τ_{minor} = 9.59 min, τ_{major} = 27.42 min.

Compound 28: Prepared according to GP-III, combining *p*-QM **1y** (23.2 mg, 0.1 mmol, 1.0 equiv), amide **2h** (40.5 mg, 0.1 mmol, 1.0 equiv), **3g** (6.3 mg, 0.015 mmol, 15.0 mol%), LiHMDS (12.0 μL, 0.012 mmol, 12.0 mol%) and 4Å MS (70.0 mg) in toluene (0.05 M, 2.0 mL) at -78°C for 18 h. The crude product was purified by column chromatography (SiO_2**,** 10%



28

EtOAc-Hexane, R_f = 0.4 for the product) to afford the title compound **28** (42.0 mg, 66%; combined yield) as white solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.05 (s, $1H_{minor}$), 7.81 (d, *J* = 8.0 Hz, $1H_{minor}$), 7.65-7.57 (m, $3H_{major+minor}$), 7.57-7.53 (m, $2H_{major+minor}$), 7.46 (dd, *J* = 7.5, 1.5 Hz, $1H_{major}$), 7.26-7.22 (m, $2H_{major+minor}$), 7.22-7.16 (m, $9H_{major+minor}$), 7.16-7.12 (m, $2H_{major+minor}$), 7.11-7.04 (m, $7H_{major+minor}$), 6.98-6.92 (m, $2H_{major+minor}$), 6.92-6.87 (m, $4H_{major+minor}$), 6.87-6.77 (m, $6H_{major+minor}$), 5.11 (s, $1H_{minor}$), 5.06 (s, $1H_{major}$), 3.49 (d, *J* = 11.5 Hz, $1H_{minor}$), 3.39 (d, *J* = 10.0 Hz, $1H_{major}$), 3.27-3.20 (m, $1H_{major}$), 2.97-2.87 (m, $1H_{minor}$), 2.02 (s, $3H_{major}$), 1.58 (s, $3H_{minor}$), 1.43 (s, $18H_{minor}$), 1.33 (s, $18H_{major}$), 1.20 (d, *J* = 7.0 Hz, $3H_{major}$), 1.10 (d, *J* = 7.0 Hz, $3H_{minor}$) ppm.

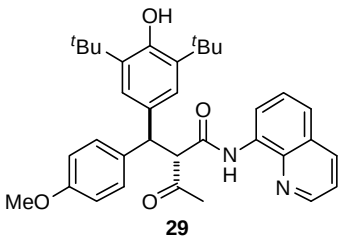
^{13}C NMR (100 MHz, $CDCl_3$) δ = 208.0, 206.9, 165.6, 165.0, 152.6, 152.5, 142.8, 142.4, 142.0, 142.0, 140.9, 140.9, 140.8, 140.7, 136.1, 135.7, 135.5, 134.9, 134.2, 134.1, 133.0, 132.8, 132.4, 132.1, 131.8, 131.1, 129.9, 129.8, 129.7, 129.6, 129.5, 129.3, 129.1, 128.6, 128.4, 127.7, 127.7, 127.6, 127.6, 127.4, 126.9, 126.8, 126.6, 126.5, 124.1, 123.7, 123.7, 123.5, 122.8, 121.3, 70.4, 69.6, 44.3, 42.0, 34.3, 34.2, 30.3, 30.2, 20.0, 19.2 ppm.

HRMS (ESI+) *m/z* calculated for $C_{44}H_{47}NO_3Na$ $[M+Na]^+$ 660.3453, found 660.3454.

IR (Neat) ν_{max} = 3645, 2957, 1683, 1584, 1520, 1435, 1233, 1157, 756, 700 cm^{-1}.

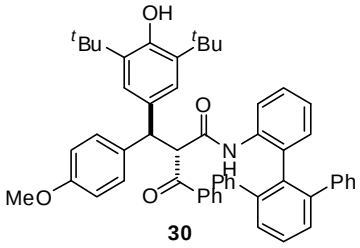
HPLC: The enantiomeric excess (% of ee = 96, minor diastereoisomer and 70, major diastereoisomer) and diastereomeric ratio (dr = 54:46) were determined by HPLC analysis using Daicel Chiralpak IA-3 column: *n*-hexane:*i*-PrOH = 98:2, flow rate 1.0 mL/min, λ = 254 nm: τ_{major} = 8.61 min, τ_{minor} = 9.23 min for minor diastereoisomer and τ_{minor} = 6.54 min, τ_{major} = 7.24 min for major diastereoisomer.

Compound 29: Prepared according to GP-III, combining *p*-QM **1a** (32.4 mg, 0.1 mmol, 1.0 equiv), amide **2i** (22.8 mg, 0.1 mmol, 1.0 equiv), **3g** (6.3 mg, 0.015 mmol, 15.0 mol%), LiHMDS (12.0 µL, 0.012 mmol, 12.0 mol%) and 4Å MS (70.0 mg) in toluene (0.05 M, 2.0 mL) at -40°C for 24 h. The crude product was purified by column chromatography (SiO_2**,** 20% EtOAc-Hexane, R_f = 0.45 for the product) to afford the title compound **29** containing 98:2 mixture of two diastereomers (confirmed by HPLC analysis) with combined yield (47.0 mg, 85%) and 97% ee as white solid.



29

Compound 30: Prepared according to GP-III, combining *p*-QM **1a** (32.4 mg, 0.1 mmol, 1.0 equiv), amide **2j** (46.8 mg, 0.1 mmol, 1.0 equiv), **3g** (6.3 mg, 0.015 mmol, 15.0 mol%), LiHMDS (12.0 µL, 0.012 mmol, 12.0 mol%) and 4Å MS (70.0 mg) in toluene (0.05 M, 2.0 mL) at -40°C for 24 h. The crude product was purified by column chromatography (SiO_2**,** 10% EtOAc-Hexane, R_f = 0.5 for the product) to afford the title compound **30** (60.0 mg, 76%) as white solid.



30

^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.69 (d, *J* = 8.0 Hz, 2H), 7.54-7.45 (m, 2H), 7.34-7.28 (m, 4H), 7.25-7.19 (m, 5H), 7.19-7.15 (m, 2H), 6.88-6.73 (m, 9H), 6.72-6.65 (m, 1H), 6.63 (d, *J* = 8.5 Hz, 2H), 6.50 (d, *J* = 7.5 Hz, 2H), 4.98-4.91 (m, 2H), 4.38 (d, *J* = 12.0 Hz, 1H), 3.61 (s, 3H), 1.22 (s, 18H) ppm.

^{13}C NMR (75 MHz, $CDCl_3$) δ = 197.2, 164.2, 157.9, 152.5, 142.6, 141.3, 140.7, 140.7, 136.3, 135.4, 134.5, 134.4, 134.2, 133.6, 131.9, 131.9, 131.4, 129.8, 129.7, 129.7, 129.0, 128.5, 128.5, 128.4, 128.1, 127.8, 127.3, 127.2, 127.2, 126.1, 124.8, 123.9, 122.9, 113.9, 63.7, 55.1, 52.5, 34.2, 30.2 ppm.

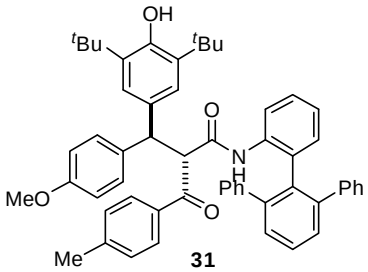
HRMS (ESI+) *m/z* calculated for $C_{55}H_{53}NO_4Na$ $[M+Na]^+$ 814.3872, found 814.3870.

IR (Neat) ν_{max} = 3622, 3357, 2954, 2925, 1693, 1674, 1583, 1512, 1439, 1237, 757, 703 cm^{-1}.

$[\alpha]_D^{25}$ = -171.98 (c = 0.40, $CHCl_3$).

HPLC: The enantiomeric excess (% of ee = 90) and diastereomeric ratio (dr = 99:1) were determined by HPLC analysis using Daicel Chiralpak IE-3 column: *n*-hexane:*i*-PrOH = 97:3, flow rate 1.0 mL/min, λ = 254 nm: τ_{minor} = 7.45 min, τ_{major} = 11.61 min.

Compound 31: Prepared according to GP-III, combining *p*-QM **1a** (32.4 mg, 0.1 mmol, 1.0 equiv), amide **2k** (48.2 mg, 0.1 mmol, 1.0 equiv), **3g** (6.3 mg, 0.015 mmol, 15.0 mol%), LiHMDS (12.0 µL, 0.012 mmol, 12.0 mol%) and 4Å MS (70.0 mg) in toluene (0.05 M, 2.0 mL) at -40°C for 24 h. The crude product was purified by column chromatography (SiO_2**,** 10% EtOAc-Hexane, R_f = 0.5 for the product) to afford the title compound **31** (56.0 mg, 70%) as white solid.



31

^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.60 (d, *J* = 8.0 Hz, 2H), 7.53-7.46 (m, 2H), 7.35 (s, 1H), 7.31 (d, *J* = 7.5 Hz, 2H), 7.25-7.15 (m, 4H), 7.06 (d, *J* = 8.0 Hz, 2H), 7.01 (d, *J* = 8.0 Hz, 2H), 6.89-6.81 (m, 3H), 6.80-6.73 (m, 5H), 6.71-6.65 (m, 1H), 6.63 (d, *J* = 7.5 Hz, 2H), 6.50 (d, *J* = 7.0 Hz, 2H), 4.95-4.89 (m, 2H, OH, CH-aliphatic), 4.38 (d, *J* = 11.5 Hz, 1H), 3.61 (s, 3H), 2.18 (s, 3H, CH_3), 1.21 (s, 18H) ppm.

^{13}C NMR (75 MHz, $CDCl_3$) δ = 196.8, 164.3, 157.9, 152.5, 144.6, 142.6, 141.3, 140.8, 140.7, 135.4, 134.6, 134.5, 134.2, 133.9, 131.9, 131.7, 131.5, 129.9, 129.7, 129.7, 129.1, 129.0, 128.7, 128.4, 128.1, 127.8, 127.2, 127.1, 126.1, 124.8, 123.7, 122.8, 113.9, 63.4, 55.1, 52.5, 34.2, 30.2, 21.5 ppm.

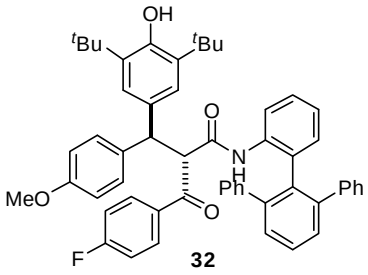
HRMS (ESI+) *m/z* calculated for $C_{56}H_{55}NO_4Na$ $[M+Na]^+$ 828.4029, found 828.4028.

IR (Neat) ν_{max} = 3619, 3366, 2961, 2923, 1690, 1670, 1511, 1436, 1236, 1179, 756, 704 cm^{-1}.

$[\alpha]_D^{25}$ = -113.54 (c = 0.31, $CHCl_3$).

HPLC: The enantiomeric excess (% of ee = 79) and diastereomeric ratio (dr = 99:1) were determined by HPLC analysis using Daicel Chiralpak ID-3 column: *n*-hexane:*i*-PrOH = 97:3, flow rate 1.0 mL/min, λ = 280 nm: τ_{minor} = 7.55 min, τ_{major} = 8.44 min.

Compound 32: Prepared according to GP-III, combining *p*-QM **1a** (32.4 mg, 0.1 mmol, 1.0 equiv), amide **2l** (48.6 mg, 0.1 mmol, 1.0 equiv), **3g** (6.3 mg, 0.015 mmol, 15.0 mol%), LiHMDS (12.0 µL, 0.012 mmol, 12.0 mol%) and 4Å MS (70.0 mg) in toluene (0.05 M, 2.0 mL) at -40°C for 24 h. The crude product was purified by column chromatography (SiO_2, 10% EtOAc-Hexane, R_f = 0.5 for the product) to afford the title compound **32** (66.0 mg, 81%) as white solid.



32

^{1}H NMR (500 MHz, $CDCl_3$) δ = 7.82 (dd, *J* = 8.5, 5.5 Hz, 2H), 7.61-7.53 (m, 2H), 7.39 (d, *J* = 7.0 Hz, 2H), 7.34-7.27 (m, 4H), 7.14 (d, *J* = 8.5 Hz, 2H), 6.96 (t, *J* = 7.5 Hz, 3H), 6.90 (t, *J* = 7.5 Hz, 3H), 6.87-6.82 (m, 4H), 6.78 (t, *J* = 7.5 Hz, 1H), 6.73 (d, *J* = 8.0 Hz, 2H), 6.61 (d, *J* = 7.5 Hz, 2H), 5.03 (s, 1H), 4.98 (d, *J* = 12.0 Hz, 1H), 4.45 (d, *J* = 12.0 Hz, 1H), 3.70 (s, 3H), 1.30 (s, 18H) ppm.

^{13}C NMR (75 MHz, $CDCl_3$) δ = 195.4, 164.2, 158.0, 152.5, 142.5, 141.3, 140.7, 135.5, 134.4, 134.2, 132.7, 132.7, 132.1, 131.9, 131.4, 131.3, 129.8, 129.7, 129.7, 128.9, 128.4, 128.1, 127.8, 127.3, 127.3, 126.2, 124.7, 124.1, 123.2, 115.7, 115.4, 113.9, 63.7, 55.1, 52.3, 34.2, 30.2 ppm.

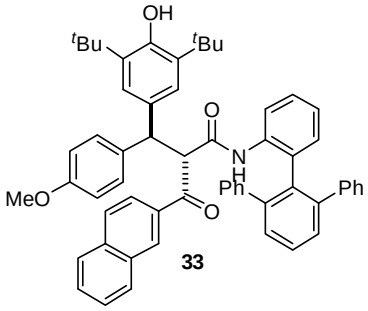
HRMS (ESI+) *m/z* calculated for $C_{55}H_{52}FNO_4Na$ $[M+Na]^+$ 832.3778, found 832.3779.

IR (Neat) ν_{max} = 3619, 3372, 2961, 2922, 1693, 1674, 1599, 1512, 1436, 1236, 756, 703 cm^{-1}.

$[\alpha]_D^{25}$ = -172.92 (c = 0.34, $CHCl_3$).

HPLC: The enantiomeric excess (% of ee = 94) and diastereomeric ratio (dr = 99:1) were determined by HPLC analysis using Daicel Chiralpak IE-3 column: *n*-hexane:*i*-PrOH = 97:3, flow rate 1.0 mL/min, λ = 254 nm: τ_{minor} = 5.89 min, τ_{major} = 9.38 min.

Compound 33: Prepared according to GP-III, combining *p*-QM **1a** (32.4 mg, 0.1 mmol, 1.0 equiv), amide **2m** (51.8 mg, 0.1 mmol, 1.0 equiv), **3g** (6.3 mg, 0.015 mmol, 15.0 mol %), LiHMDS (12.0 μL, 0.012 mmol, 12.0 mol%) and 4Å MS (70.0 mg) in toluene (0.05 M, 2.0 mL) at -40°C for 24 h. The crude product was purified by column chromatography (SiO_2**,** 10% EtOAc-Hexane, R_f = 0.5 for the product) to afford the title compound **33** (76.0 mg, 90%) as white solid.



33

^{1}H NMR (300 MHz, $CDCl_3$) δ = 8.36 (s, 1H), 7.87 (d, *J* = 7.5 Hz, 1H), 7.70-7.60 (m, 3H), 7.56-7.40 (m, 5H), 7.33 (d, *J* = 6.9 Hz, 2H), 7.25-7.15 (m, 3H), 7.09 (d, *J* = 8.4 Hz, 3H), 6.92-6.82 (m, 2H), 6.82-6.67 (m, 5H), 6.67-6.57 (m, 4H), 6.43 (d, *J* = 7.5 Hz, 2H), 5.09 (d, *J* = 12.0 Hz, 1H), 4.96 (s, 1H), 4.45 (d, *J* = 12.0 Hz, 1H), 3.57 (s, 3H), 1.23 (s, 18H) ppm.

^{13}C NMR (75 MHz, $CDCl_3$) δ = 197.3, 164.4, 157.9, 152.5, 142.5, 141.3, 140.8, 140.5, 135.7, 135.5, 134.5, 134.1, 133.9, 132.2, 132.0, 131.7, 131.5, 130.7, 129.8, 129.7, 129.7, 128.8, 128.7, 128.5, 128.4, 128.2, 127.8, 127.6, 127.2, 127.0, 126.6, 126.0, 124.8, 123.8, 122.8, 113.9, 63.6, 55.0, 52.9, 34.2, 30.2 ppm.

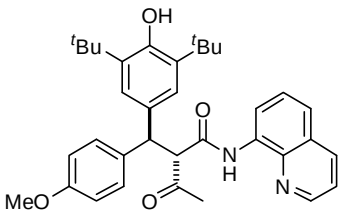
HRMS (ESI+) *m/z* calculated for $C_{59}H_{55}NO_4Na$ $[M+Na]^+$ 864.4029, found 864.4026.

IR (Neat) ν_{max} = 3639, 3379, 2954, 2925, 1669, 1584, 1510, 1436, 1177, 754, 700 cm^{-1}.

$[\alpha]_D^{25}$ = -175.74 (c = 0.33, $CHCl_3$).

HPLC: The enantiomeric excess (% of ee = 88) and diastereomeric ratio (dr = 99:1) were determined by HPLC analysis using Daicel Chiralpak IE-3 column: *n*-hexane:*i*-PrOH = 97:3, flow rate 1.0 mL/min, λ = 254 nm: τ_{minor} = 8.50 min, τ_{major} = 12.71 min.

7. Gram Scale Experiment: To a flame dried 250 mL schlenk flask equipped with a magnetic stir bar, carbene precursor **3g** (189.0 mg, 0.45 mmol, 0.15 equiv), activated 4Å MS (1.6 g) and toluene (24.0 mL) were placed under argon. To the resulting heterogeneous mixture, LiHMDS (360.0 µL, 0.36 mmol, 0.12 equiv, 1(M) in THF) was added and stirred at 25 °C for 1h under argon. The reaction mixture was cooled to -50 °C prior to the addition of a solution of amide **2i** (685.0 mg, 3.0 mmol, 1.0 equiv) in 24.0 mL toluene and stirred for 10 min. To the cold reaction mixture, a solution of *p*-QM **1a** (973.0 mg, 3.0 mmol, 1.0 equiv) in 12.0 mL toluene was added dropwise. The reaction was continued for 43 h, while maintaining the reaction temperature at -50 °C. The reaction mixture was quenched with 30.0 mL water. The 4Å MS was filtered and aqueous layer was extracted with EtOAc (3x40 mL). The combined organic layer was dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The solid residue was purified by gradient column chromatography from 1:3 EtOAc:Hexane to 1:4:6 DCM:EtOAc:Hexane (20% EtOAc-Hexane, R_f = 0.45) to afford the desired compound **29** containing 98:2 mixture of two diastereomers (confirmed by HPLC analysis) with combined yield (1.25 g, 75%) as white solid.



29

^{1}H NMR (300 MHz, $CDCl_3$) δ = 9.88 (s, 1H), 8.78 (dd, *J* = 4.2, 1.2 Hz, 1H), 8.57 (t, *J* = 4.5 Hz, 1H), 8.13-8.06 (m, 1H), 7.49-7.36 (m, 3H), 7.31 (d, *J* = 8.4 Hz, 2H), 7.08 (s, 2H), 6.86 (d, *J* = 8.4 Hz, 2H), 4.88-4.77 (m, 2H), 4.42 (d, *J* = 12.0 Hz, 1H), 3.78 (s, 3H), 2.22 (s, 3H), 1.17 (s, 18H) ppm.

^{13}C NMR (75 MHz, $CDCl_3$) δ = 205.0, 165.6, 158.3, 152.3, 148.2, 138.2, 136.0, 135.6, 134.0, 133.7, 131.9, 129.0, 127.7, 127.0, 124.2, 121.7, 121.5, 116.2, 114.1, 70.4, 55.1, 51.5, 34.1, 29.9, 29.4 ppm.

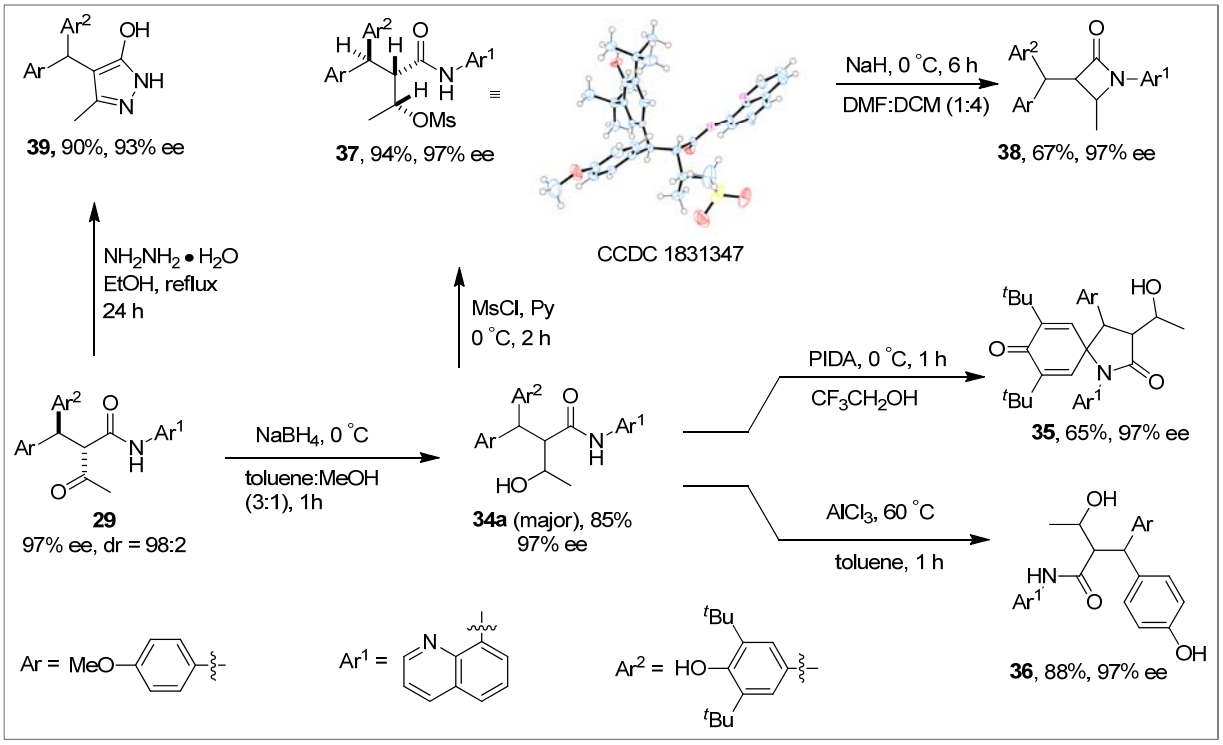
HRMS (ESI+) *m/z* calculated for $C_{35}H_{41}N_2O_4$ $[M+H]^+$ 553.3066, found 553.3058.

IR (Neat) ν_{max} = 3629, 3331, 2961, 1714, 1681, 1527, 1512, 1249, 829, 799, 760 cm^{-1}.

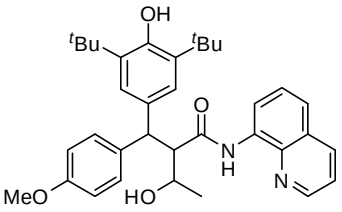
$[\alpha]_D^{25}$ = -131.10 (c = 0.36, $CHCl_3$).

HPLC: The enantiomeric excess (% of ee = 97) and diastereomeric ratio (dr = 98:2) were determined by HPLC analysis using Daicel Chiralpak IA-3 column: *n*-hexane:*i*-PrOH = 96:4, flow rate 1.0 mL/min, λ = 254 nm: τ_{major} = 16.75 min, τ_{minor} = 27.93 min.

8. Synthetic Application:



Compound 34a: $NaBH_4$ (68.0 mg, 1.8 mmol, 1.5 equiv) was added to a stirred solution of compound **29** (665.0 mg, 1.2 mmol, 1.0 equiv) in toluene (0.06 M, 20.0 mL) under argon atmosphere at 0 °C. To the resulting heterogeneous mixture, CH_3OH (6.0 mL) was added slowly with stirring and the reaction was continued for 1 h at 0 °C. After complete consumption of the starting material, volatile materials were removed under reduced pressure. The solid residue was dissolved in EtOAc and the resulting solution was neutralized with 2 (N) HCl. The organic layer was separated and aqueous layer was extracted with EtOAc (twice). The combined organic layer was dried over anhydrous Na_2SO_4, filtered and concentrated. The crude material was purified by column chromatography (SiO_2**,** 30% EtOAc-Hexane, R_f = 0.5 for the product) to afford the title compound **34a** (567.0 mg, 85%, major diastereoisomer) as white solid. Compound **34a** was crystallized by slow evaporation from a mixture of MeOH:$CHCl_3$ (10:1).



34a (*major diastereoisomer*)

^{1}H NMR (300 MHz, $CDCl_3$) δ = 9.74 (s, 1H), 8.76 (dd, *J* = 4.2, 1.2 Hz, 1H), 8.51 (dd, *J* = 5.1, 3.9 Hz, 1H), 8.07 (dd, *J* = 8.1, 1.2 Hz, 1H), 7.43-7.32 (m, 5H), 7.16 (s, 2H), 6.88 (d, *J* = 8.7 Hz, 2H), 4.76 (s, 1H), 4.35 (d, *J* = 11.7 Hz, 1H), 4.12-4.02 (m, 1H), 3.79 (s, 3H), 3.68 (dd, *J* = 11.7, 4.5 Hz, 1H), 2.59 (s, br., 1H), 1.31 (d, *J* = 6.3 Hz, 3H), 1.20 (s, 18H) ppm.

^{13}C NMR (75 MHz, $CDCl_3$) δ = 171.4, 158.2, 151.9, 148.0, 138.2, 136.1, 135.4, 134.9, 134.1, 133.6, 129.1, 127.7, 127.0, 124.1, 121.3, 116.4, 114.2, 68.5, 59.4, 55.2, 50.3, 34.1, 30.0, 19.3 ppm.

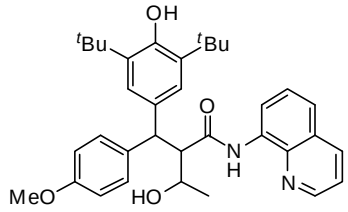
HRMS (ESI+) *m/z* calculated for $C_{35}H_{42}N_2O_4Na$ $[M+ Na]^+$ 577.3042, found 577.3043.

IR (Neat) ν_{max} = 3632, 3580, 3363, 3333, 2957, 2919, 1682, 1535, 1512, 1435, 1322, 1245, 1118, 826, 791, 638 cm^{-1}.

$[\alpha]_D^{25}$ = +25.21 (c = 0.46, $CHCl_3$).

HPLC: The enantiomeric excess (% of ee = 97) and diastereomeric ratio (dr = 99:1) were determined by HPLC analysis using Daicel Chiralpak IA-3 column: *n*-hexane:*i*-PrOH = 95:5, flow rate 1.0 mL/min, λ = 254 nm: τ_{minor} = 18.18 min, τ_{major} = 19.83 min.

Compound 34b: The reaction (sodium borohydride reduction of compound **29)** also afforded the minor diasteroisomer **34b** (34.0 mg, 5 %, SiO_2**,** 30% EtOAc-Hexane, R_f = 0.55 for the product) as white solid.



34b (*minor diastereoisomer*)

^{1}H NMR (500 MHz, $CDCl_3$) δ = 9.58 (s, 1H), 8.74 (d, *J* = 3.0 Hz, 1H), 8.64-8.59 (m, 1H), 8.10 (d, *J* = 8.5 Hz, 1H), 7.46-7.43 (m, 2H), 7.43-7.37 (m, 3H), 7.13 (s, 2H), 6.90 (d, *J* = 8.0 Hz, 2H), 4.69 (s, 1H), 4.61 (d, *J* = 11.5 Hz, 1H), 4.08 (d, *J* = 9.5 Hz, 1H), 3.80 (s, 4H), 3.10 (d, *J* = 11.5 Hz, 1H), 1.30 (d, *J* = 6.5 Hz, 1H), 1.15 (s, 18H) ppm.

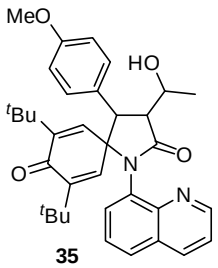
^{13}C NMR (100 MHz, $CDCl_3$) δ = 173.5, 158.2, 152.0, 148.1, 138.1, 136.2, 135.5, 134.2, 133.7, 133.0, 129.4, 127.7, 127.1, 124.3, 121.6, 121.4, 116.4, 114.1, 66.5, 59.4, 55.2, 50.7, 34.0, 29.9, 22.7 ppm.

HRMS (ESI+) *m/z* calculated for $C_{35}H_{43}N_2O_4$ $[M+ H]^+$ 555.3217, found 555.3215.

$[\alpha]_D^{25}$ = -47.78 (c = 0.23, $CHCl_3$).

HPLC: The enantiomeric excess (% of ee = 94) and diastereomeric ratio (dr = 98:2) were determined by HPLC analysis using Daicel Chiralpak IA-3 column: *n*-hexane:*i*-PrOH = 95:5, flow rate 1.0 mL/min, λ = 254 nm: τ_{major} = 15.34 min, τ_{minor} = 16.38 min.

Compound 35: To a solution of **34a** (55.4 mg, 0.1 mmol, 1.0 equiv) in CF_3CH_2OH (0.1 M, 1.0 mL), $PhI(OAc)_2$ (39.0 mg, 0.12 mmol, 1.2 equiv) was added at 0 °C. The resulting solution was stirred for 1 h at 0 °C. After complete consumption of the starting material, the reaction mixture was neutralized with saturated $NaHCO_3$ and extracted with EtOAc. The combined organic layers was dried over anhydrous Na_2SO_4, filtered and concentrated. The crude residue was purified by column chromatography (SiO_2**,** 50% EtOAc-Hexane, R_f = 0.4 for the product) to afford the title compound **35** (36.0 mg, 65%, major diastereoisomer) as brown solid. The trace amount of the minor diastereoisomer was separated during purification.



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^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.87-8.82 (m, 1H), 8.21-8.15 (m, 1H), 7.58-7.49 (m, 2H), 7.44 (dd, *J* = 8.4, 4.0 Hz, 1H), 7.32 (dd, *J* = 6.8, 1.6 Hz, 1H), 6.98 (d, *J* = 8.4 Hz, 2H), 6.76 (d, *J* = 8.4 Hz, 2H), 6.35 (d, *J* = 2.8 Hz, 1H), 6.31 (d, *J* = 2.8 Hz, 1H), 4.92-4.85 (m, 1H), 4.03 (d, *J* = 10.8 Hz, 1H), 3.80-3.70 (m, 4H), 1.09 (s, 9H), 1.05 (d, *J* = 6.4 Hz, 3H), 0.91 (s, 9H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$) δ = 184.8, 164.0, 159.1, 148.9, 148.0, 147.7, 144.8, 140.3, 138.2, 136.7, 136.0, 129.1, 129.1, 127.1, 127.0, 122.6, 121.3, 118.8, 113.8, 84.5, 68.0, 55.2, 51.0, 50.0, 34.6, 34.4, 29.1, 28.7, 19.8 ppm.

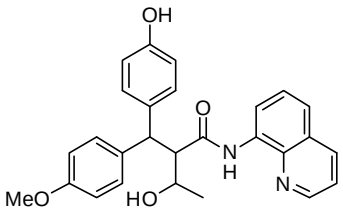
HRMS (ESI+) *m/z* calculated for $C_{35}H_{40}N_2O_4Na$ $[M+Na]^+$ 553.3061, found 553.3062.

IR (Neat) ν_{max} = 2957, 2919, 1708, 1646, 1514, 1463, 1365, 1250, 1178, 974, 831, 794 cm^{-1}.

$[\alpha]_D^{25}$ = -184.98 (c = 0.69, $CHCl_3$).

HPLC: The enantiomeric excess (% of ee = 97) was determined by HPLC analysis using Daicel Chiralpak IE-3 column: *n*-hexane:*i*-PrOH = 95:5, flow rate 1.0 mL/min, λ = 220 nm: τ_{major} = 16.09 min, τ_{minor} = 18.32 min.

Compound 36: Anhydrous aluminium chloride ($AlCl_3$) (133.3 mg, 1.0 mmol, 10.0 equiv) was added to a stirred solution of compound **34a** (55.4 mg, 0.1 mmol, 1.0 equiv) in toluene (0.025 M, 4.0 mL) under argon atmosphere at 25 °C. The resulting heterogeneous mixture was stirred and heated



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at 60 °C (preheated oil bath) for 1 h under argon atmosphere. After complete consumption of the starting material, the reaction mixture was cooled to room temperature. Then the reaction mixture was diluted with 5.0 mL water and extracted with EtOAc. The combined organic layers was dried over anhydrous Na_2SO_4, filtered and concentrated. The solid residue was purified by column chromatography (SiO_2**,** 50% EtOAc-Hexane, R_f = 0.5 for the product) to afford the title compound **36** (39.0 mg, 88%) as white solid.

^{1}H NMR (500 MHz, acetone-d_6) δ = 10.15 (s, 1H), 8.88-8.84 (m, 1H), 8.68 (d, *J* = 8.0 Hz, 1H), 8.30 (d, *J* = 8.0 Hz, 1H), 7.93 (s, br., 1H), 7.58-7.54 (m, 1H), 7.53 (d, *J* = 8.5 Hz, 1H), 7.46 (t, *J* = 8.0 Hz, 1H), 7.41 (d, *J* = 8.5 Hz, 2H), 7.33 (d, *J* = 8.5 Hz, 2H), 6.88 (d, *J* = 8.5 Hz, 2H), 6.63 (d, *J* = 8.5 Hz, 2H), 4.32 (d, *J* = 11.5 Hz, 1H), 4.14 (s, 1H), 3.95-3.87 (m, 2H), 3.76 (s, 3H), 1.21 (d, *J* = 6.0 Hz, 3H) ppm.

^{13}C NMR (100 MHz, acetone-d_6) δ = 172.2, 160.1, 157.2, 150.2, 140.2, 138.1, 137.7, 137.6, 137.2, 130.9, 130.4, 129.9, 128.9, 123.6, 122.8, 117.6, 116.8, 115.8, 68.4, 60.0, 56.4, 51.0, 19.2 ppm.

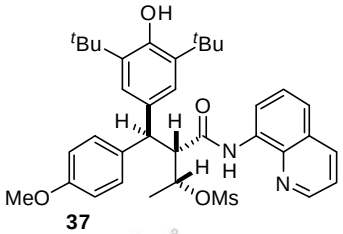
HRMS (ESI+) *m/z* calculated for $C_{27}H_{26}N_2O_4Na$ $[M+Na]^+$ 465.1790, found 465.1789.

IR (Neat) ν_{max} = 3476, 3335, 3257, 2937, 1637, 1608, 1514, 1486, 1256, 822, 786 cm^{-1}.

$[\alpha]_D^{25}$ = 115.18 (c = 0.63, CH_3COCH_3).

HPLC: The enantiomeric excess (% of ee = 97) and diastereomeric ratio (dr = 99:1) were determined by HPLC analysis using Daicel Chiralpak IA-3 column: *n*-hexane:*i*-PrOH = 85:15, flow rate 1.0 mL/min, λ = 254 nm: τ_{minor} = 23.22 min, τ_{major} = 25.53 min.

Compound 37: Methanesulfonyl chloride (MsCl) (78.0 µL, 1.0 mmol, 2.0 equiv) was added to a stirred solution of compound **34a** (280.0 mg, 0.51 mmol, 1.0 equiv) in pyridine (0.7 M, 0.8 mL) under argon atmosphere at 0 °C. The resulting heterogeneous mixture was stirred for 2 h and slowly warmed up to room temperature. After complete consumption of the starting material, pyridine was removed under reduced pressure. 5.0 mL water and 25.0 mL EtOAc were added successively to dissolve the resultant solid residue. The organic layer was separated and aqueous layer extracted with EtOAc (twice). The combined organic layers washed with brine, dried over anhydrous Na_2SO_4, filtered and



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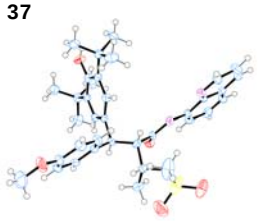
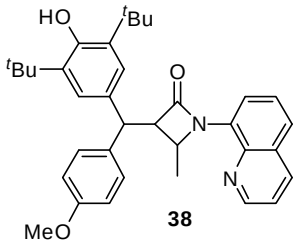


concentrated. The solid residue was purified by column chromatography (SiO_2**,** 30% EtOAc-Hexane, R_f = 0.52 for the product) to afford the title compound **37** (300.0 mg, 94%) as white solid. Compound **37** was crystallized by slow evaporation from a mixture of EtOAc:^{i}PrOH (1:5). Absolute configuration of the compound **37** was unambiguously determined by the single-crystal X-ray analysis.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 9.72 (s, 1H), 8.75 (d, *J* = 2.4 Hz, 1H), 8.63 (dd, *J* = 6.0, 2.4 Hz, 1H), 8.10 (d, *J* = 8.0 Hz, 1H), 7.48-7.33 (m, 5H), 7.11 (s, 2H), 6.92 (d, *J* = 8.0 Hz, 2H), 5.09-5.00 (m, 1H), 4.78 (s, 1H), 4.29 (d, *J* = 12.0 Hz, 1H), 3.88 (dd, *J* = 12.0, 4.4 Hz, 1H), 3.81 (s, 3H), 2.94 (s, 3H), 1.59 (d, *J* = 6.8 Hz, 3H), 1.19 (s, 18H) ppm.
^{13}C NMR (100 MHz, $CDCl_3$) δ = 168.8, 158.5, 152.1, 148.1, 138.2, 136.1, 135.5, 134.2, 132.8, 132.6, 129.1, 127.8, 127.1, 124.1, 121.5, 121.4, 116.4, 114.5, 78.2, 57.4, 55.2, 50.4, 38.5, 34.1, 30.0, 15.9 ppm.
HRMS (ESI+) *m/z* calculated for $C_{36}H_{44}N_2O_6SNa$ $[M+Na]^+$ 655.2818, found 655.2820.
IR (Neat) ν_{max} = 3639, 3609, 3350, 2958, 1681, 1527, 1512, 1324, 1177, 917, 897, 792 cm^{-1}.
$[\alpha]_D^{25}$ = -36.03 (c = 0.54, $CHCl_3$).
HPLC: The enantiomeric excess (% of ee = 97) and diastereomeric ratio (dr = 99:1) were determined by HPLC analysis using Daicel Chiralpak IA-3 column: *n*-hexane:*i*-PrOH = 95:5, flow rate 1.0 mL/min, λ = 254 nm: τ_{major} = 14.01 min, τ_{minor} = 17.99 min.

Compound 38: A solution of the compound **37** (63.2 mg, 0.1 mmol, 1.0 equiv) in 10.0 mL of DMF-CH_2Cl_2 (1:4) was added over 30 min to a mixture of NaH (13.1 mg, 0.3 mmol, 3.0 equiv; 55% mineral oil dispersion) in 10 mL of DMF-CH_2Cl_2 (1:4) at 0 °C while stirring under argon atmosphere. The resulting heterogeneous mixture was allowed to warm to 25 °C and stirring was continued for 6 h. After complete consumption of the starting material, CH_2Cl_2 was removed under reduced pressure. To the residue, saturated NH_4Cl solution was added. The aqueous layer was extracted with EtOAc (twice), the combined organic layer was washed with water and finally brine, dried over anhydrous Na_2SO_4, filtered and concentrated. The oily residue was purified by column chromatography (SiO_2**,** 15% EtOAc-Hexane, R_f = 0.4 for the product) to afford the title compound **38** (36.0 mg, 67%, major



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diastereoisomer) as white solid. The trace amount of the minor diastereoisomer was separated during purification.

^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.76 (d, *J* = 3.0 Hz, 1H), 8.28 (d, *J* = 7.5 Hz, 1H), 8.07 (d, *J* = 8.5 Hz, 1H), 7.53 (d, *J* = 8.0 Hz, 1H), 7.47 (t, *J* = 8.0 Hz, 1H), 7.36-7.29 (m, 3H), 7.16 (s, 2H), 6.88 (d, *J* = 8.5 Hz, 2H), 5.04 (s, 1H), 4.93-4.87 (m, 1H), 4.47 (d, *J* = 9.0 Hz, 1H), 3.79 (s, 3H), 3.66 (dd, *J* = 9.0, 2.0 Hz, 1H), 1.40 (s, 18H), 1.36 (d, *J* = 6.0 Hz, 3H) ppm.

^{13}C NMR (75 MHz, $CDCl_3$) δ = 168.0, 158.1, 152.2, 148.7, 140.6, 135.7, 135.3, 135.1, 133.5, 133.1, 129.5, 128.9, 126.5, 125.1, 123.6, 121.5, 121.0, 113.7, 62.7, 58.0, 55.1, 50.0, 34.3, 30.3, 19.4 ppm.

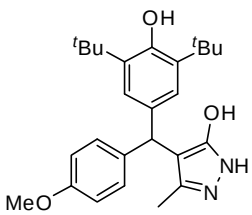
HRMS (ESI+) *m/z* calculated for $C_{35}H_{40}N_2O_3Na$ $[M+Na]^+$ 559.2937, found 559.2934.

IR (Neat) ν_{max} = 3637, 2957, 1734, 1505, 1405, 1252, 1152, 757 cm^{-1}.

$[\alpha]_D^{25}$ = 0.43 (c = 0.94, $CHCl_3$).

HPLC: The enantiomeric excess (% of ee = 97) was determined by HPLC analysis using Daicel Chiralpak IC-3 column: *n*-hexane:*i*-PrOH = 97:3, flow rate 1.0 mL/min, λ = 254 nm: τ_{minor} = 12.06 min, τ_{major} = 14.06 min.

Compound 39: To the suspension of compound **29** (55.2 mg, 0.1 mmol, 1.0 equiv) in EtOH (0.25 M, 0.4 mL) was added hydrazine hydrate (15.0 μL, 0.3 mmol, 3.0 equiv). The resulting suspension was heated to reflux for 24 h. Then the reaction mixture was allowed to cool to ambient temperature and EtOH was removed under reduced pressure. The oily residue was purified by gradient column chromatography from 50% EtOAc-Hexane to EtOAc (SiO_2**,** 60% EtOAc-Hexane, R_f = 0.5 for the product) to afford the title compound **39** (38.0 mg, 90%) as yellow solid.



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^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.07 (d, *J* = 8.4 Hz, 2H), 6.99 (s, 2H), 6.80 (d, *J* = 8.4 Hz, 2H), 5.24 (s, 1H), 3.78 (m, 3H), 1.78 (s, 3H), 1.36 (s, 18H) ppm.

^{13}C NMR (100 MHz, $CDCl_3$) δ = 161.20, 157.74, 152.02, 138.64, 136.17, 135.54, 133.60, 129.70, 125.52, 113.44, 105.85, 55.20, 44.15, 34.33, 30.36, 11.11 ppm.

HRMS (ESI+) *m/z* calculated for $C_{26}H_{35}N_2O_3$ $[M+H]^+$ 423.2642, found 423.2641.

IR (Neat) ν_{max} = 2961, 2873, 1609, 1508, 1246, 1178, 769 cm^{-1}.

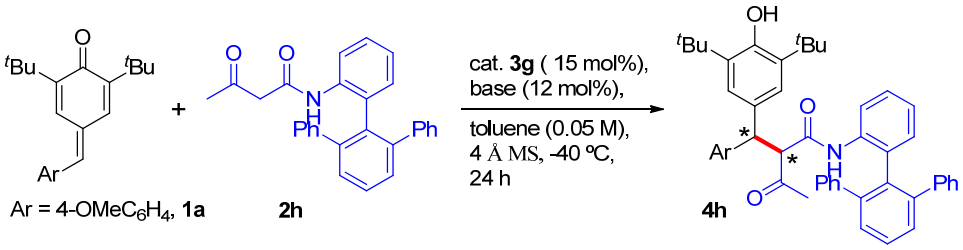
$[\alpha]_D^{25}$ = 11.78 (c = 0.92, $CHCl_3$).

HPLC: The enantiomeric excess (% of ee = 93) was determined by HPLC analysis using Daicel Chiralpak IA-3 column: *n*-hexane:*i*-PrOH = 90:10, flow rate 1.0 mL/min, λ = 220 nm: τ_{major} = 12.26 min, τ_{minor} = 17.34 min.

9. Control Experiments:

a) Effect of metal ions present in the base:

To understand the role of the metal ion present in the base, we carried out the catalytic reaction using NaHMDS and KHMDS instead of LiHMDS using *p*-QM **1a** and amide **2h** under standard reaction conditions. It was observed that both the reactions afforded the product **4h** in a similar efficiency. These results indicate that the metal ion in the base may not have any considerable effect in the reaction outcome.



Entry[a]	Base	Conv. (%)	ee (%)	dr.
1	NaHMDS	90	98	98:2
2	KHMDS	90	97	98:2

[a]Reaction conditions: **1a** (0.05 mmol), **2h** (0.05 mmol) and 4Å MS (35 mg) in 1.0 mL toluene; reaction conversion determined by ^{1}H NMR analysis.

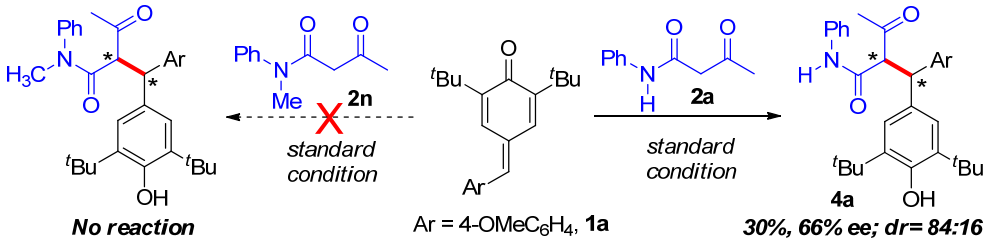
b) The catalytic reaction using preformed NHC:

To a flame dried schlenk tube equipped with a magnetic stir bar, carbene precursor **3g** (4.2 mg, 0.01 mmol, 0.2 equiv), activated 4Å MS (20.0 mg), toluene (0.5 mL) and LiHMDS (10.0 µL, 0.01 mmol, 0.2 equiv, 1(M) in THF) were placed under argon atmosphere and stirred at 25 °C for 1h (solution 1). In a separate flame dried schlenk tube equipped with a magnetic stir bar, amide **2h** (20.2 mg, 0.05 mmol, 1.0 equiv), activated 4Å MS (35.0 mg) and toluene (0.5 mL) were placed under argon. To the solution, the preformed carbene solution (prepared earlier, solution 1) was transferred via cannulation. The reaction mixture was cooled to 0 °C prior to the addition of *p*-QM **1a** (16.2 mg, 0.05 mmol, 1.0 equiv). The reaction was continued for another 12 h while stirring. The reaction mixture was quenched with 0.5 mL water and extracted with EtOAc (twice), the combined organic layer was dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The solid residue was purified by column chromatography

(SiO_2, 15% EtOAc-Hexane, R_f = 0.5 for the product) to afford the desired compound **4h** in 30% isolated yield with 82% ee and dr = 98:2.

c) Role of free N-H of ketoamide:

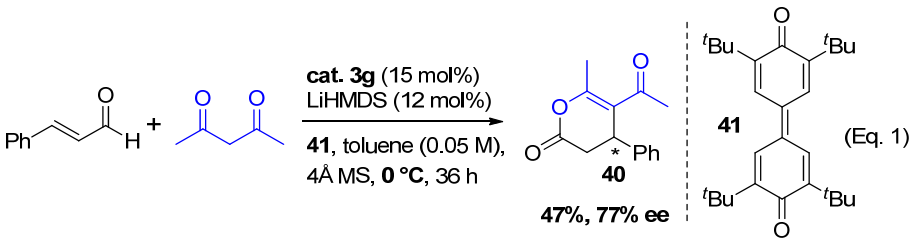
To confirm the role of free N-H of the ketoamide in the catalytic reaction, we carried out the addition reaction using *p*-QM **1a** and *N*-methyl-3-oxo-*N*-phenylbutanamide **2n** under standard reaction conditions. Unlike the ketoamide **2a**, its alkyl analogue resulted in complete inhibition of the catalysis suggesting a crucial role for the free-N-H group of the amide in this catalytic conjugate addition reaction (Scheme 1).



Scheme 1: NHC-Catalyzed 1,6-conjugate addition reaction using N-H and N-Me ketoamide.

d) Confirmation of the in situ formation of NHC:

In order to ensure the involvement of carbene as catalyst in our 1,6-conjugate addition reaction, we performed the well established NHC catalyzed oxidative annulations reaction between commercially available cinnamaldehyde and acetyl acetone under our optimized reaction conditions in presence of oxidant **41** (Eq. 1). The desired product **40** was isolated in moderate yield and enantioselectivity, confirming the formation of NHC species under the reaction conditions.



To a flame dried schlenk tube equipped with a magnetic stir bar, carbene precursor **3g** (3.2 mg, 0.0075 mmol, 0.15 equiv), activated 4Å MS (35.0 mg) and toluene (1.0 mL) were placed under argon. To the resulting heterogeneous mixture, LiHMDS (6.0 µL, 0.006 mmol, 0.12 equiv, 1(M)

in THF) was added and stirred at 25 °C for 1h under argon. Then acetyl acetone (7.8 μL, 0.075 mmol, 1.5 equiv) and bis-quinone oxidant **41** (20.4 mg, 0.05 mmol, 1.0 equiv) were added successively to the reaction mixture and stirred for another 5 min. The reaction mixture was cooled to 0 °C. To the cold solution, cinnamaldehyde (6.4 μL, 0.05 mmol, 1.0 equiv) was added and the reaction was continued for 36 h while maintaining the reaction temperature at 0 °C. The crude product was purified by column chromatography (SiO_2, 30% EtOAc-Hexane, R_f = 0.5 for the product) to afford the desired product **40** (5.4 mg, 47%) with 77% ee.[9]

HPLC: The enantiomeric excess (% of ee = 77) was determined by HPLC analysis using Daicel Chiralpak IE-3 column: *n*-hexane:*i*-PrOH = 94:6, flow rate 1.0 mL/min, λ = 254 nm: τ_{minor} = 16.3 min, τ_{major} = 18.2 min.

e) ^{1}H NMR study:

To understand the role of NHC in this 1,6-conjugate addition reaction, we performed ^{1}H NMR studies. It was observed that ^{1}H NMR signal at 10.76 ppm that corresponds to iminium C2-H of the azolium salt **3g** was disappeared when the azolium salt **3g** was treated with an equimolar amount of LiHMDS (**Fig. 1**, sepctram **b**). Interestingly, the signal was reappeared by adding the ketoamide **2h** into the solution (**Fig. 1**, sepctram **c**). This result may suggest that the in situ generated NHC (pK_a ~ 17-19) deprotonates the acidic N-H of ketoamide (pK_a ~ 10-12) thus forming a chiral ion pair consisting of azolium and enolate.

Experimental Procedure: The azolium salt **3g** (8.4 mg, 0.02 mmol, 1 equiv) was placed to a dry NMR tube inside a glove box. The tube was sealed properly with a septum. To have a homogenous solution of the salt, a mixture of deuterated solvents (0.4 mL of d_8-toluene and 0.1 mL of CD_3CN) was added to the NMR tube under argon atmosphere. ^{1}H NMR spectra of the solution was recorded (**Fig. 1**, sepctram **a**). To the resulting solution, LiHMDS (20.0 μL, 0.02 mmol, 1 equiv, 1(M) in THF) was added under argon and shaken for 5 min before ^{1}H NMR spectra of the solution was recorded (**Fig. 1**, sepctram **b**). Then a solution of ketoamide **2h** (8.4 mg, 0.02 mmol, 1 equiv) in 0.1 mL of d_8-toluene was added to the preformed NHC solution and ^{1}H NMR spectra was recorded (**Fig. 1**, sepctram **c**).

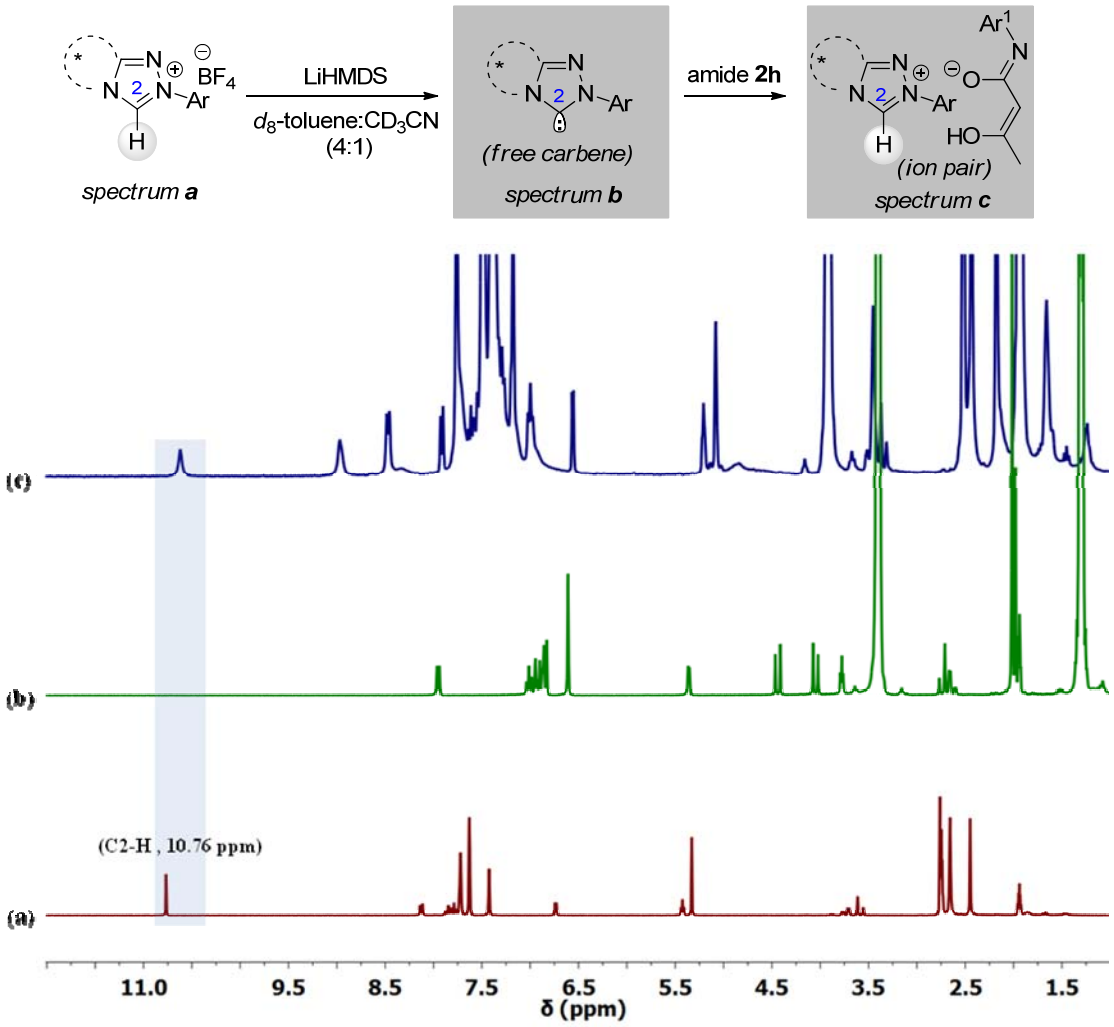


Figure 1: ^{1}H NMR spectra are recorded in a mixture of solvents using d_8-toluene and CD_3CN (4:1). ^{1}H NMR spectra of the azolium salt **3g** (a); ^{1}H NMR spectra of a 1:1 mixture of azolium salt **3g** and LiHMDS (b); ^{1}H NMR spectra of a 1:1 mixture of azolium salt **3g** and LiHMDS after adding equimolar amount of the amide **2h** (c).

10. References:

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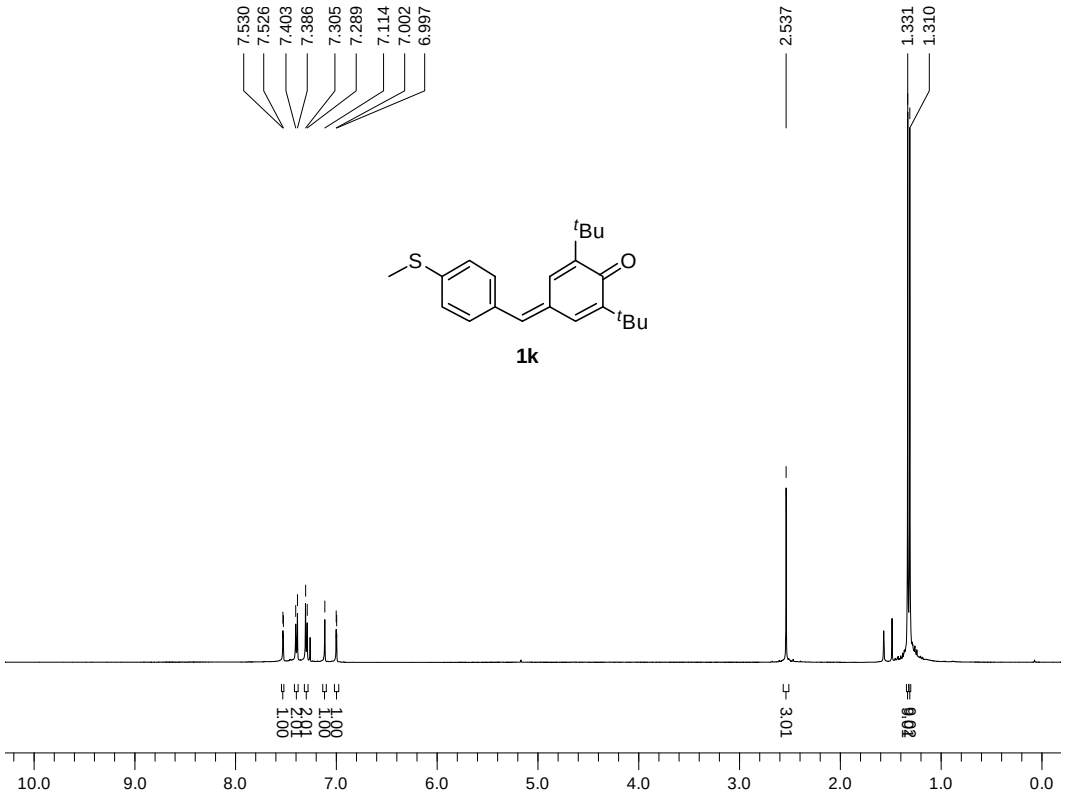
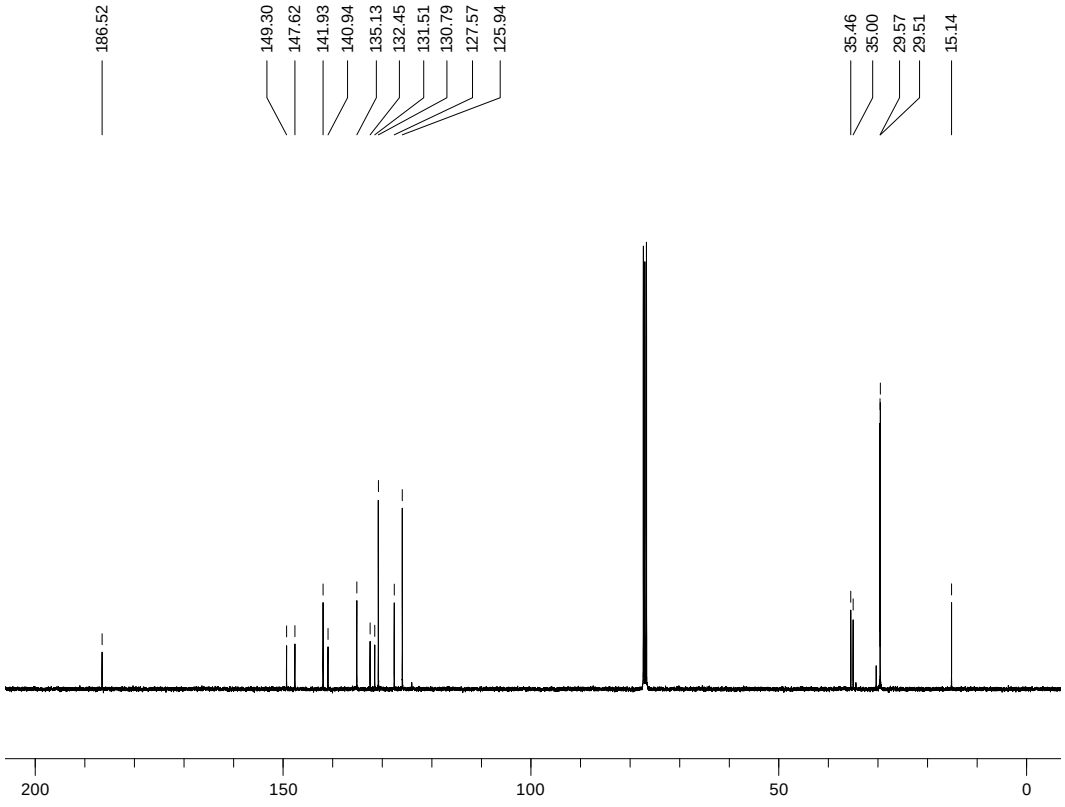
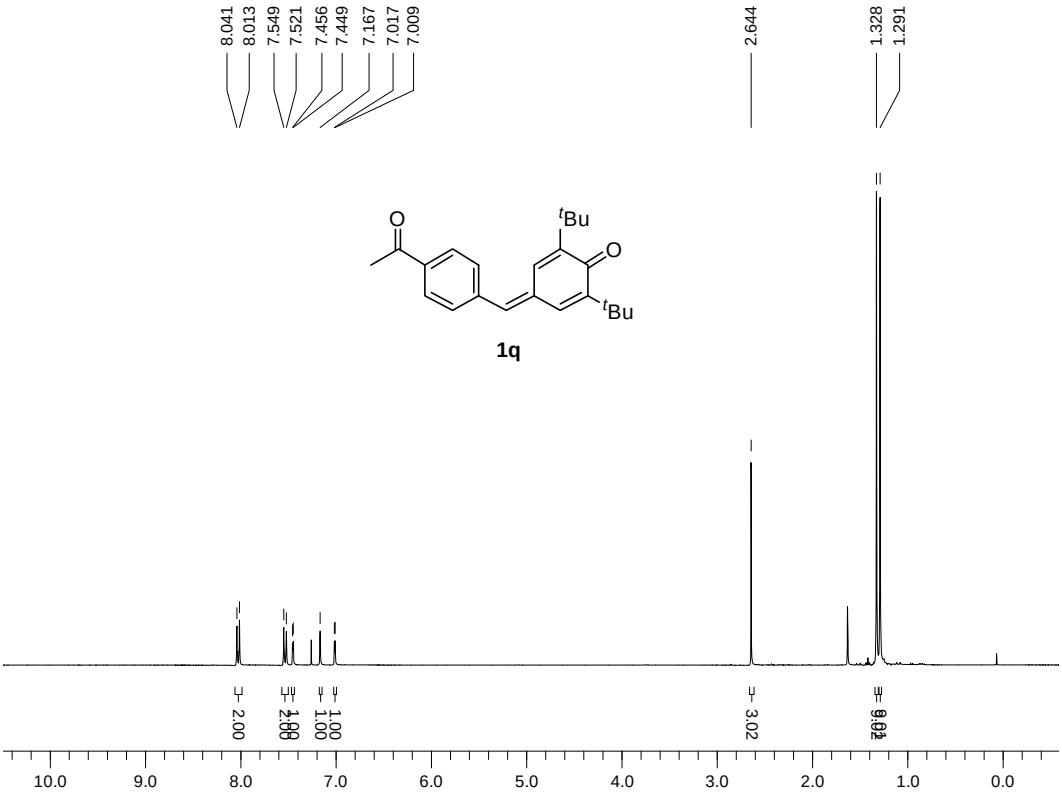
11. X-Ray Crystallographic Data of the Compounds 11, 34a and 37

Compound reference	**11**	**34a**	**37**
Chemical formula	$C_{49}H_{48}BrNO_3$	$C_{70}H_{82}N_4O_8$	$C_{36}H_{43}N_2O_6S$
Formula Mass	778.79	1107.4	631.78
Crystal system	Orthorhombic	Monoclinic	Monoclinic
a/Å	10.118(1)	14.151(3)	11.571(3)
b/Å	14.0353(14)	14.717(4)	25.090(6)
c/Å	28.194(3)	16.184(3)	11.915(4)
α/°	90.00	90.00	90.00
β/°	90.00	111.316(6)	90.00
γ/°	90.00	90.00	90.00
Unit cell volume/Å^3	4003.8(7)	3139.9(12)	3459.1(17)
Temperature/K	100(2)	100(2)	100
Space group	P 21 2121	P 21	P 21
No. of formula units per unit cell, *Z*	4	2	4
Radiation type	MoKα	MoKα	MoKα
Absorption coefficient, μ/mm^{-1}	1.070	0.076	0.140
No. of reflections measured	9989	18150	10699
No. of independent reflections	7602	9257	6162
R_{int}	0.0537	0.0679	0.0701
Final R_1 values ($I > 2\sigma(I)$)	0.0537	0.0679	0.0701
Final $wR(F^2)$ values ($I > 2\sigma(I)$)	0.1295	0.1771	0.1512
Final R_1 values (all data)	0.0714	0.0722	0.1280
Final $wR(F^2)$ values (all data)	0.1392	0.1835	0.1747
Goodness of fit on F^2	1.040	0.951	0.933
Flack parameter	0.075(9)	0.3(9)	0.26(9)
CCDC number	1831345	1831346	1831347

12. ^{1}H and ^{13}C NMR Spectra



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tBu
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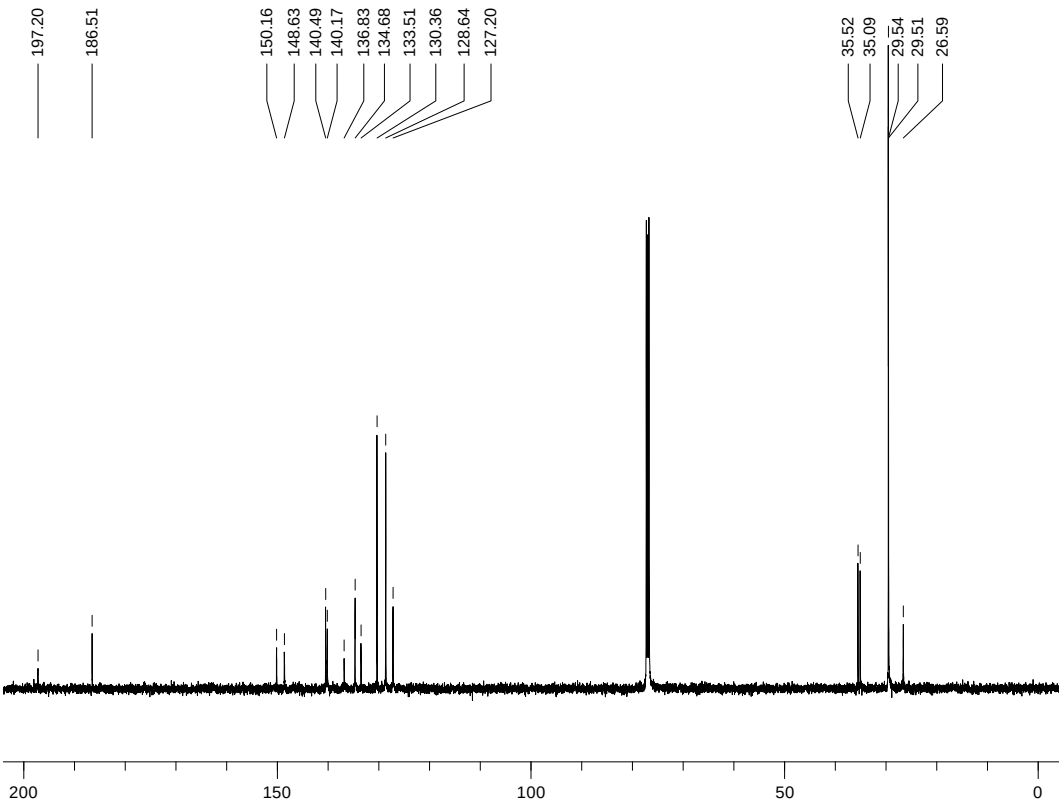
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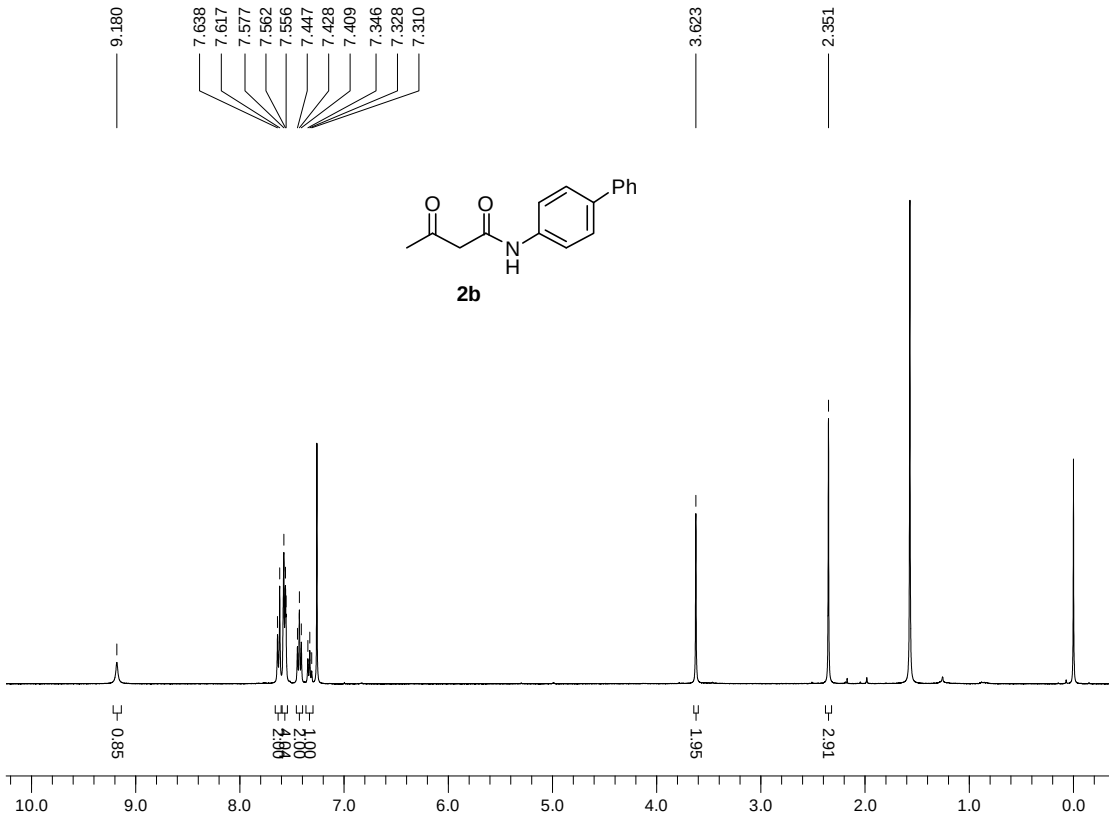
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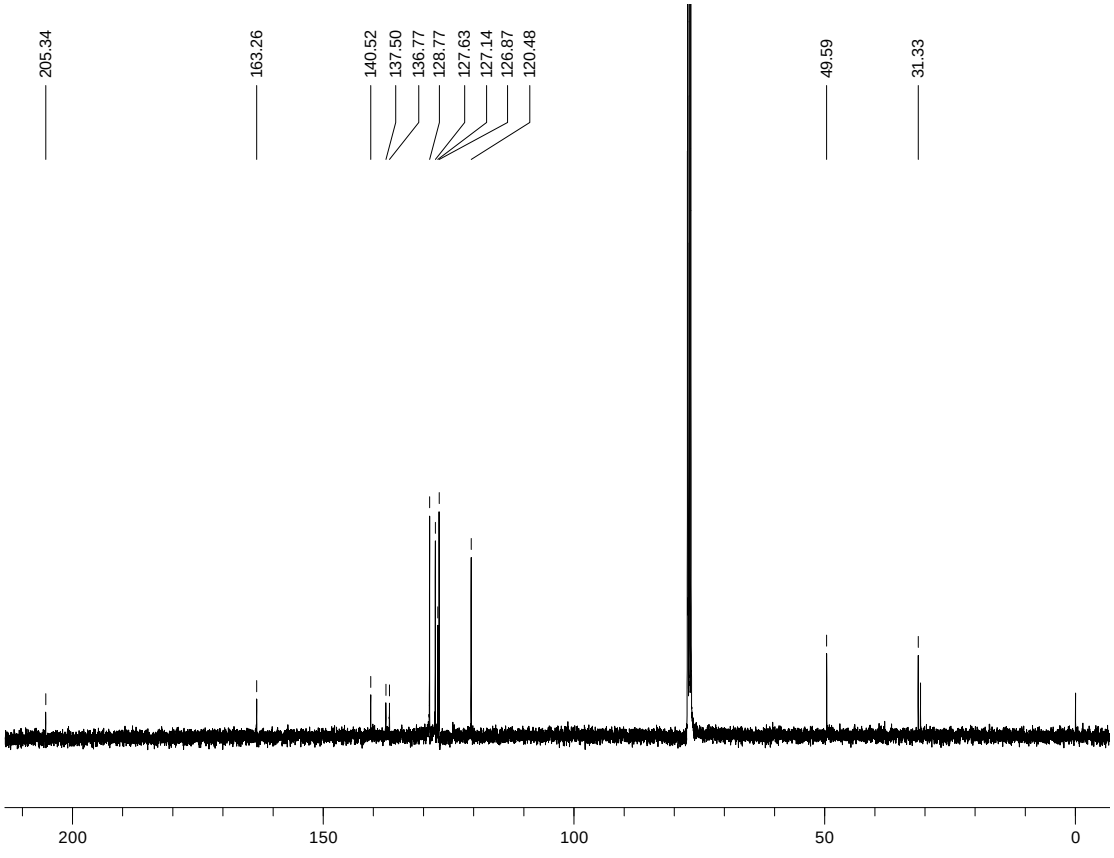
2b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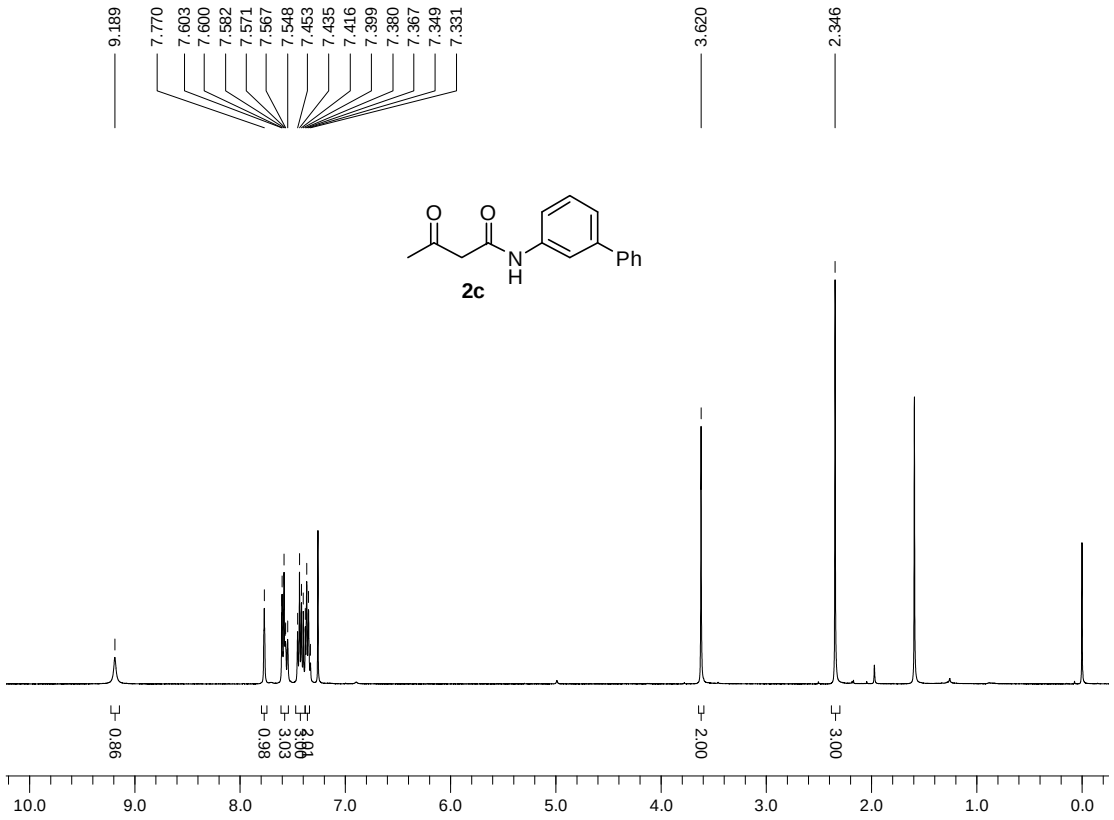
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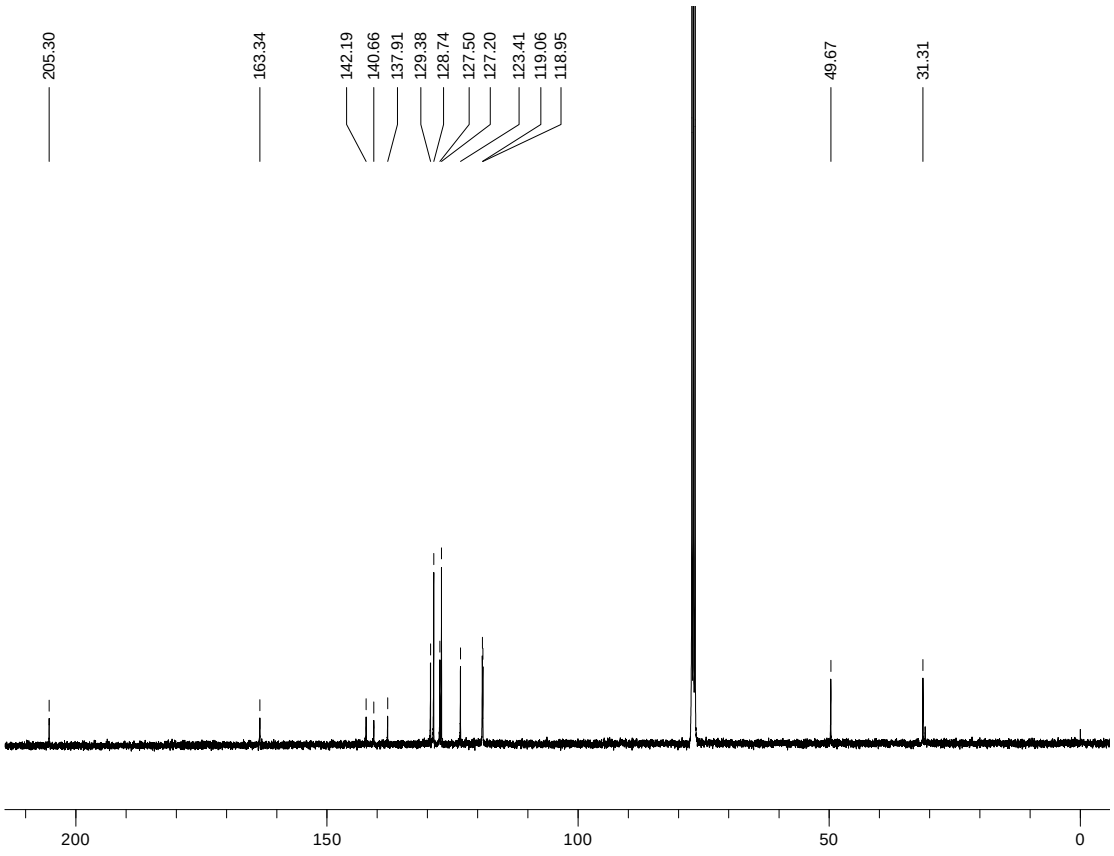
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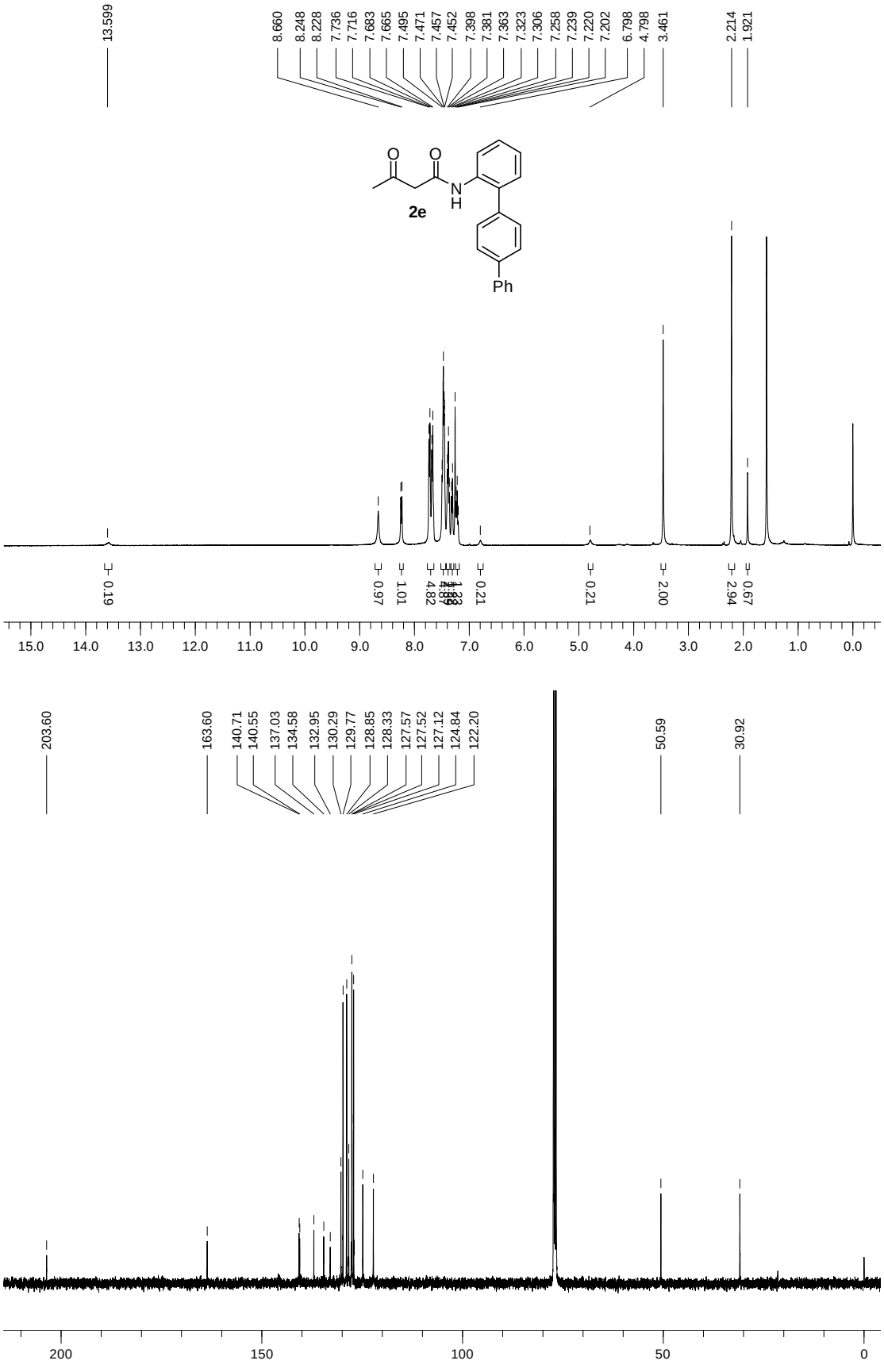
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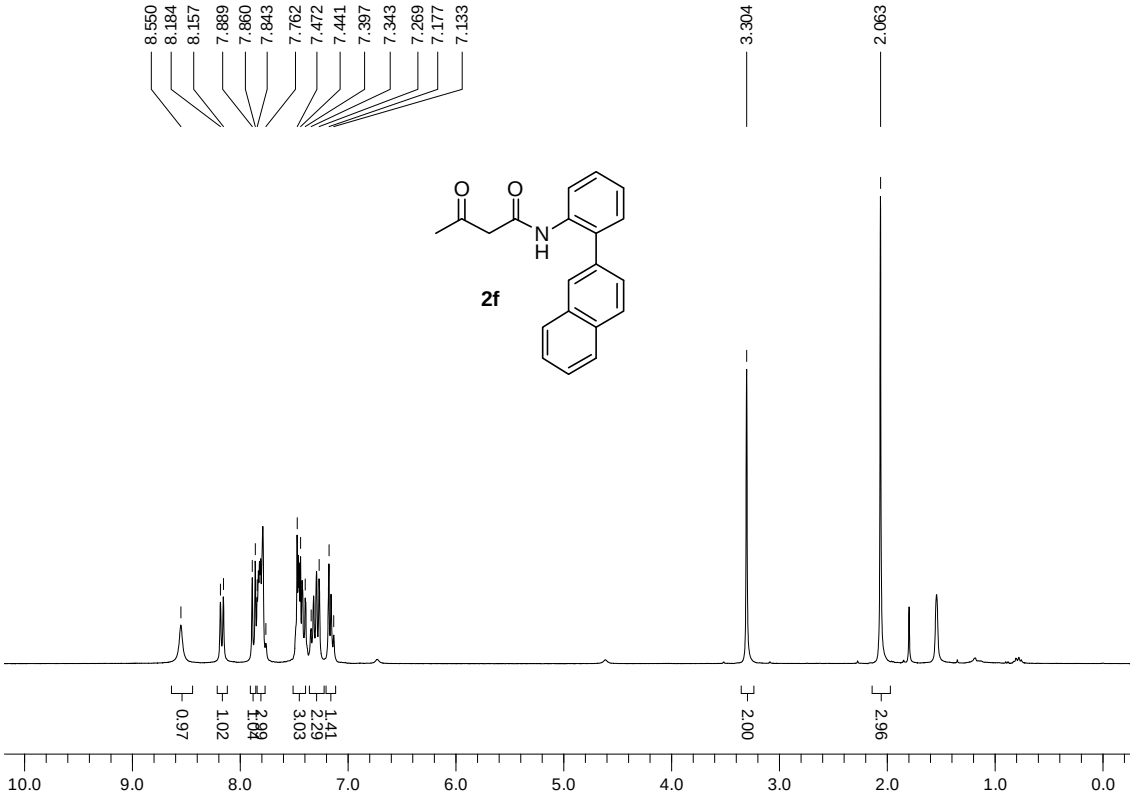
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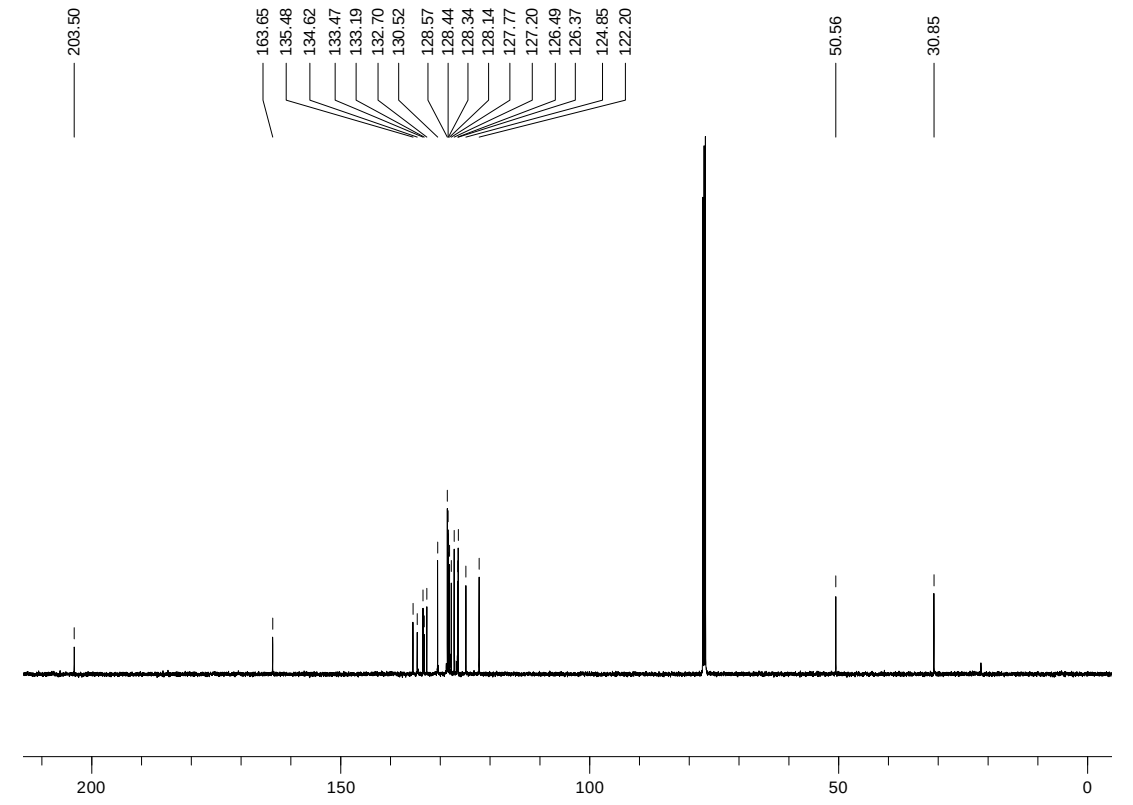
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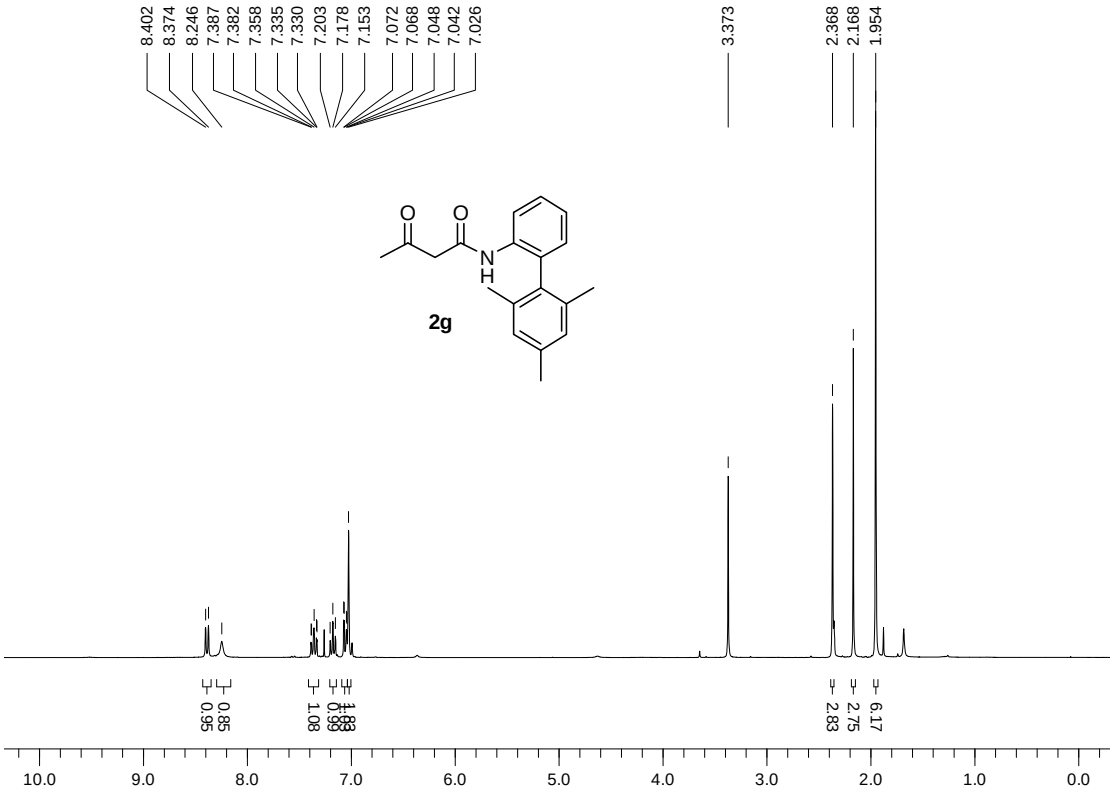
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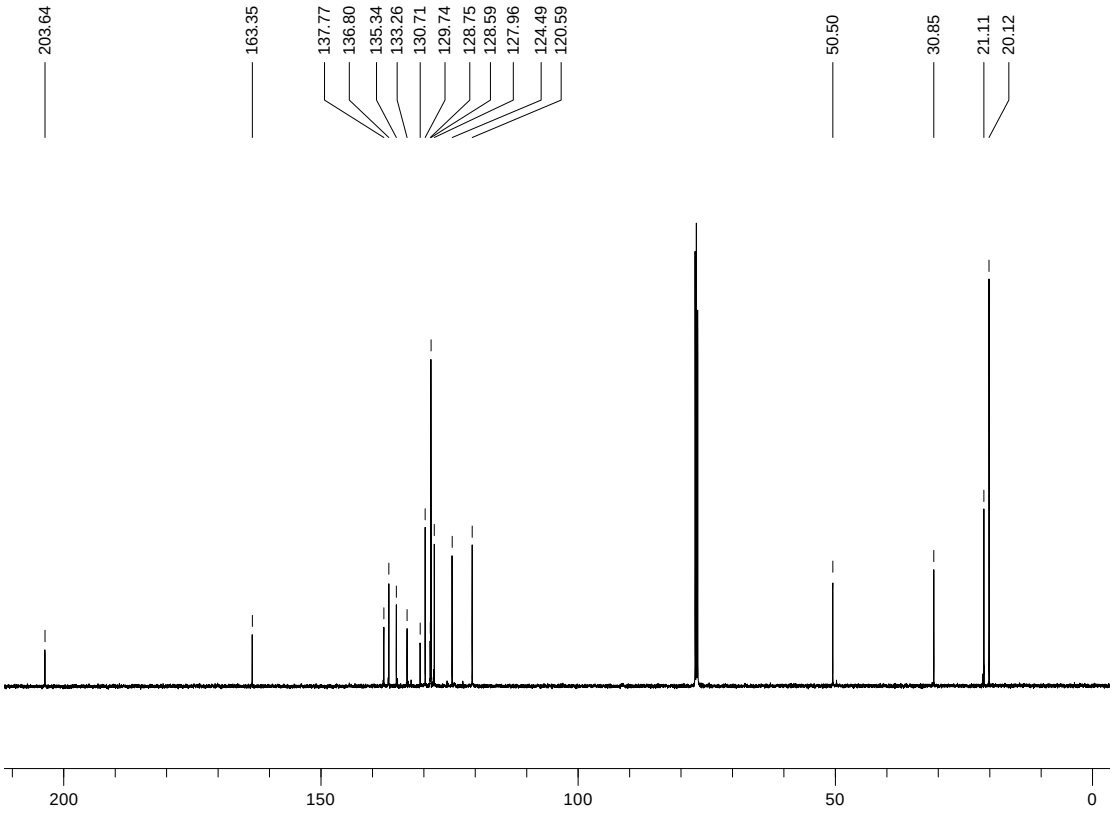
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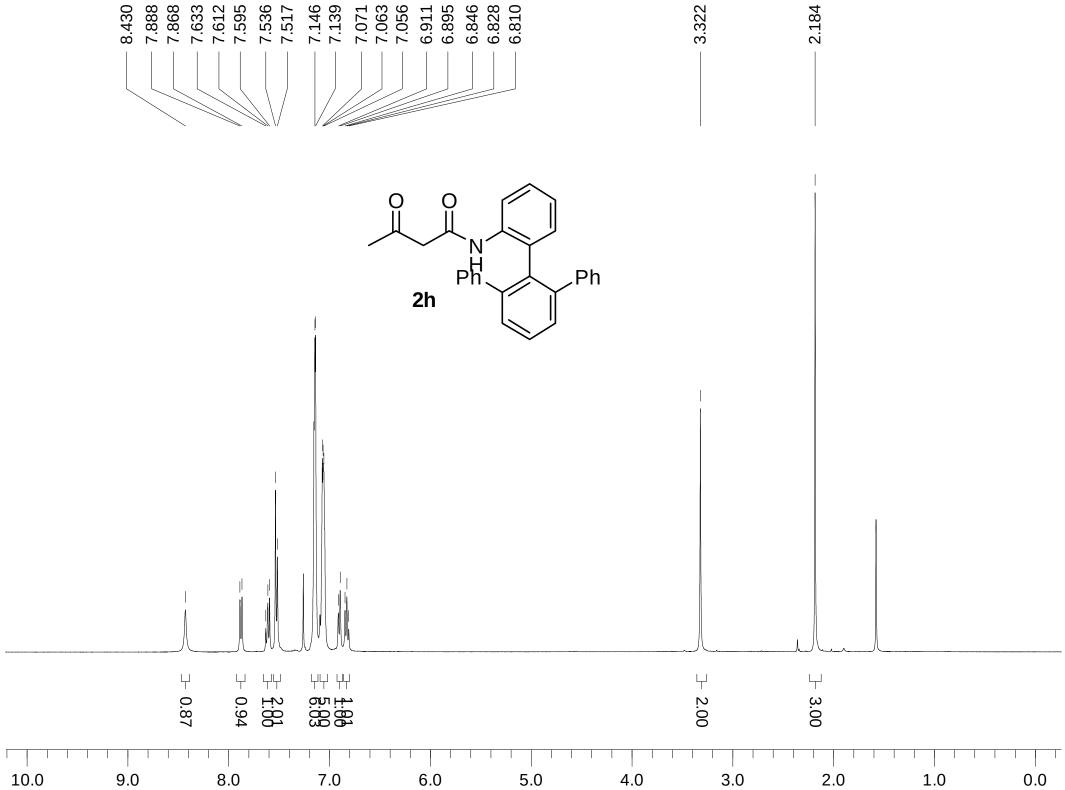
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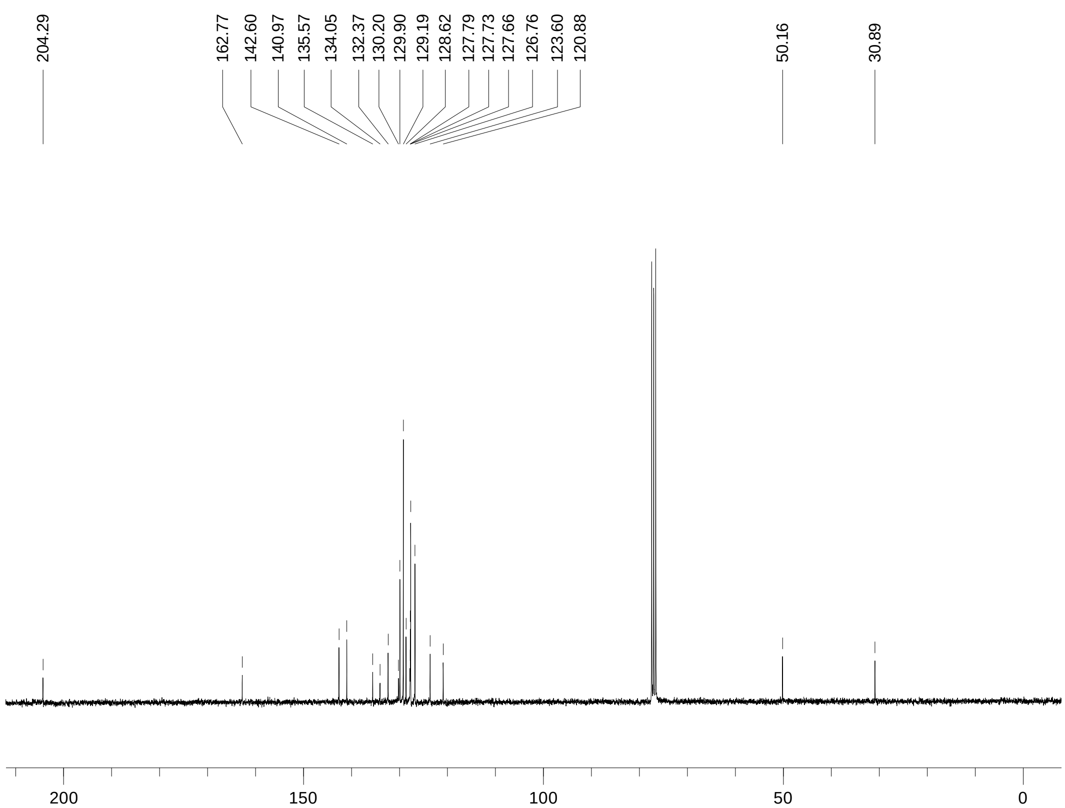
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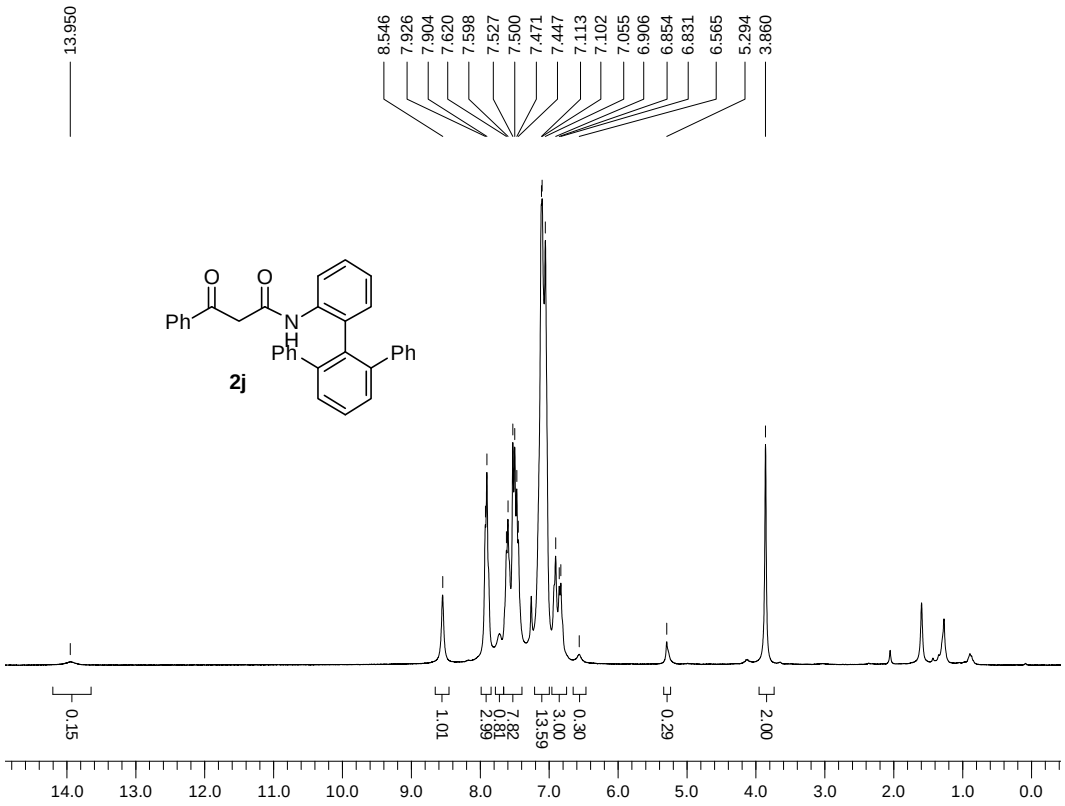
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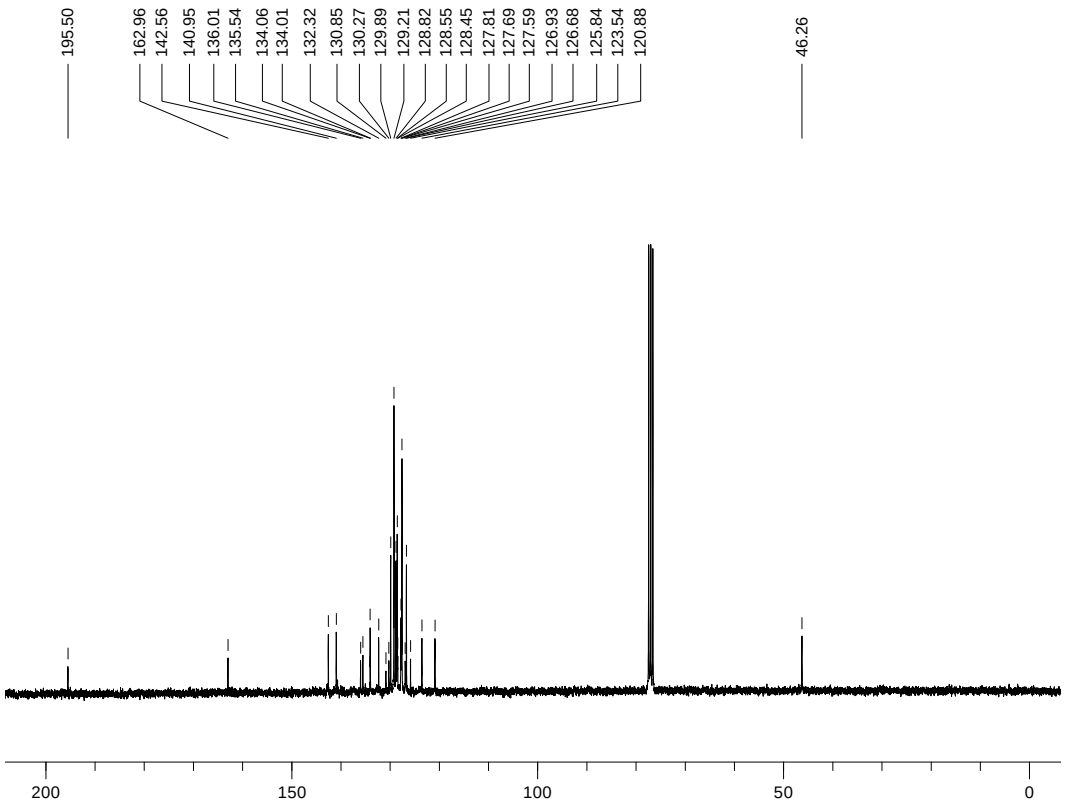
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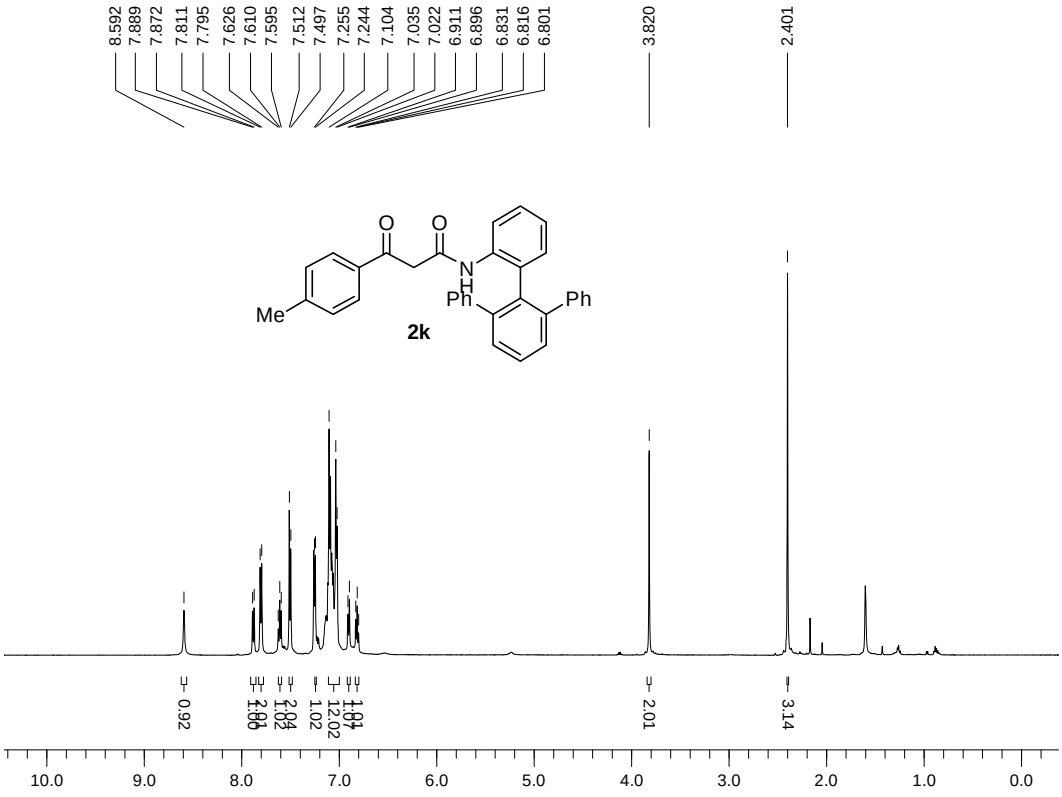
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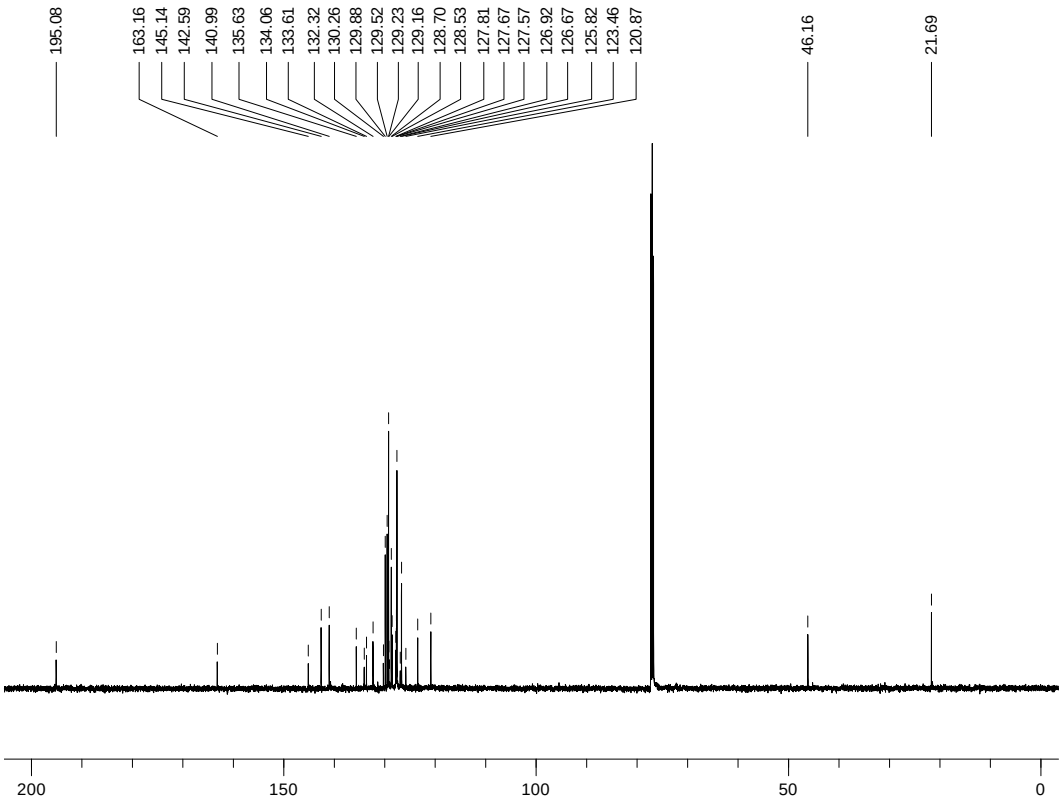
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129.23
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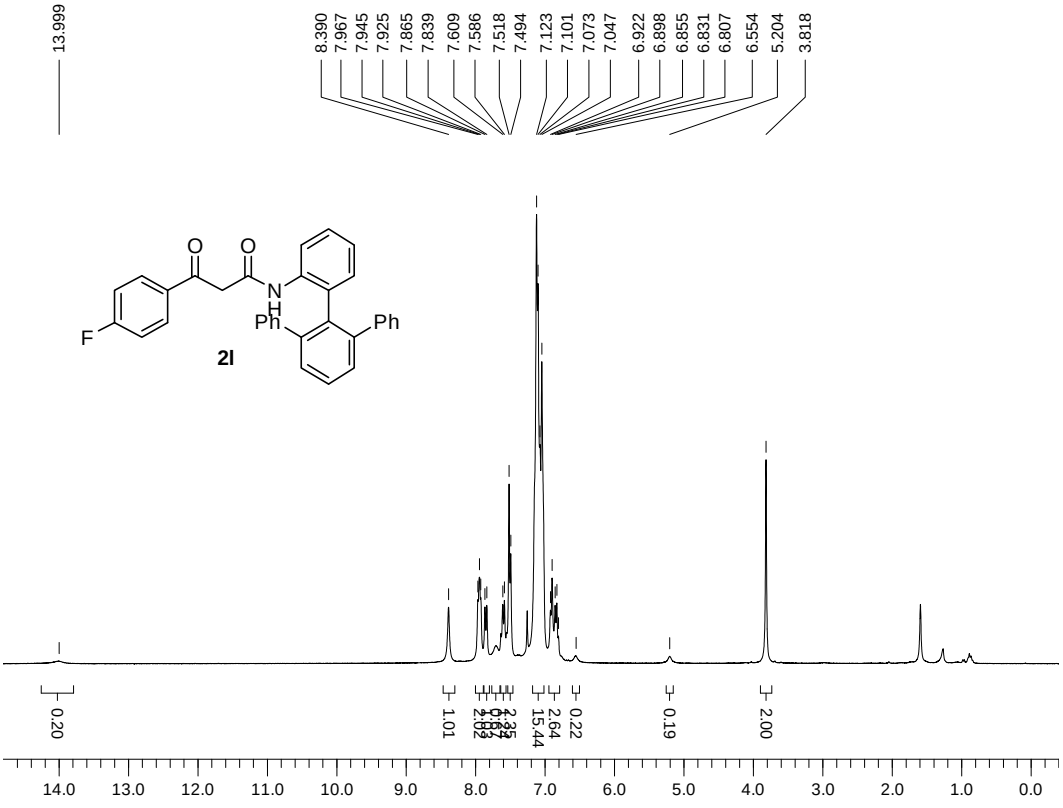
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7.123
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7.073
7.047
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6.898
6.855
6.831
6.807
6.554
5.204
3.818
O
O
N
H
Ph
Ph
F
2l
0.20
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15.44
2.94
0.22
0.19
2.00
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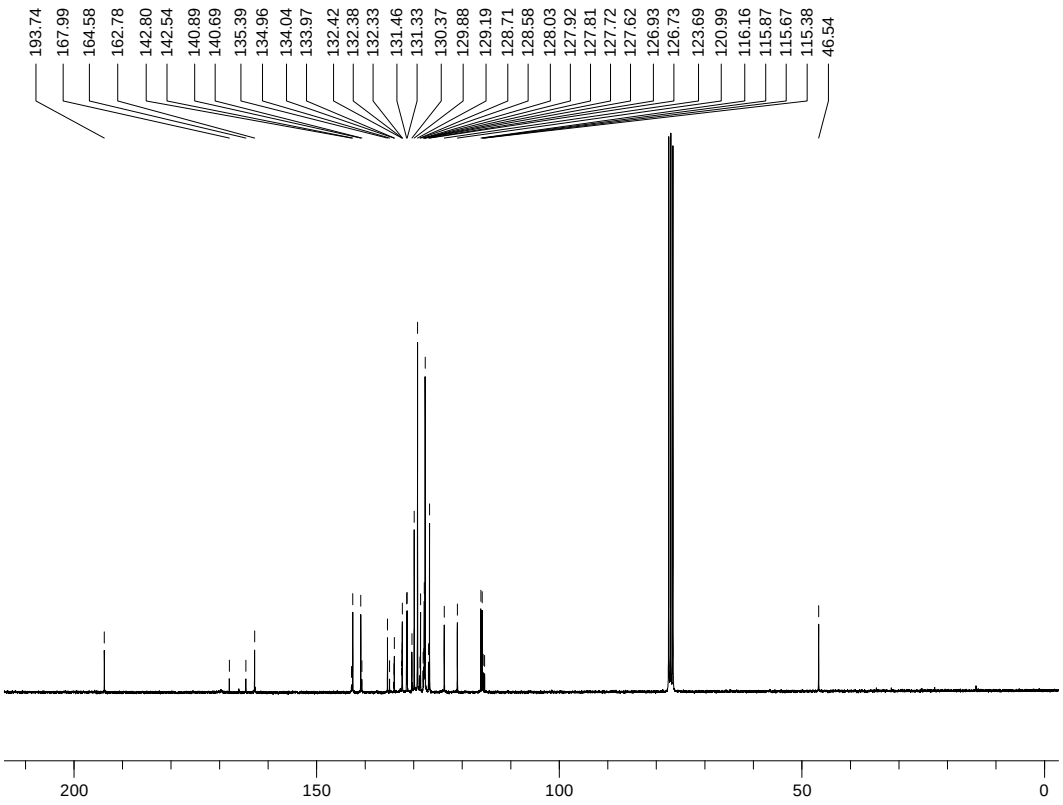
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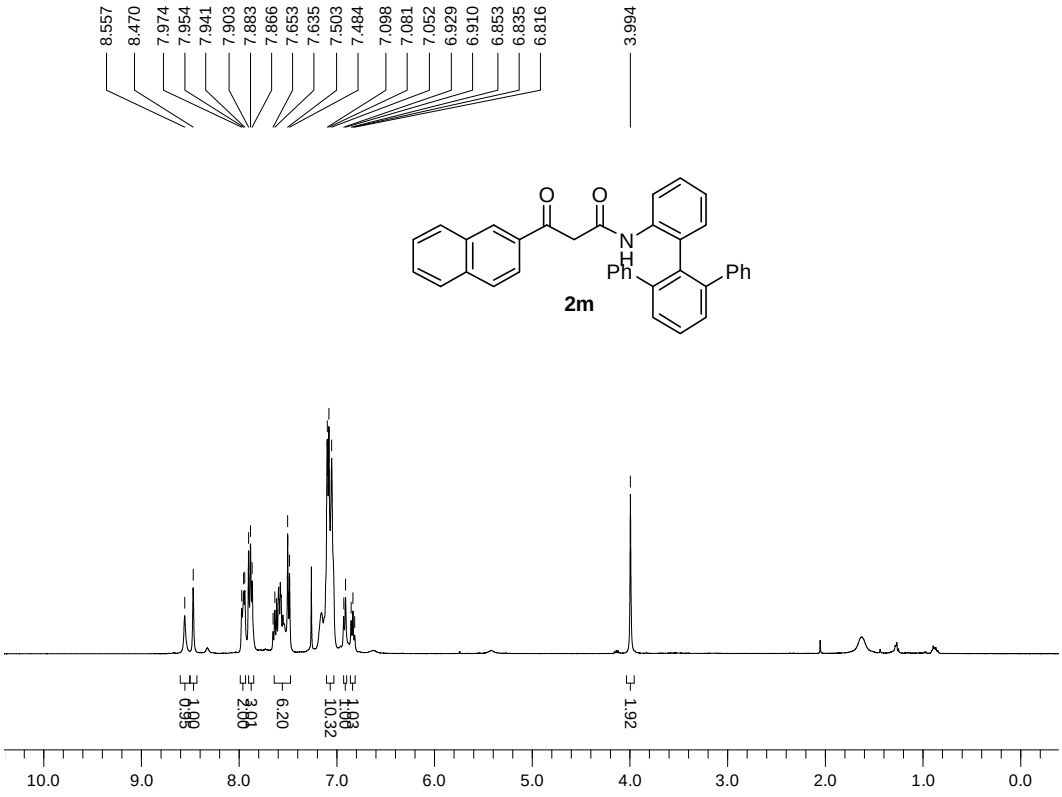
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7.484
7.098
7.081
7.052
6.929
6.910
6.853
6.835
6.816
3.994
O
O
N
H
Ph
Ph
2m
1.00
2.01
6.20
10.32
11.03
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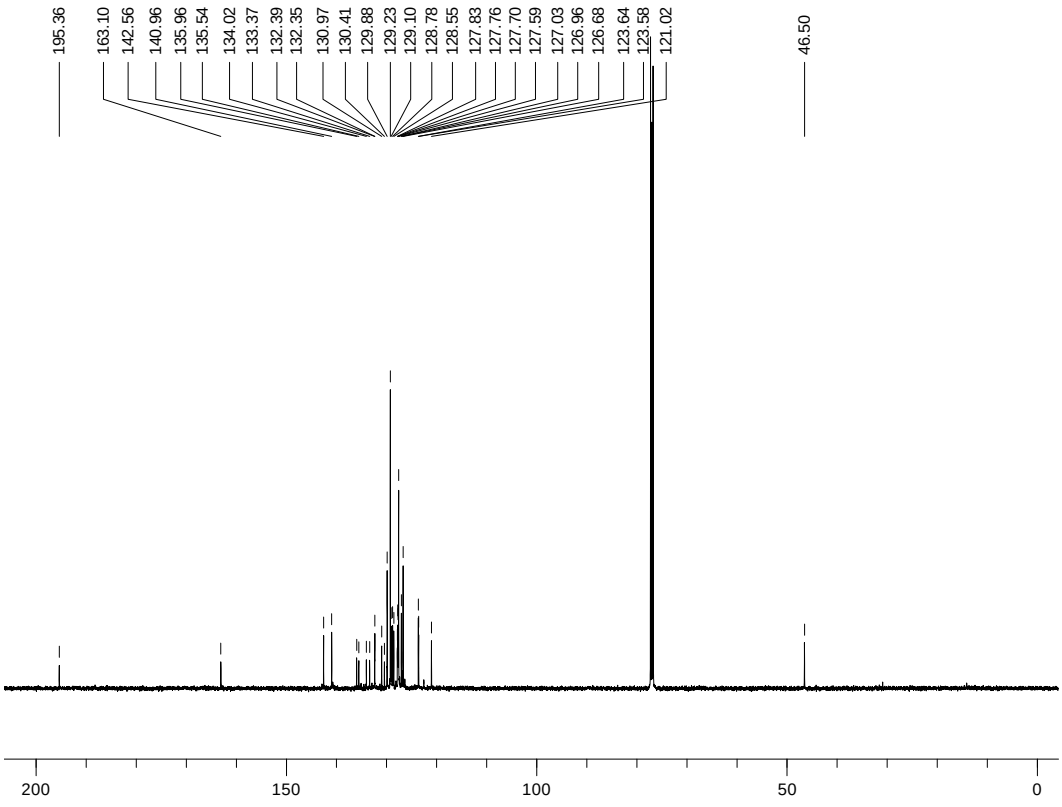
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135.54
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129.23
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128.78
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127.83
127.76
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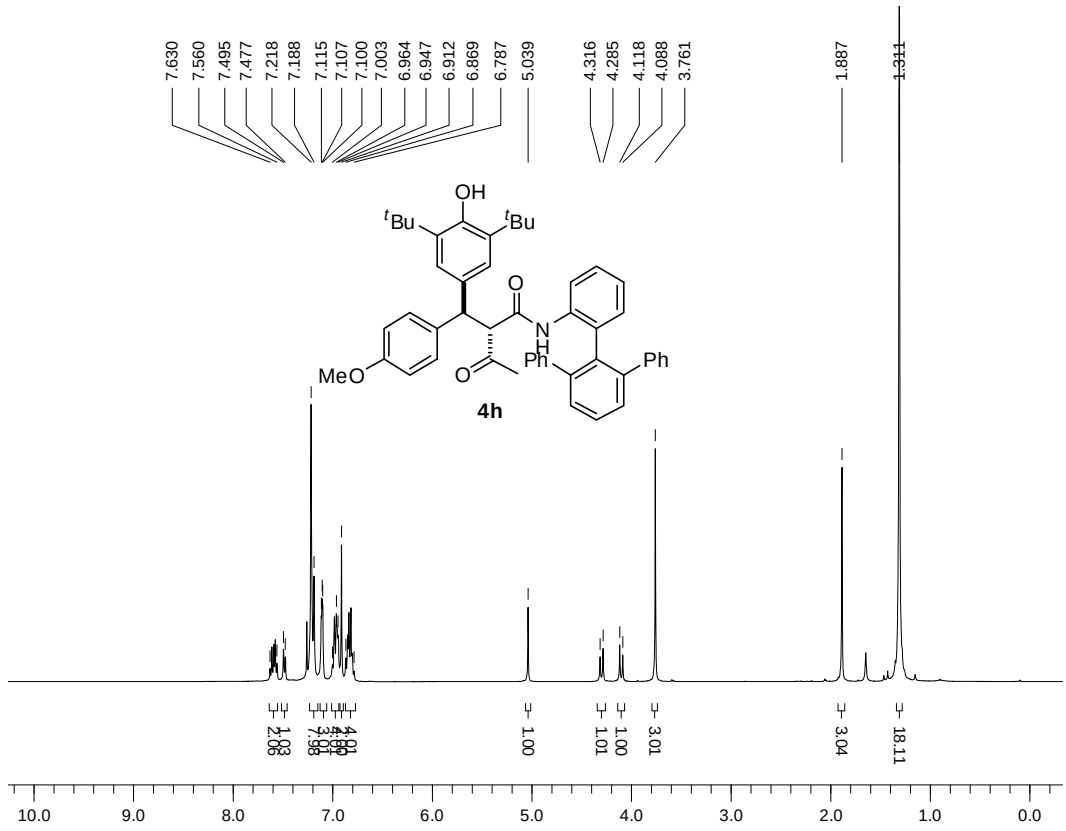
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7.495
7.477
7.218
7.188
7.115
7.107
7.100
7.003
6.964
6.947
6.912
6.869
6.787
5.039
4.316
4.285
4.118
4.088
3.761
1.887
1.311
OH
tBu
tBu
O
N
H
Ph
Ph
MeO
O
4h
2.08
1.03
3.01
1.00
1.01
1.00
3.01
3.04
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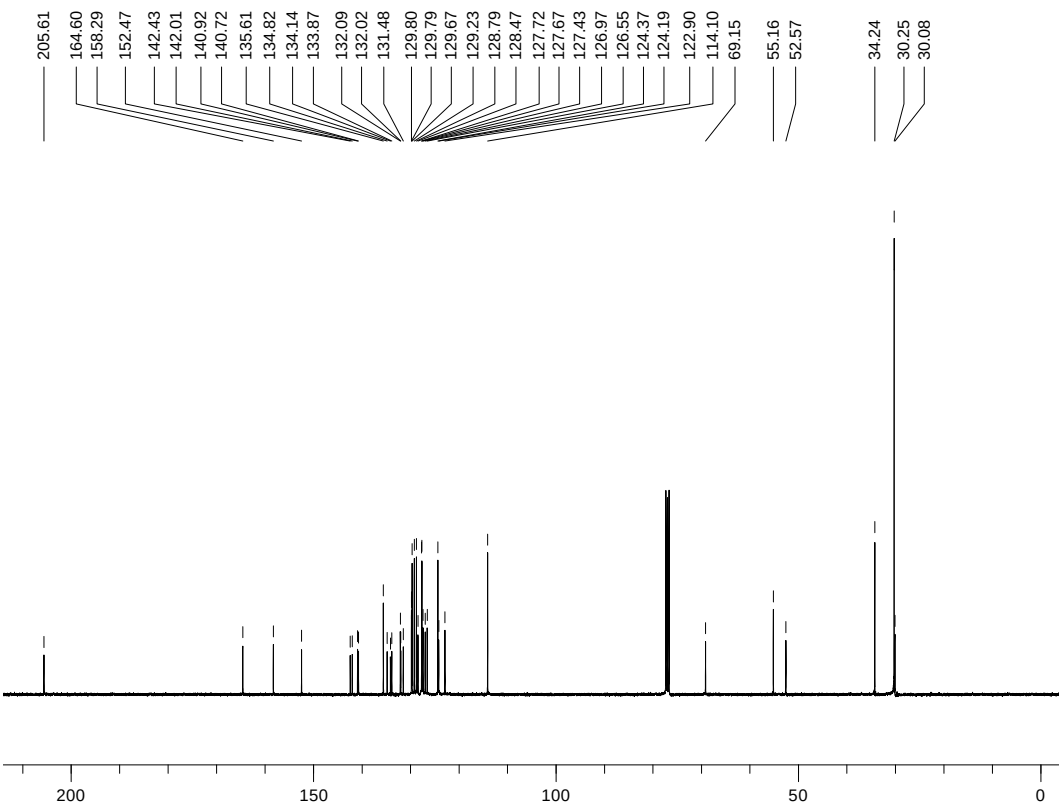
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133.87
132.09
132.02
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129.80
129.79
129.67
129.23
128.79
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127.72
127.67
127.43
126.97
126.55
124.37
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52.57
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30.25
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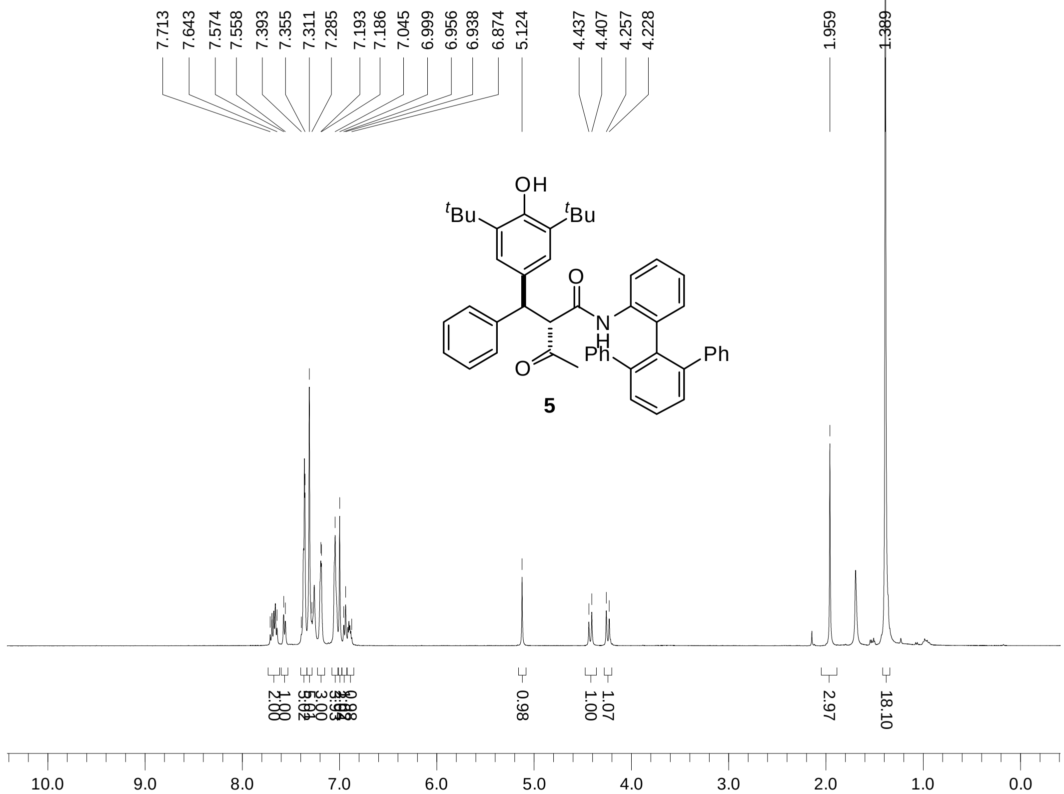
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7.558
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7.355
7.311
7.285
7.193
7.186
7.045
6.999
6.956
6.938
6.874
5.124
4.437
4.407
4.257
4.228
1.959
1.389
OH
tBu
tBu
O
N
H
Ph
Ph
O
5
2.00
1.00
3.00
0.98
1.00
1.07
2.97
18.10
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8.0
7.0
6.0
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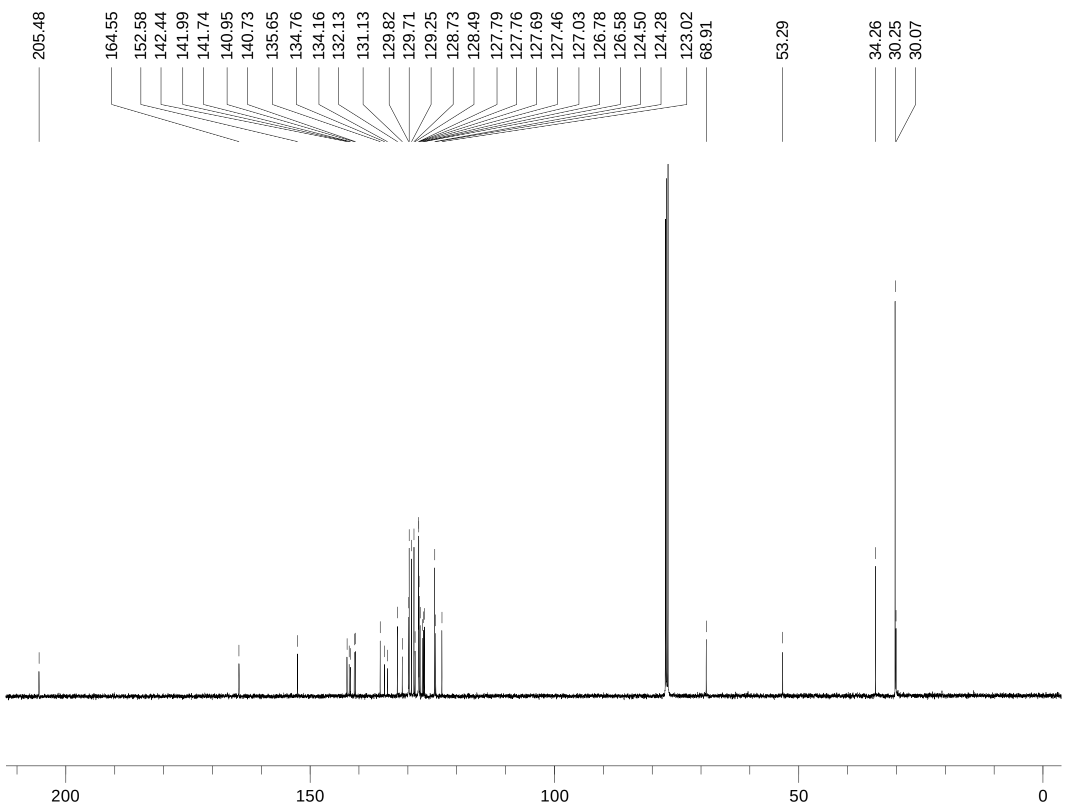
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129.71
129.25
128.73
128.49
127.79
127.76
127.69
127.46
127.03
126.78
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124.28
123.02
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30.25
30.07
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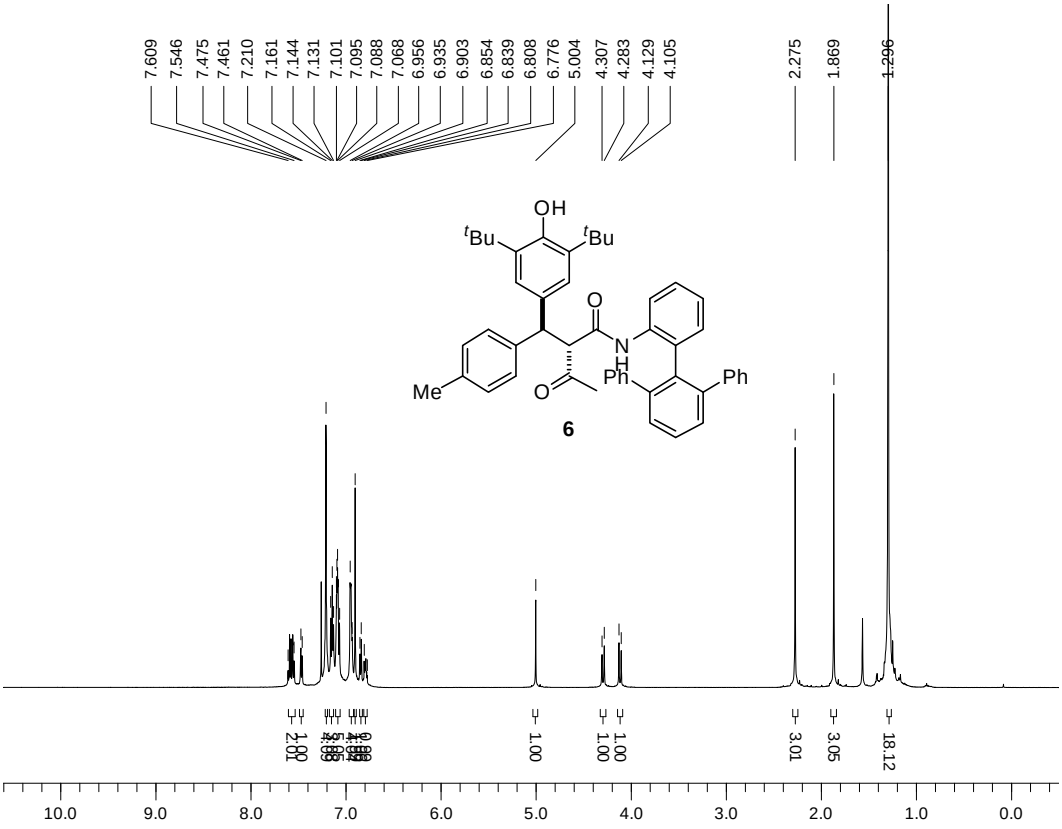
150
100
50
0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7.161
7.144
7.131
7.101
7.095
7.088
7.068
6.956
6.935
6.903
6.854
6.839
6.808
6.776
5.004
4.307
4.283
4.129
4.105
2.275
1.869
1.296
OH
tBu
tBu
O
N
H
Ph
Ph
Me
O
6
2.01
1.00
1.00
1.00
3.01
3.05
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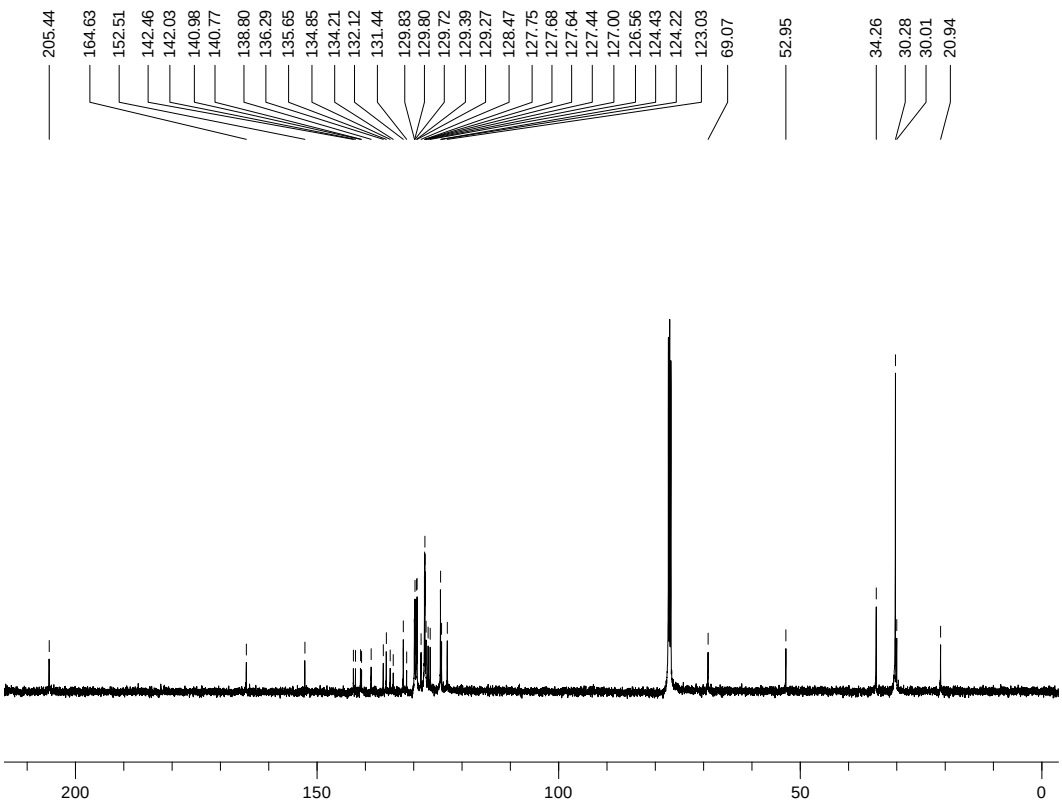
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129.80
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129.39
129.27
128.47
127.75
127.68
127.64
127.44
127.00
126.56
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69.07
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34.26
30.28
30.01
20.94
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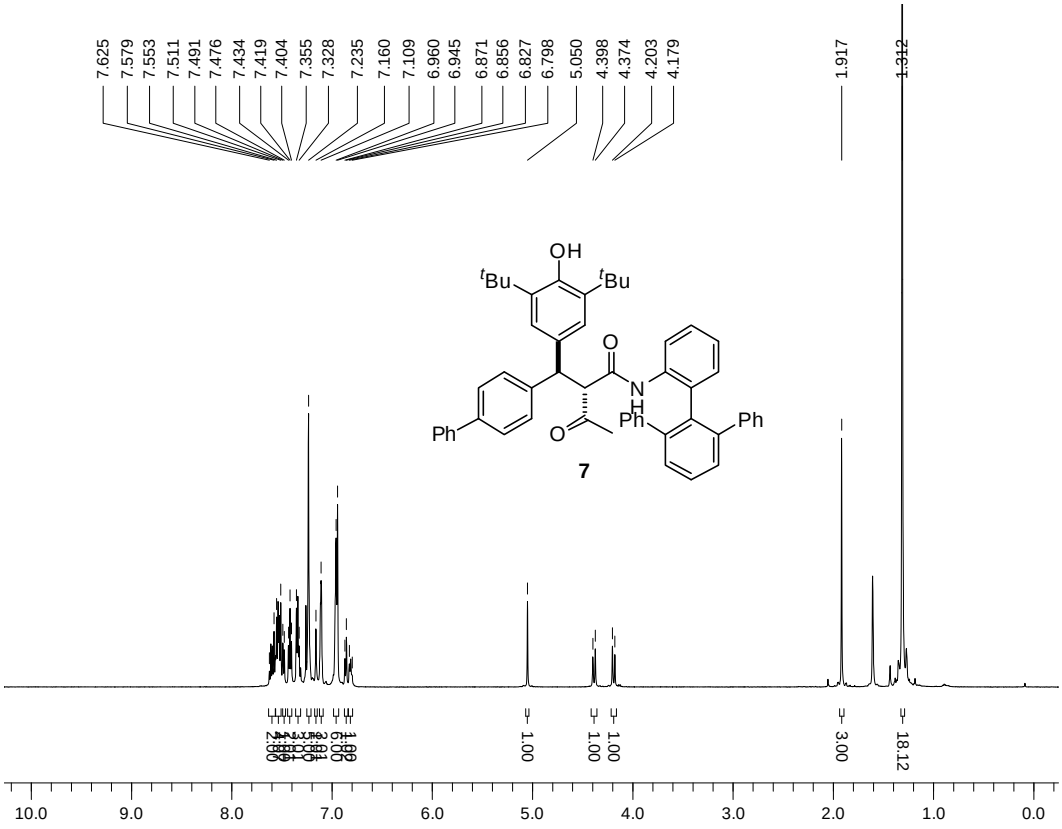
150
100
50
0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7.419
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7.328
7.235
7.160
7.109
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6.945
6.871
6.856
6.827
6.798
5.050
4.398
4.374
4.203
4.179
1.917
1.312
OH
tBu
tBu
O
N
H
Ph
Ph
Ph
O
7
1.00
1.00
1.00
3.00
18.12
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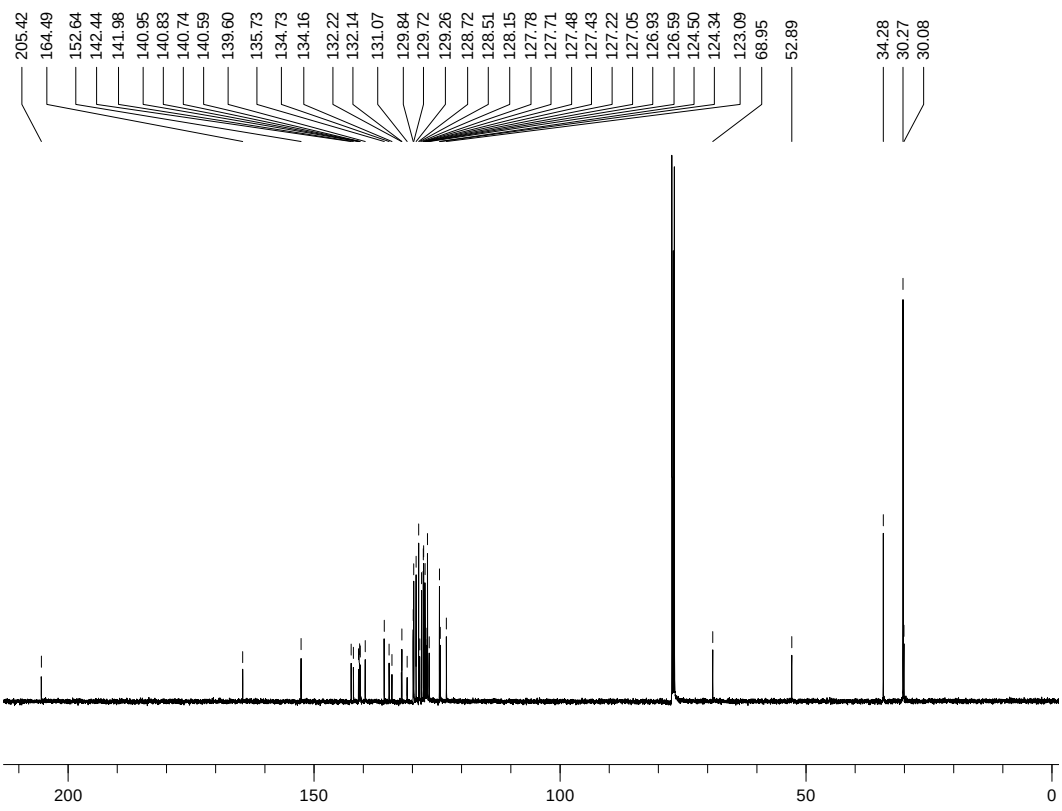
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134.16
132.22
132.14
131.07
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129.72
129.26
128.72
128.51
128.15
127.78
127.71
127.48
127.43
127.22
127.05
126.93
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123.09
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30.27
30.08
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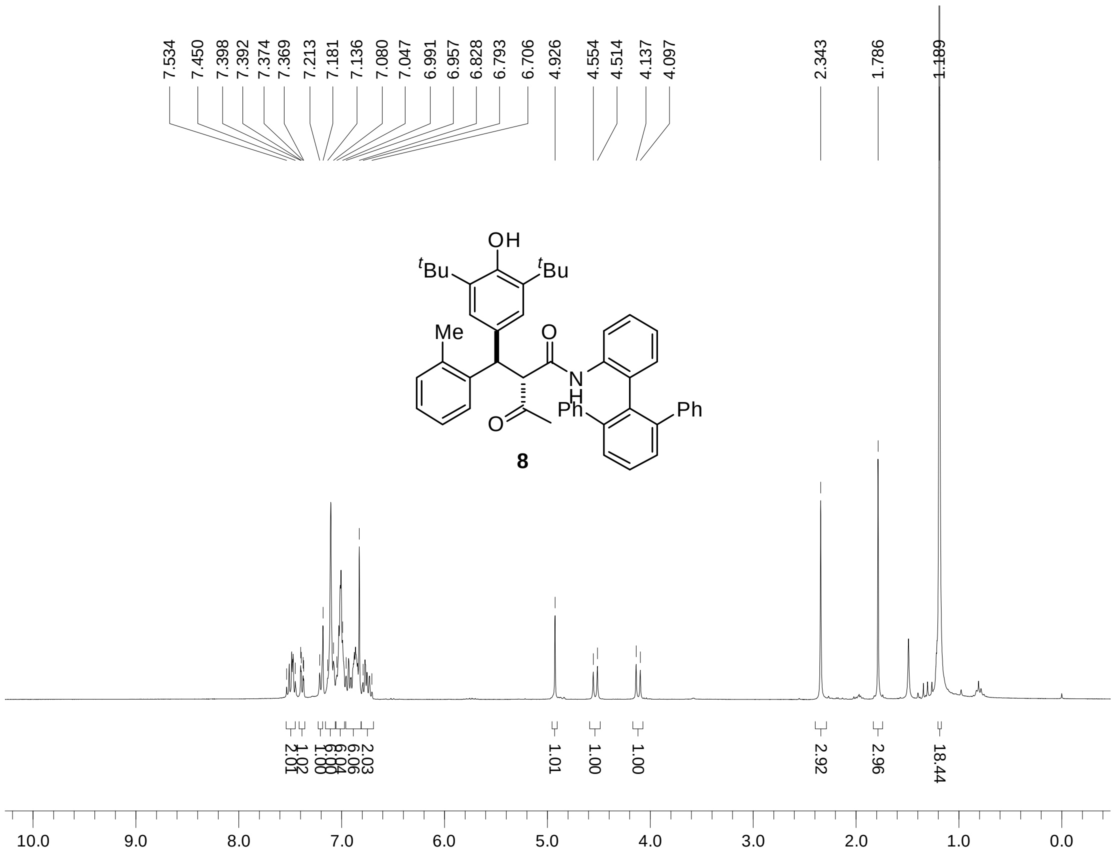
100
50
0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7.080
7.047
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6.706
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4.514
4.137
4.097
2.343
1.786
1.189
OH
^{t}Bu
^{t}Bu
Me
O
N
H
Ph
Ph
O
8
2.01
1.02
1.00
6.04
6.06
2.03
1.01
1.00
1.00
2.92
2.96
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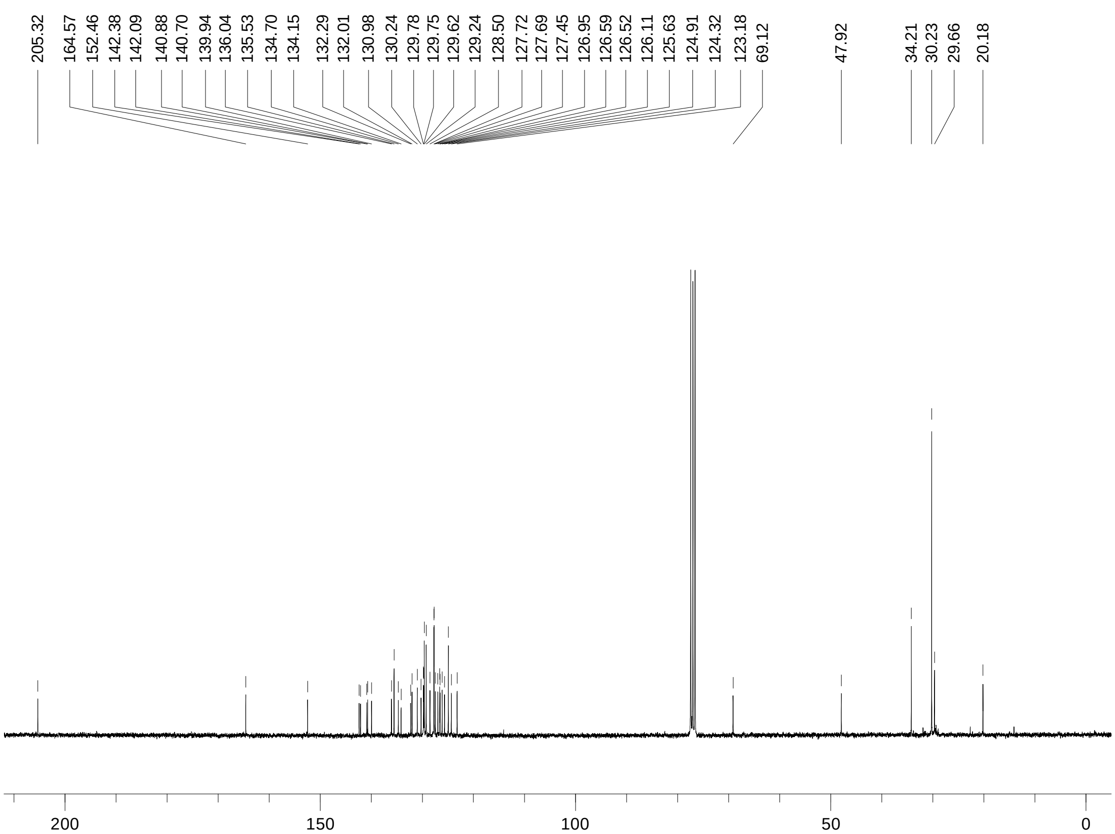
0.0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129.24
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126.52
126.11
125.63
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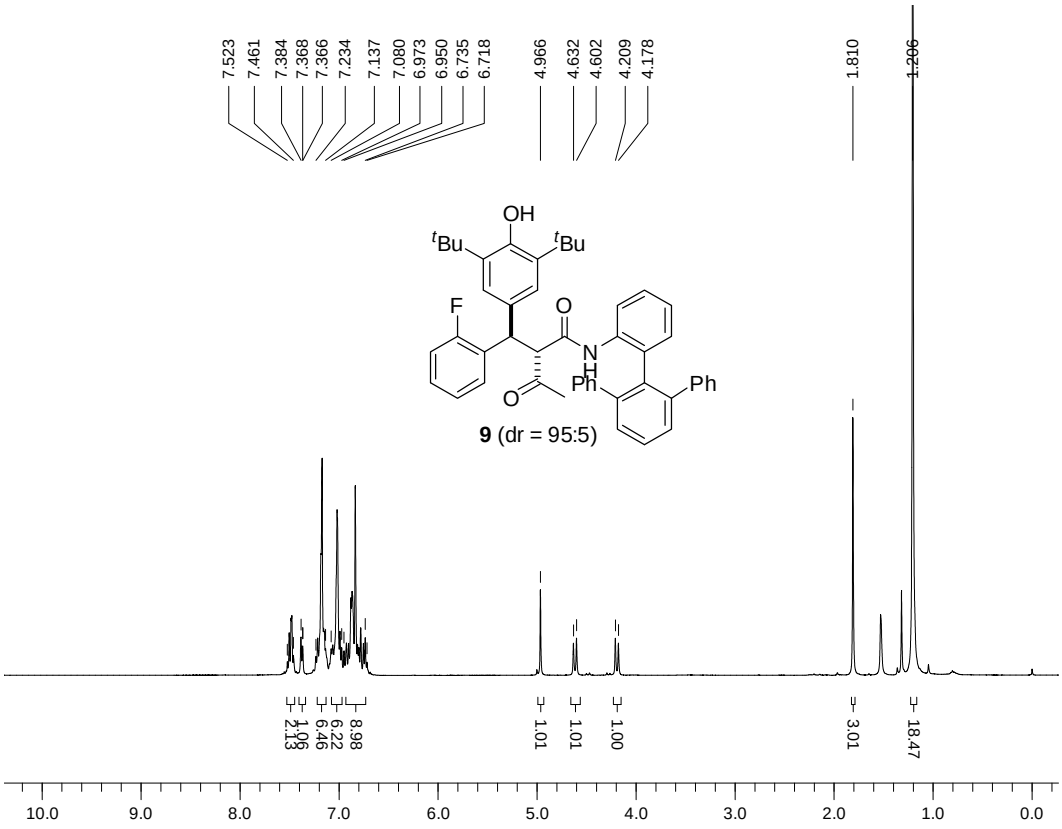
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4.632
4.602
4.209
4.178
1.810
1.206
OH
tBu
tBu
F
O
N
H
Ph
Ph
O
9 (dr = 95:5)
2.13
1.08
6.46
6.22
8.98
1.01
1.01
1.00
3.01
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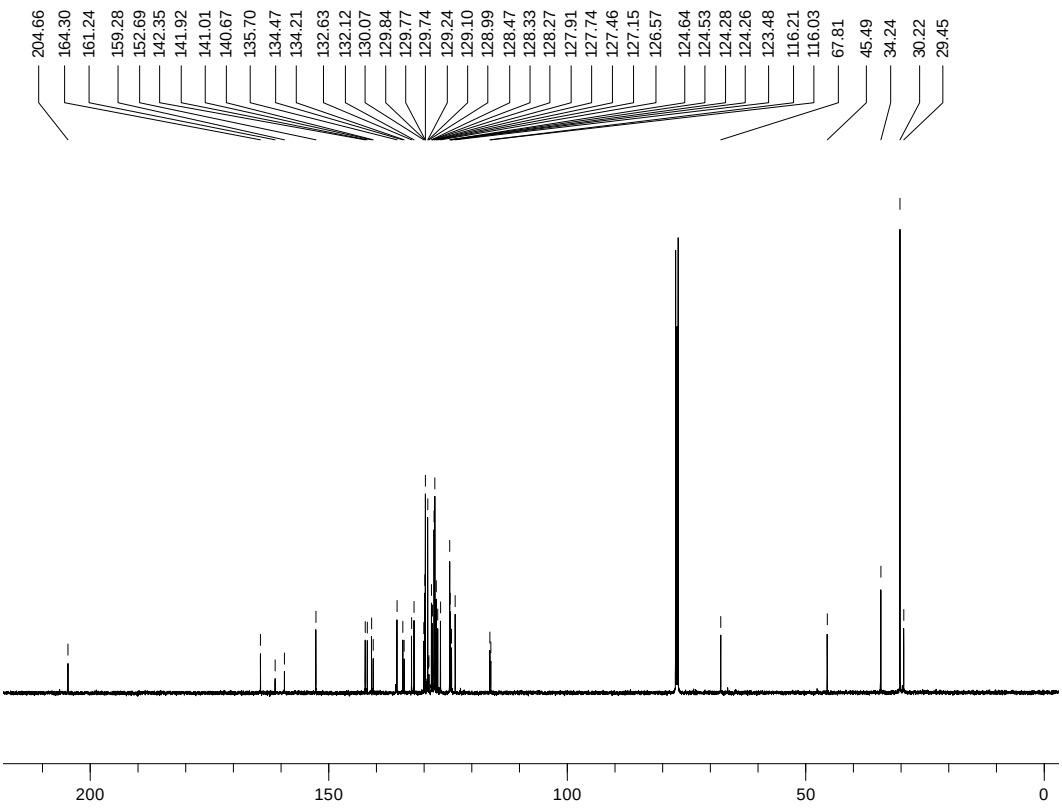
0.0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127.15
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124.64
124.53
124.28
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116.03
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45.49
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30.22
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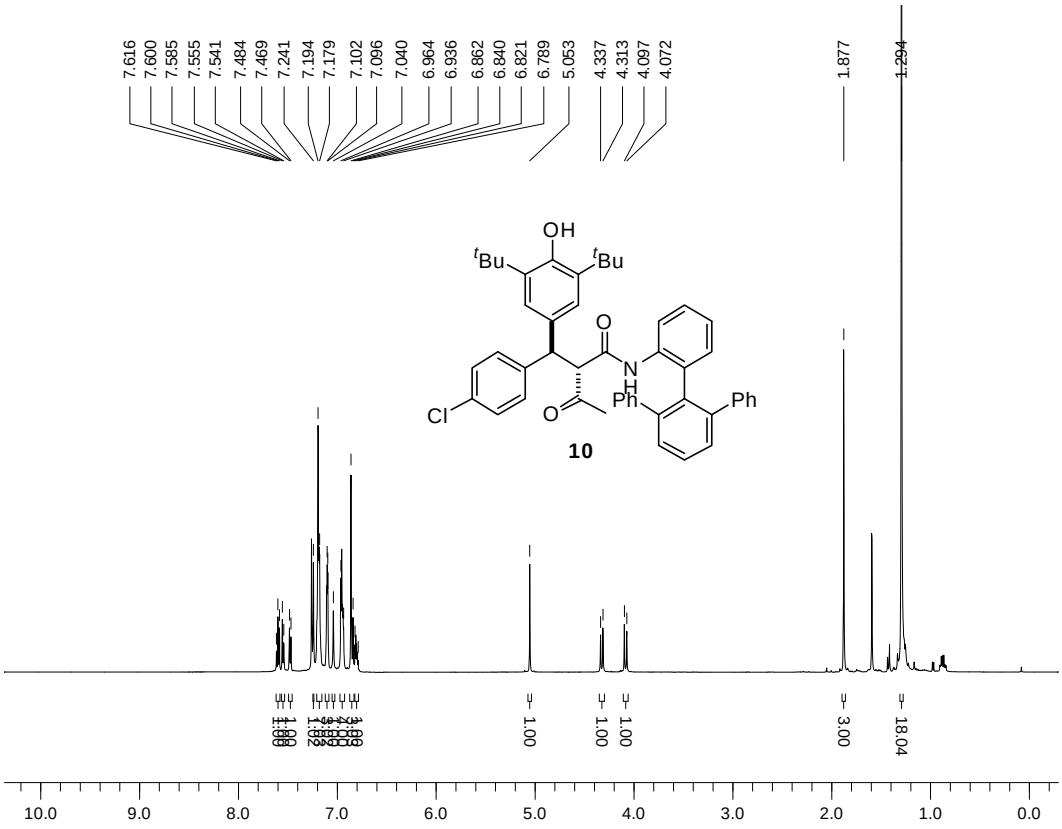
50
0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7.040
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6.789
5.053
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4.313
4.097
4.072
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1.294
OH
tBu
tBu
O
N
H
Ph
Ph
Cl
O
10
1.00
1.00
1.00
3.00
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4.0
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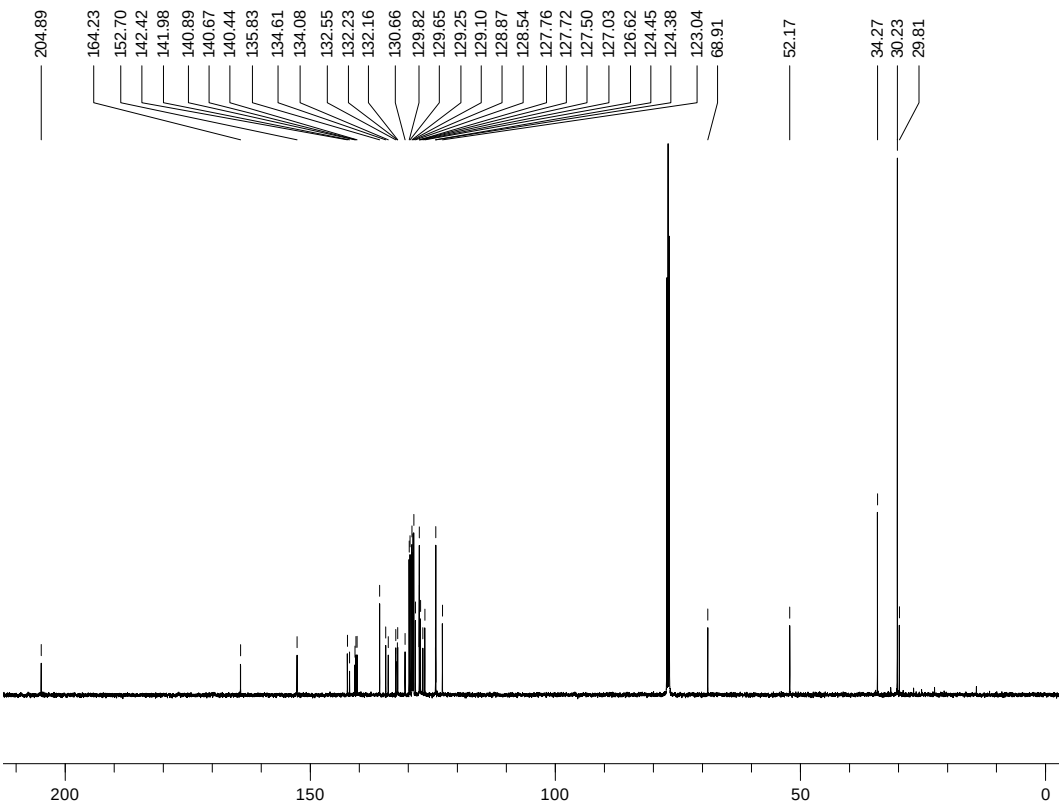
0.0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129.82
129.65
129.25
129.10
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127.76
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127.50
127.03
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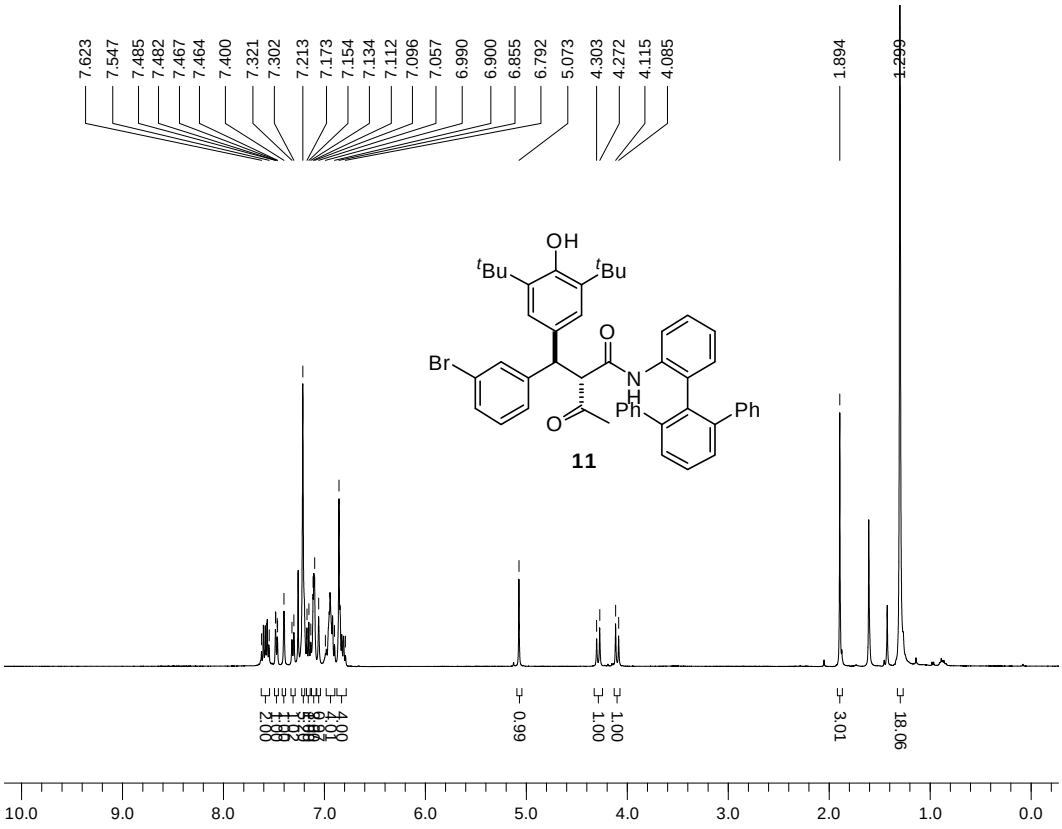
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7.112
7.096
7.057
6.990
6.900
6.855
6.792
5.073
4.303
4.272
4.115
4.085
1.894
1.299
OH
tBu
tBu
O
Br
N
H
Ph
Ph
O
11
0.99
1.00
1.00
3.01
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4.0
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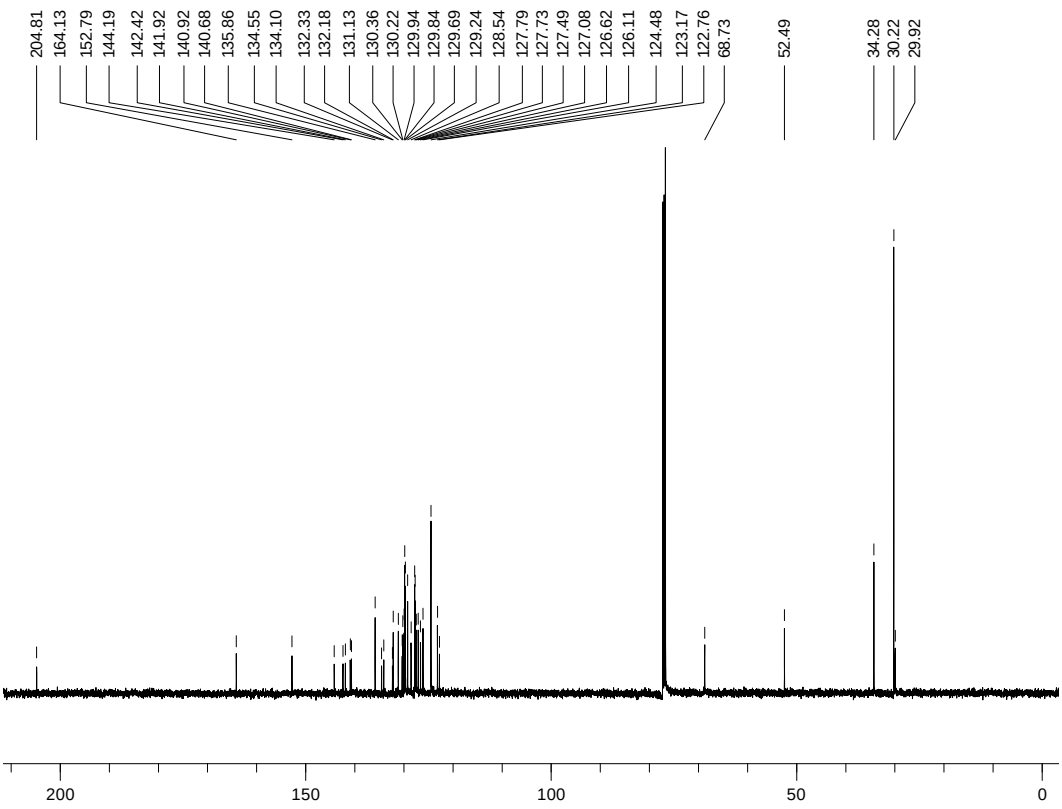
2.0
1.0
0.0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130.22
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129.84
129.69
129.24
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127.73
127.49
127.08
126.62
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150
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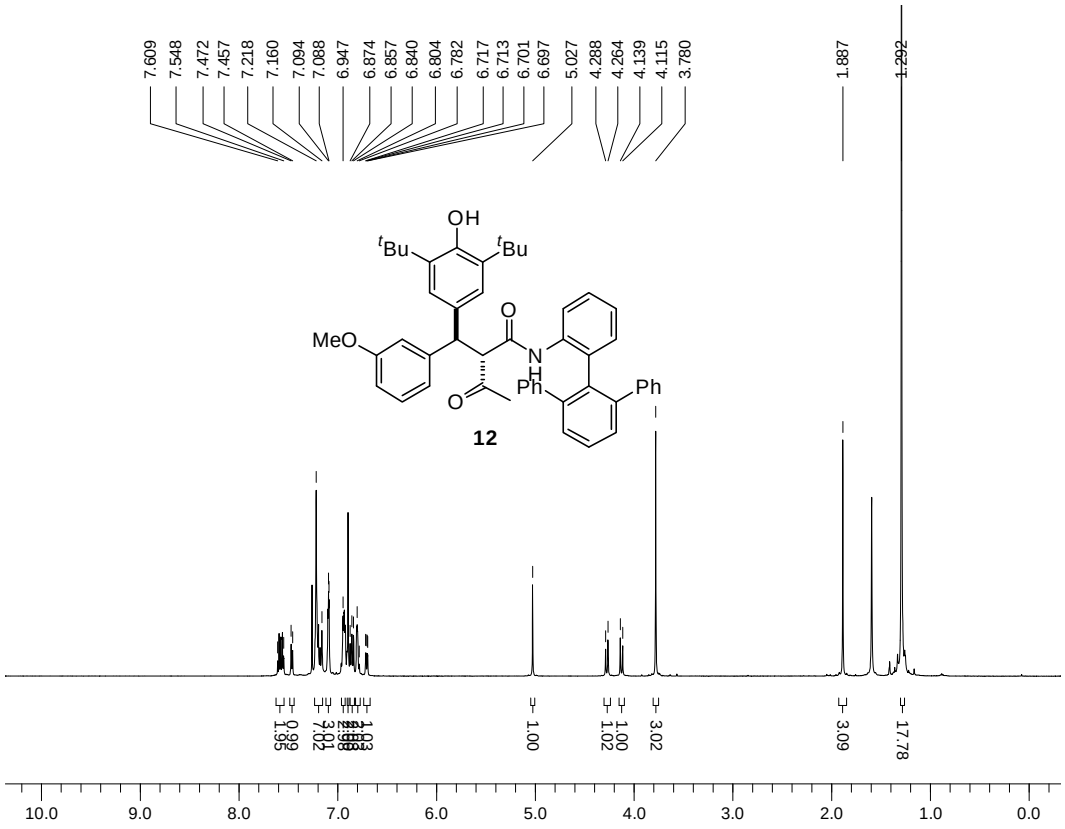
50
0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6.804
6.782
6.717
6.713
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5.027
4.288
4.264
4.139
4.115
3.780
1.887
1.292
OH
tBu
tBu
MeO
O
N
H
Ph
Ph
O
12
0.98
1.95
3.02
1.00
1.02
1.00
3.02
3.09
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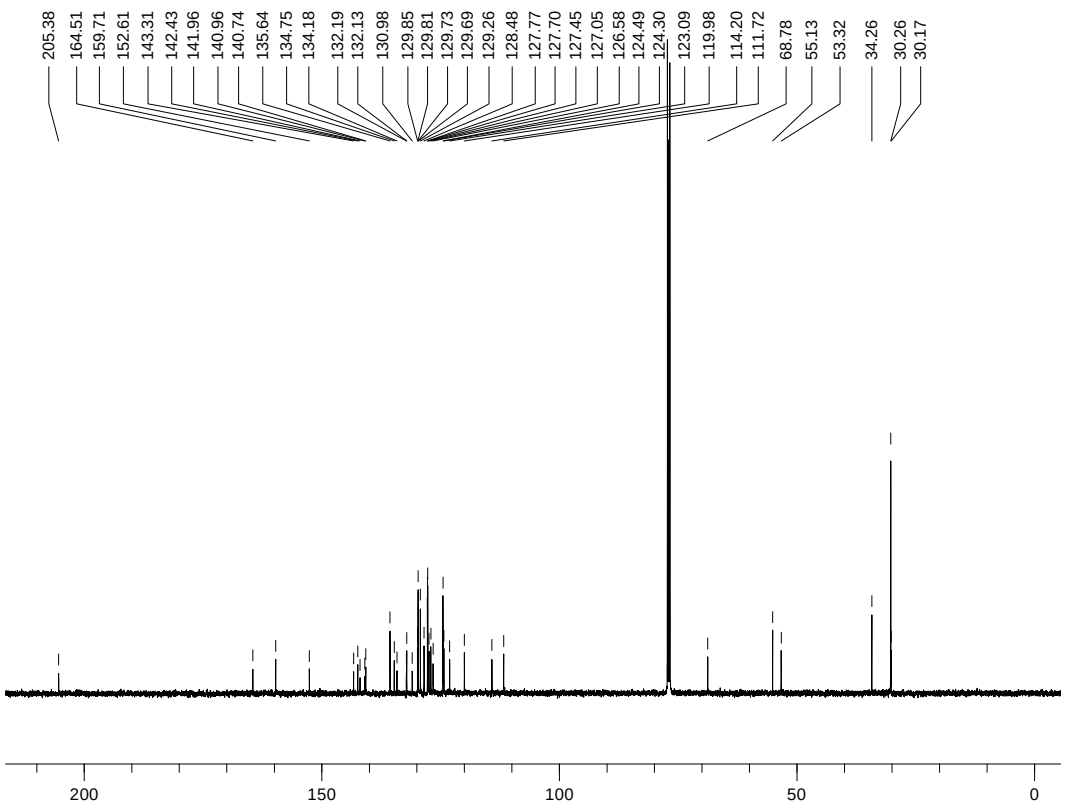
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129.69
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127.70
127.45
127.05
126.58
124.49
124.30
123.09
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68.78
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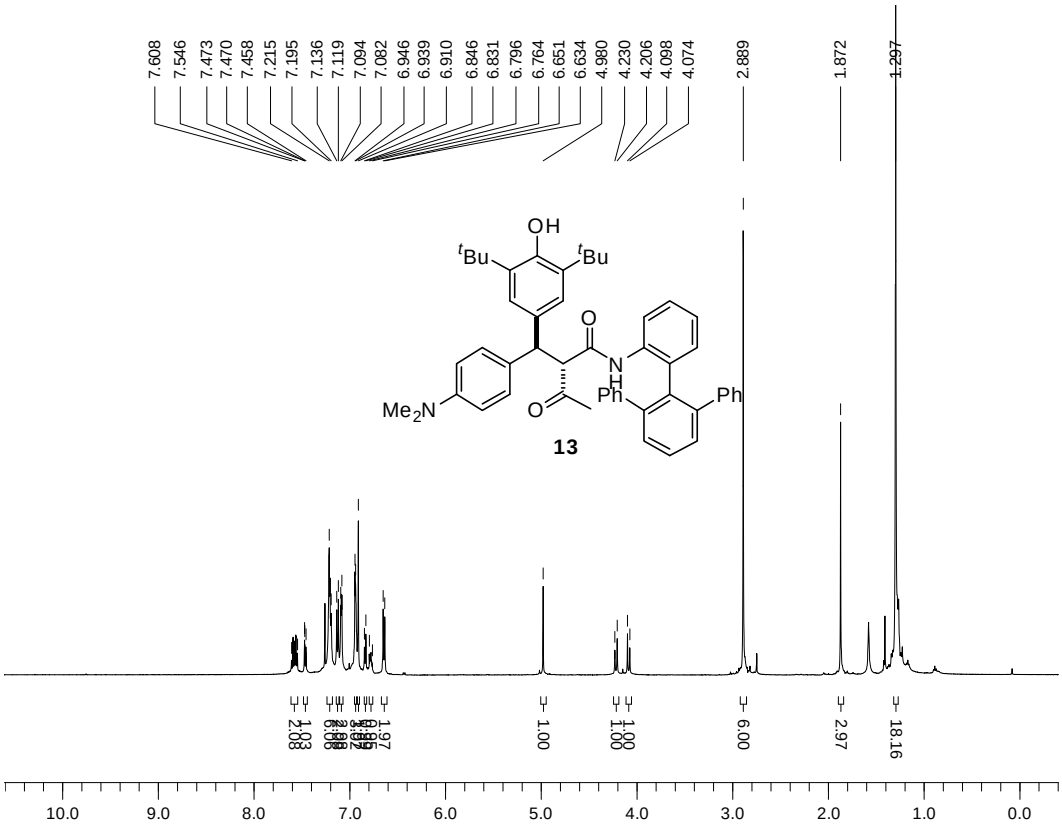
30.26
30.17
200
150
100
50
0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6.939
6.910
6.846
6.831
6.796
6.764
6.651
6.634
4.980
4.230
4.206
4.098
4.074
2.889
1.872
1.297
OH
tBu
tBu
O
N
H
Ph
Ph
Me2N
O
13
2.08
1.97
1.00
1.00
6.00
2.97
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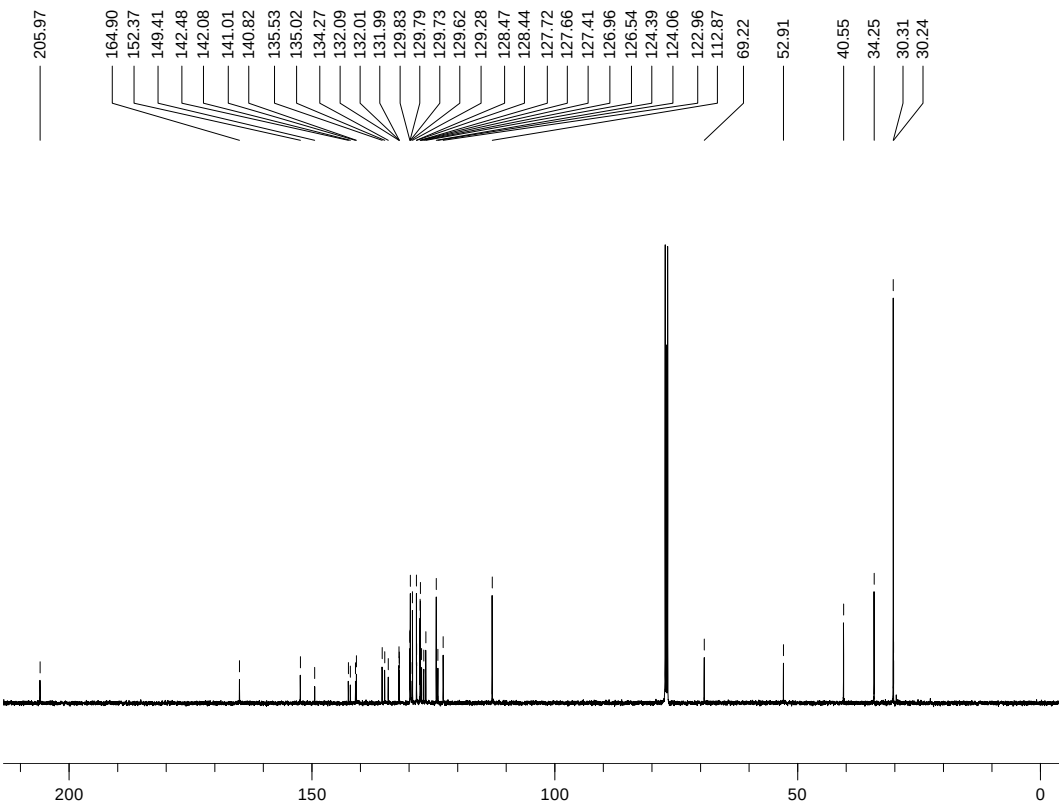
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135.02
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132.09
132.01
131.99
129.83
129.79
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129.62
129.28
128.47
128.44
127.72
127.66
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126.54
124.39
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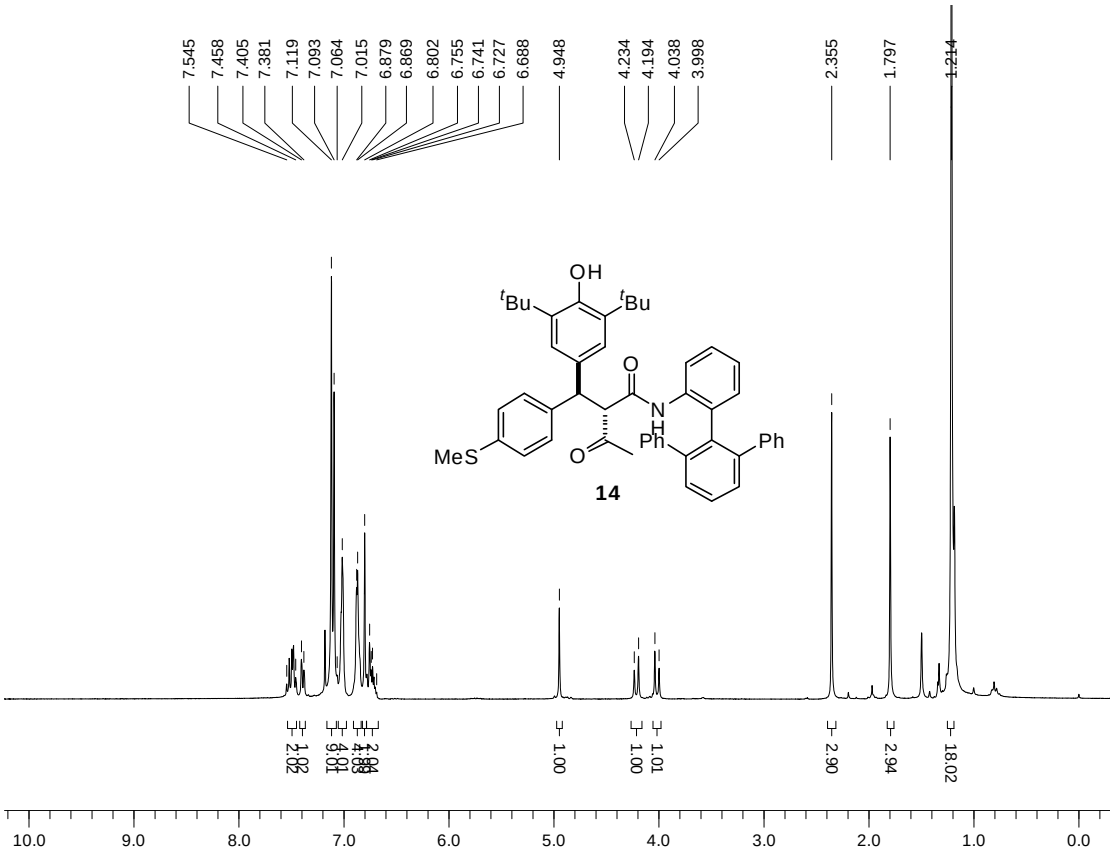
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7.064
7.015
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6.869
6.802
6.755
6.741
6.727
6.688
4.948
4.234
4.194
4.038
3.998
2.355
1.797
1.214
OH
tBu
tBu
O
N
H
Ph
Ph
MeS
O
14
2.02
1.00
1.00
1.01
2.90
2.94
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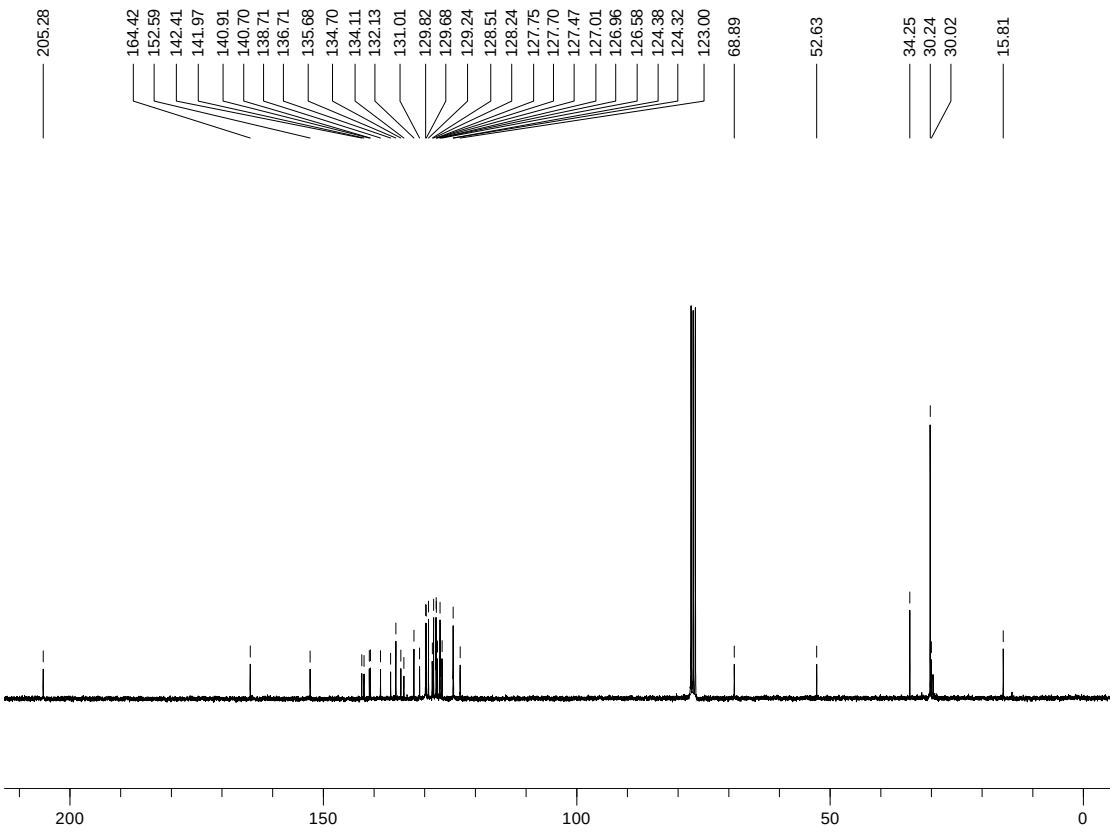
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129.68
129.24
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128.24
127.75
127.70
127.47
127.01
126.96
126.58
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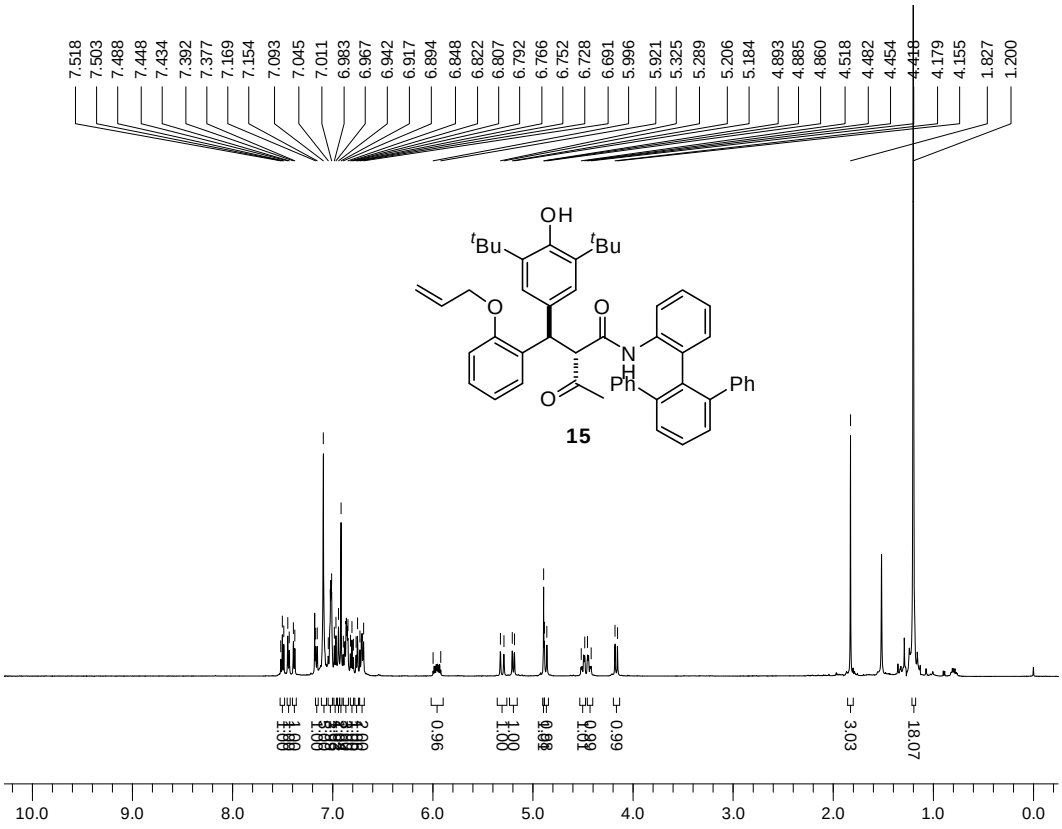
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7.169
7.154
7.093
7.045
7.011
6.983
6.967
6.942
6.917
6.894
6.848
6.822
6.807
6.792
6.766
6.752
6.728
6.691
5.996
5.921
5.325
5.289
5.206
5.184
4.893
4.885
4.860
4.518
4.482
4.454
4.418
4.179
4.155
1.827
1.200
OH
tBu
tBu
O
O
N
H
Ph
Ph
O
15
0.96
1.00
1.00
0.99
3.03
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8.0
7.0
6.0
5.0
4.0
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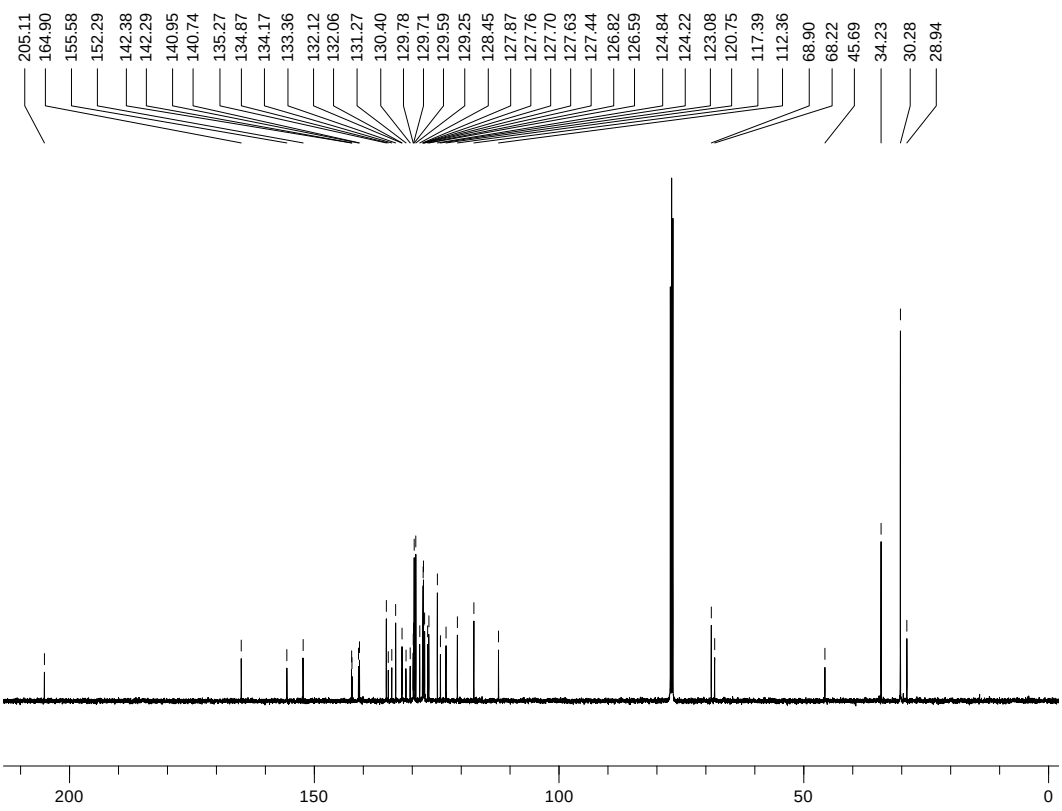
0.0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140.74
135.27
134.87
134.17
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132.12
132.06
131.27
130.40
129.78
129.71
129.59
129.25
128.45
127.87
127.76
127.70
127.63
127.44
126.82
126.59
124.84
124.22
123.08
120.75
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112.36
68.90
68.22
45.69
34.23
30.28
28.94
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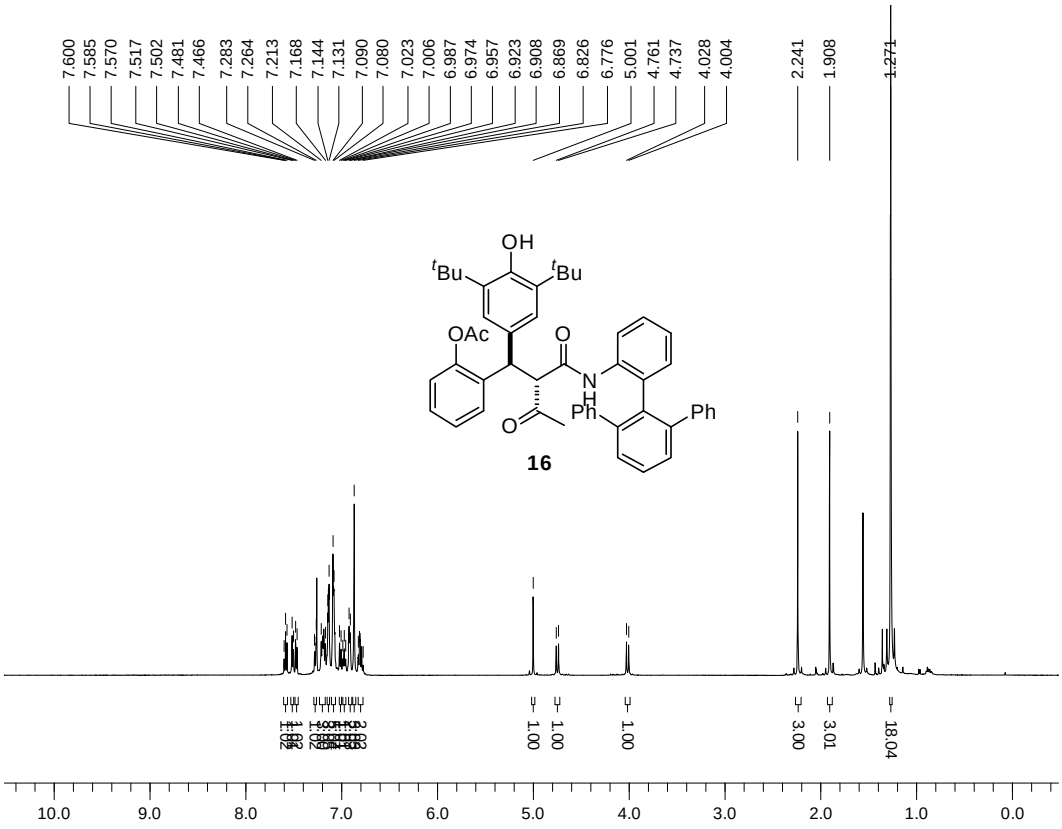
150
100
50
0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7.517
7.502
7.481
7.466
7.283
7.264
7.213
7.168
7.144
7.131
7.090
7.080
7.023
7.006
6.987
6.974
6.957
6.923
6.908
6.869
6.826
6.776
5.001
4.761
4.737
4.028
4.004
2.241
1.908
1.271
OH
tBu
tBu
OAc
O
N
H
Ph
Ph
O
16
1.00
1.00
1.00
3.00
3.01
18.04
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9.0
8.0
7.0
6.0
5.0
4.0
3.0
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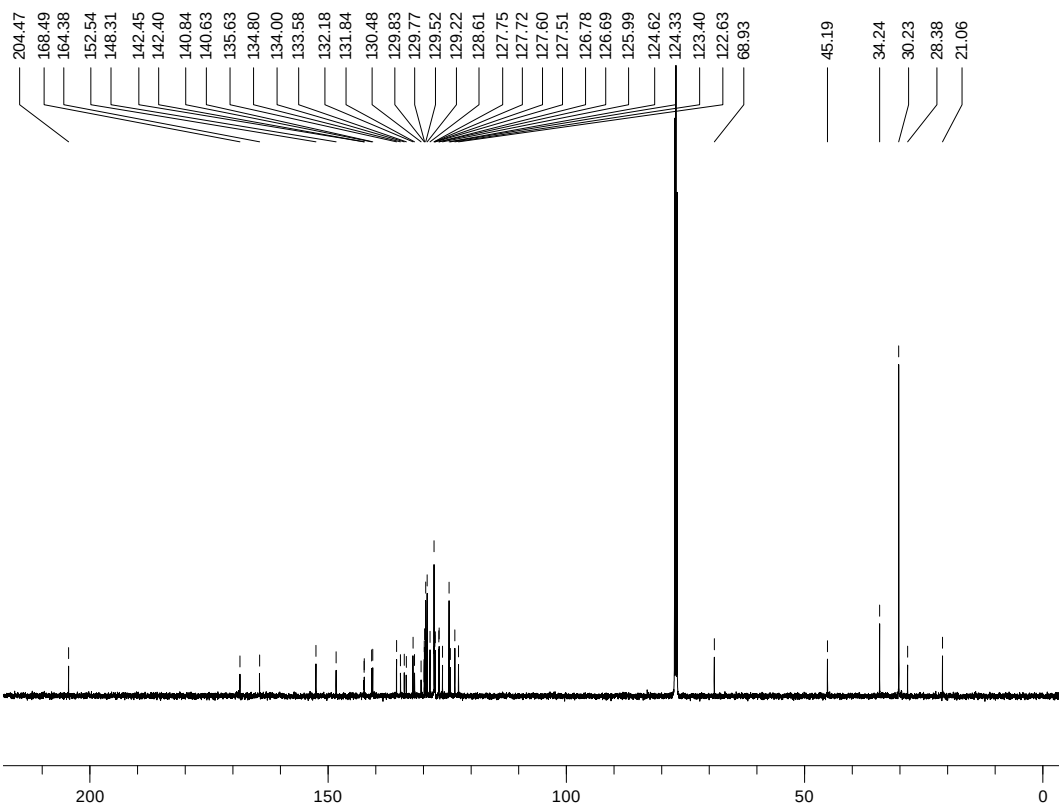
0.0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135.63
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129.83
129.77
129.52
129.22
128.61
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127.72
127.60
127.51
126.78
126.69
125.99
124.62
124.33
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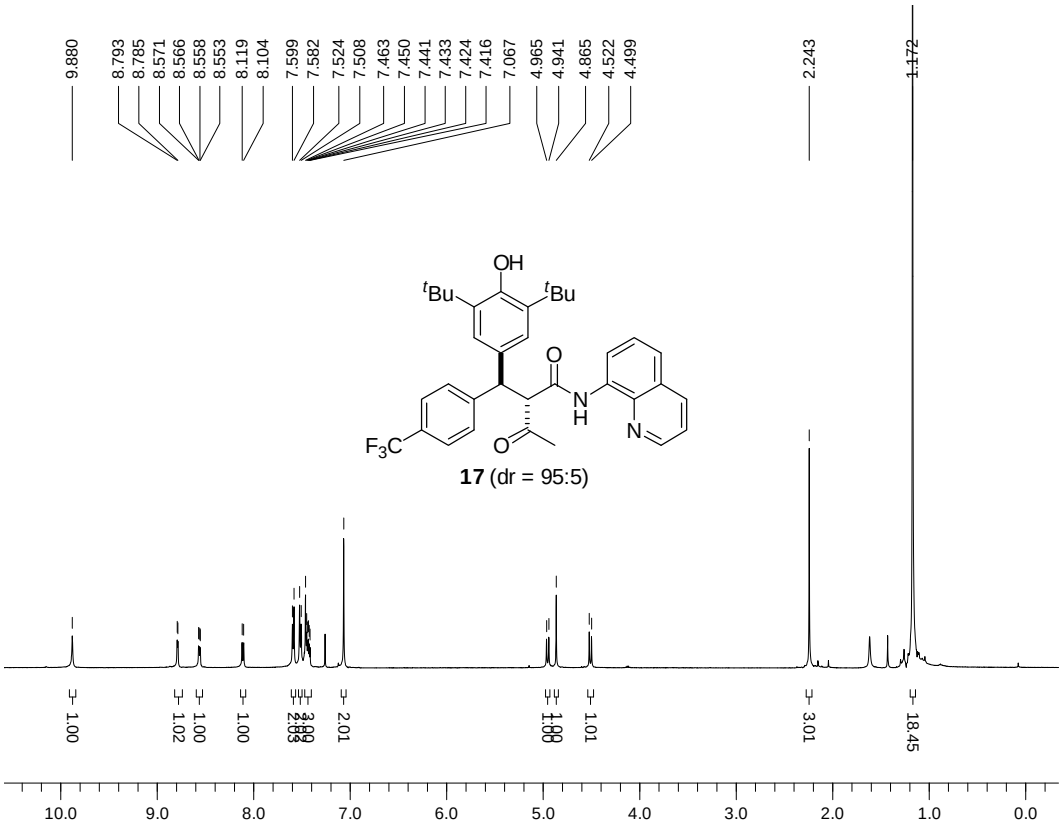
122.63
68.93
45.19
34.24
30.23
28.38
21.06
200
150
100
50
0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8.553
8.119
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7.582
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7.508
7.463
7.450
7.441
7.433
7.424
7.416
7.067
4.965
4.941
4.865
4.522
4.499
2.243
1.172
OH
tBu
tBu
O
N
H
N
F3C
O
1.00
1.02
1.00
1.00
2.01
1.00
1.01
3.01
18.45
10.0
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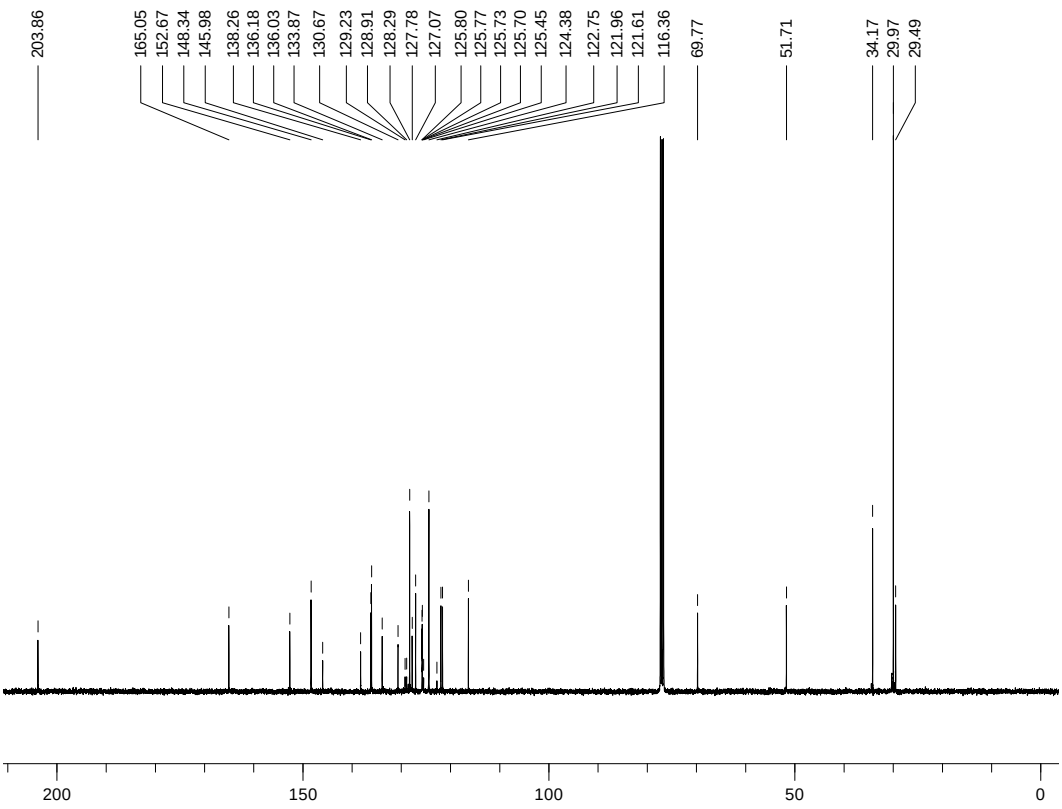
17 (dr = 95:5)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128.91
128.29
127.78
127.07
125.80
125.77
125.73
125.70
125.45
124.38
122.75
121.96
121.61
116.36
69.77
51.71
34.17
29.97
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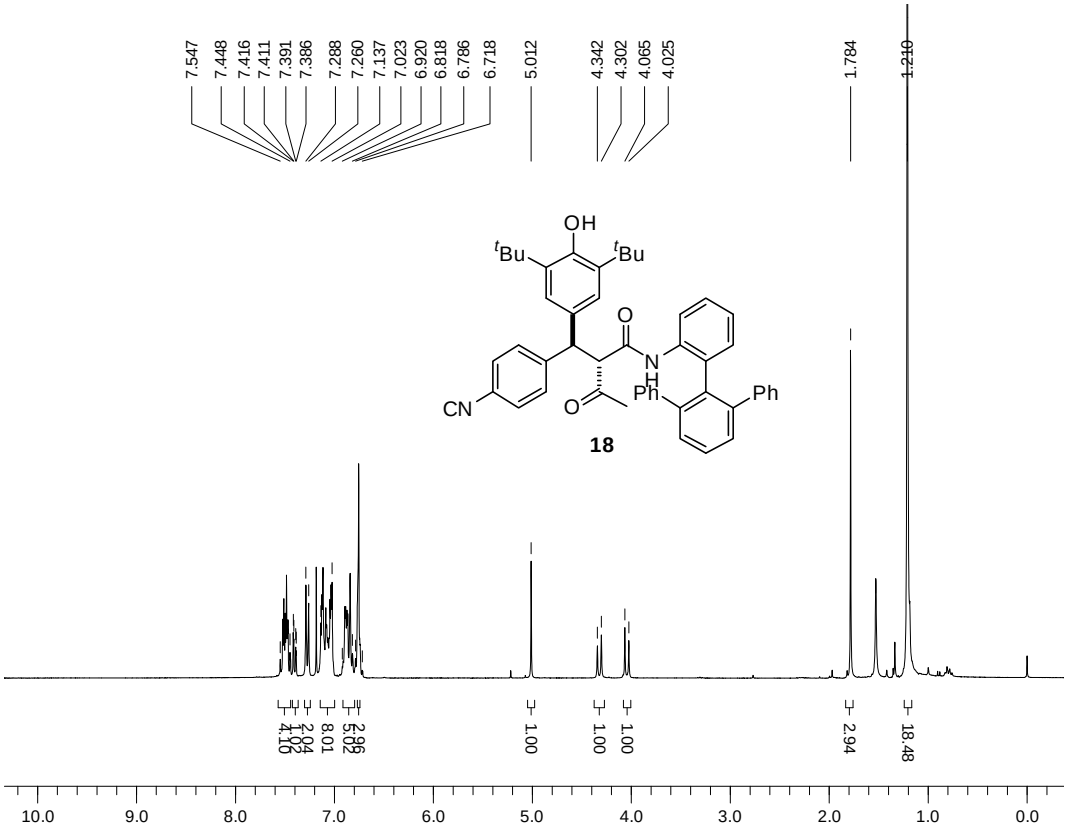
200
150
100
50
0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6.920
6.818
6.786
6.718
5.012
4.342
4.302
4.065
4.025
1.784
1.210
OH
tBu
tBu
O
N
H
Ph
Ph
CN
O
18
1.00
1.00
1.00
2.94
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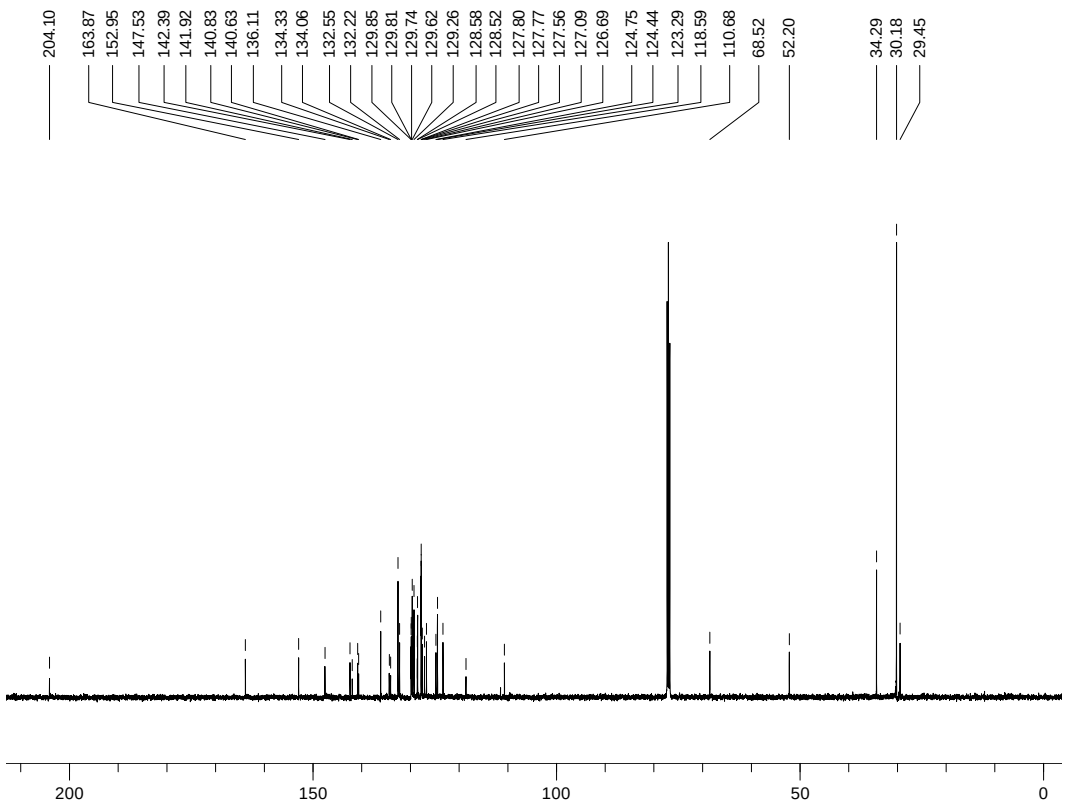
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0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134.06
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132.22
129.85
129.81
129.74
129.62
129.26
128.58
128.52
127.80
127.77
127.56
127.09
126.69
124.75
124.44
123.29
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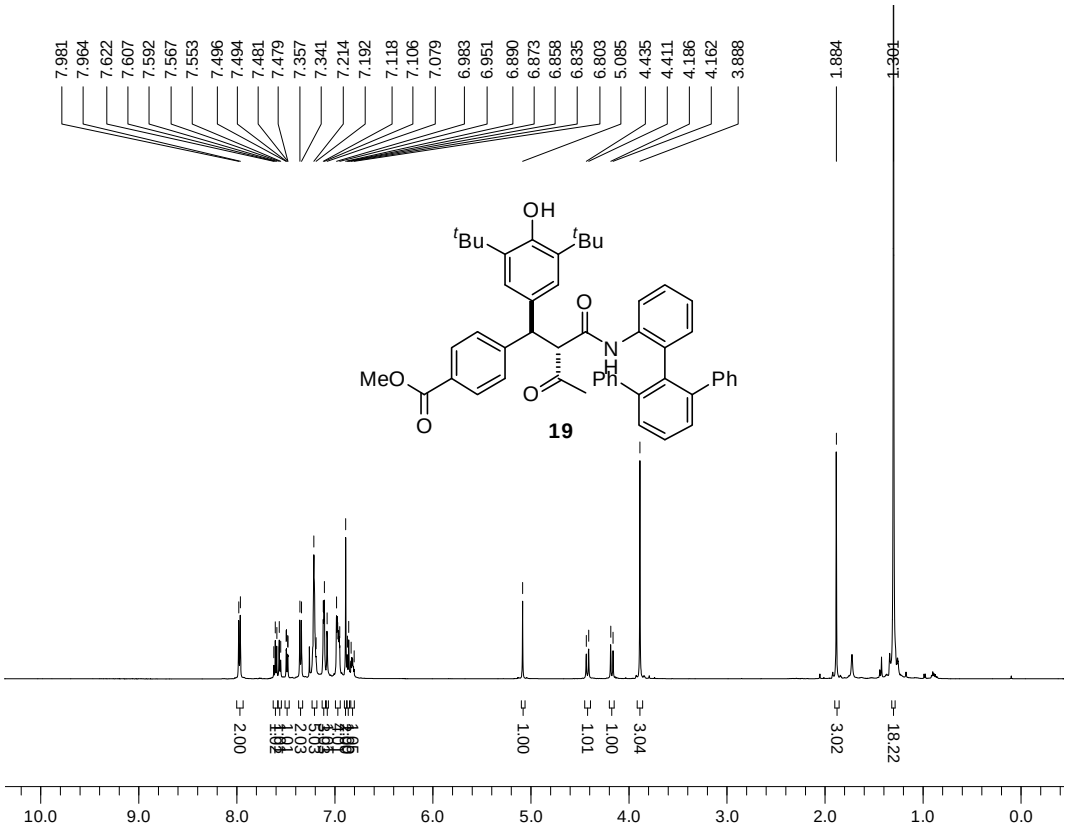
52.20
34.29
30.18
29.45
200
150
100
50
0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7.494
7.481
7.479
7.357
7.341
7.214
7.192
7.118
7.106
7.079
6.983
6.951
6.890
6.873
6.858
6.835
6.803
5.085
4.435
4.411
4.186
4.162
3.888
1.884
1.301
OH
tBu
tBu
O
NH
MeO
O
O
Ph
Ph
19
2.00
1.00
1.01
1.00
3.04
3.02
18.22
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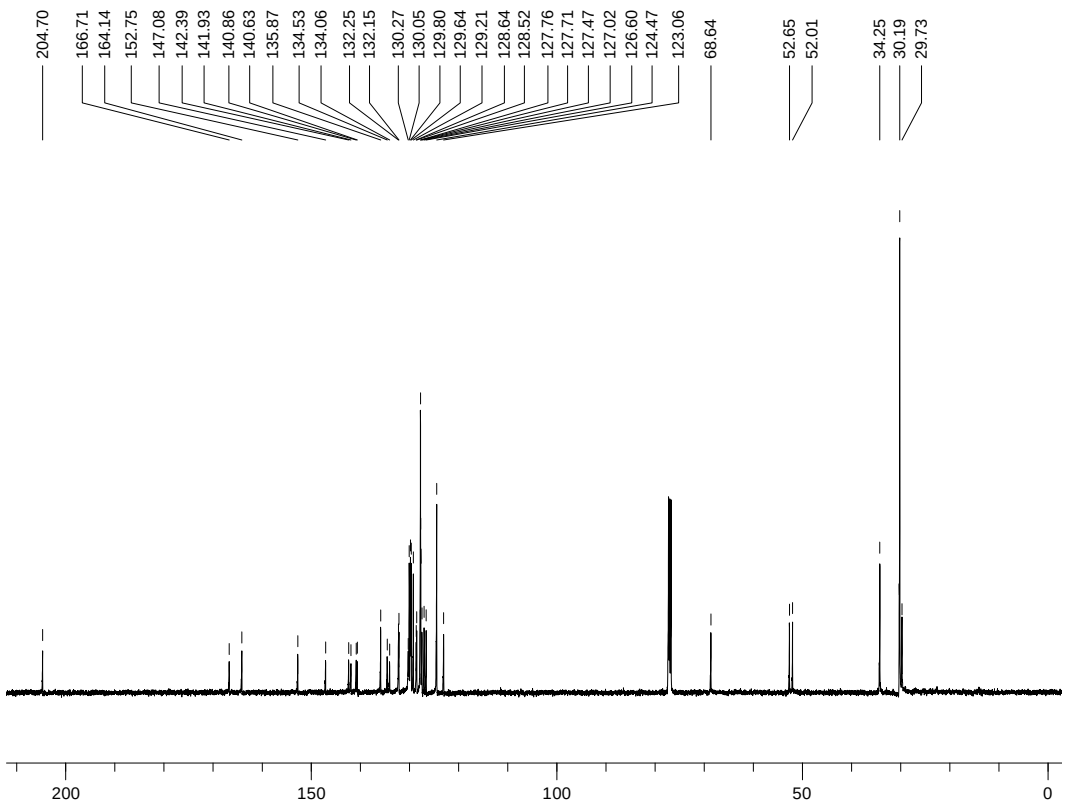
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0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130.05
129.80
129.64
129.21
128.64
128.52
127.76
127.71
127.47
127.02
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30.19
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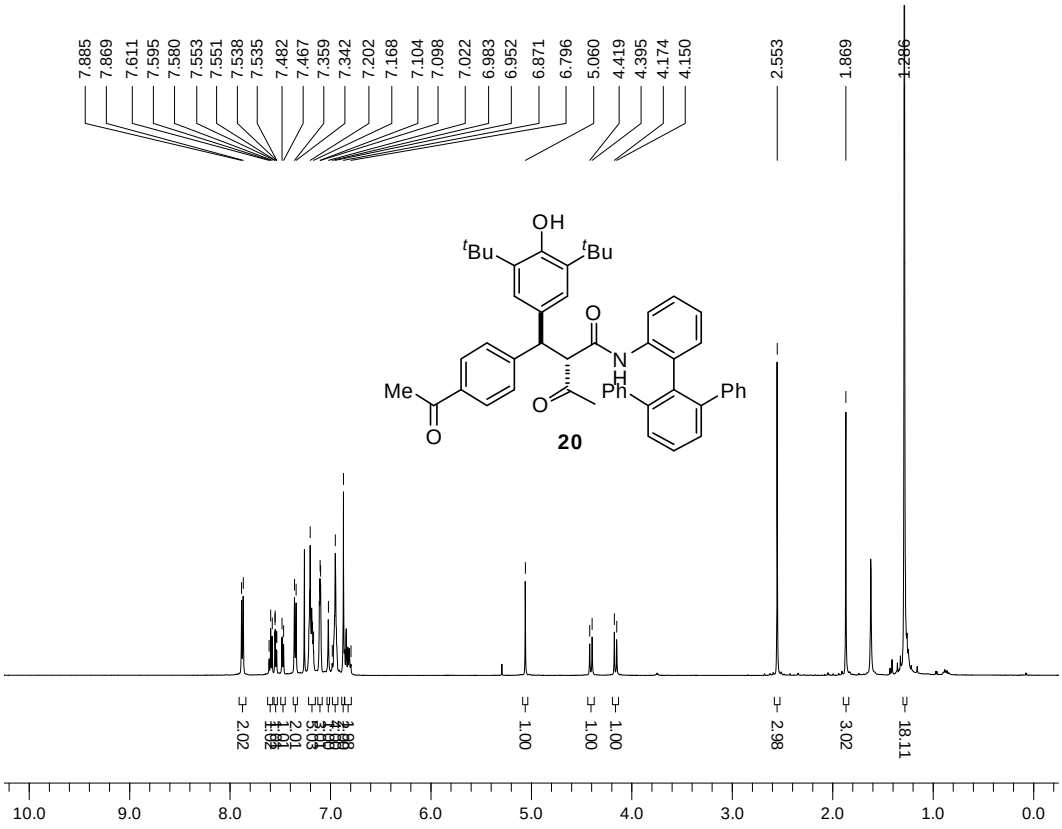
100
50
0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7.342
7.202
7.168
7.104
7.098
7.022
6.983
6.952
6.871
6.796
5.060
4.419
4.395
4.174
4.150
2.553
1.869
1.286
OH
tBu
tBu
O
N
H
Ph
Ph
Me
O
O
20
2.02
1.00
1.00
1.00
2.98
3.02
18.11
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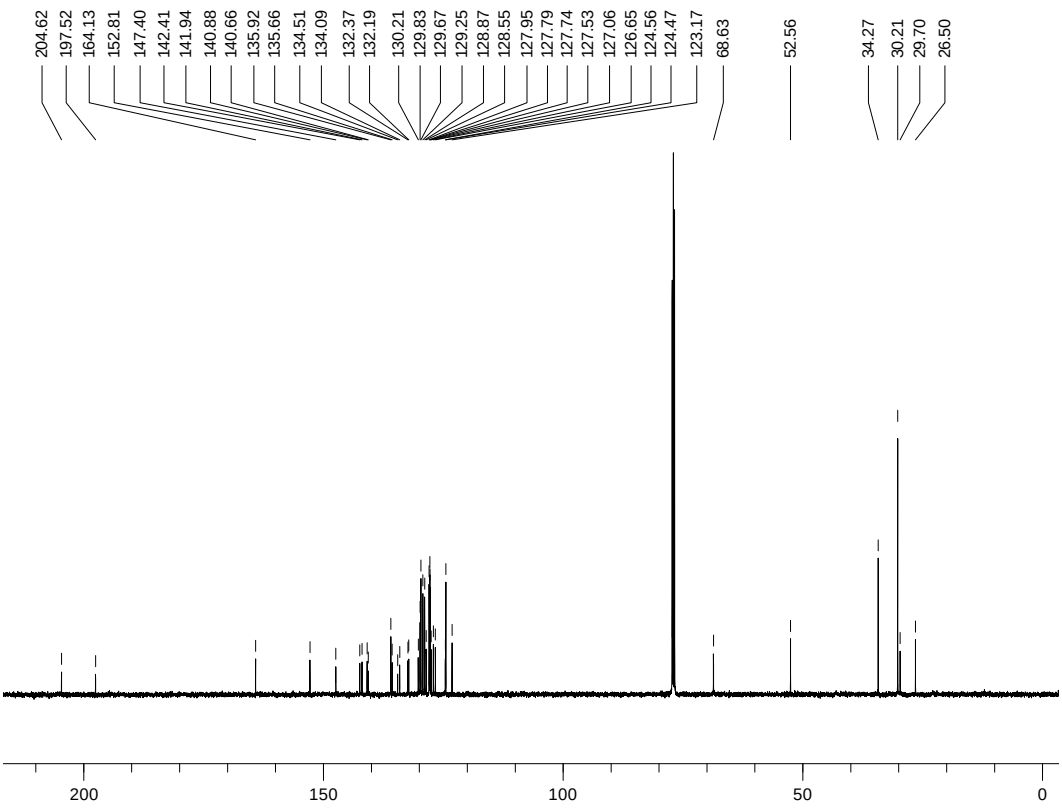
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0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134.51
134.09
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132.19
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129.83
129.67
129.25
128.87
128.55
127.95
127.79
127.74
127.53
127.06
126.65
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123.17
68.63
52.56
34.27
30.21
29.70
26.50
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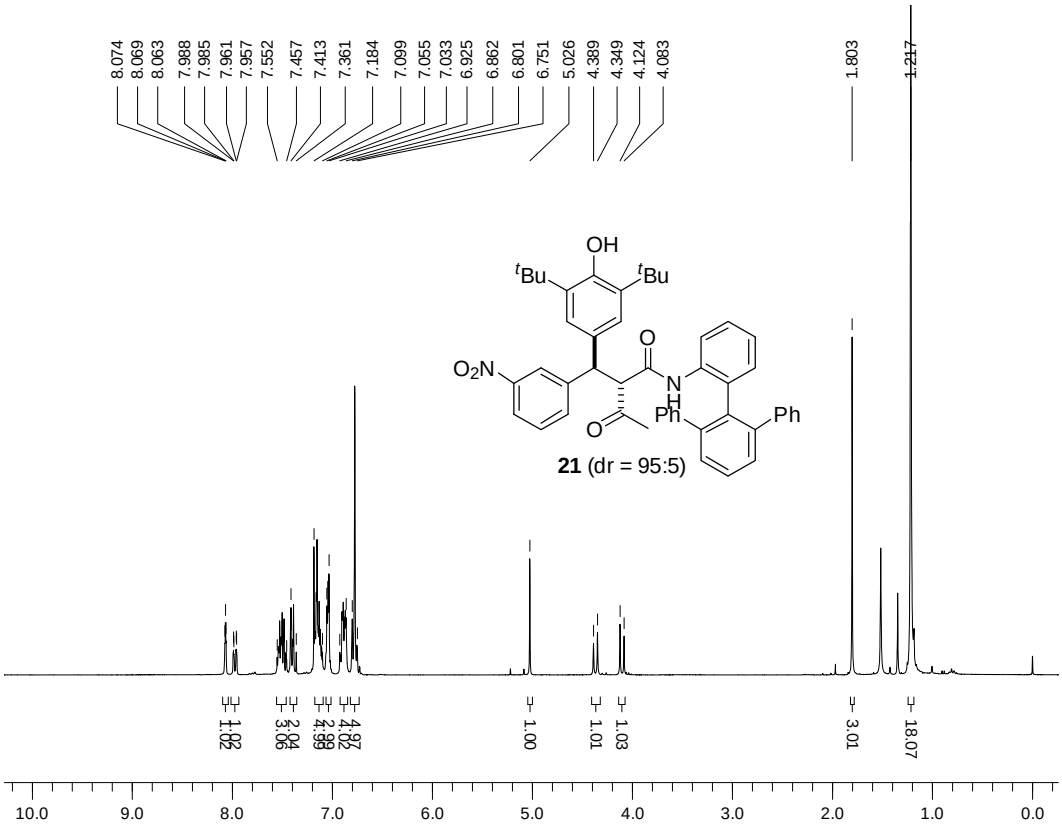
150
100
50
0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7.099
7.055
7.033
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6.862
6.801
6.751
5.026
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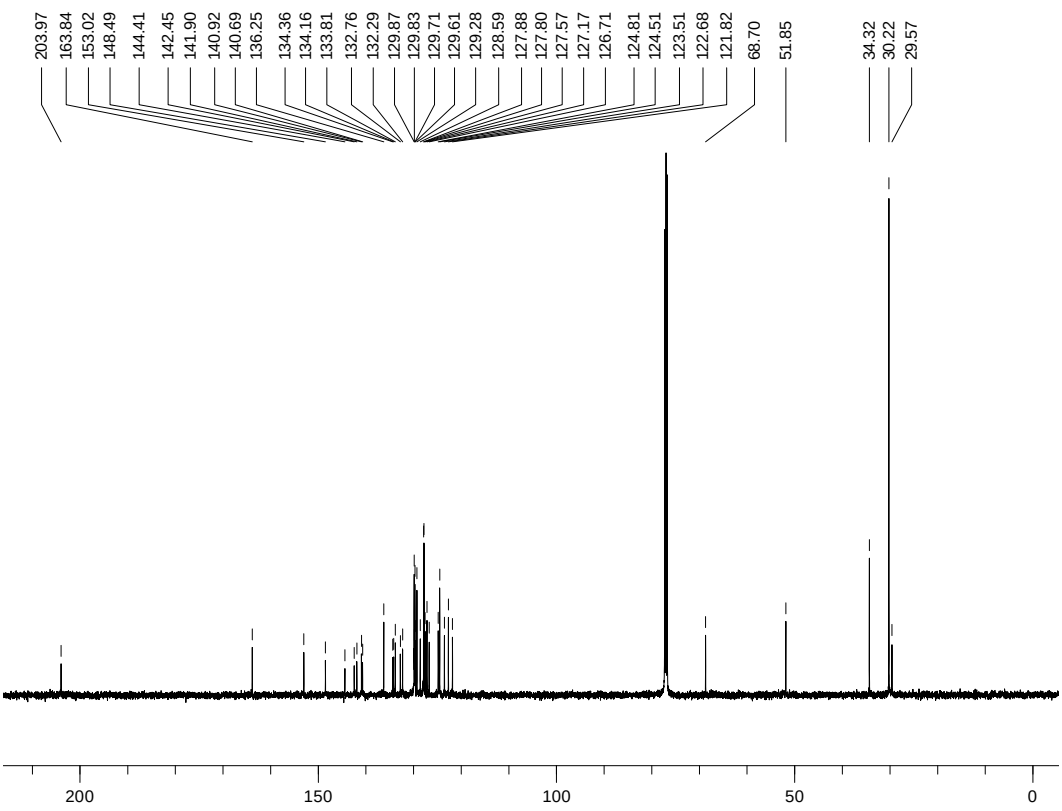
4.349
4.124
4.083
1.803
1.217
OH
tBu
tBu
O
O2N
N
H
Ph
Ph
O
21 (dr = 95:5)
1.00
1.01
1.03
3.01
18.07
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0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142.45
141.90
140.92
140.69
136.25
134.36
134.16
133.81
132.76
132.29
129.87
129.83
129.71
129.61
129.28
128.59
127.88
127.80
127.57
127.17
126.71
124.81
124.51
123.51
122.68
121.82
68.70
51.85
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30.22
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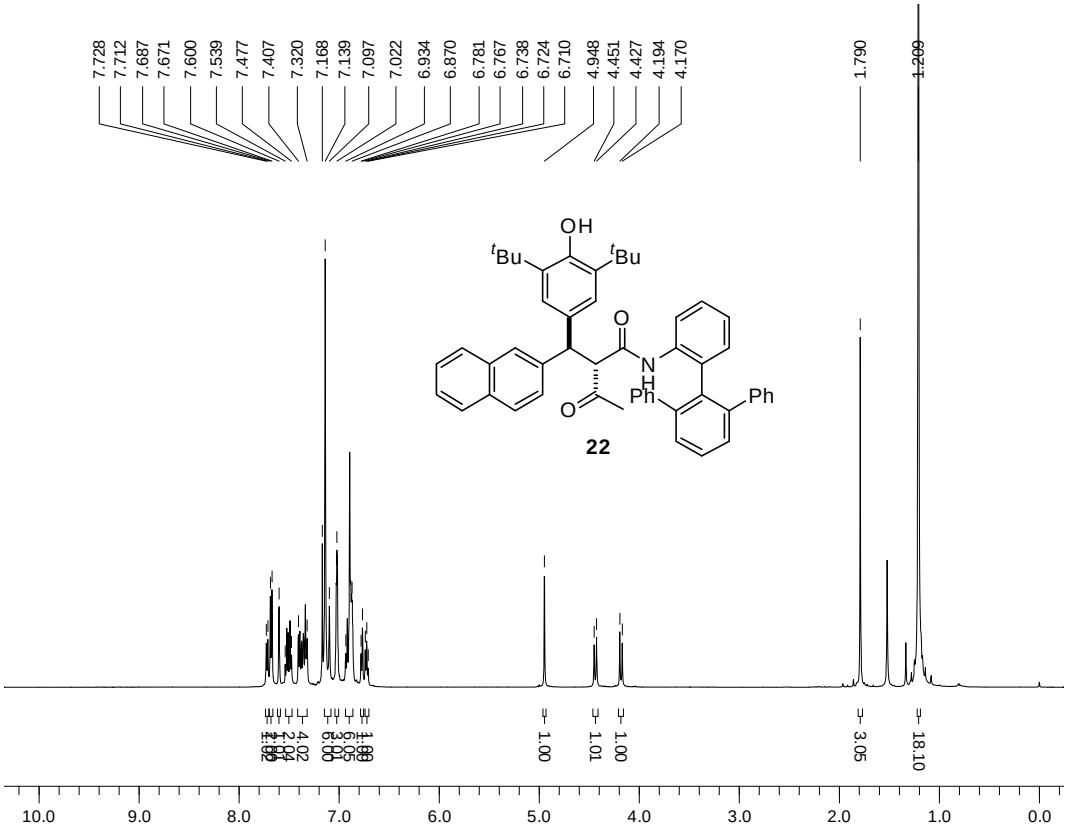
200
150
100
50
0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7.539
7.477
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7.168
7.139
7.097
7.022
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6.781
6.767
6.738
6.724
6.710
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4.451
4.427
4.194
4.170
1.790
1.209
OH
tBu
tBu
O
N
H
Ph
Ph
O
22
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1.01
1.00
3.05
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8.0
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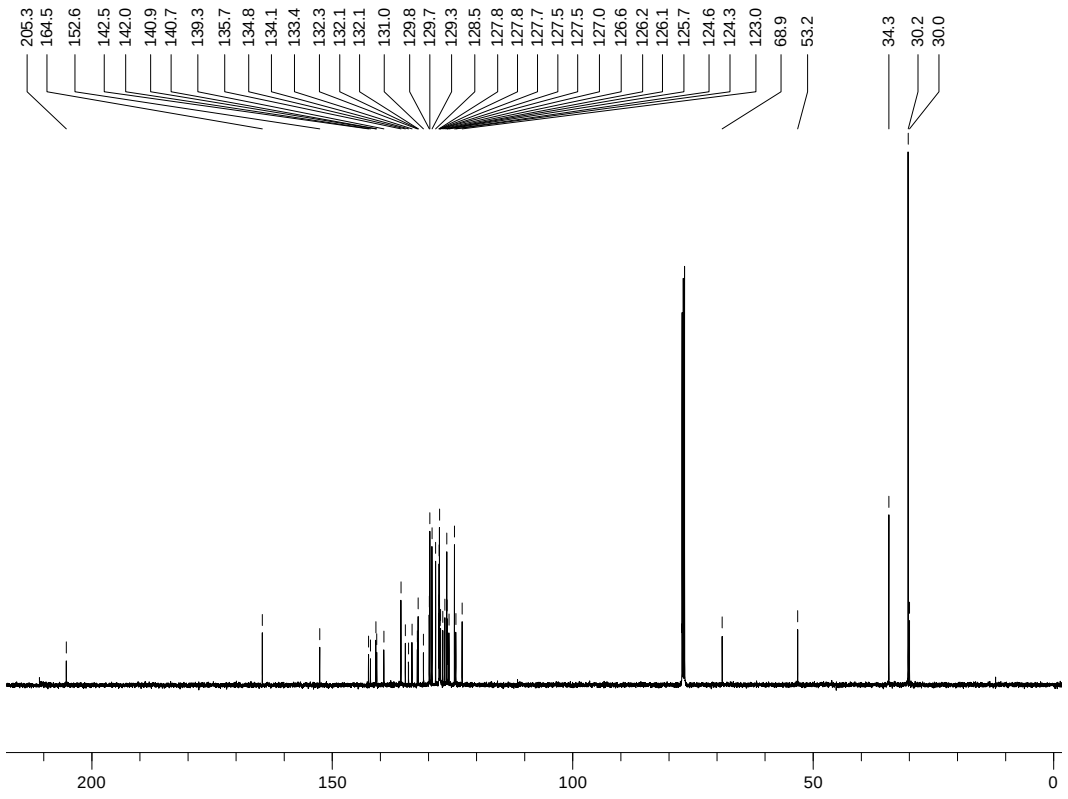
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132.1
132.1
131.0
129.8
129.7
129.3
128.5
127.8
127.8
127.7
127.5
127.5
127.0
126.6
126.2
126.1
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124.3
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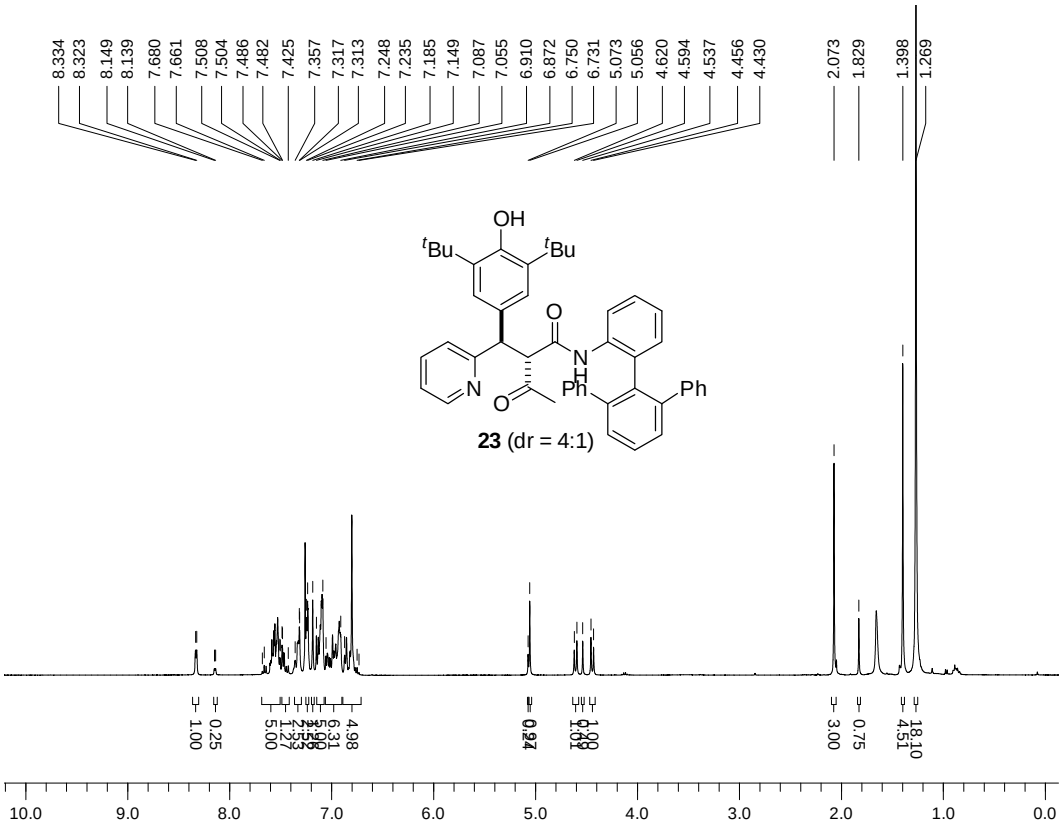
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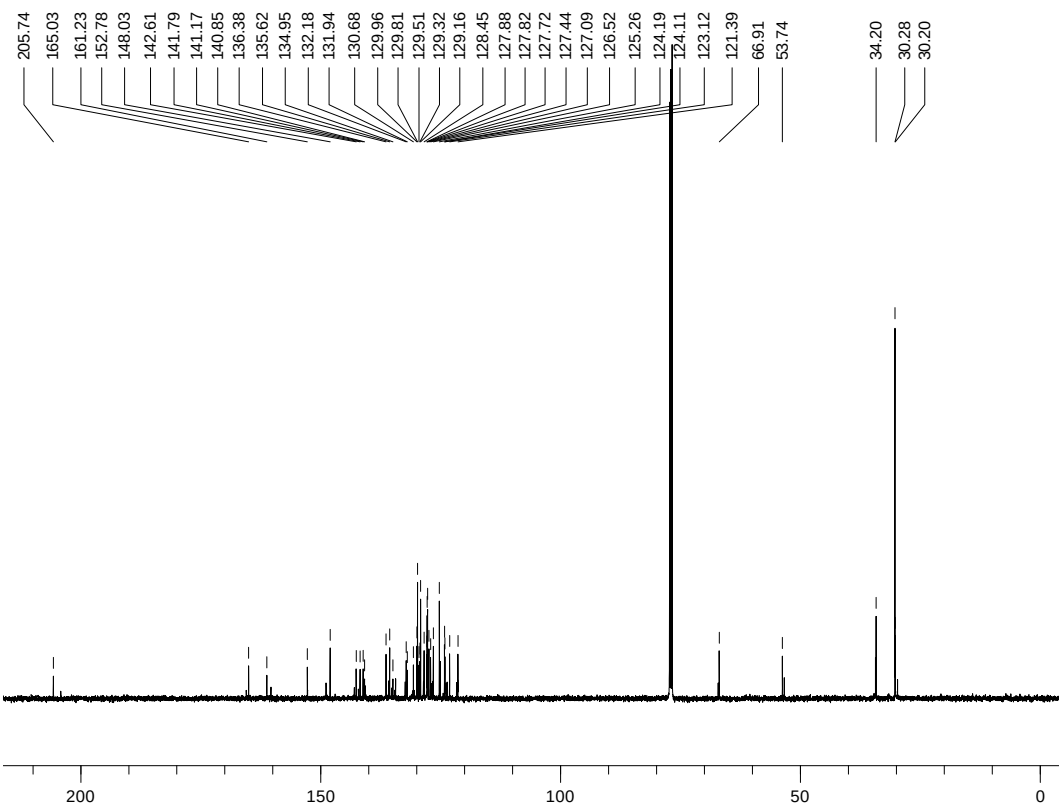
7.425
7.357
7.317
7.313
7.248
7.235
7.185
7.149
7.087
7.055
6.910
6.872
6.750
6.731
5.073
5.056
4.620
4.594
4.537
4.456
4.430
2.073
1.829
1.398
1.269
OH
tBu
tBu
O
N
H
Ph
Ph
N
O
23 (dr = 4:1)
1.00
0.25
5.00
4.98
0.94
1.01
1.00
3.00
0.75
18.10
4.51
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0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148.03
142.61
141.79
141.17
140.85
136.38
135.62
134.95
132.18
131.94
130.68
129.96
129.81
129.51
129.32
129.16
128.45
127.88
127.82
127.72
127.44
127.09
126.52
125.26
124.19
124.11
123.12
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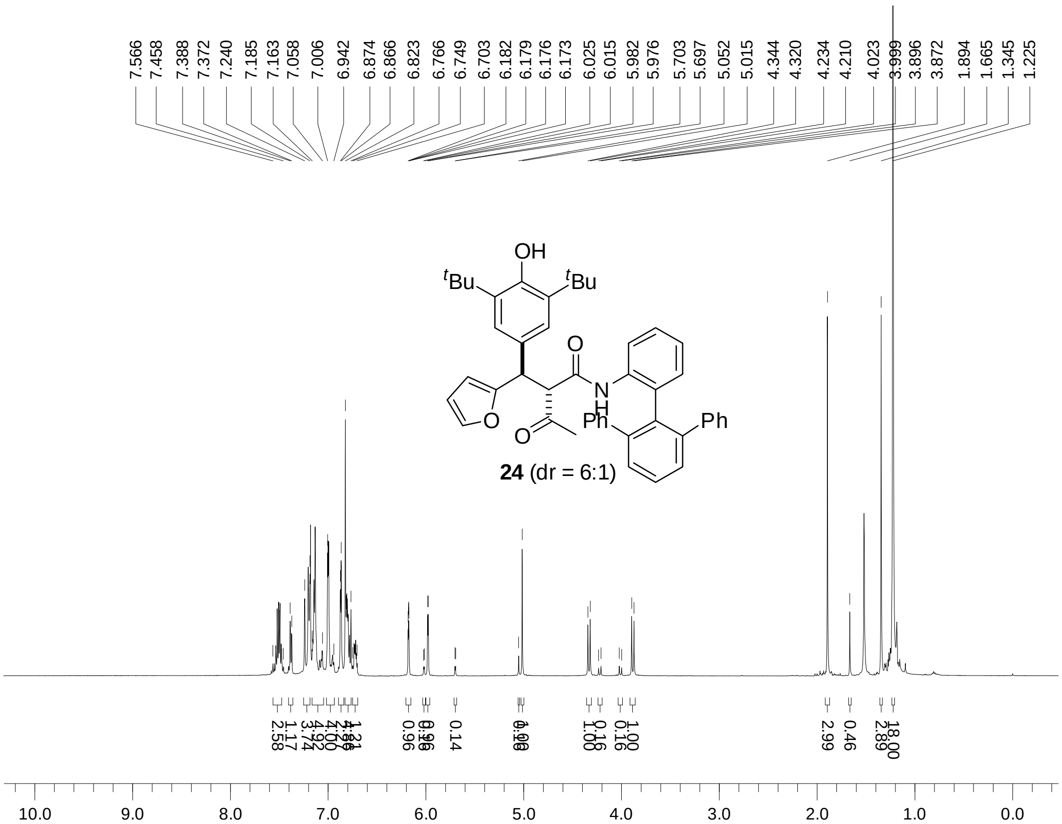
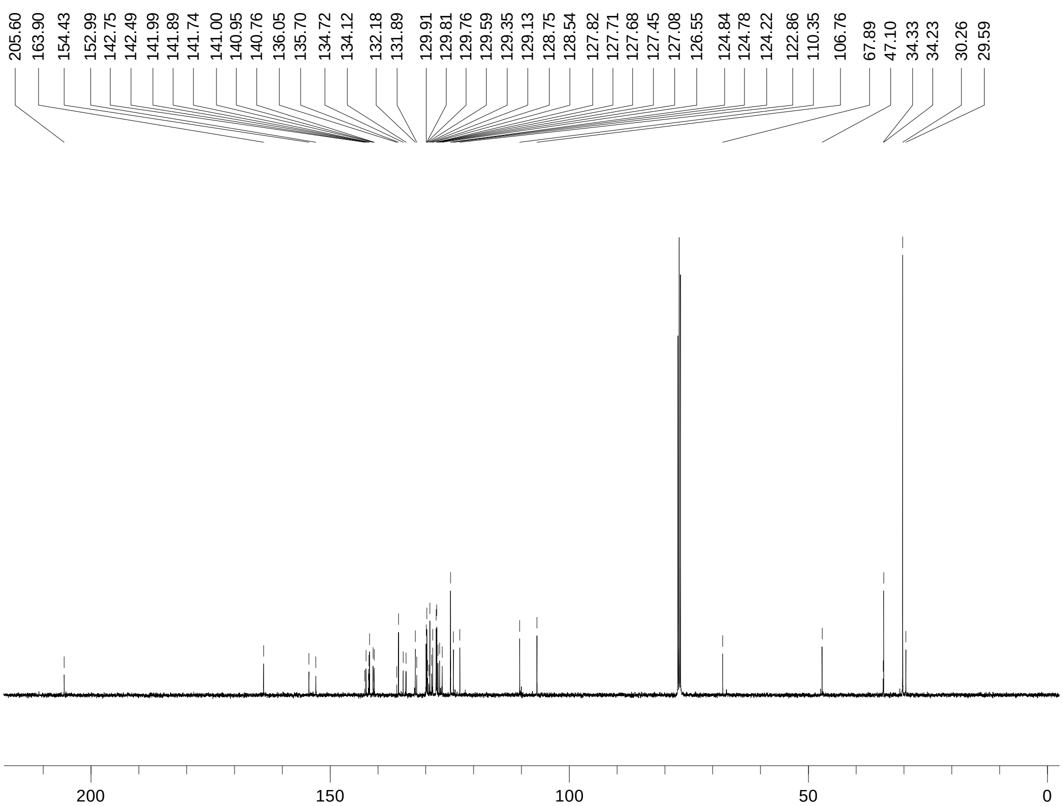
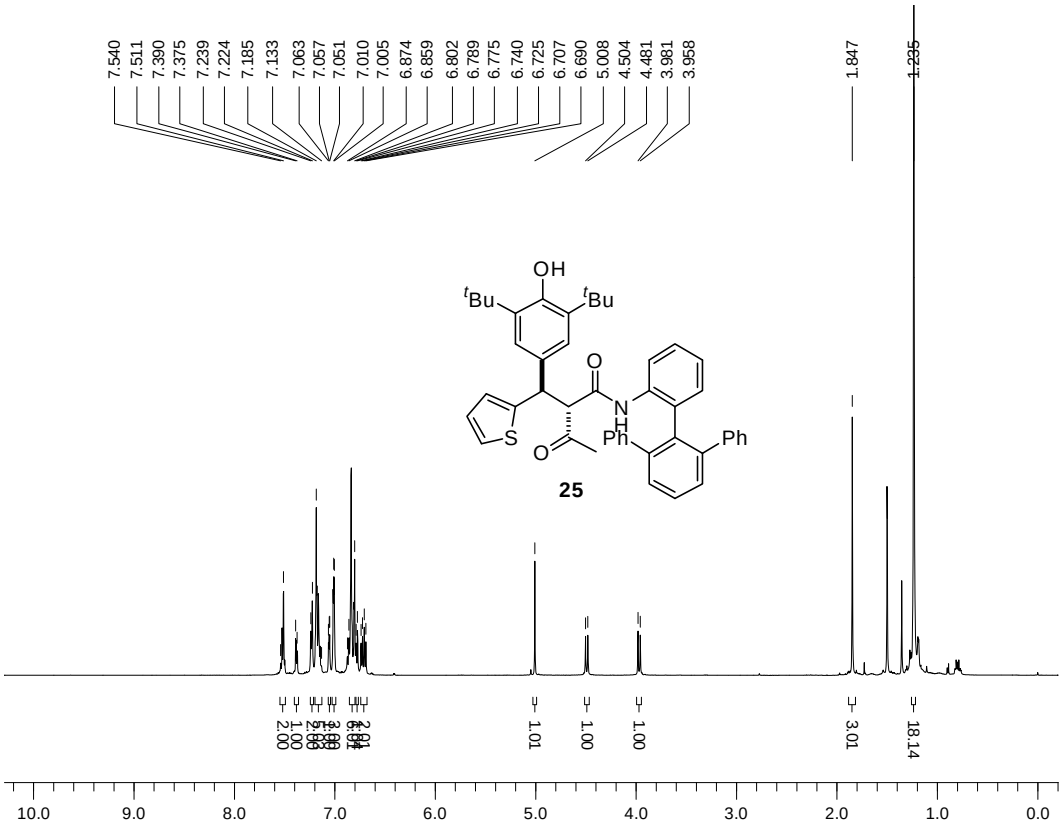
30.28
30.20
200
150
100
50
0

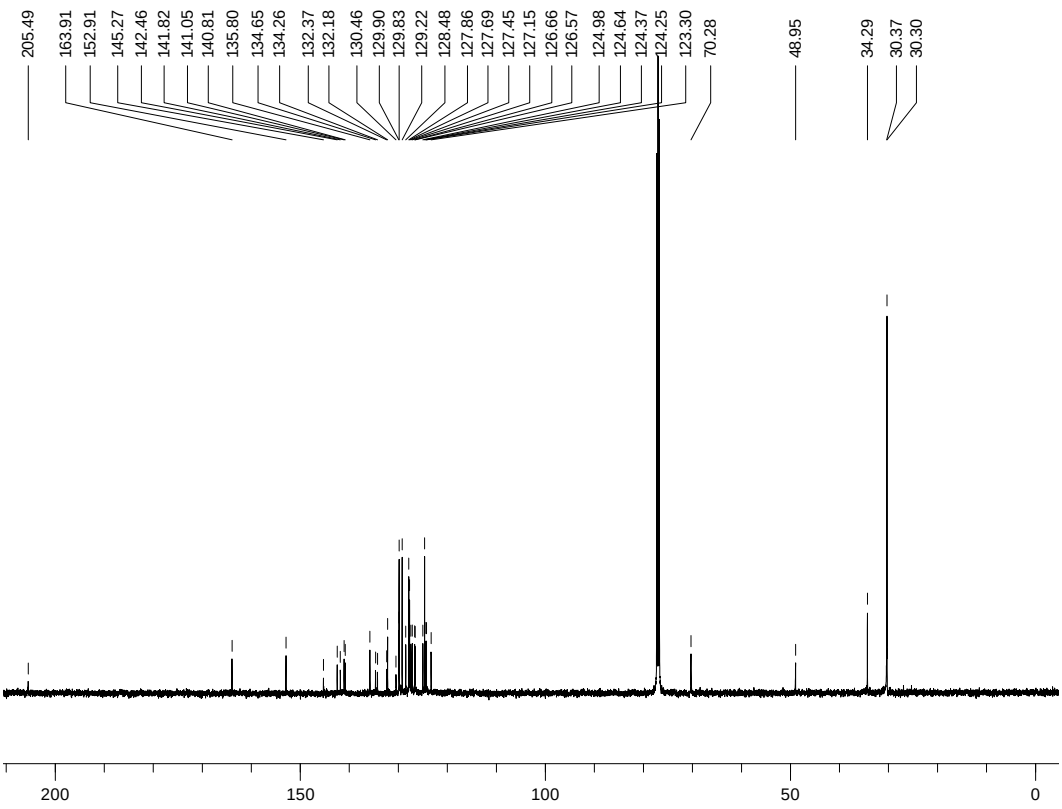


7.566 7.458 7.388 7.372 7.240 7.185 7.163 7.058 7.006 6.942 6.874 6.866 6.823 6.766 6.749 6.703 6.182 6.179 6.176 6.173 6.025 6.015 5.982 5.976 5.703 5.697 5.052 5.015 4.344 4.320 4.234 4.210 4.023 3.999 3.896 3.872 1.894 1.665 1.345 1.225
OH
tBu
tBu
O
N
H
O
Ph
Ph
O
24 (dr = 6:1)
2.58 1.17 3.74 4.92 4.00 0.96 0.14 1.00 0.16 1.00 2.99 0.46 2.89 18.00
10.0 9.0 8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0 0.0



205.60 163.90 154.43 152.99 142.75 142.49 141.99 141.89 141.74 141.00 140.95 140.76 136.05 135.70 134.72 134.12 132.18 131.89 129.91 129.81 129.76 129.59 129.35 129.13 128.75 128.54 127.82 127.71 127.68 127.45 127.08 126.55 124.84 124.78 124.22 122.86 110.35 106.76 67.89 47.10 34.33 34.23 30.26 29.59
200 150 100 50 0


7.540
7.511
7.390
7.375
7.239
7.224
7.185
7.133
7.063
7.057
7.051
7.010
7.005
6.874
6.859
6.802
6.789
6.775
6.740
6.725
6.707
6.690
5.008
4.504
4.481
3.981
3.958
1.847
1.235
OH
tBu
tBu
O
N
H
S
O
Ph
Ph
25
2.00
1.00
1.01
1.00
1.00
3.01
18.14
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0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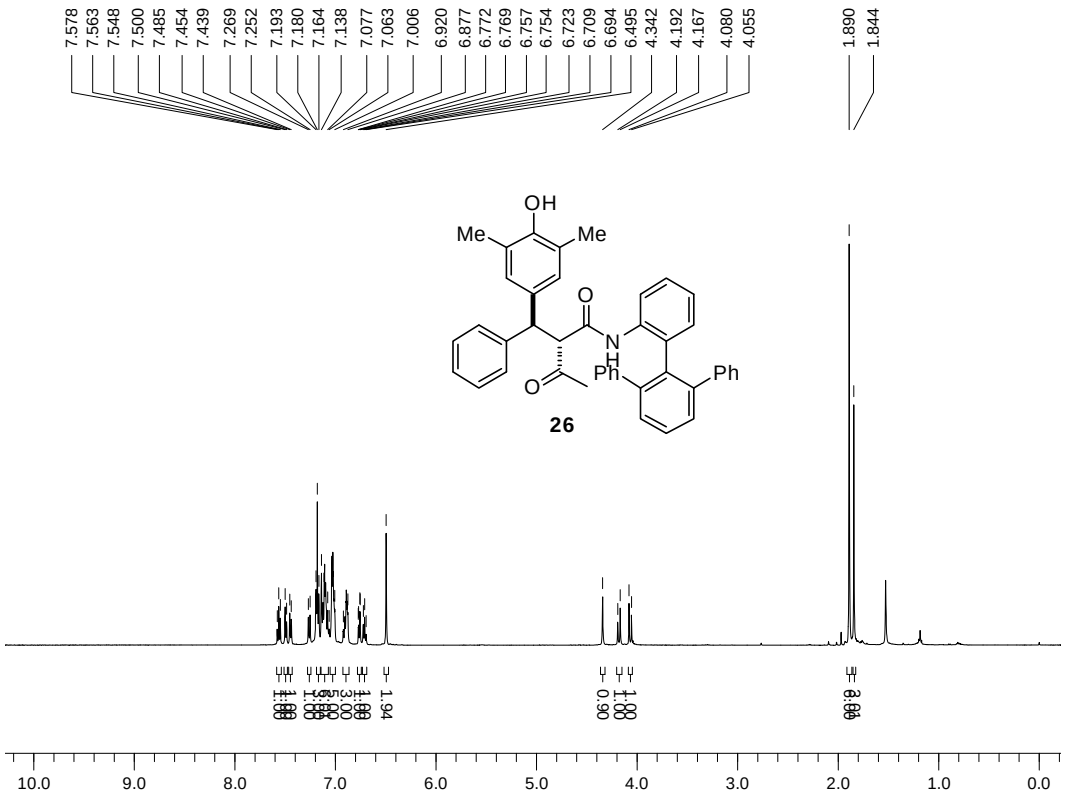
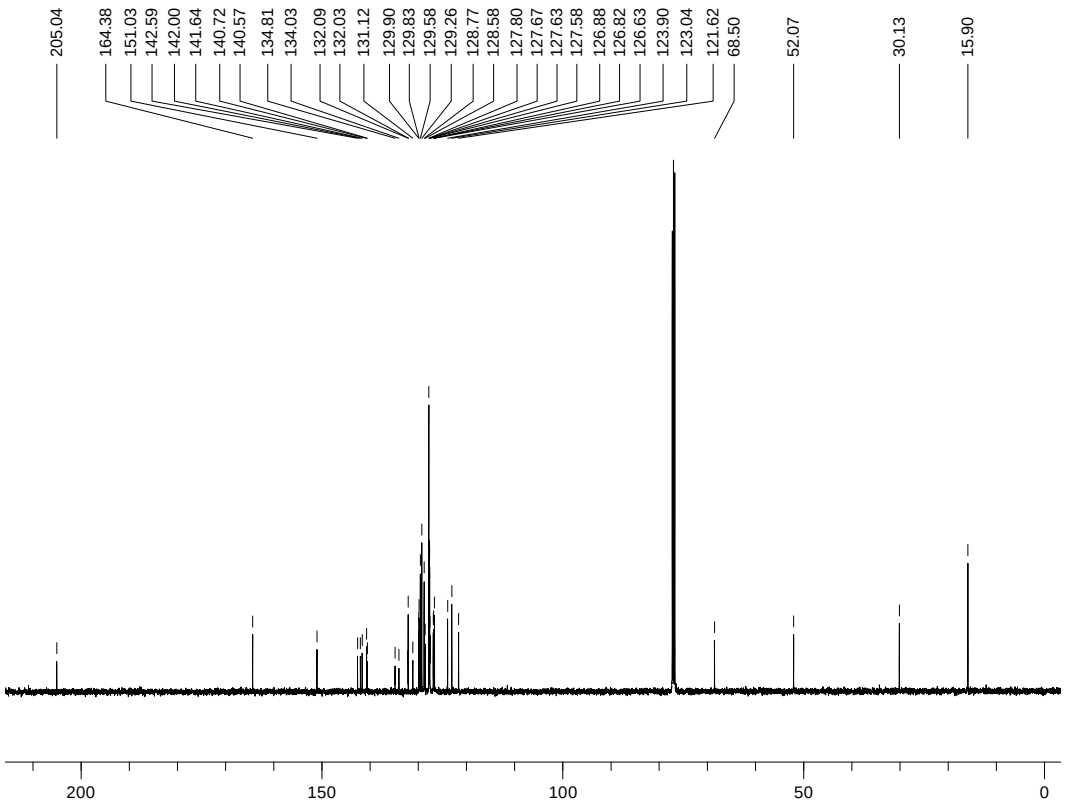
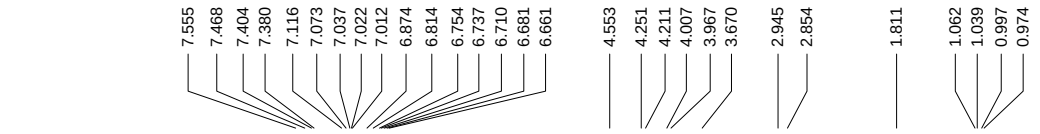
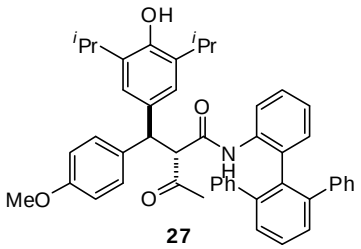
163.91
152.91
145.27
142.46
141.82
141.05
140.81
135.80
134.65
134.26
132.37
132.18
130.46
129.90
129.83
129.22
128.48
127.86
127.69
127.45
127.15
126.66
126.57
124.98
124.64
124.37
124.25
123.30
70.28
48.95
34.29
30.37
30.30
200
150
100
50
0

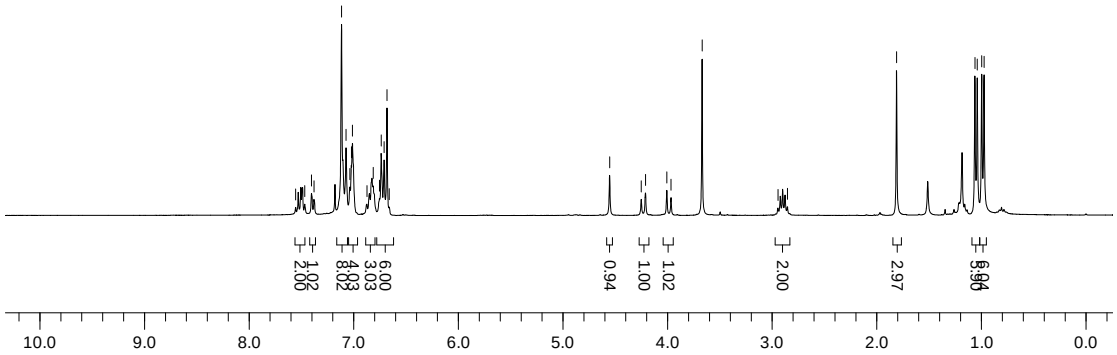

7.578
7.563
7.548
7.500
7.485
7.454
7.439
7.269
7.252
7.193
7.180
7.164
7.138
7.077
7.063
7.006
6.920
6.877
6.772
6.769
6.757
6.754
6.723
6.709
6.694
6.495
4.342
4.192
4.167
4.080
4.055
1.890
1.844
OH
Me
Me
O
N
H
Ph
Ph
O
26
1.94
0.90
6.00
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0

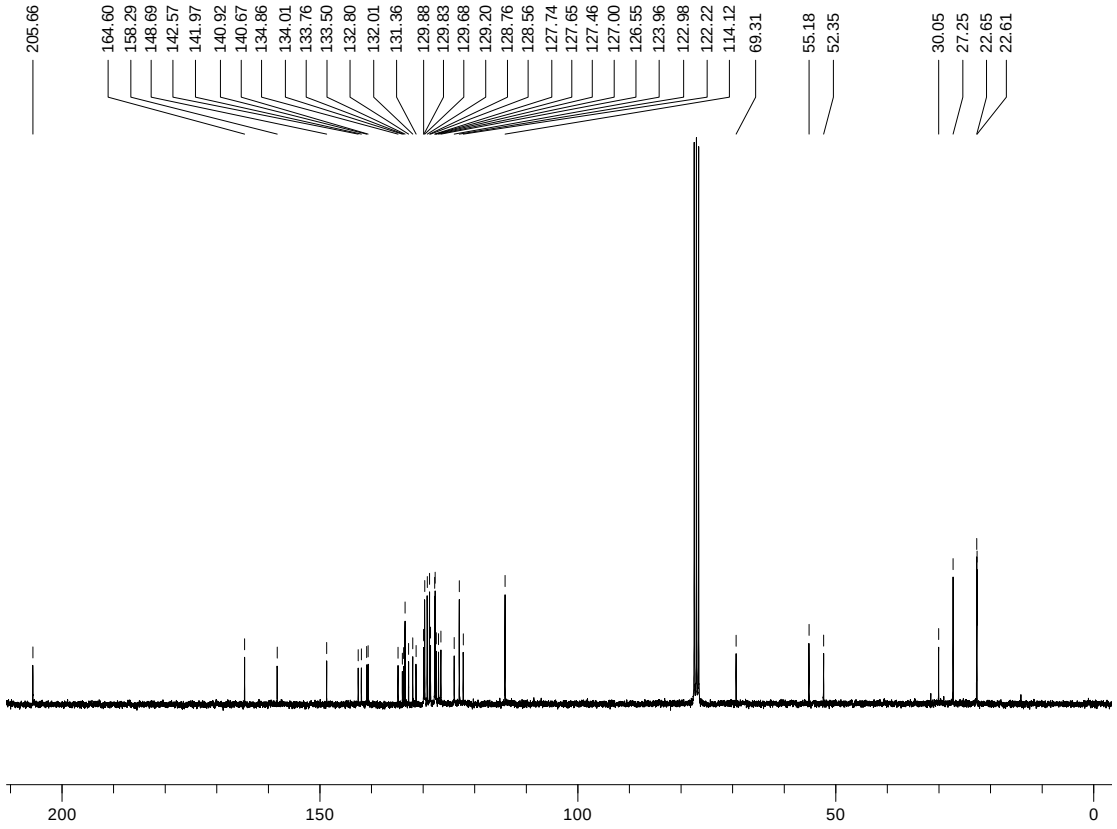

205.04
164.38
151.03
142.59
142.00
141.64
140.72
140.57
134.81
134.03
132.09
132.03
131.12
129.90
129.83
129.58
129.26
128.77
128.58
127.80
127.67
127.63
127.58
126.88
126.82
126.63
123.90
123.04
121.62
68.50
52.07
30.13
15.90
200
150
100
50
0

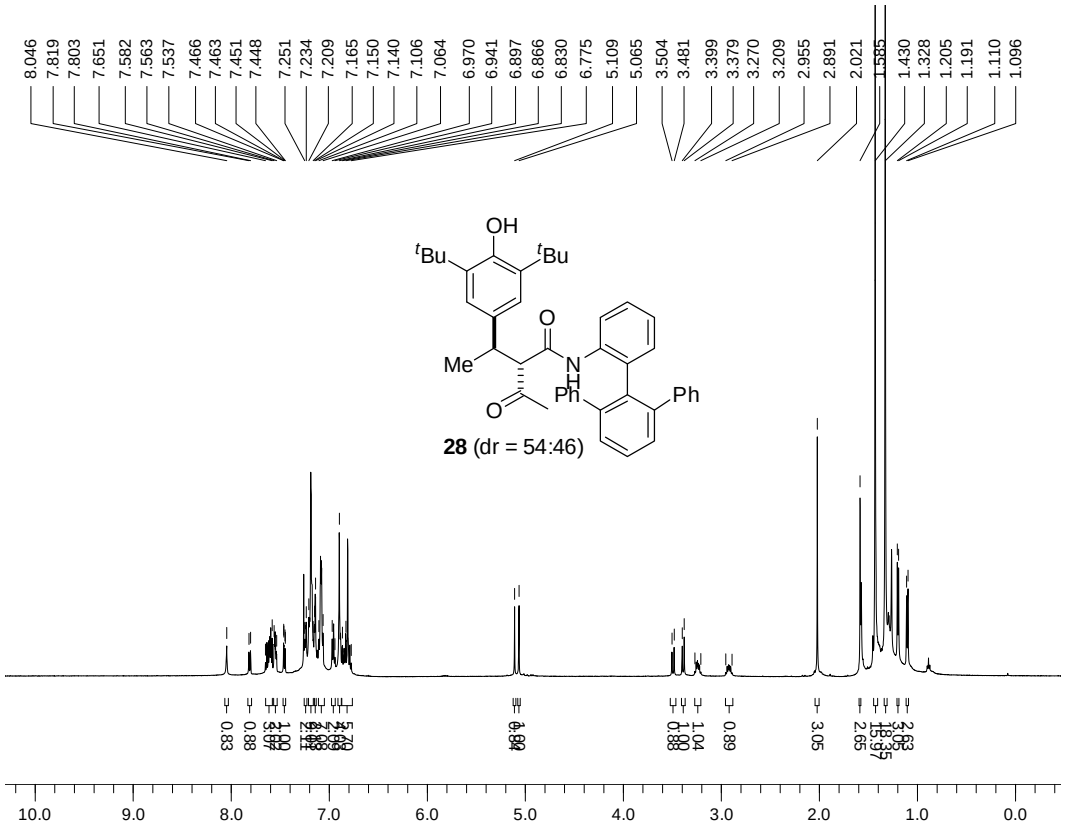

7.555
7.468
7.404
7.380
7.116
7.073
7.037
7.022
7.012
6.874
6.814
6.754
6.737
6.710
6.681
6.661
4.553
4.251
4.211
4.007
3.967
3.670
2.945
2.854
1.811
1.062
1.039
0.997
0.974

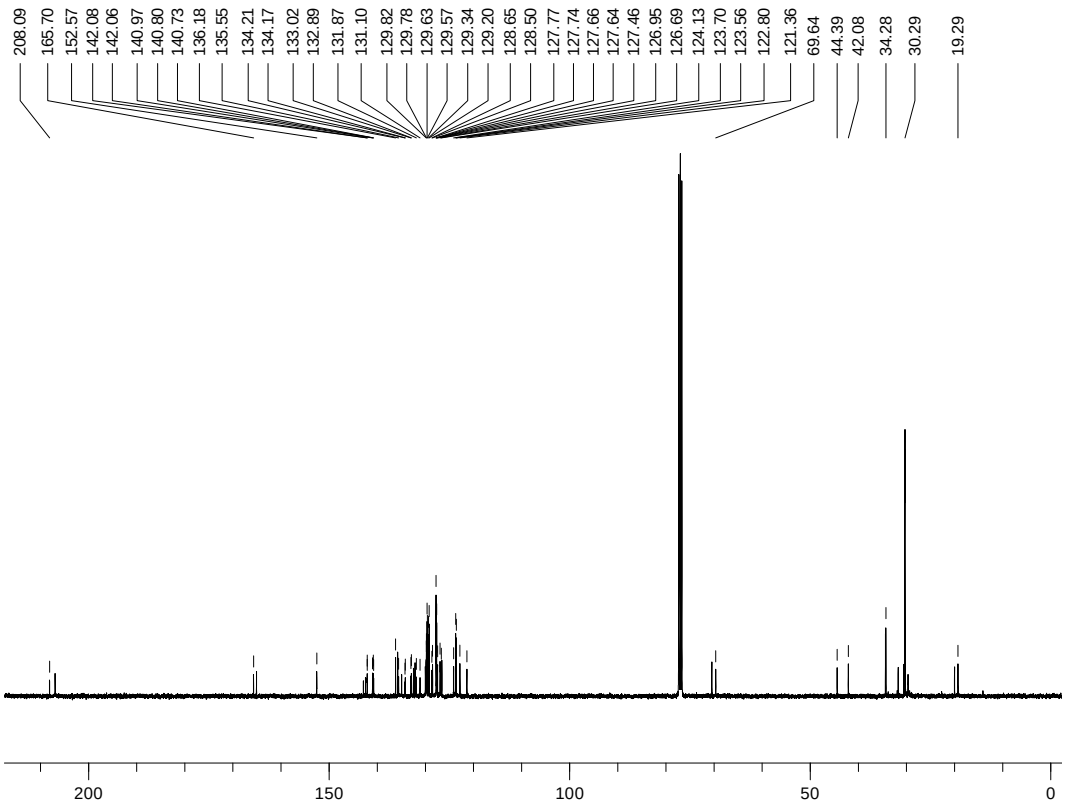

OH
iPr
iPr
O
N
H
Ph
Ph
MeO
O

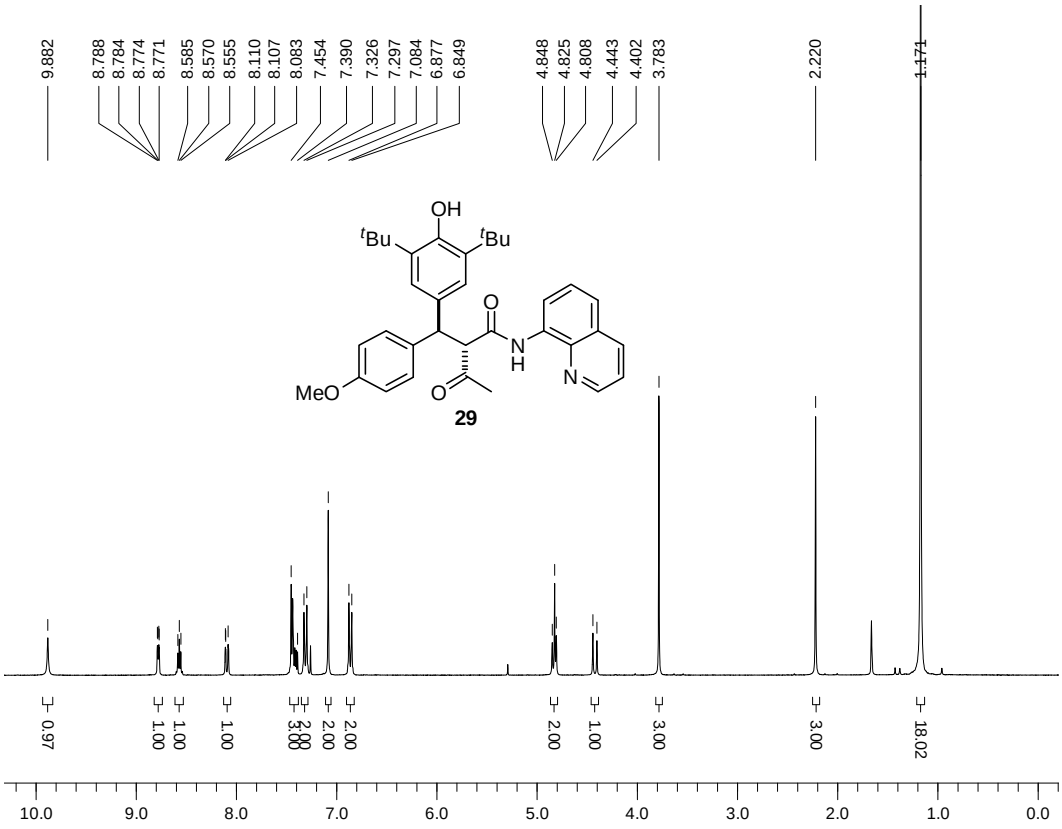
27

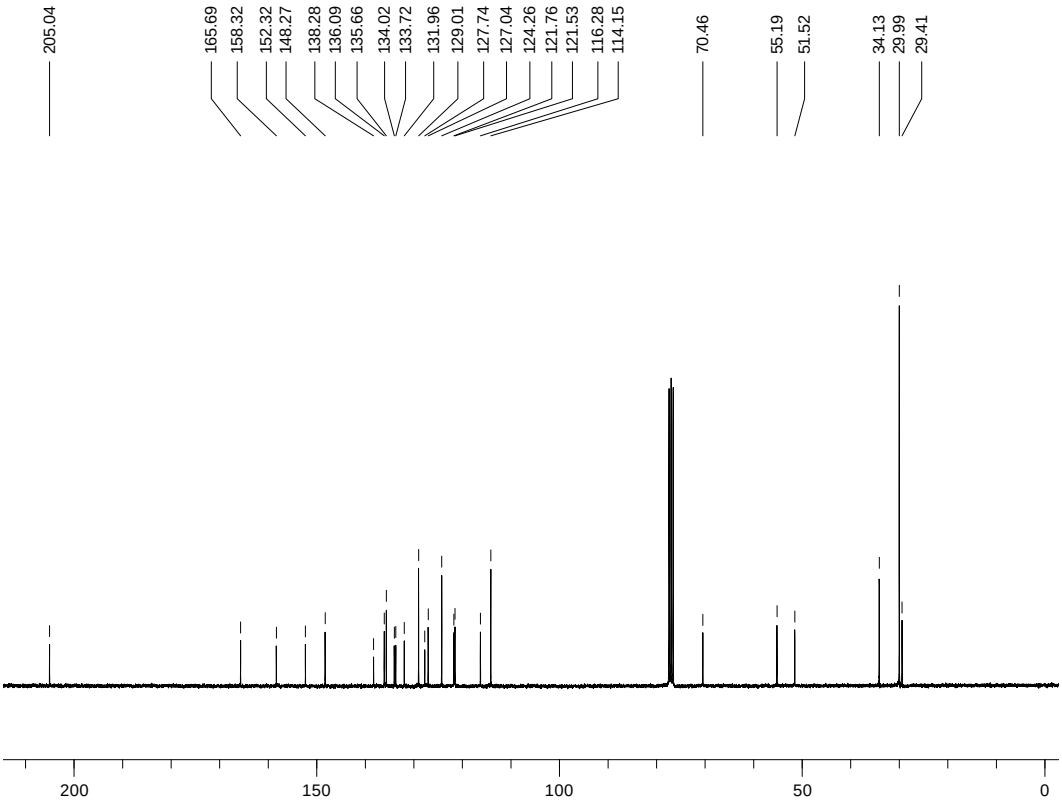

2.00
1.02
4.02
4.03
6.00
0.94
1.00
1.02
2.00
2.97
6.00
6.04
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0

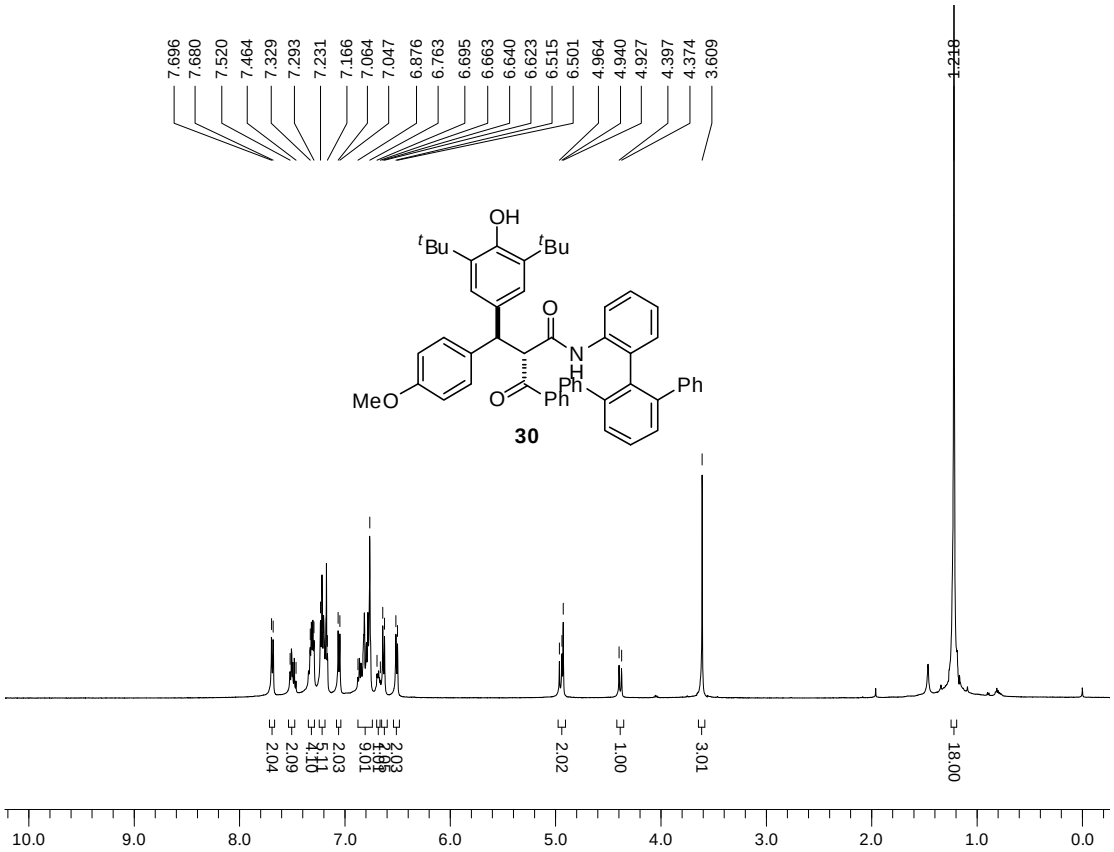

205.66
164.60
158.29
148.69
142.57
141.97
140.92
140.67
134.86
134.01
133.76
133.50
132.80
132.01
131.36
129.88
129.83
129.68
129.20
128.76
128.56
127.74
127.65
127.46
127.00
126.55
123.96
122.98
122.22
114.12
69.31
55.18
52.35
30.05
27.25
22.65
22.61
200
150
100
50
0

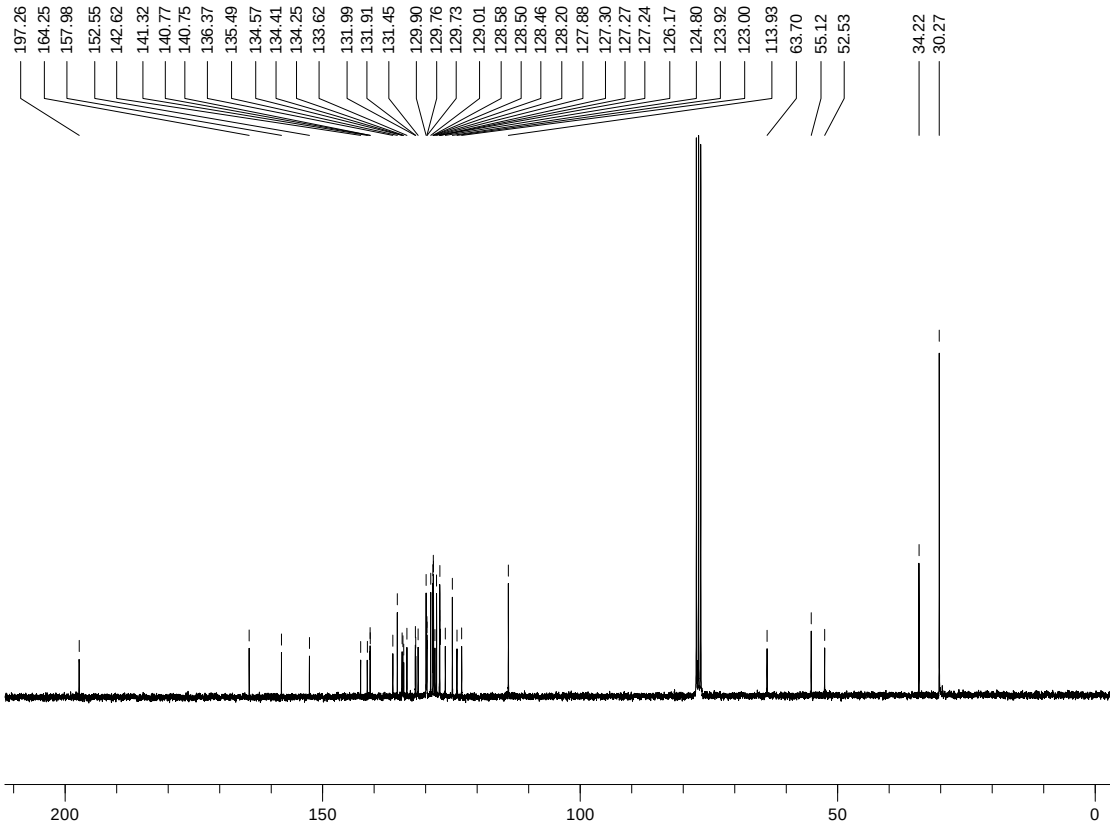

8.046
7.819
7.803
7.651
7.582
7.563
7.537
7.466
7.463
7.451
7.448
7.251
7.234
7.209
7.165
7.150
7.140
7.106
7.064
6.970
6.941
6.897
6.886
6.830
6.775
5.109
5.065
3.504
3.481
3.399
3.379
3.270
3.209
2.955
2.891
2.021
1.585
1.430
1.328
1.205
1.191
1.110
1.096
OH
tBu
tBu
O
Me
N
H
Ph
Ph
O
28 (dr = 54:46)
0.83
0.88
0.89
3.06
2.66
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0

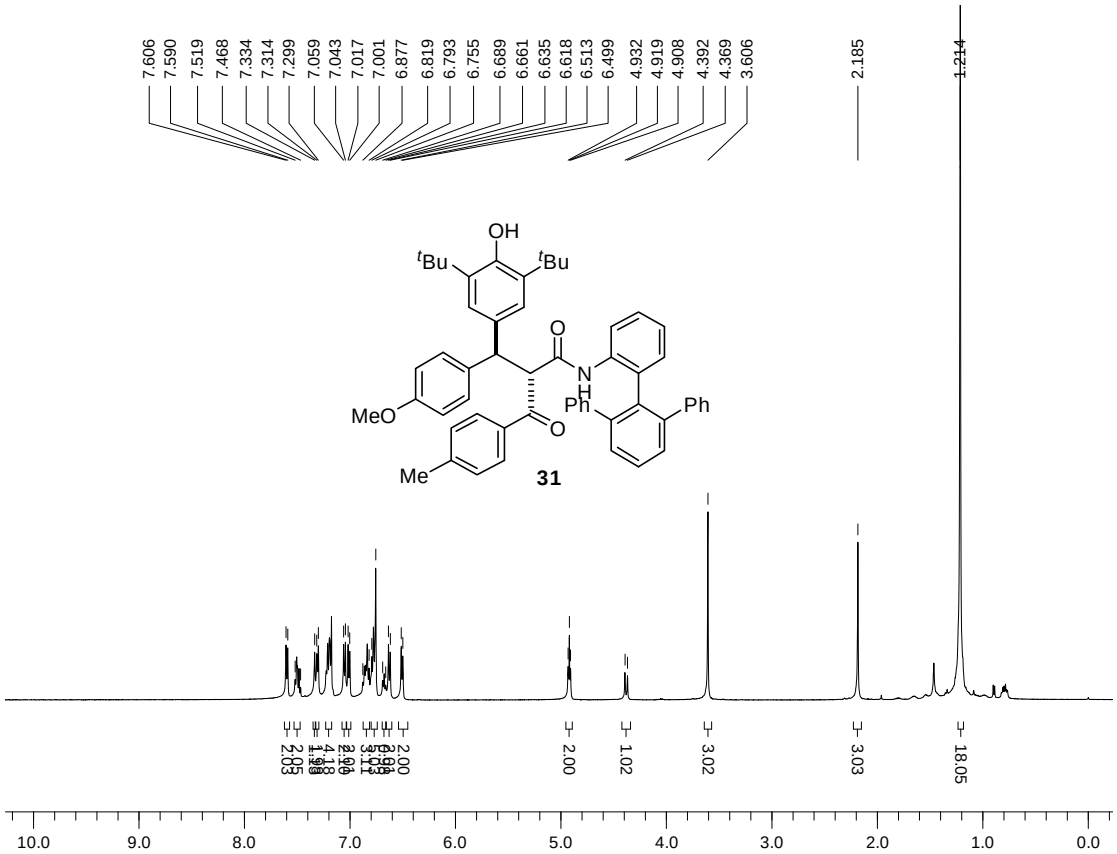

208.09
165.70
152.57
142.08
142.06
140.97
140.80
140.73
136.18
135.55
134.21
134.17
133.02
132.89
131.87
131.10
129.82
129.78
129.63
129.57
129.34
129.20
128.65
128.50
127.77
127.74
127.66
127.64
127.46
126.95
126.69
124.13
123.70
123.56
122.80
121.36
69.64
44.39
42.08
34.28
30.29
19.29
200
150
100
50
0

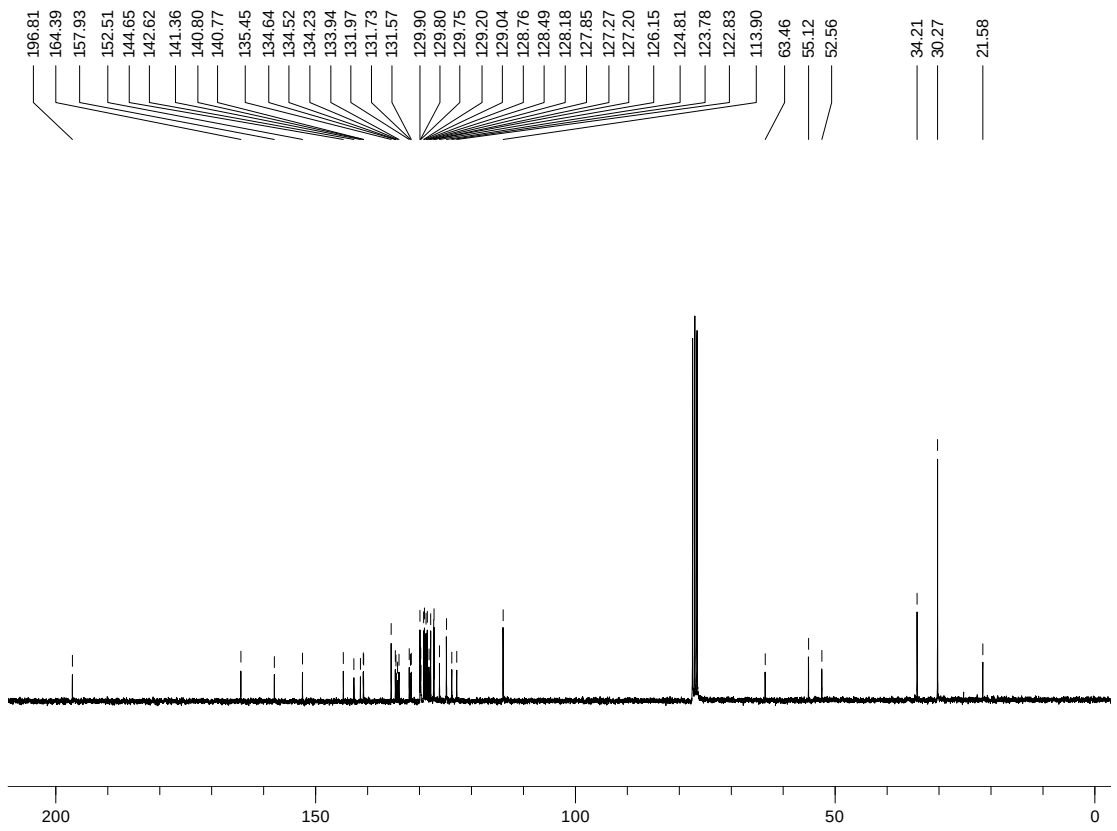

9.882
8.788
8.784
8.774
8.771
8.585
8.570
8.555
8.110
8.107
8.083
7.454
7.390
7.326
7.297
7.084
6.877
6.849
4.848
4.825
4.808
4.443
4.402
3.783
2.220
1.171
OH
tBu
tBu
O
N
H
MeO
O
N
29
0.97
1.00
1.00
1.00
3.30
2.00
2.00
2.00
1.00
3.00
3.00
18.02
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0

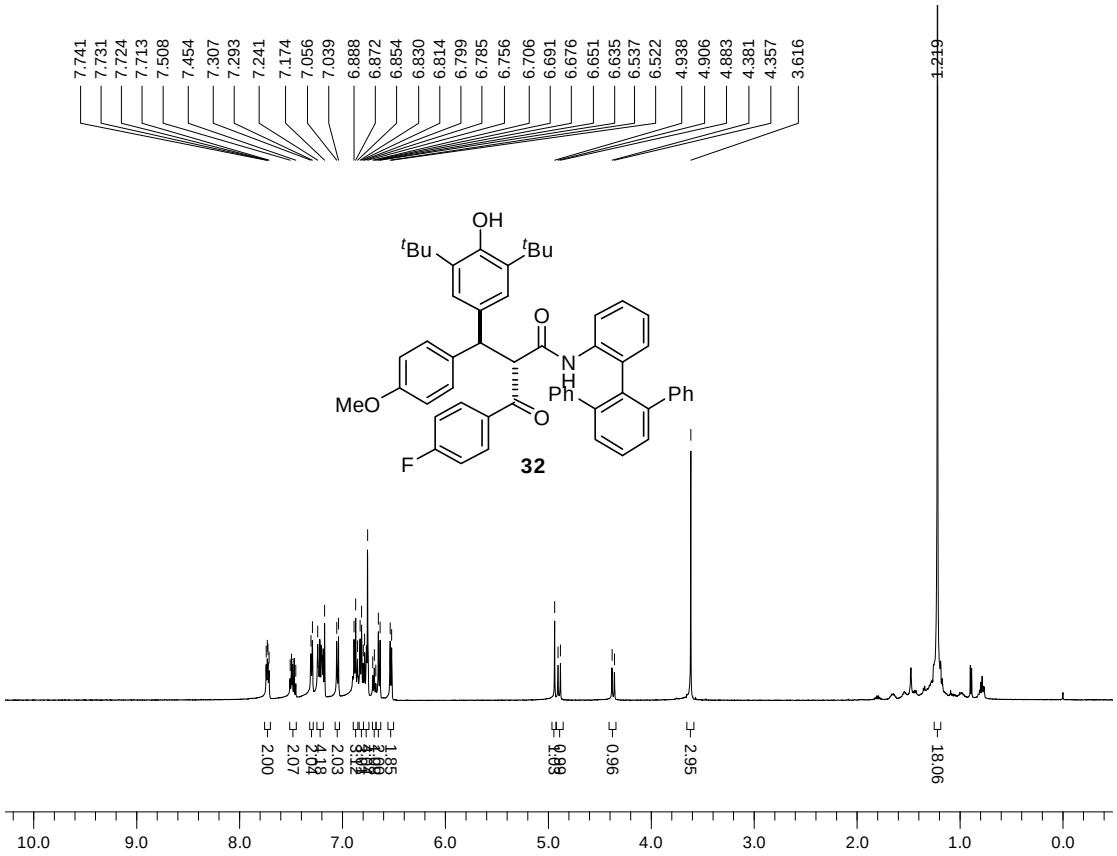

205.04
165.69
158.32
152.32
148.27
138.28
136.09
135.66
134.02
133.72
131.96
129.01
127.74
127.04
124.26
121.76
121.53
116.28
114.15
70.46
55.19
51.52
34.13
29.99
29.41
200
150
100
50
0

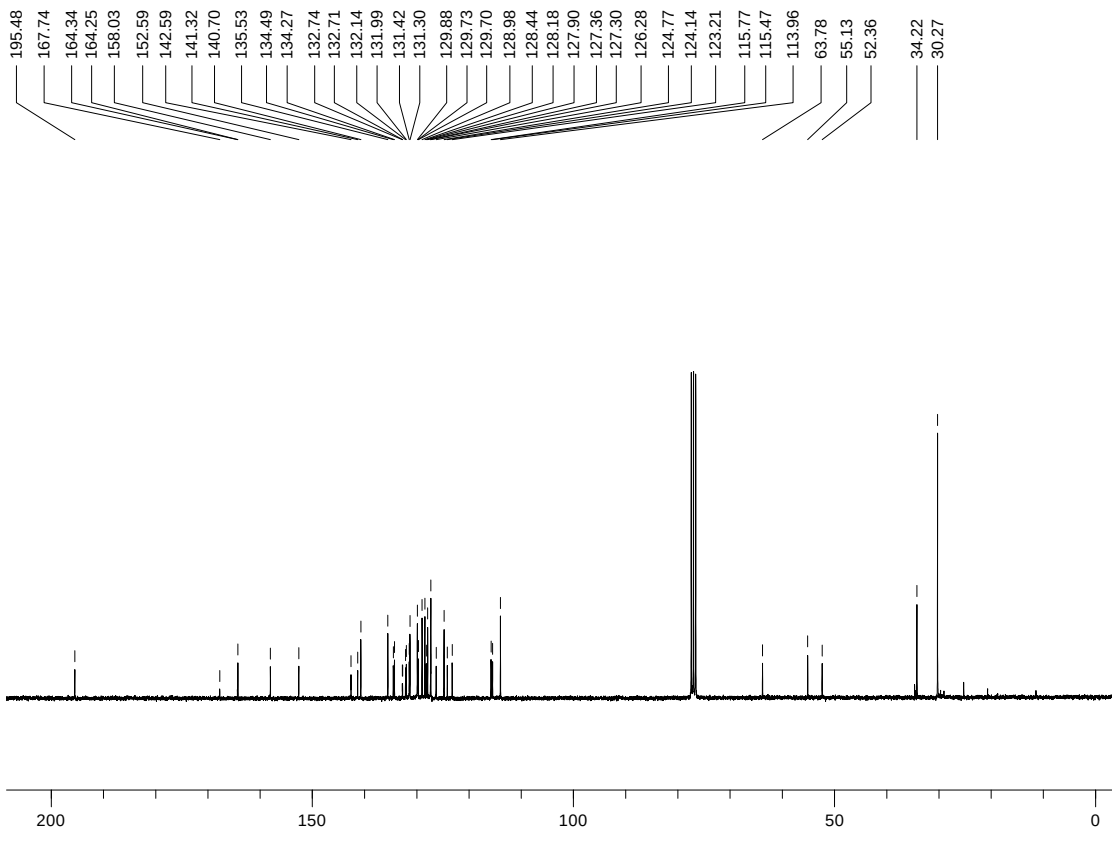

7.696
7.680
7.520
7.464
7.329
7.293
7.231
7.166
7.064
7.047
6.876
6.763
6.695
6.663
6.640
6.623
6.515
6.501
4.964
4.940
4.927
4.397
4.374
3.609
1.218
OH
tBu
tBu
O
N
H
Ph
Ph
MeO
O
Ph
30
2.04
2.09
2.03
2.02
1.00
3.01
18.00
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0

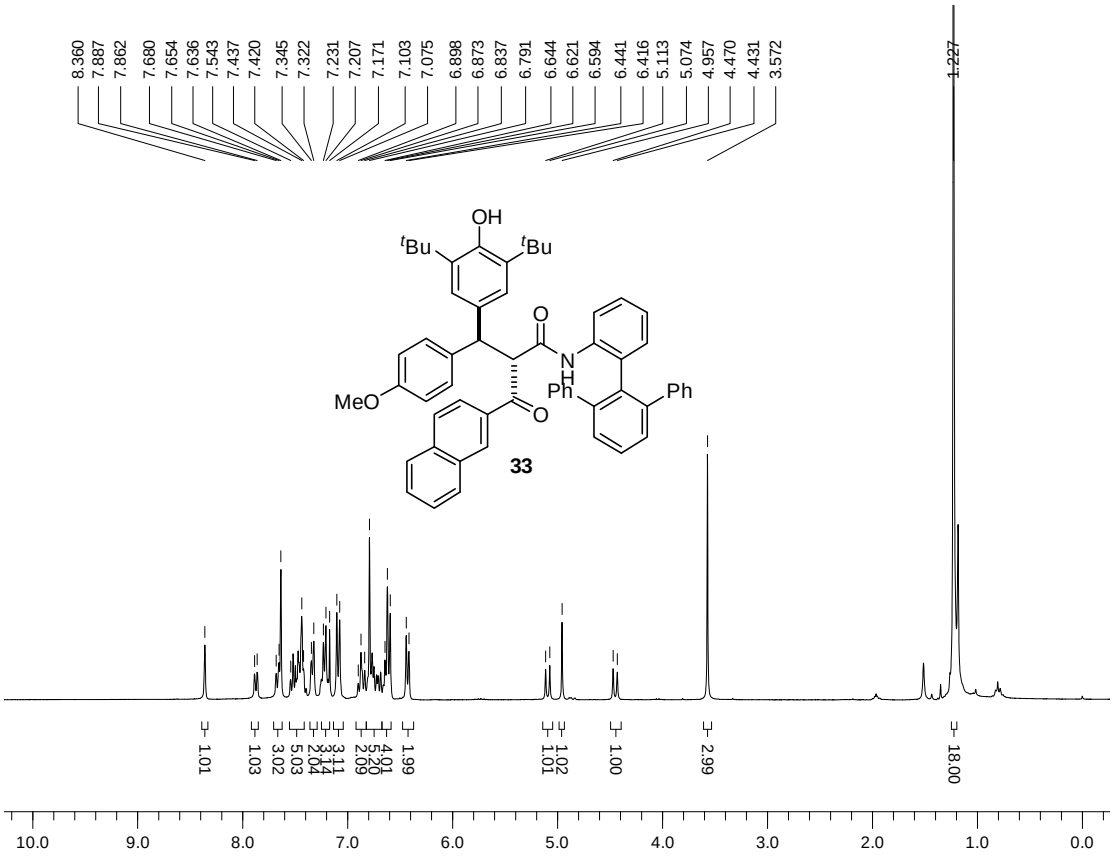

197.26
164.25
157.98
152.55
142.62
141.32
140.77
140.75
136.37
135.49
134.57
134.41
134.25
133.62
131.99
131.91
131.45
129.90
129.76
129.73
129.01
128.58
128.50
128.46
128.20
127.88
127.30
127.27
127.24
126.17
124.80
123.92
123.00
113.93
63.70
55.12
52.53
34.22
30.27
200
150
100
50
0

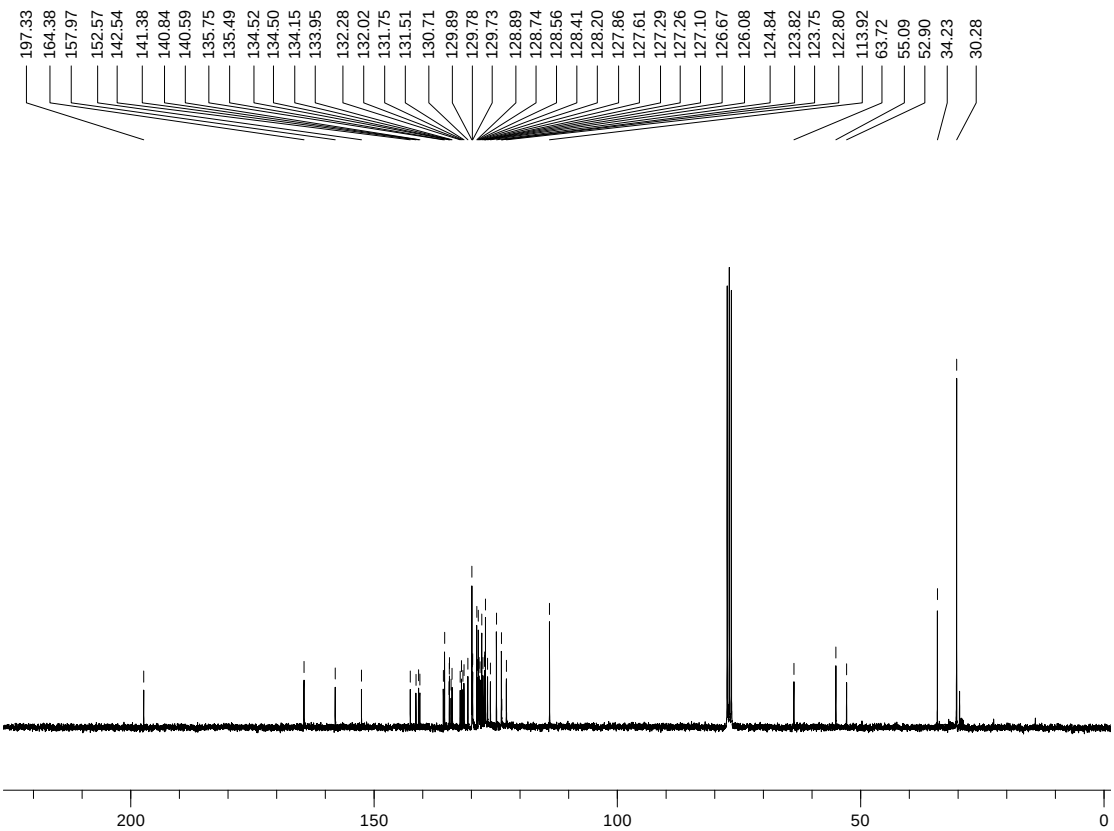

7.606
7.590
7.519
7.468
7.334
7.314
7.299
7.059
7.043
7.017
7.001
6.877
6.819
6.793
6.755
6.689
6.661
6.635
6.618
6.513
6.499
4.932
4.919
4.908
4.392
4.369
3.606
2.185
1.214
OH
tBu
tBu
O
N
H
Ph
Ph
MeO
O
Me
31
2.03
2.00
1.02
3.02
3.03
18.05
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0

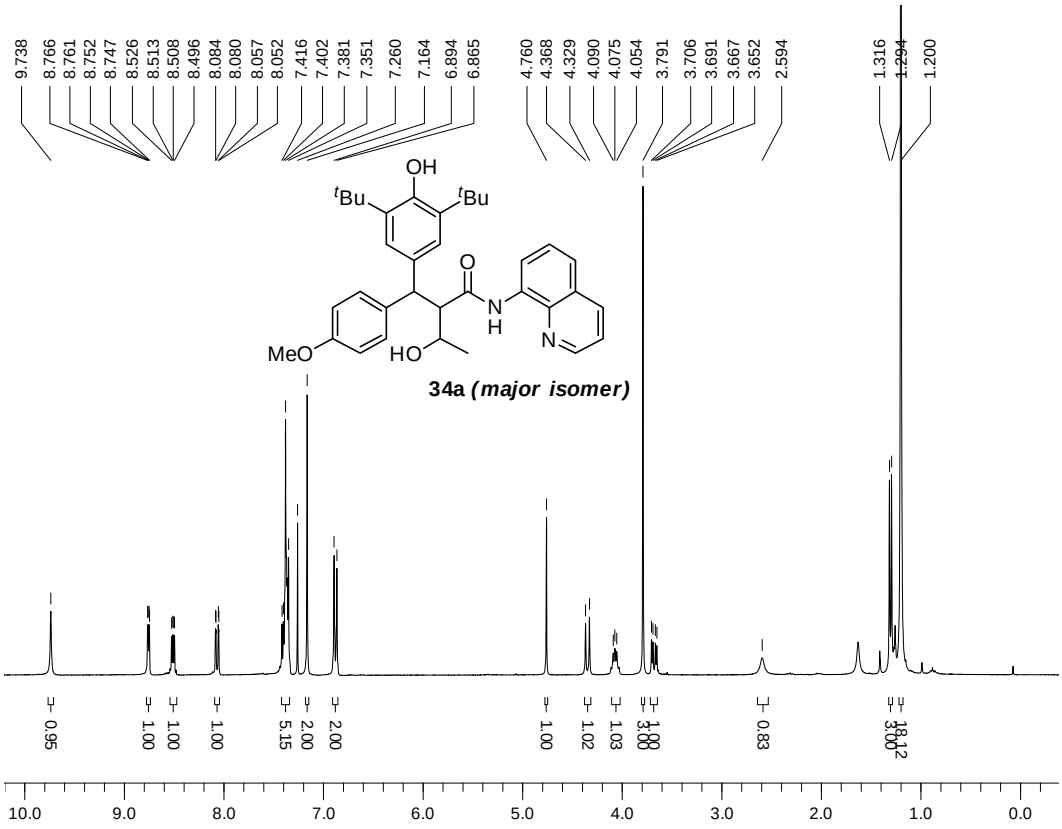

196.81
164.39
157.93
152.51
144.65
142.62
141.36
140.80
140.77
135.45
134.64
134.52
134.23
133.94
131.97
131.73
131.57
129.90
129.80
129.75
129.20
129.04
128.76
128.49
128.18
127.85
127.27
127.20
126.15
124.81
123.78
122.83
113.90
63.46
55.12
52.56
34.21
30.27
21.58
200
150
100
50
0

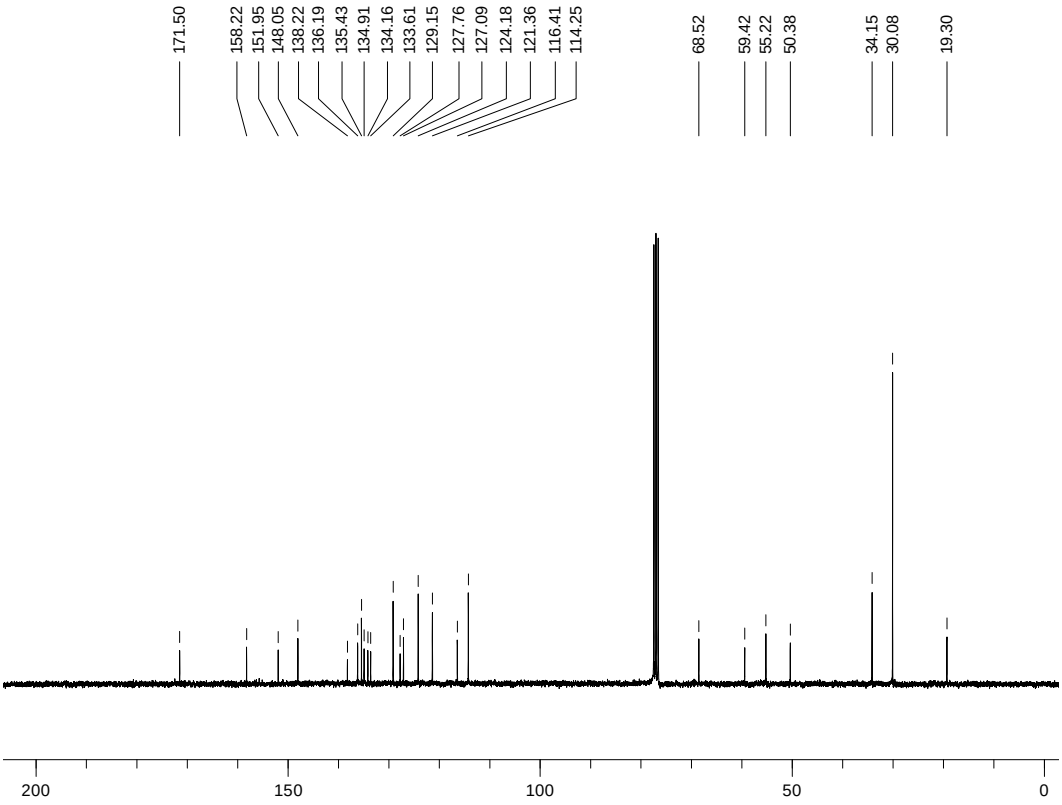

7.741
7.731
7.724
7.713
7.508
7.454
7.307
7.293
7.241
7.174
7.056
7.039
6.888
6.872
6.854
6.830
6.814
6.799
6.785
6.756
6.706
6.691
6.676
6.651
6.635
6.537
6.522
4.938
4.906
4.883
4.381
4.357
3.616
1.219
OH
tBu
tBu
O
N
H
Ph
Ph
MeO
O
F
32
2.00
2.07
2.18
2.03
1.85
1.00
0.96
2.95
18.06
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0

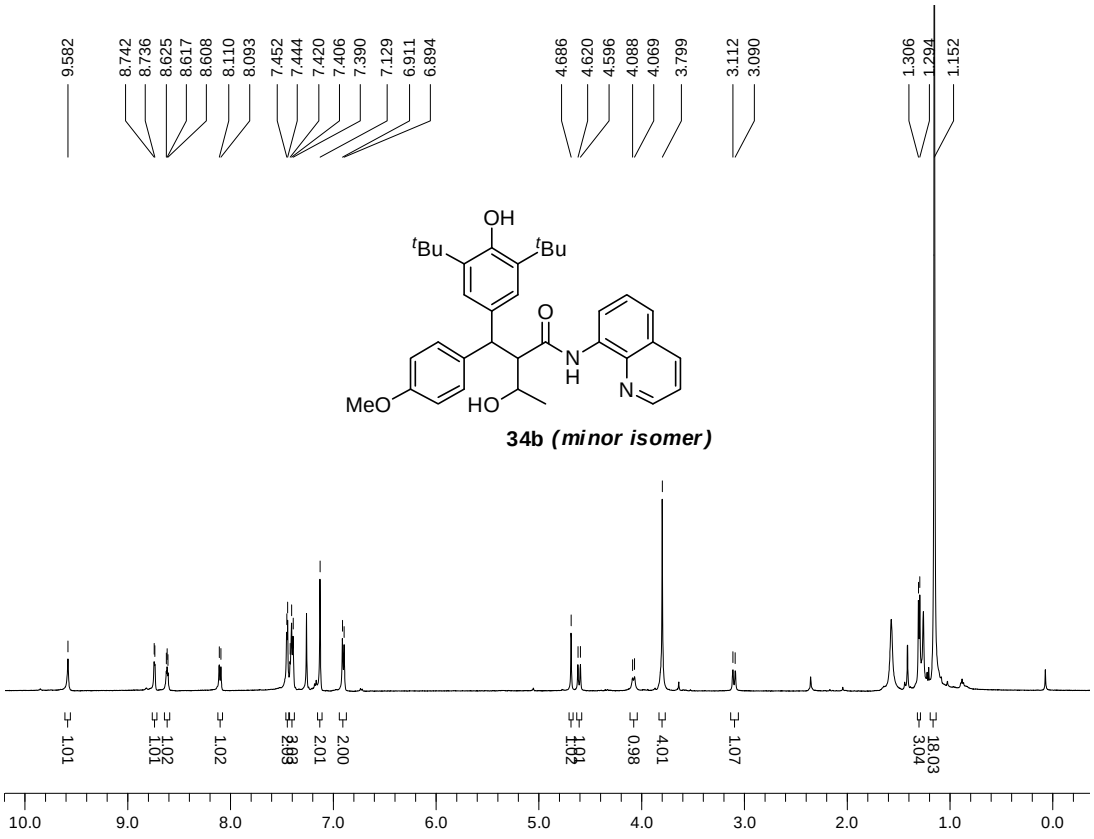

195.48
167.74
164.34
164.25
158.03
152.59
142.59
141.32
140.70
135.53
134.49
134.27
132.74
132.71
132.14
131.99
131.42
131.30
129.88
129.73
129.70
128.98
128.44
128.18
127.90
127.36
127.30
126.28
124.77
124.14
123.21
115.77
115.47
113.96
63.78
55.13
52.36
34.22
30.27
200
150
100
50
0


8.360
7.887
7.862
7.680
7.654
7.636
7.543
7.437
7.420
7.345
7.322
7.231
7.207
7.171
7.103
7.075
6.898
6.873
6.837
6.791
6.644
6.621
6.594
6.441
6.416
5.113
5.074
4.957
4.470
4.431
3.572
1.227
OH
tBu
tBu
O
N
H
Ph
Ph
MeO
O
33
1.01
1.03
1.02
3.03
3.02
3.44
3.14
3.11
2.09
5.01
4.01
1.99
1.01
1.02
1.00
2.99
18.00
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0

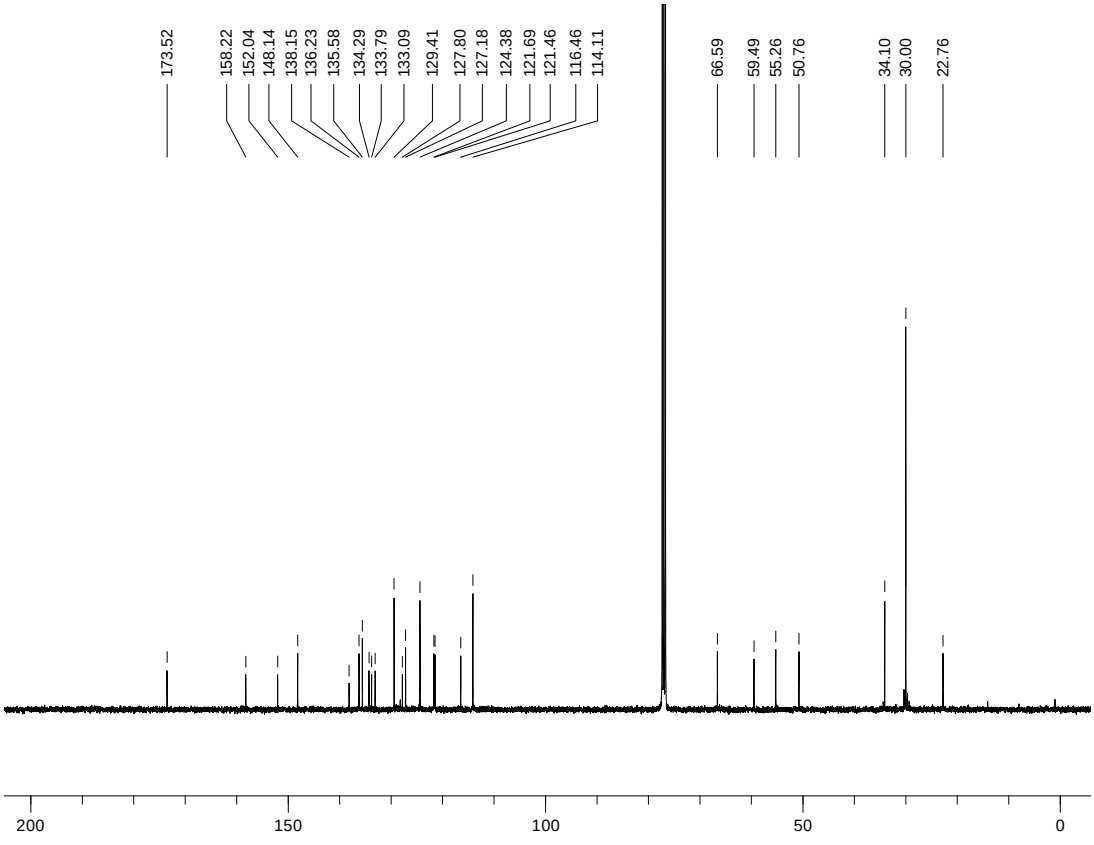

197.33
164.38
157.97
152.57
142.54
141.38
140.84
140.59
135.75
135.49
134.52
134.50
134.15
133.95
132.28
132.02
131.75
131.51
130.71
129.89
129.78
129.73
128.89
128.74
128.56
128.41
128.20
127.86
127.61
127.29
127.26
127.10
126.67
126.08
124.84
123.82
123.75
122.80
113.92
63.72
55.09
52.90
34.23
30.28
200
150
100
50
0

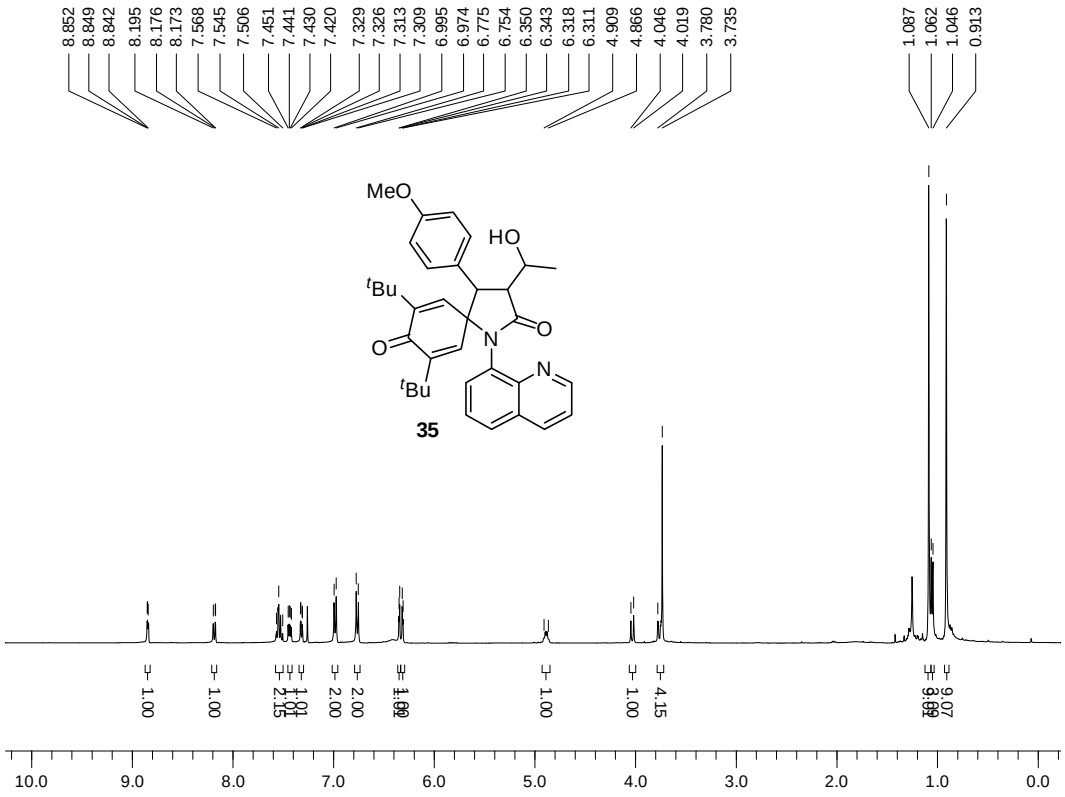

9.738
8.766
8.761
8.752
8.747
8.526
8.513
8.508
8.496
8.084
8.080
8.057
8.052
7.416
7.402
7.381
7.351
7.260
7.164
6.894
6.865
4.760
4.368
4.329
4.090
4.075
4.054
3.791
3.706
3.691
3.667
3.652
2.594
1.316
1.294
1.200
OH
tBu
tBu
O
N
H
N
MeO
HO
34a (major isomer)
0.95
1.00
1.00
1.00
5.15
2.00
2.00
1.00
1.02
1.03
3.00
3.00
0.83
18.12
3.00
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0


171.50
158.22
151.95
148.05
138.22
136.19
135.43
134.91
134.16
133.61
129.15
127.76
127.09
124.18
121.36
116.41
114.25
68.52
59.42
55.22
50.38
34.15
30.08
19.30
200
150
100
50
0



34b ***(minor isomer)***

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7.545
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7.451
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7.430
7.420
7.329
7.326
7.313
7.309
6.995
6.974
6.775
6.754
6.350
6.343
6.318
6.311
4.909
4.866
4.046
4.019
3.780
3.735
1.087
1.062
1.046
0.913
MeO
HO
tBu
tBu
O
O
N
O
N
35
1.00
1.00
2.00
2.00
1.00
1.00
4.15
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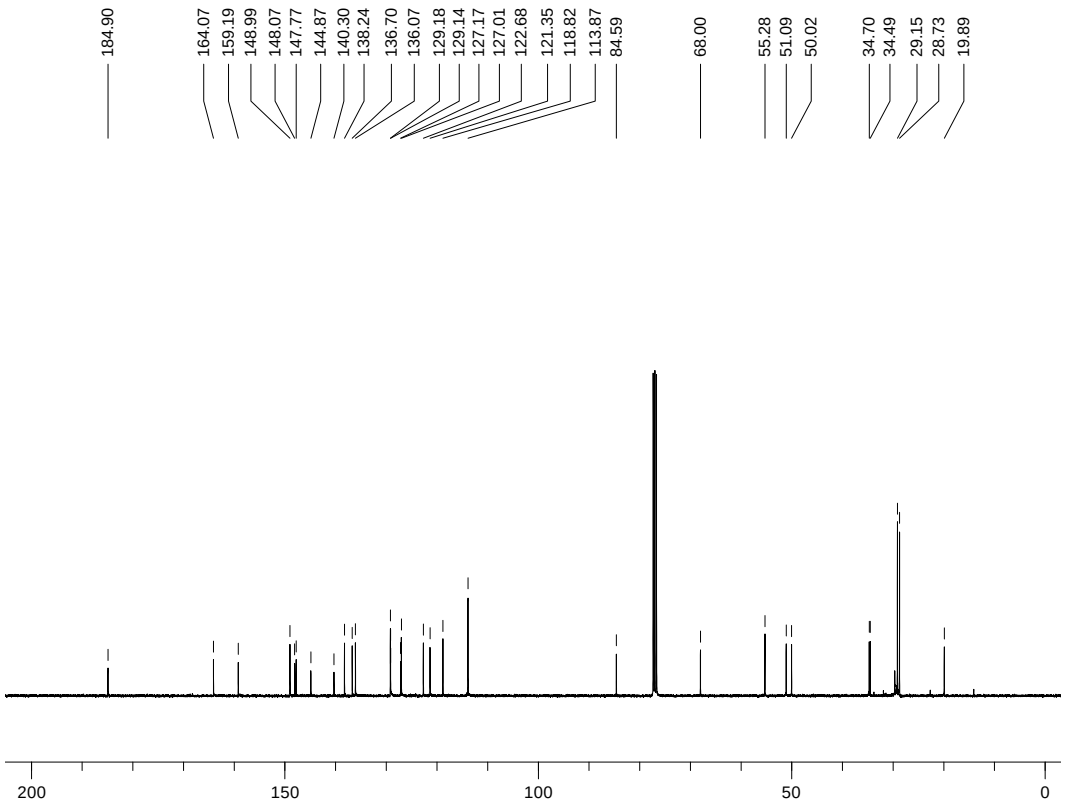
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0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140.30
138.24
136.70
136.07
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129.14
127.17
127.01
122.68
121.35
118.82
113.87
84.59
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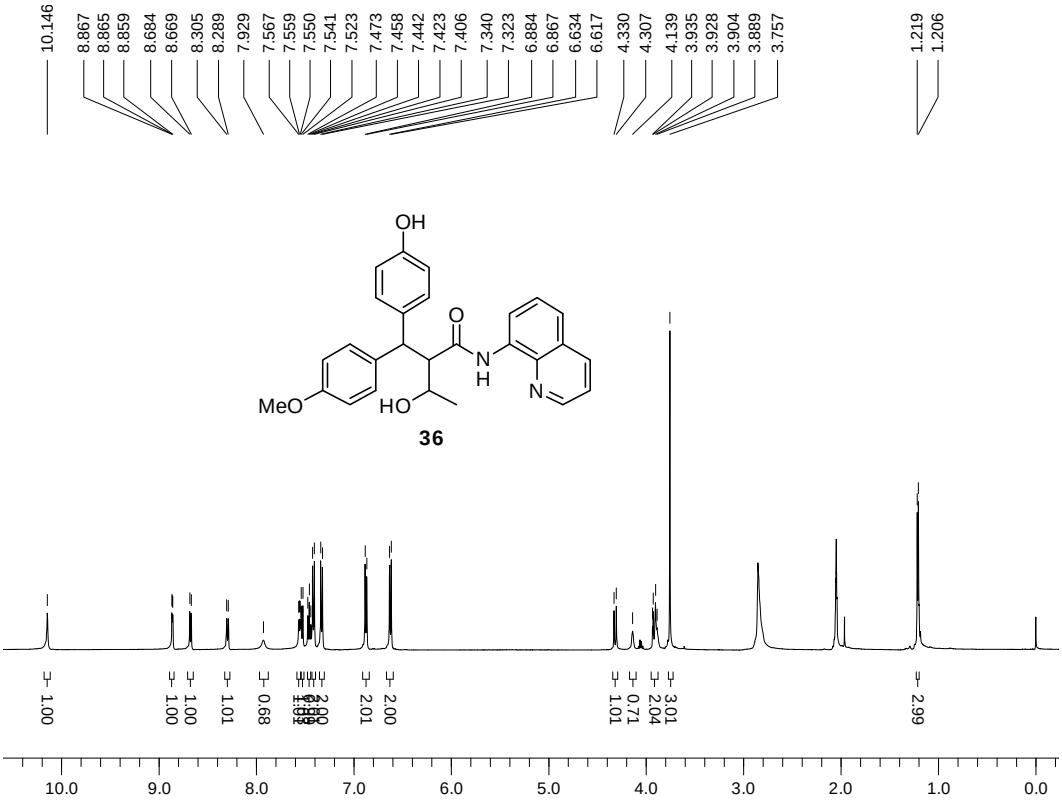
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7.550
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7.473
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7.442
7.423
7.406
7.340
7.323
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6.867
6.634
6.617
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4.307
4.139
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3.928
3.904
3.889
3.757
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1.206
OH
O
N
H
N
MeO
HO
1.00
1.00
1.00
1.01
0.68
2.01
2.00
1.01
0.71
2.04
3.01
2.99
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6.0
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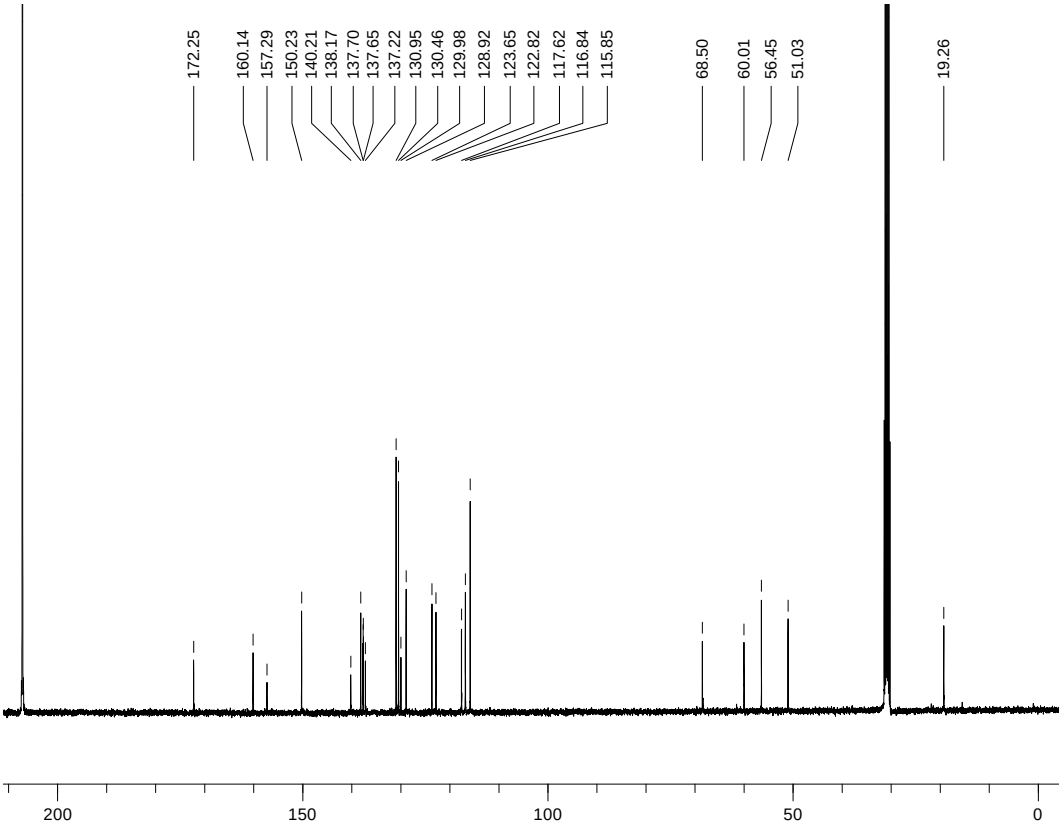
2.0
1.0
0.0

36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138.17
137.70
137.65
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130.95
130.46
129.98
128.92
123.65
122.82
117.62
116.84
115.85
68.50
60.01
56.45
51.03
19.26
200
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50
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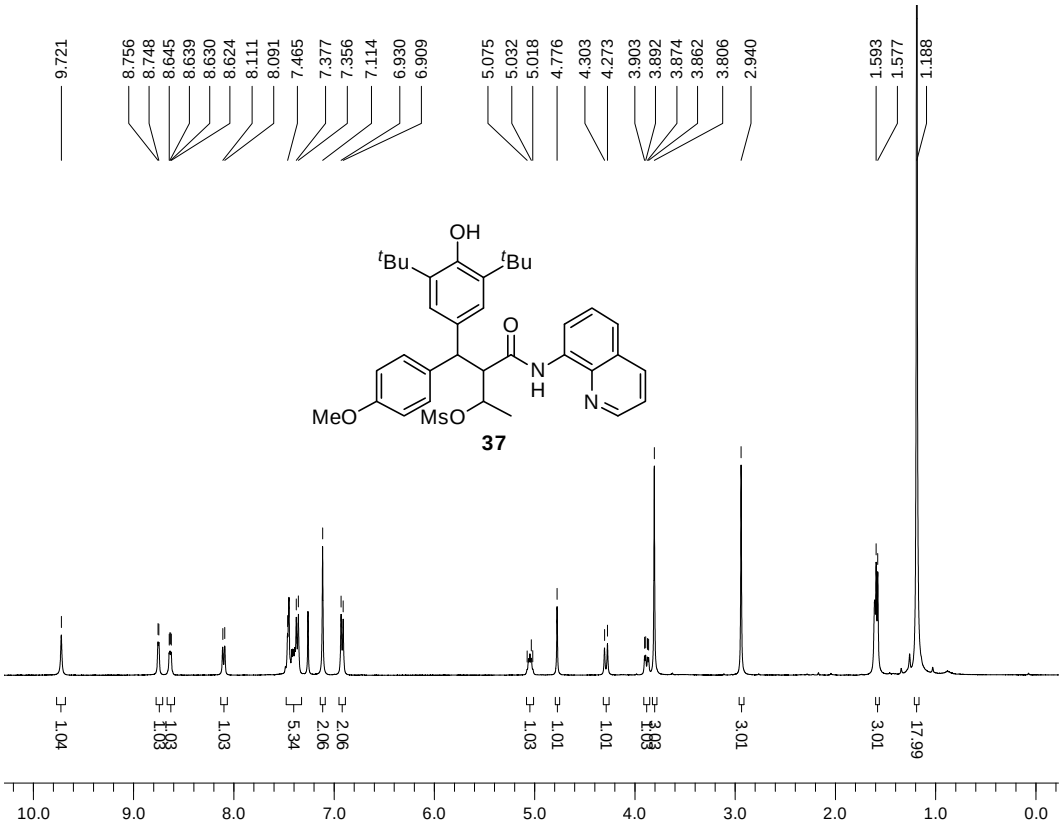
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6.909
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5.032
5.018
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4.303
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3.874
3.862
3.806
2.940
1.593
1.577
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OH
tBu
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O
N
H
N
MeO
MsO
37
1.04
1.08
1.08
1.03
5.34
2.06
2.06
1.03
1.01
1.01
1.08
1.08
3.01
3.01
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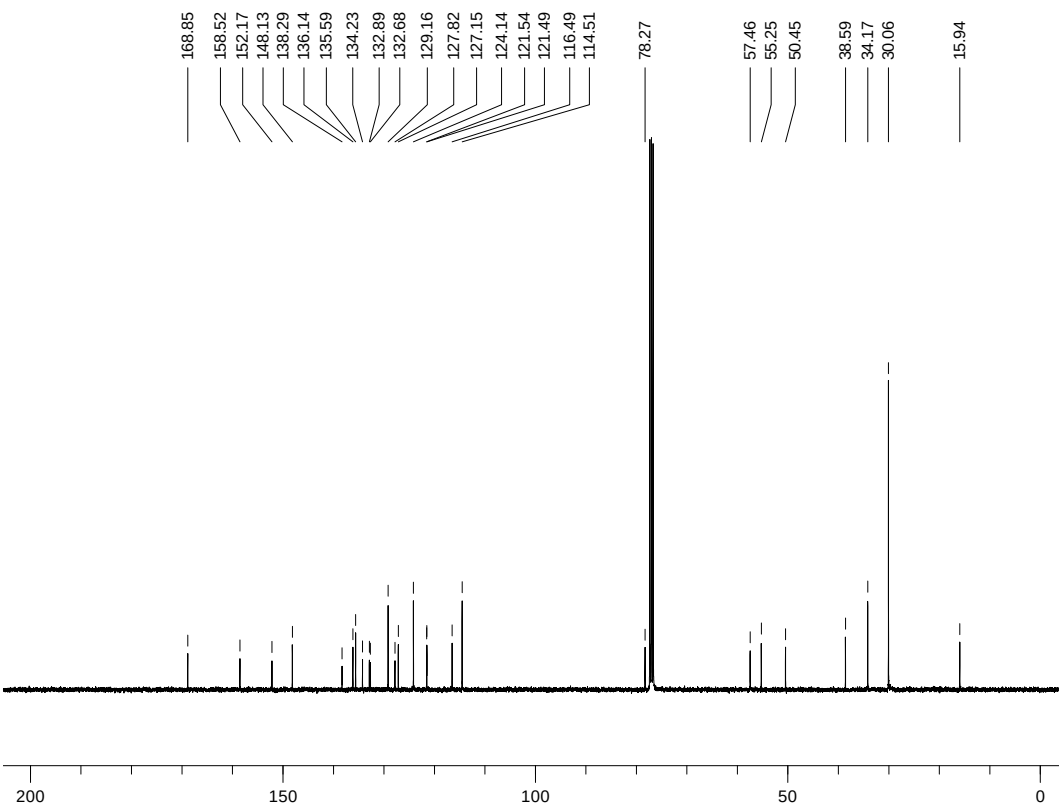
2.0
1.0
0.0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134.23
132.89
132.68
129.16
127.82
127.15
124.14
121.54
121.49
116.49
114.51
78.27
57.46
55.25
50.45
38.59
34.17
30.06
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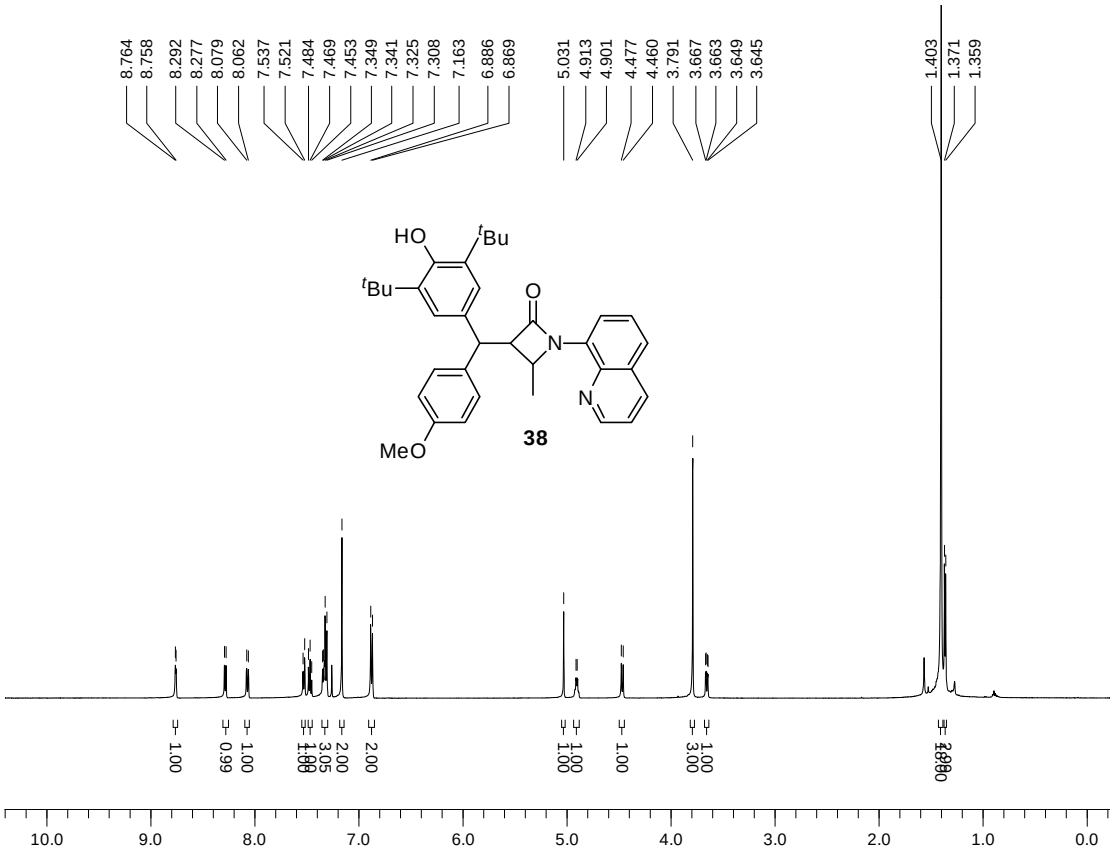
150
100
50
0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7.163
6.886
6.869
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3.791
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3.645
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1.371
1.359
HO
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tBu
O
N
N
MeO
38
1.00
0.99
1.00
1.00
3.05
2.00
2.00
1.00
1.00
3.00
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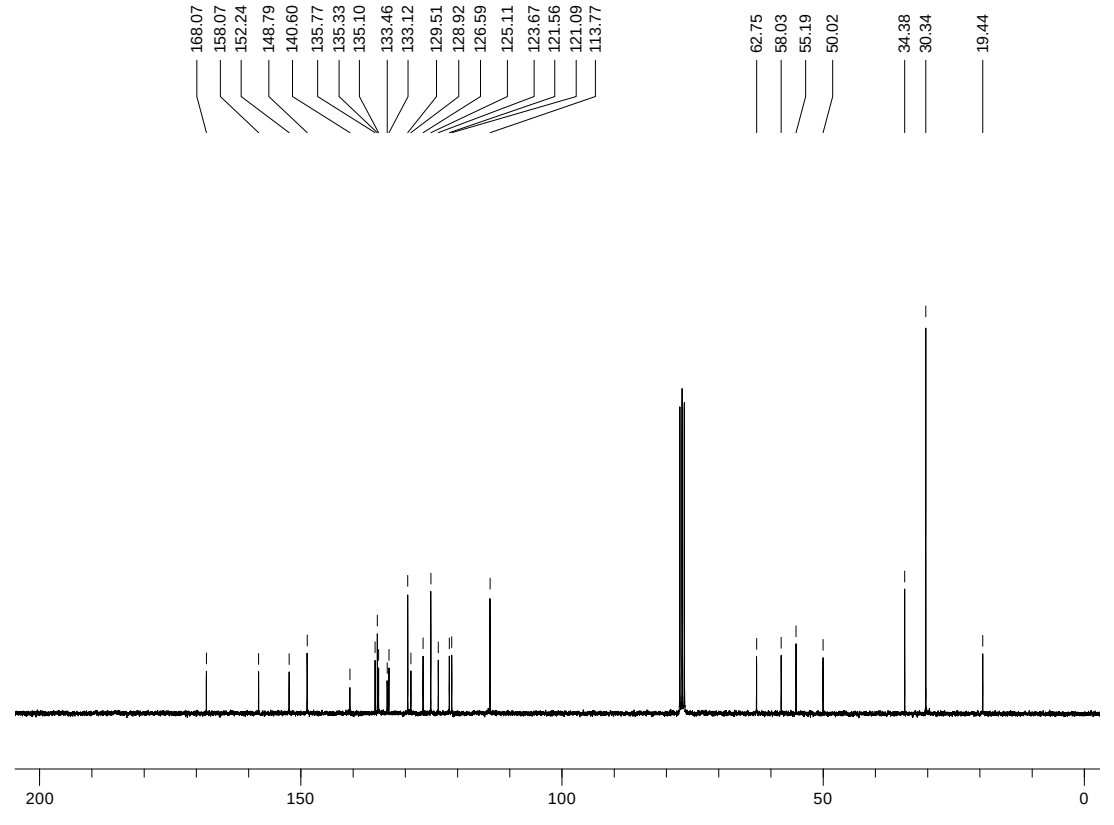
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135.10
133.46
133.12
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128.92
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125.11
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121.56
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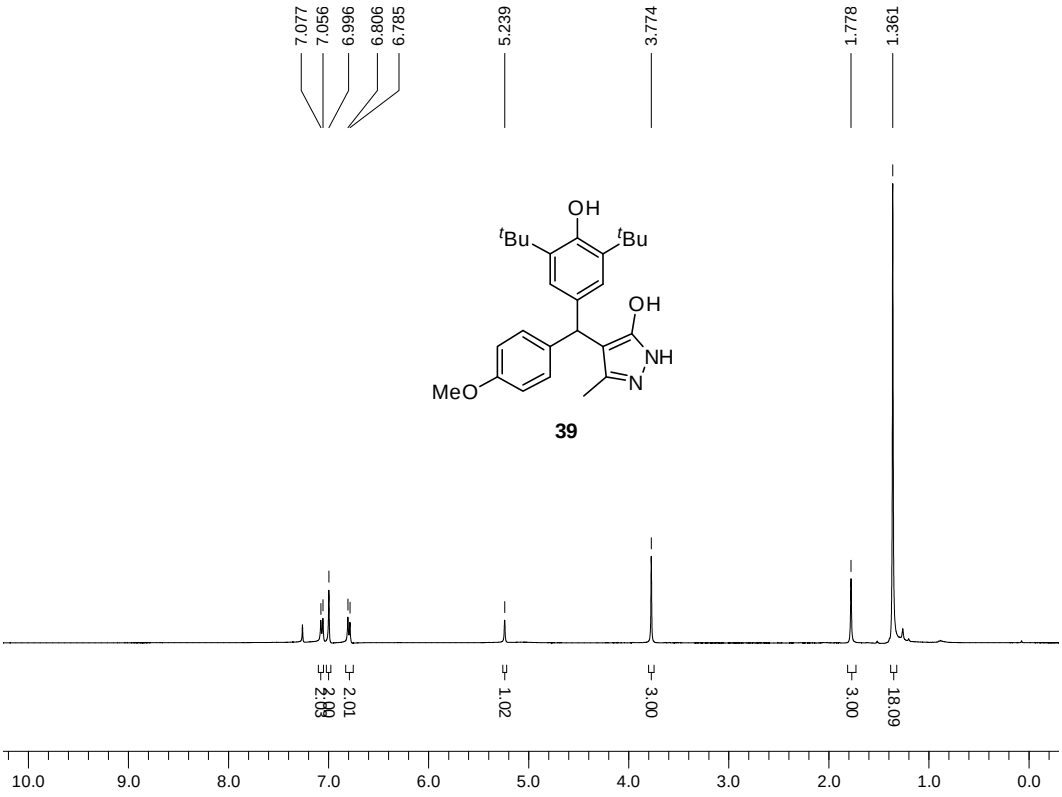
62.75
58.03
55.19
50.02
34.38
30.34
19.44
200
150
100
50
0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OH
tBu
tBu
OH
NH
N
MeO
39
2.00
2.03
2.01
1.02
3.00
3.00
18.09
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9.0
8.0
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5.0
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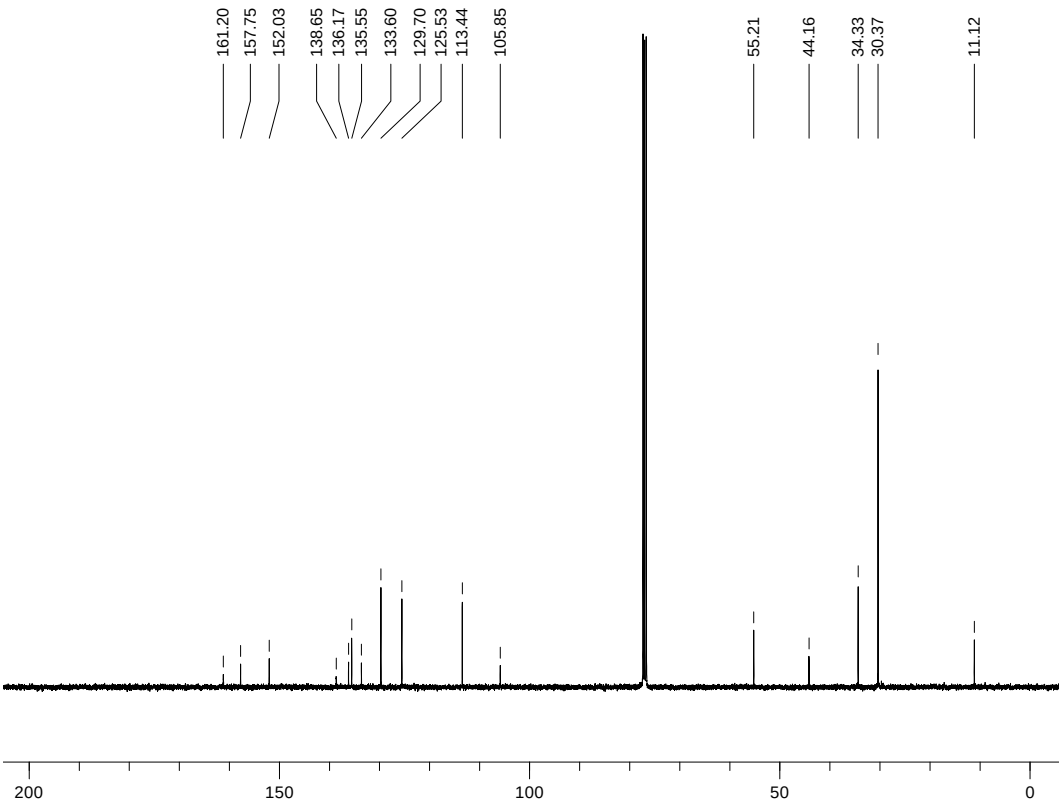
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30.37
11.12
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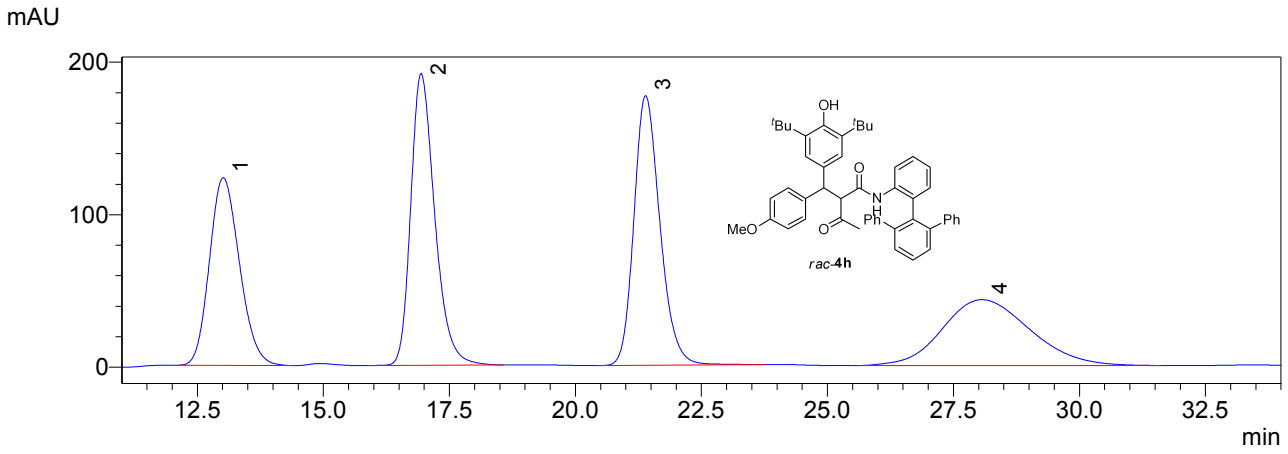
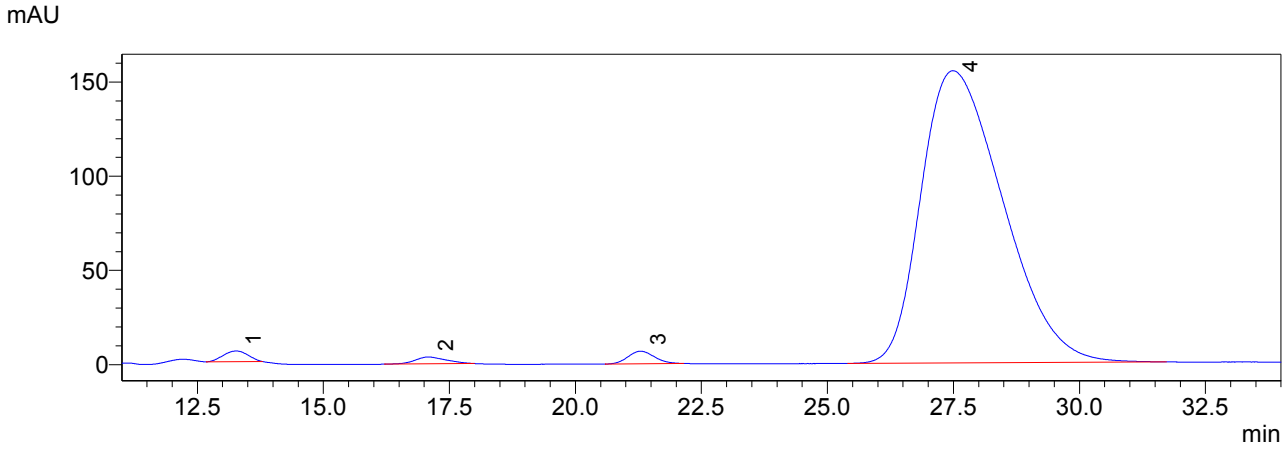
150
100
50
0

13. HPLC traces



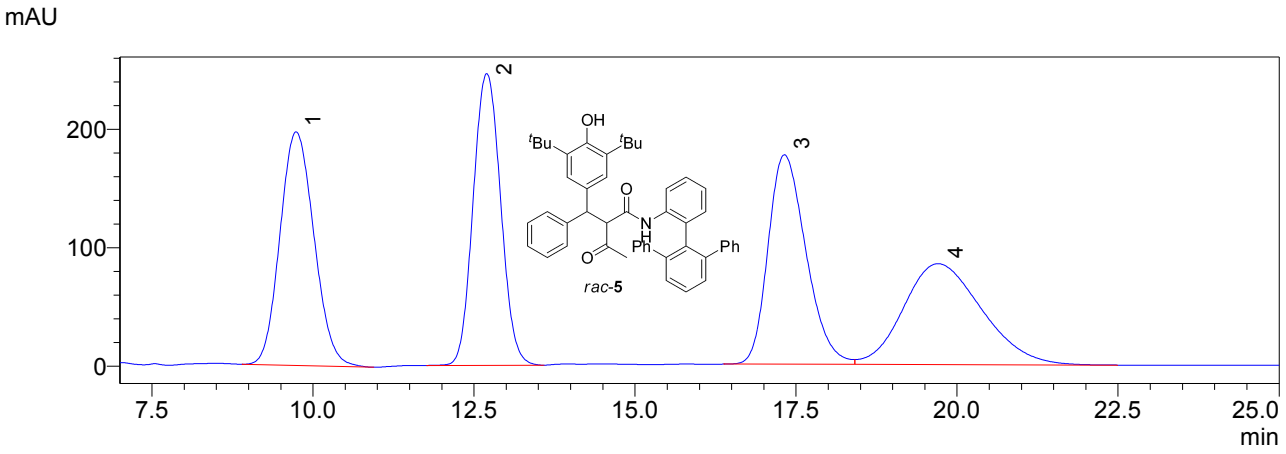
PDA Ch1 254nm

Peak#	Ret. Time	Area%
1	13.01	22.15
2	16.94	27.52
3	21.39	27.65
4	28.07	22.68
Total		100.00



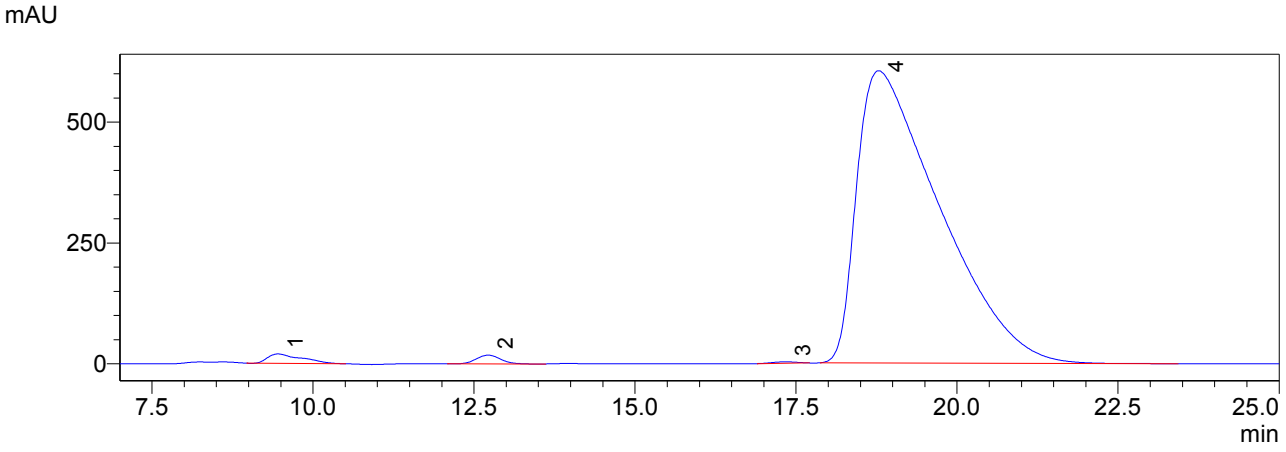
PDA Ch1 254nm

Peak#	Ret. Time	Area%
1	13.27	1.06
2	17.08	0.86
3	21.29	1.34
4	27.49	96.74
Total		100.00



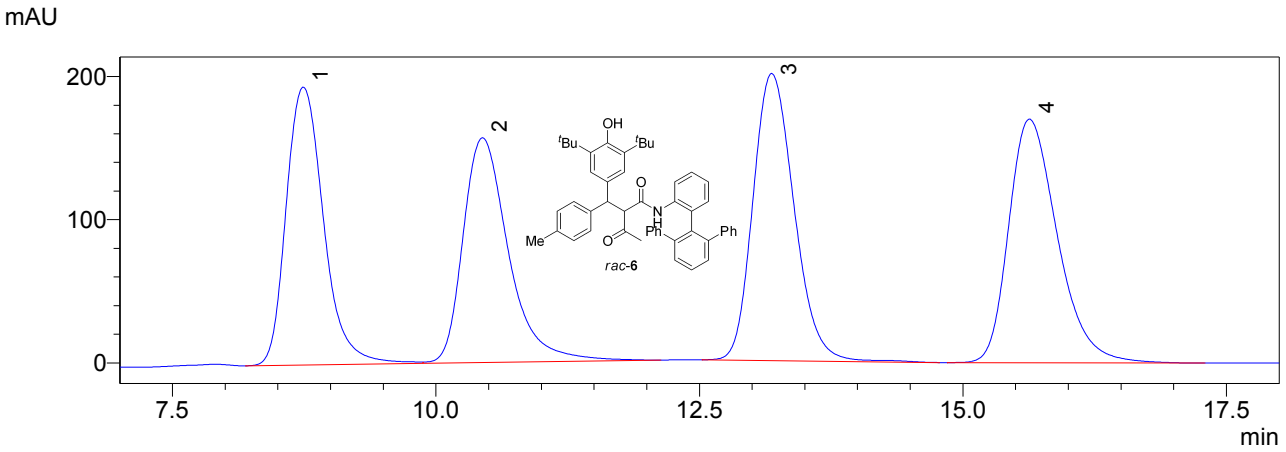
PDA Ch1 254nm

Peak#	Ret. Time	Area%
1	9.74	24.98
2	12.70	25.16
3	17.32	24.99
4	19.70	24.86
Total		100.00



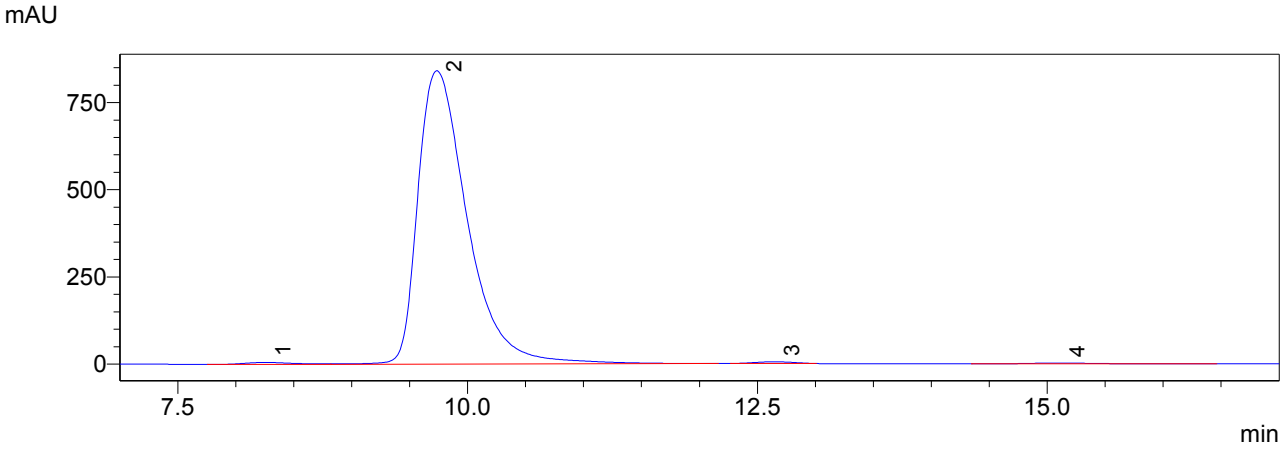
PDA Ch1 254nm

Peak#	Ret. Time	Area%
1	9.46	1.30
2	12.72	0.85
3	17.33	0.14
4	18.78	97.71
Total		100.00



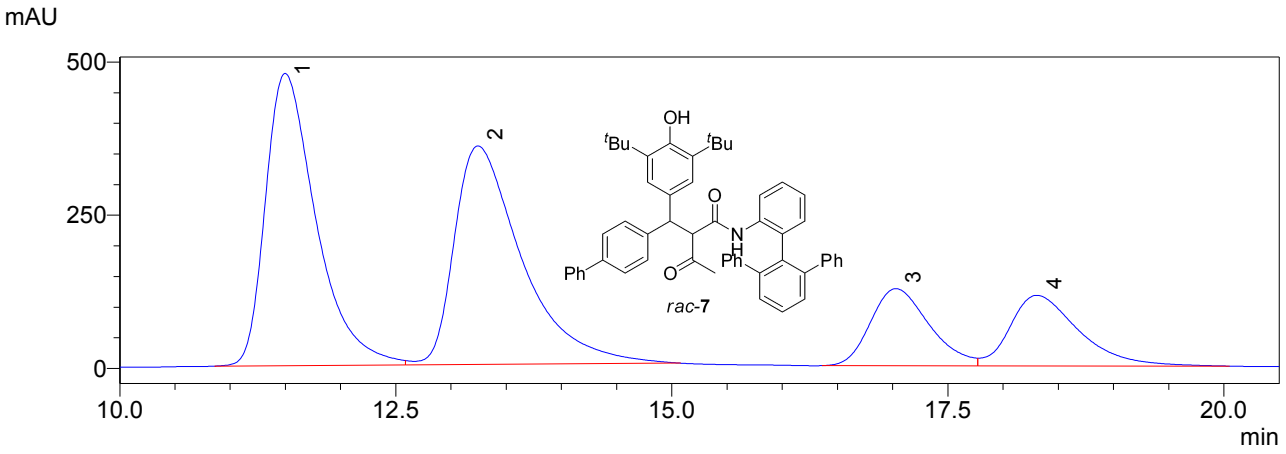
PDA Ch1 254nm

Peak#	Ret. Time	Area%
1	8.74	23.52
2	10.44	23.04
3	13.19	26.66
4	15.63	26.77
Total		100.00



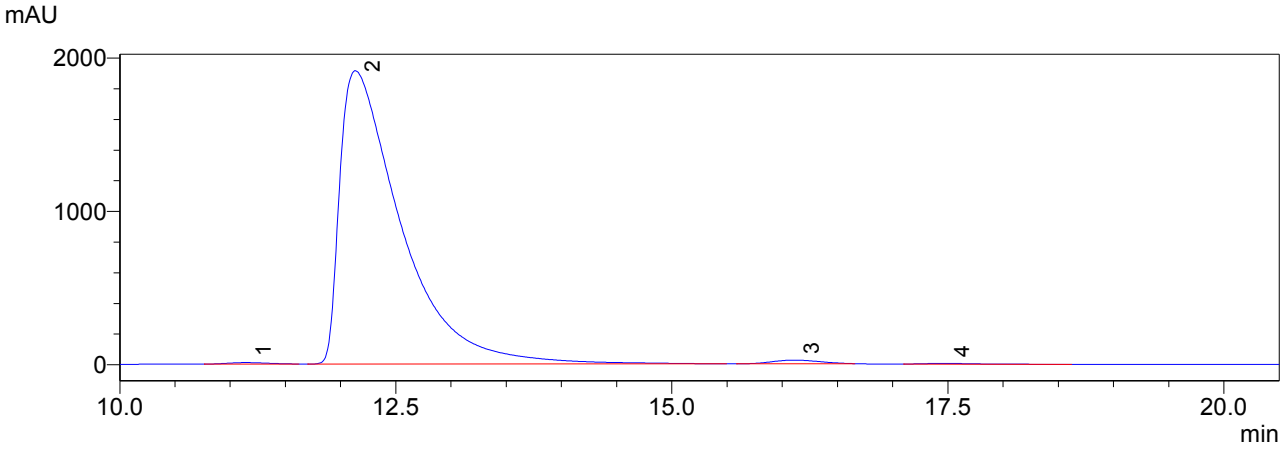
PDA Ch1 254nm

Peak#	Ret. Time	Area%
1	8.26	0.70
2	9.74	98.45
3	12.65	0.46
4	15.11	0.40
Total		100.00



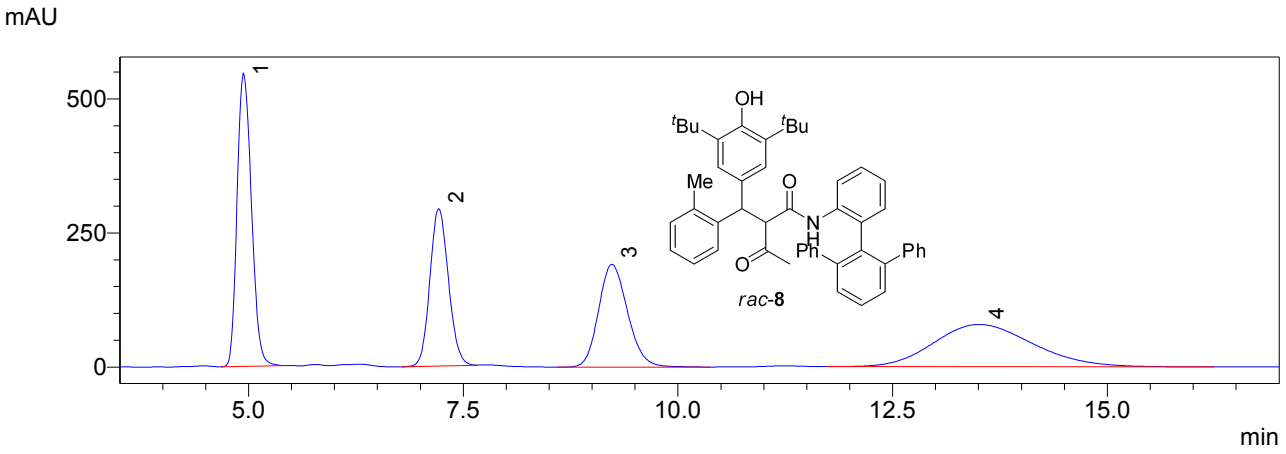
PDA Ch1 254nm

Peak#	Ret. Time	Area%
1	11.50	37.98
2	13.24	37.93
3	17.03	11.63
4	18.31	12.46
Total		100.00



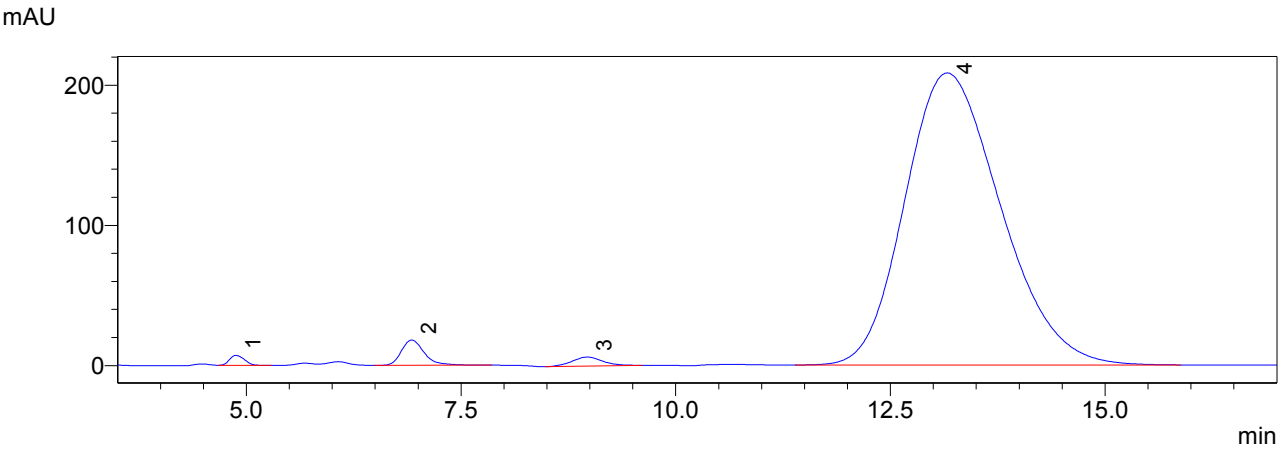
PDA Ch1 254nm

Peak#	Ret. Time	Area%
1	11.14	0.33
2	12.13	98.52
3	16.11	0.94
4	17.47	0.21
Total		100.00



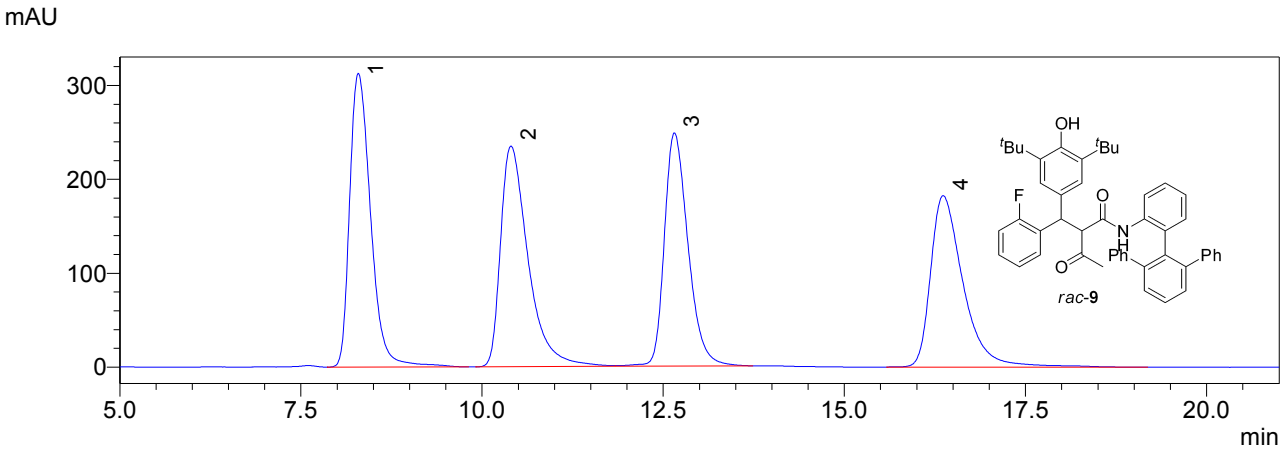
PDA Ch1 254nm

Peak#	Ret. Time	Area%
1	4.94	29.37
2	7.21	20.36
3	9.23	20.94
4	13.51	29.33
Total		100.00



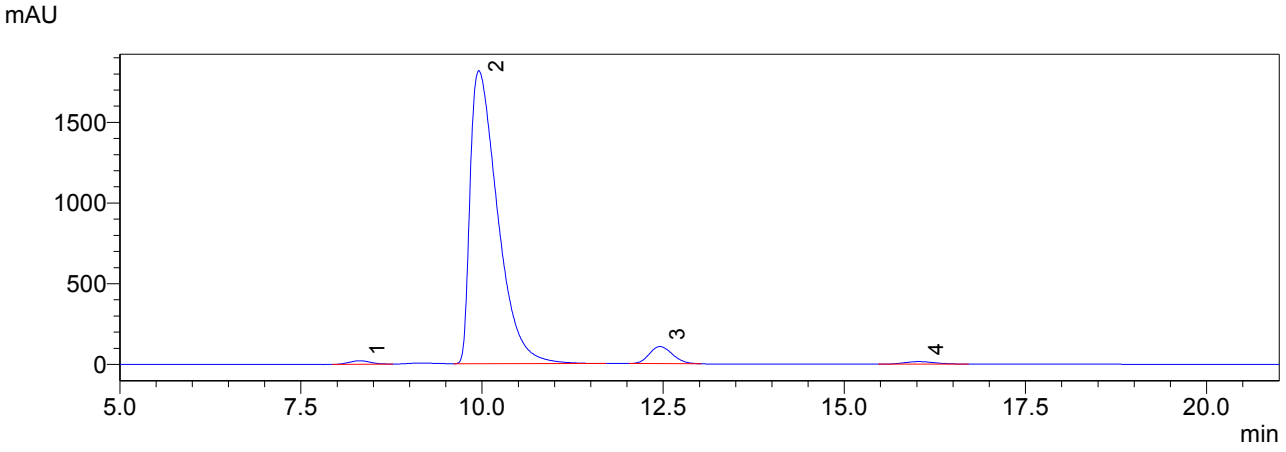
PDA Ch1 254nm

Peak#	Ret. Time	Area%
1	4.88	0.51
2	6.92	1.99
3	8.97	0.97
4	13.16	96.53
Total		100.00



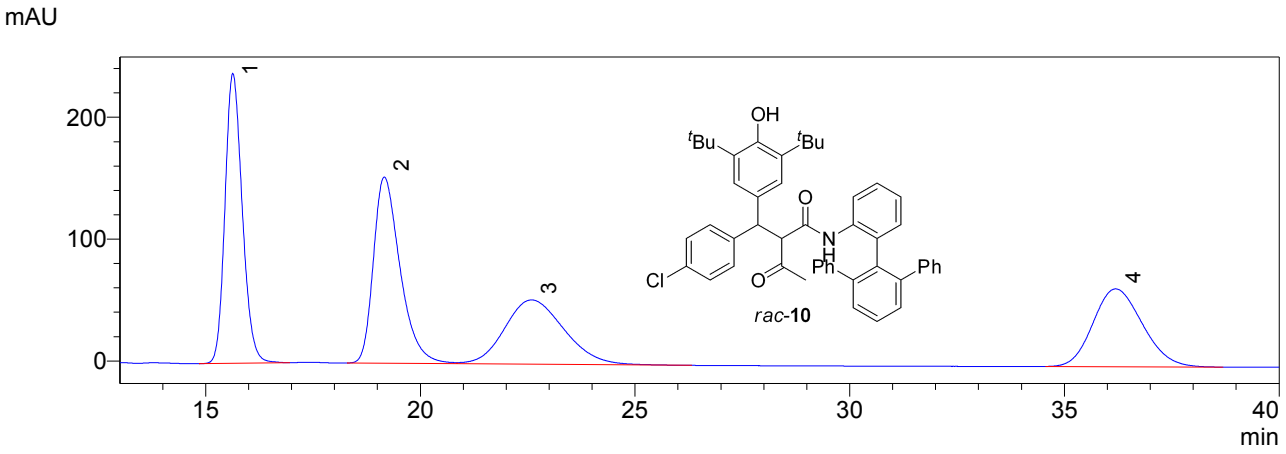
PDA Ch1 254nm

Peak#	Ret. Time	Area%
1	8.29	26.43
2	10.40	25.98
3	12.65	23.66
4	16.36	23.93
Total		100.00



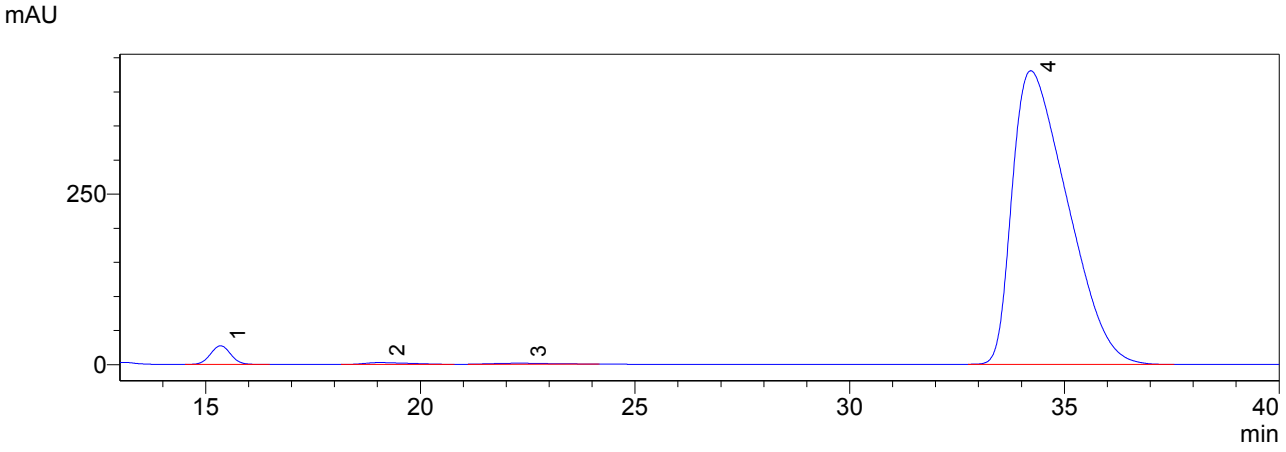
PDA Ch1 254nm

Peak#	Ret. Time	Area%
1	8.31	0.86
2	9.95	93.67
3	12.46	4.57
4	16.02	0.90
Total		100.00



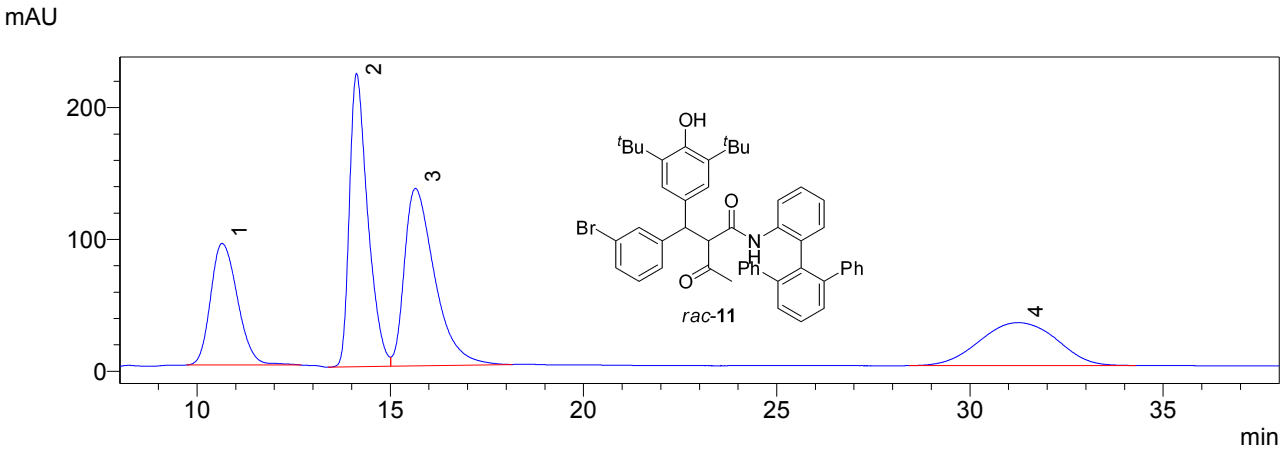
PDA Ch1 254nm

Peak#	Ret. Time	Area%
1	15.63	28.41
2	19.16	28.13
3	22.59	21.69
4	36.19	21.77
Total		100.00



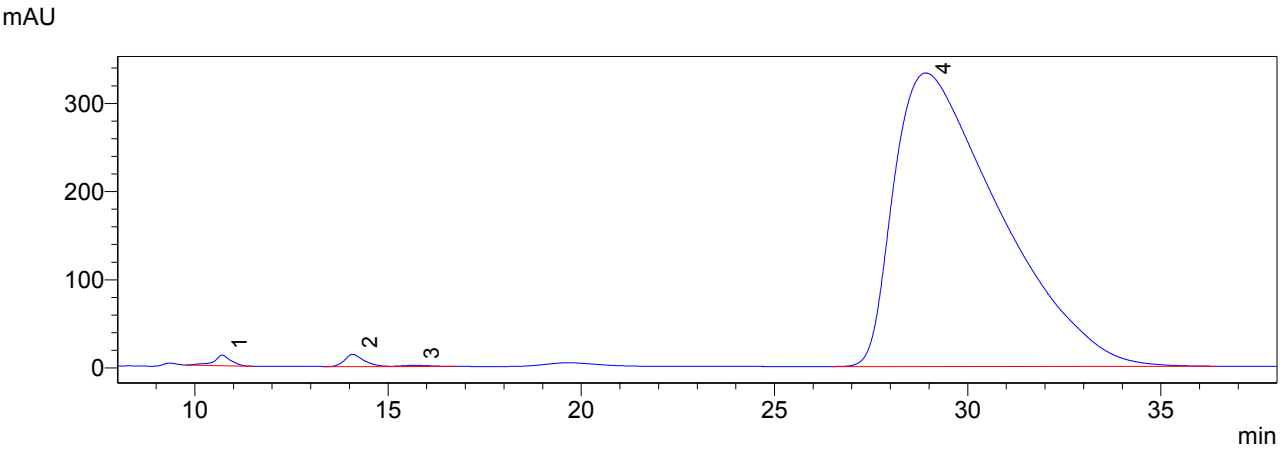
PDA Ch1 254nm

Peak#	Ret. Time	Area%
1	15.35	2.27
2	19.06	0.51
3	22.35	0.32
4	34.22	96.90
Total		100.00



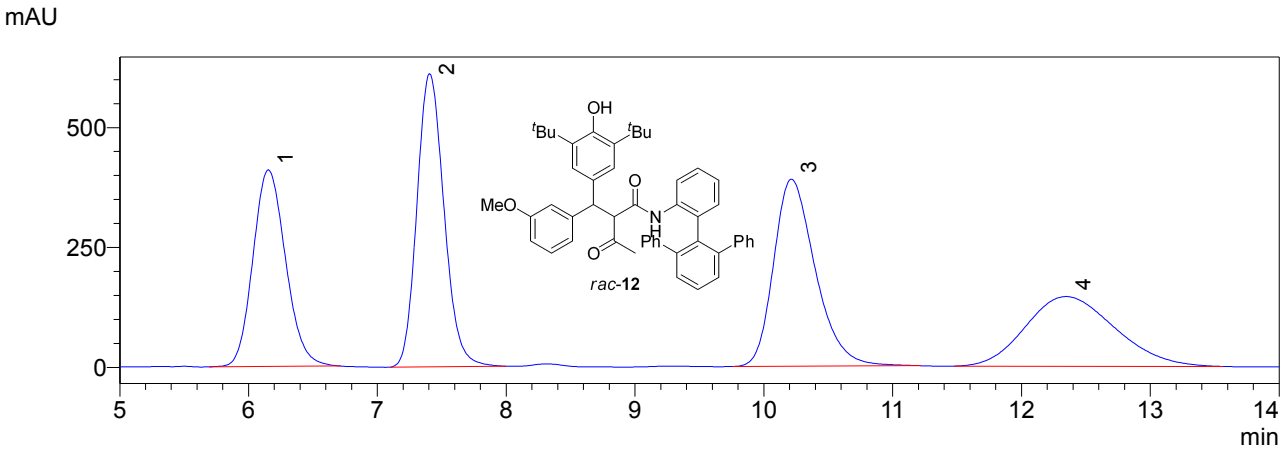
PDA Ch1 254nm

Peak#	Ret. Time	Area%
1	10.65	18.85
2	14.13	31.08
3	15.65	31.01
4	31.24	19.07
Total		100.00



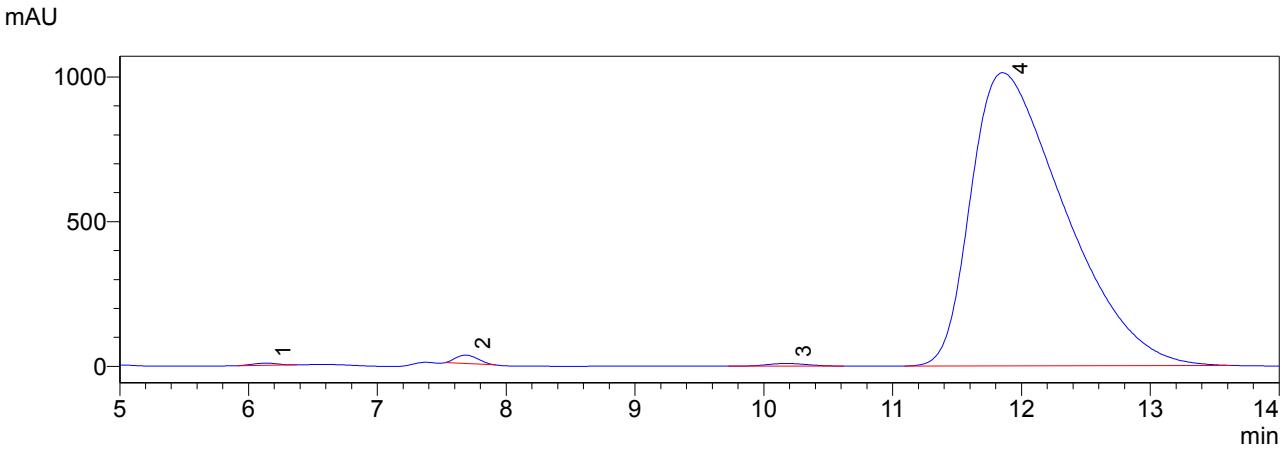
PDA Ch1 254nm

Peak#	Ret. Time	Area%
1	10.71	0.57
2	14.08	0.76
3	15.67	0.10
4	28.92	98.57
Total		100.00



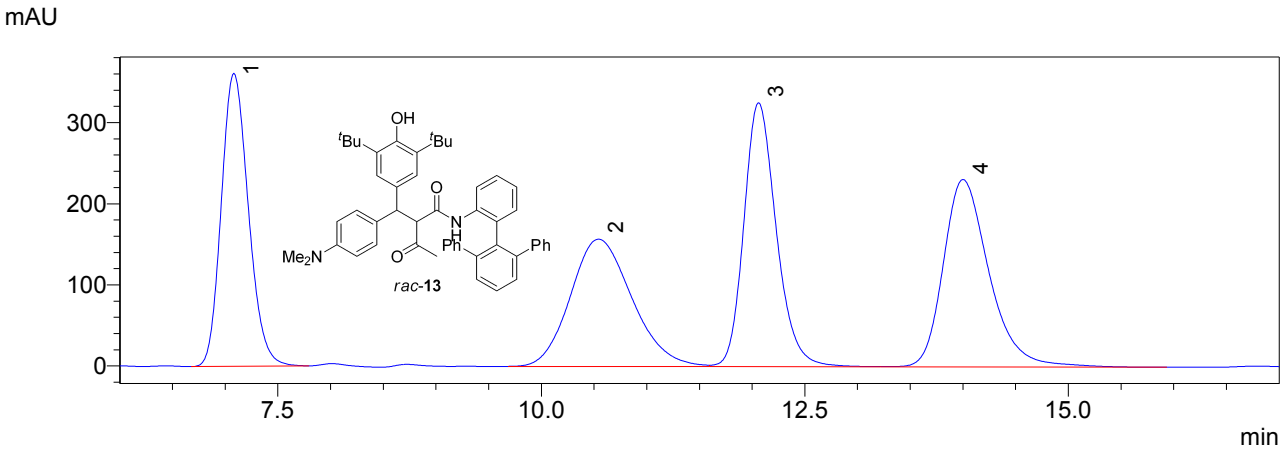
PDA Ch1 254nm

Peak#	Ret. Time	Area%
1	6.15	22.64
2	7.40	27.96
3	10.21	27.44
4	12.35	21.95
Total		100.00



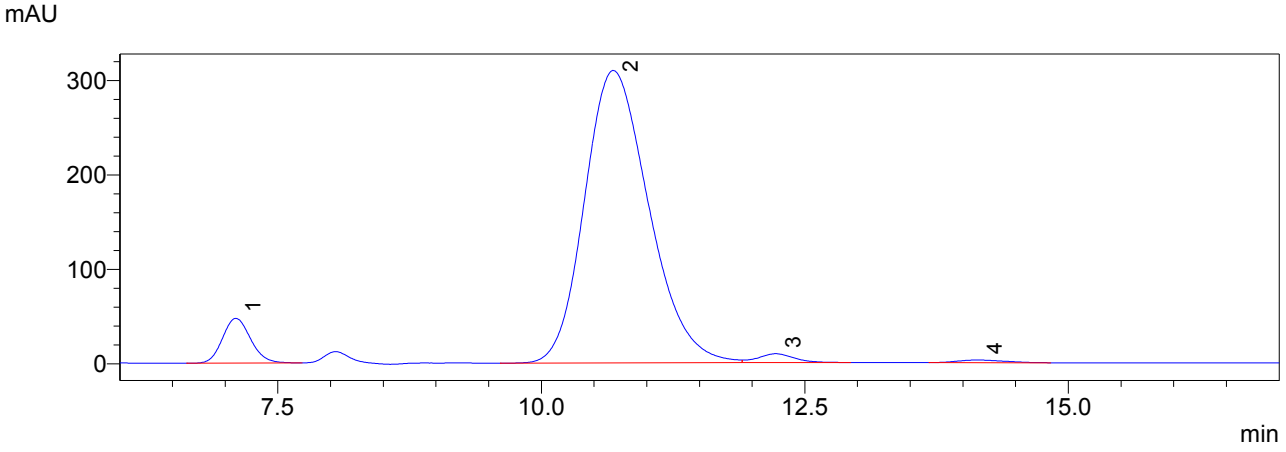
PDA Ch1 254nm

Peak#	Ret. Time	Area%
1	6.13	0.19
2	7.68	0.67
3	10.17	0.38
4	11.85	98.76
Total		100.00



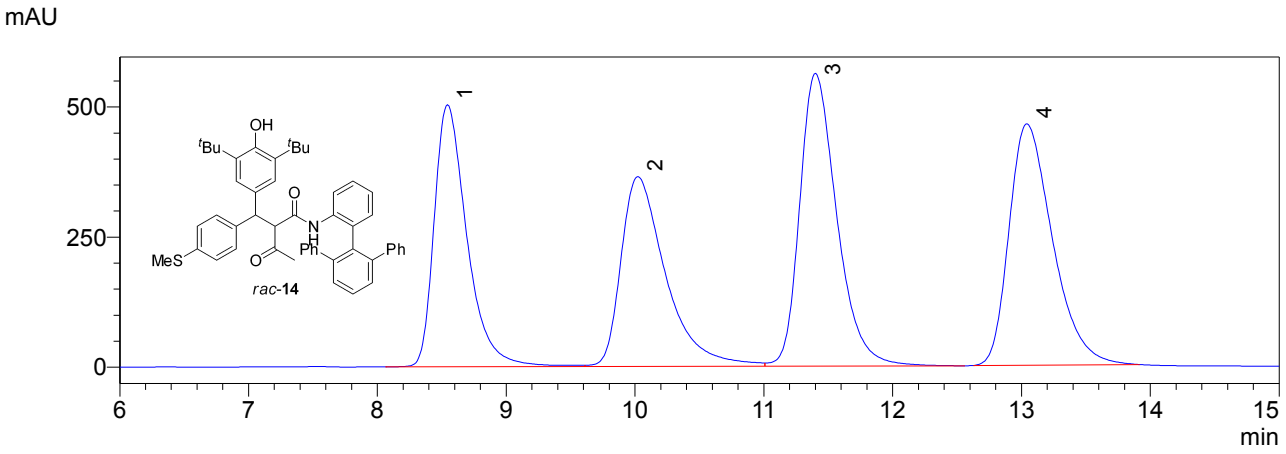
PDA Ch1 254nm

Peak#	Ret. Time	Area%
1	7.08	24.06
2	10.54	23.81
3	12.06	26.04
4	14.00	26.09
Total		100.00



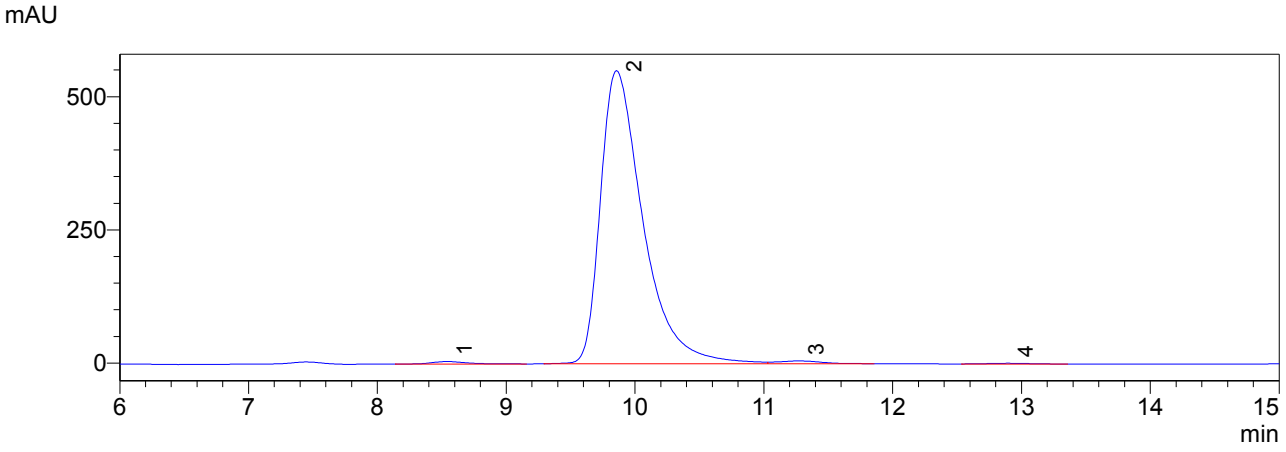
PDA Ch1 254nm

Peak#	Ret. Time	Area%
1	7.10	6.13
2	10.68	91.71
3	12.22	1.56
4	14.14	0.60
Total		100.00



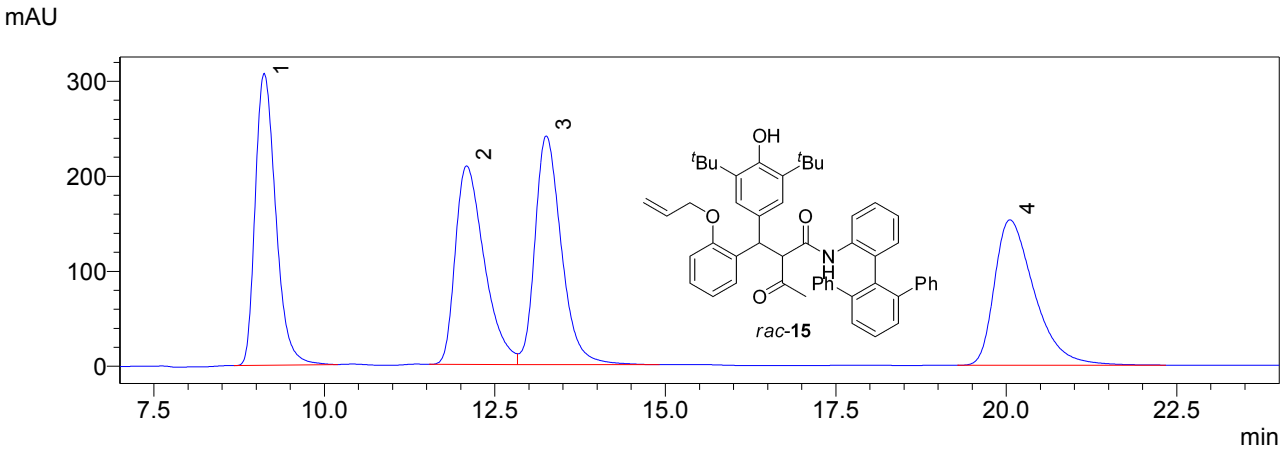
PDA Ch1 254nm

Peak#	Ret. Time	Area%
1	8.54	22.33
2	10.02	22.09
3	11.40	28.28
4	13.04	27.30
Total		100.00



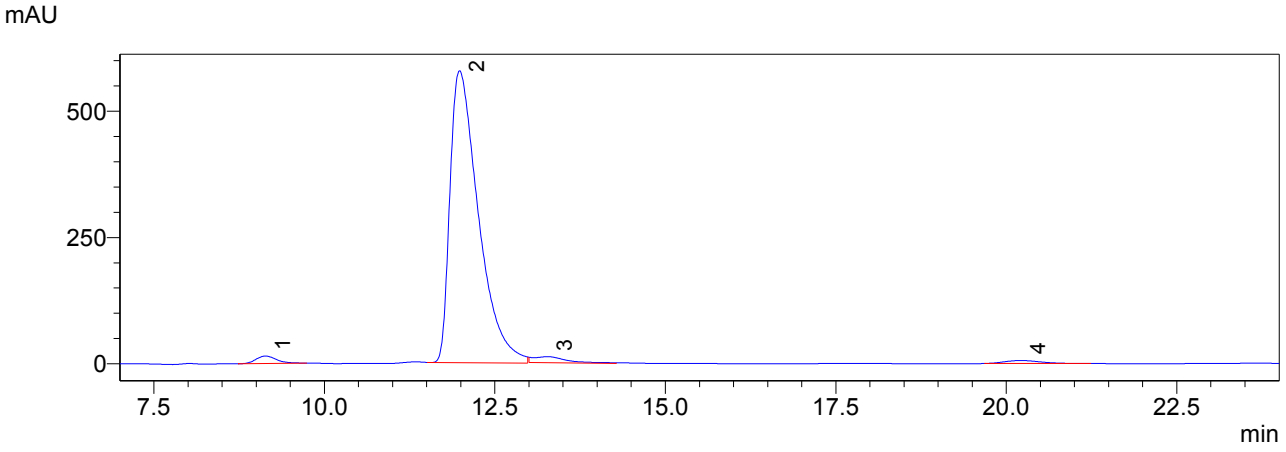
PDA Ch1 254nm

Peak#	Ret. Time	Area%
1	8.54	0.68
2	9.86	98.16
3	11.27	0.93
4	12.90	0.22
Total		100.00



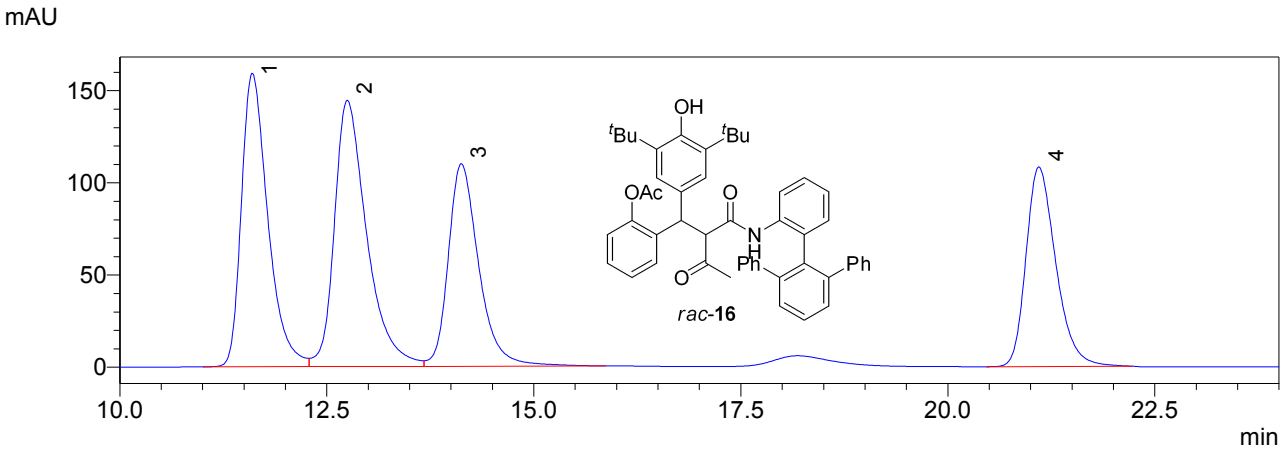
PDA Ch1 254nm

Peak#	Ret. Time	Area%
1	9.12	25.39
2	12.09	24.50
3	13.25	25.59
4	20.05	24.52
Total		100.00



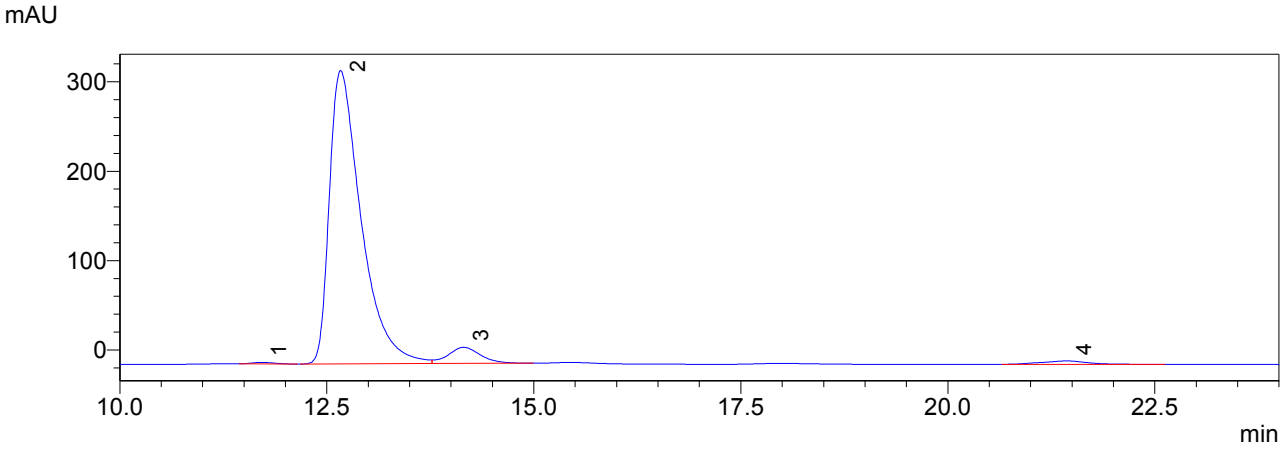
PDA Ch1 254nm

Peak#	Ret. Time	Area%
1	9.14	1.73
2	11.98	94.69
3	13.27	2.34
4	20.21	1.24
Total		100.00



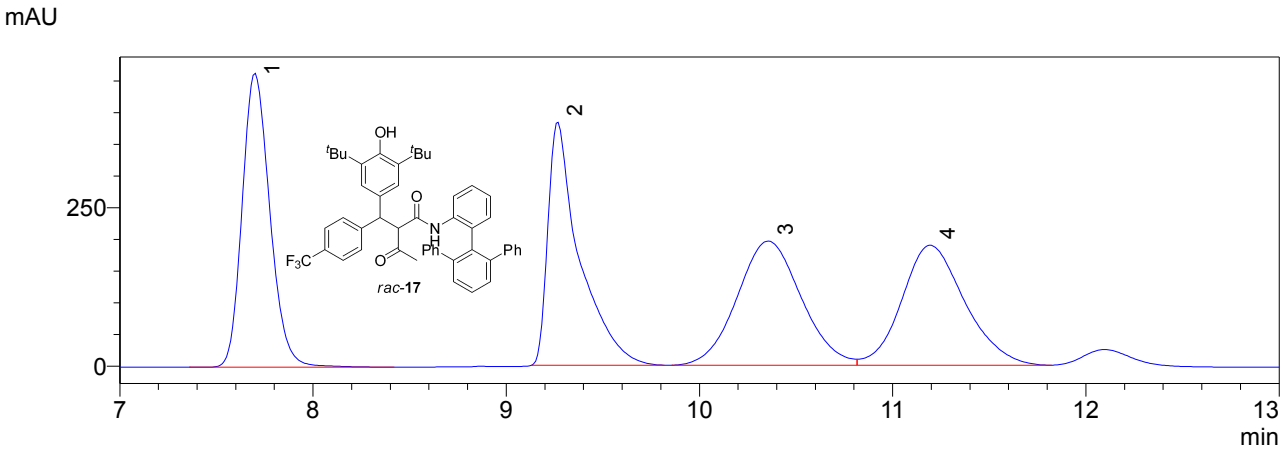
PDA Ch1 254nm

Peak#	Ret. Time	Area%
1	11.60	27.26
2	12.75	30.21
3	14.12	21.65
4	21.10	20.88
Total		100.00



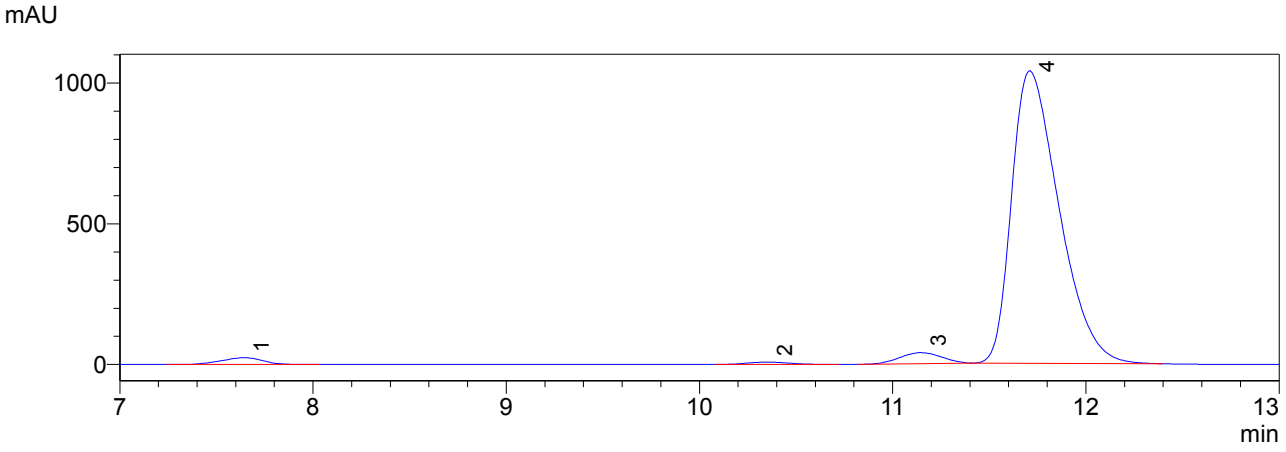
PDA Ch1 254nm

Peak#	Ret. Time	Area%
1	11.71	0.34
2	12.67	92.82
3	14.15	5.22
4	21.43	1.62
Total		100.00



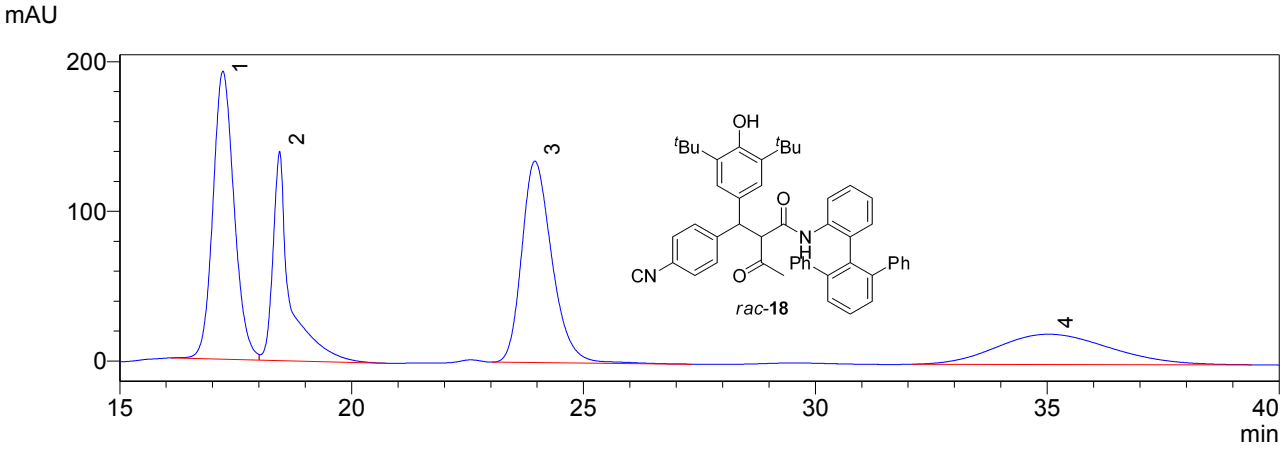
PDA Ch1 254nm

Peak#	Ret. Time	Area%
1	7.70	26.02
2	9.26	24.36
3	10.36	25.46
4	11.19	24.15
Total		100.00



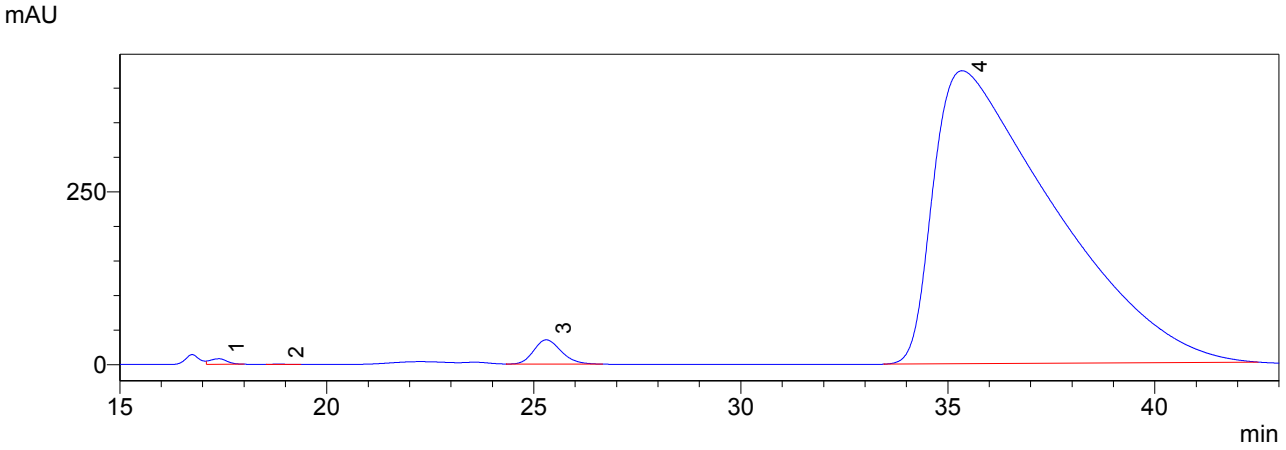
PDA Ch1 254nm

Peak#	Ret. Time	Area%
1	7.64	1.94
2	10.35	0.68
3	11.15	3.15
4	11.71	94.23
Total		100.00



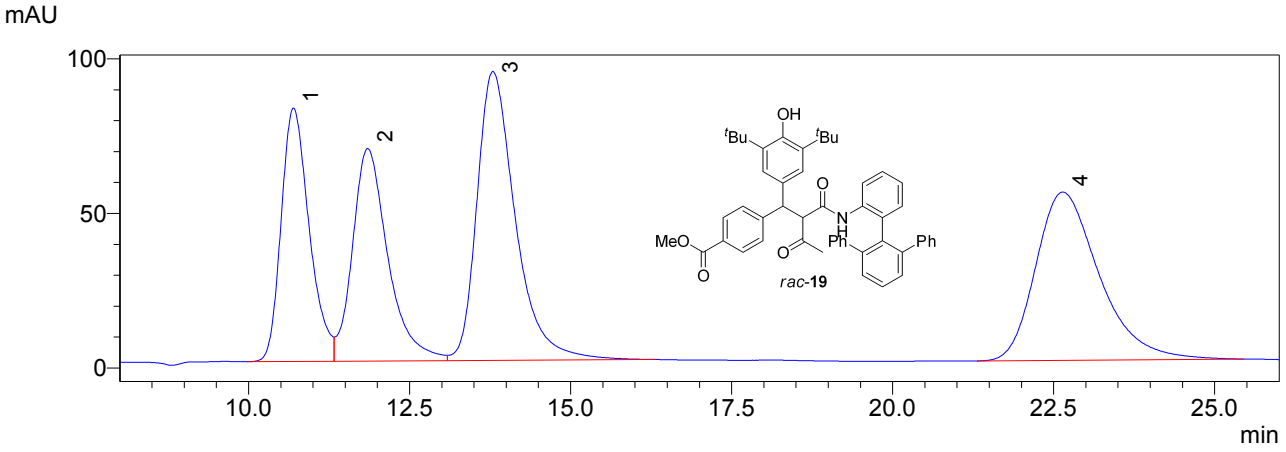
PDA Ch1 254nm

Peak#	Ret. Time	Area%
1	17.22	31.86
2	18.45	18.39
3	23.95	31.82
4	35.02	17.92
Total		100.00



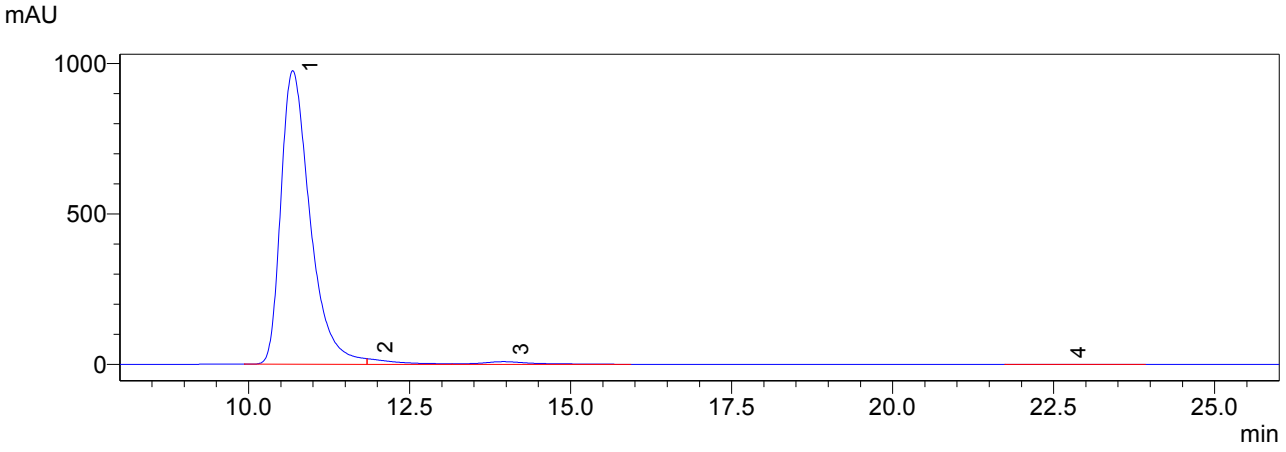
PDA Ch1 254nm

Peak#	Ret. Time	Area%
1	17.40	0.26
2	18.84	0.01
3	25.30	1.83
4	35.34	97.90
Total		100.00



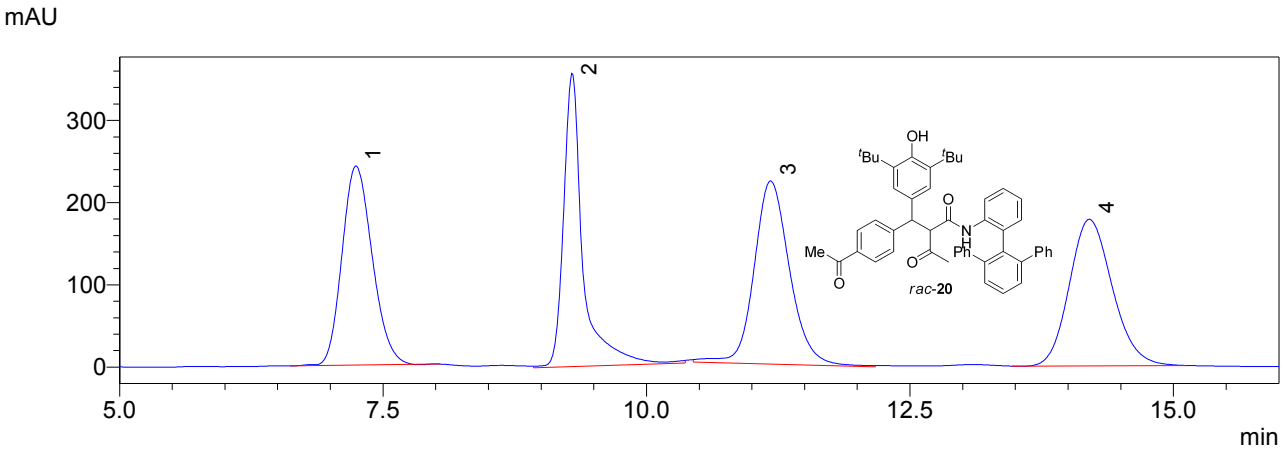
PDA Ch1 254nm

Peak#	Ret. Time	Area%
1	10.70	19.56
2	11.85	20.63
3	13.79	30.47
4	22.64	29.34
Total		100.00



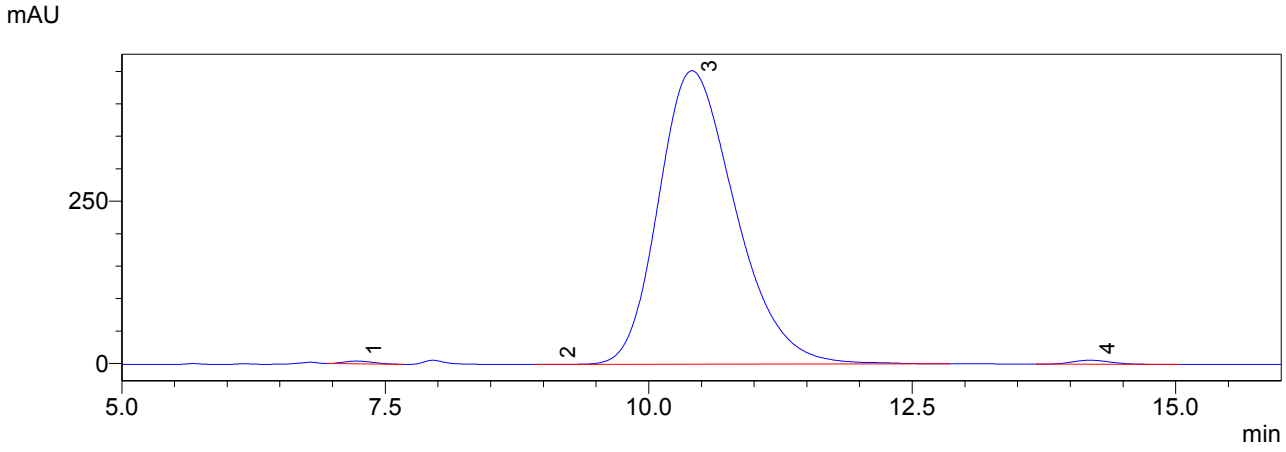
PDA Ch1 254nm

Peak#	Ret. Time	Area%
1	10.68	96.76
2	11.86	1.62
3	13.96	1.50
4	22.61	0.12
Total		100.00



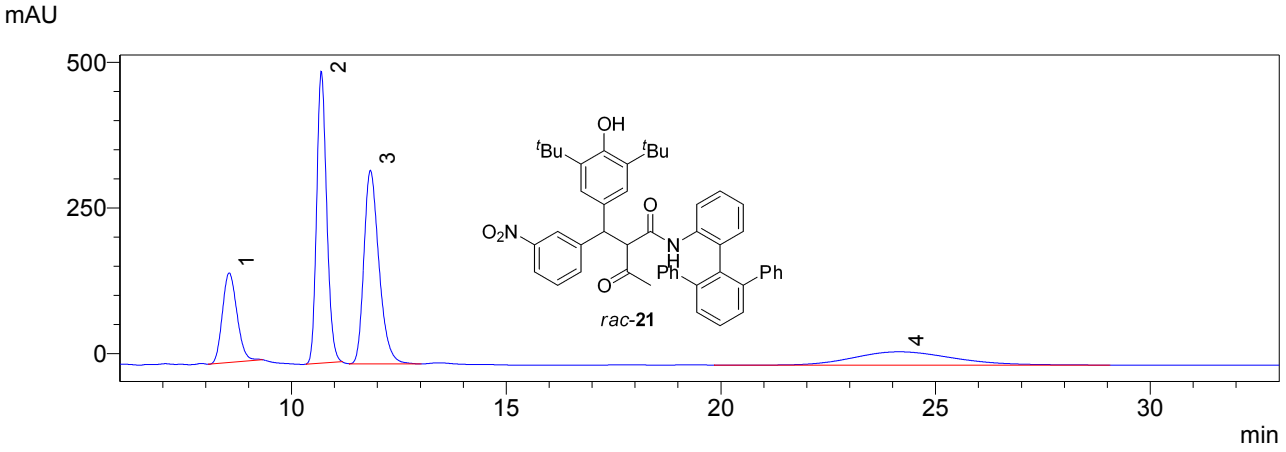
PDA Ch1 254nm

Peak#	Ret. Time	Area%
1	7.24	24.54
2	9.29	23.19
3	11.18	26.59
4	14.20	25.68
Total		100.00



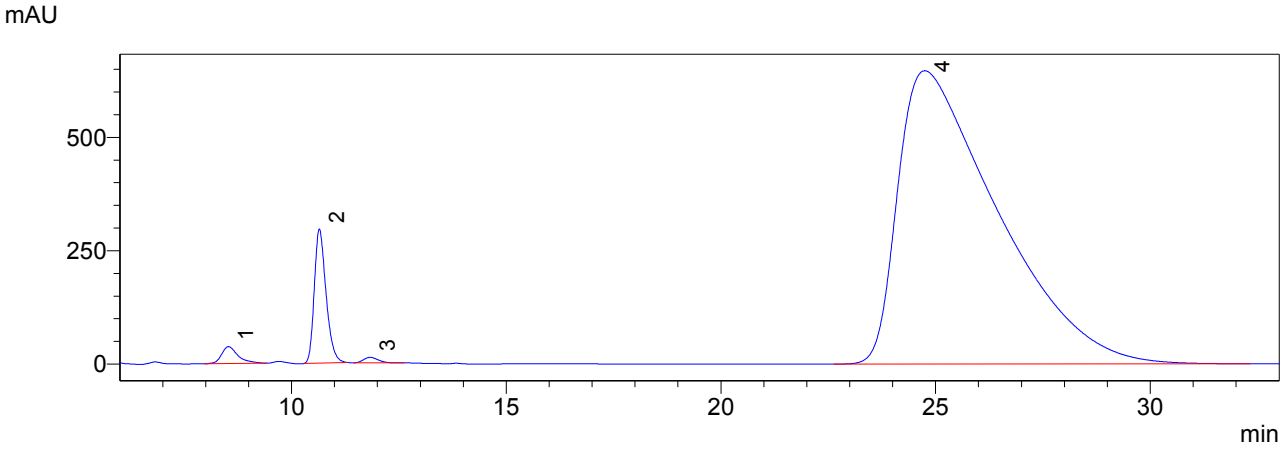
PDA Ch1 254nm

Peak#	Ret. Time	Area%
1	7.23	0.36
2	9.07	0.01
3	10.41	98.94
4	14.19	0.69
Total		100.00



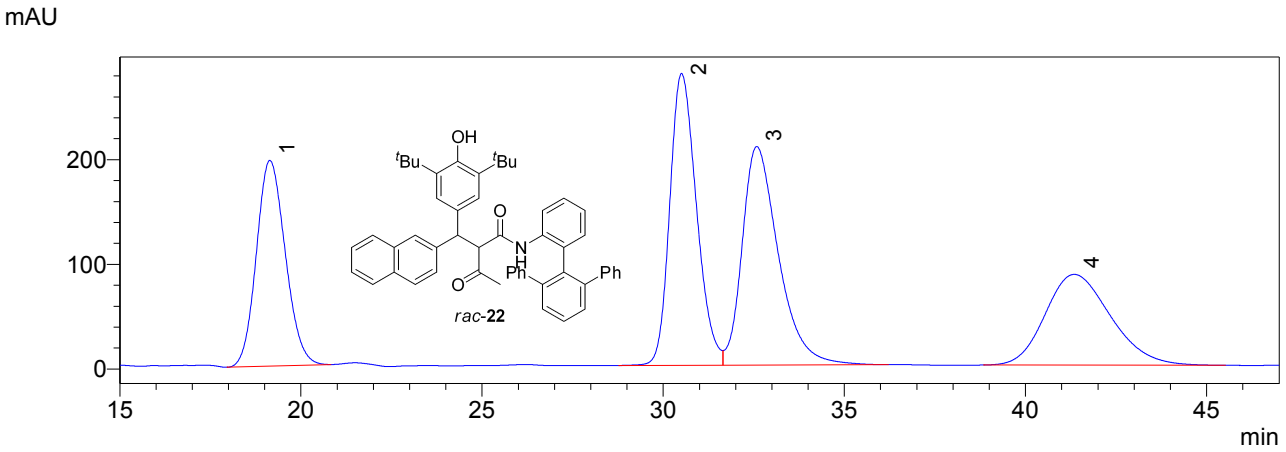
PDA Ch1 254nm

Peak#	Ret. Time	Area%
1	8.55	15.39
2	10.69	34.62
3	11.84	34.42
4	24.14	15.57
Total		100.00



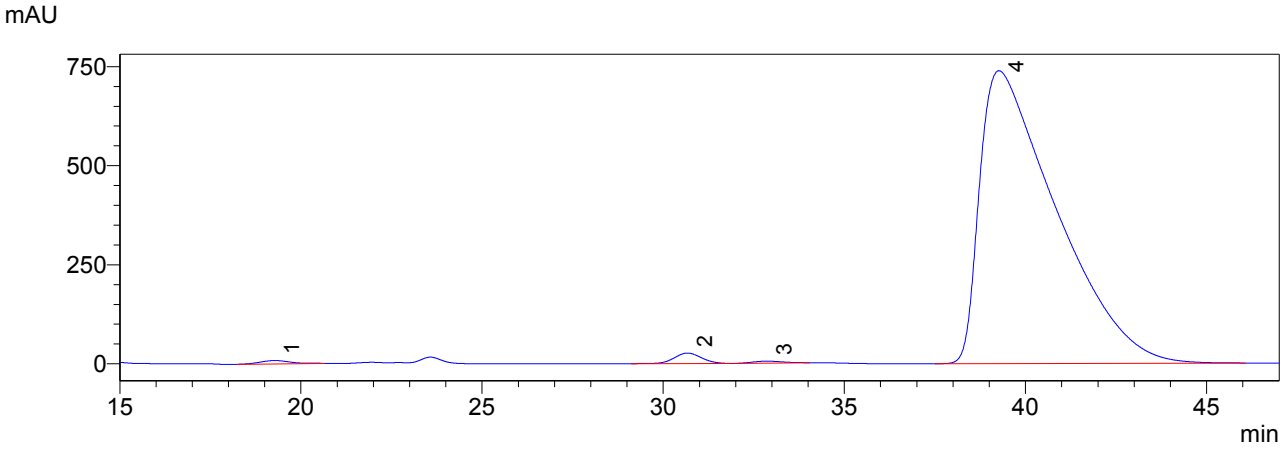
PDA Ch1 254nm

Peak#	Ret. Time	Area%
1	8.53	0.90
2	10.65	5.05
3	11.83	0.26
4	24.75	93.79
Total		100.00



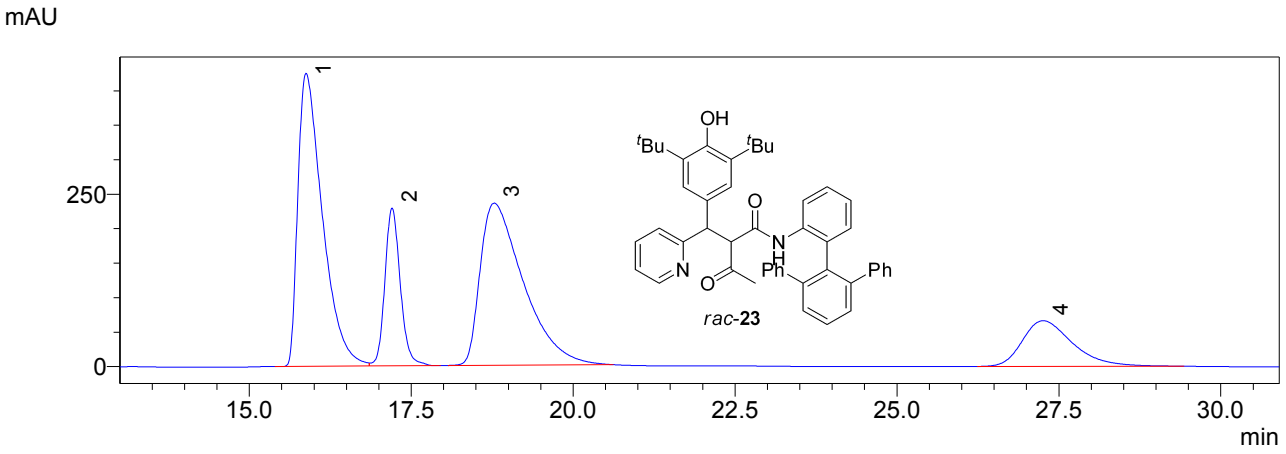
PDA Ch1 254nm

Peak#	Ret. Time	Area%
1	19.14	21.53
2	30.51	28.29
3	32.58	28.69
4	41.34	21.49
Total		100.00



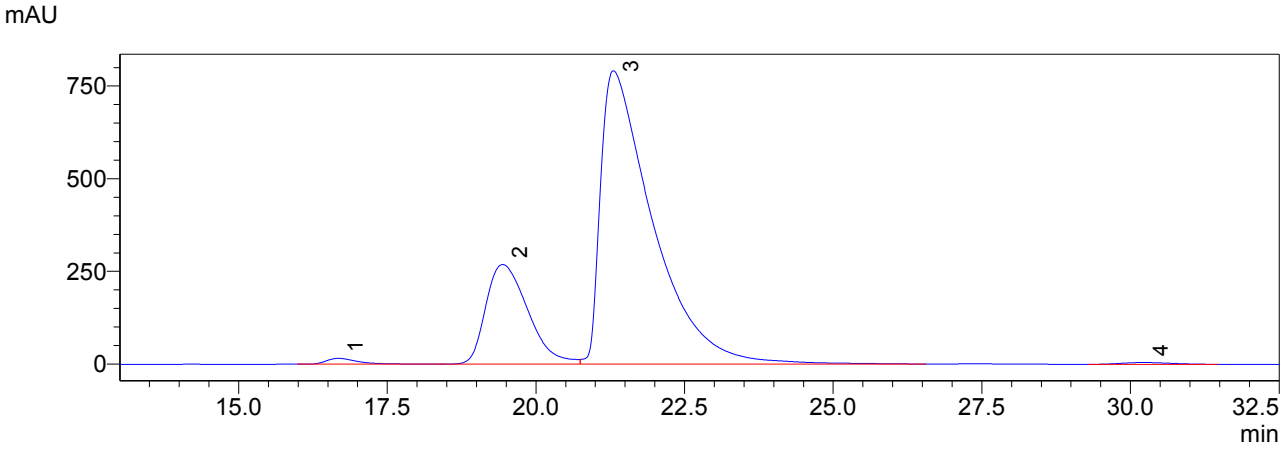
PDA Ch1 254nm

Peak#	Ret. Time	Area%
1	19.28	0.45
2	30.67	1.24
3	32.86	0.25
4	39.27	98.06
Total		100.00



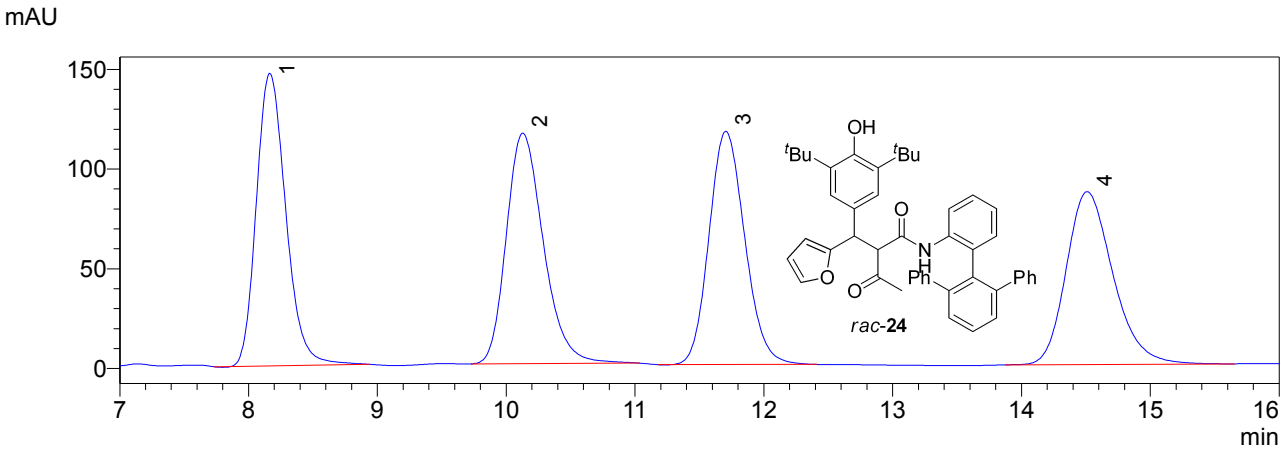
PDA Ch1 254nm

Peak#	Ret. Time	Area%
1	15.88	38.01
2	17.20	12.87
3	18.78	37.02
4	27.25	12.10
Total		100.00



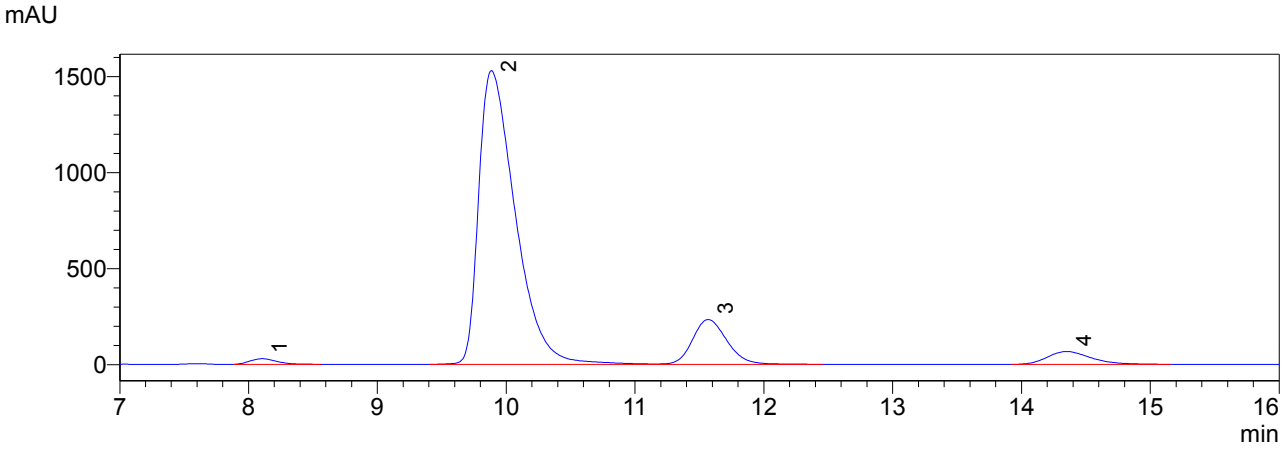
PDA Ch1 254nm

Peak#	Ret. Time	Area%
1	16.68	0.86
2	19.44	21.16
3	21.30	77.53
4	30.21	0.46
Total		100.00



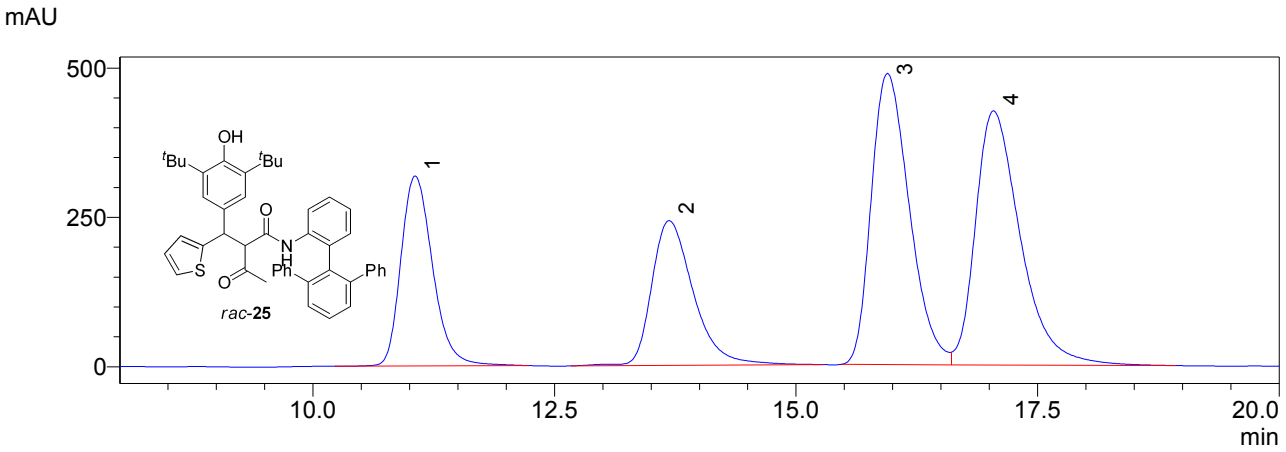
PDA Ch1 254nm

Peak#	Ret. Time	Area%
1	8.16	25.63
2	10.13	25.47
3	11.70	24.86
4	14.51	24.04
Total		100.00



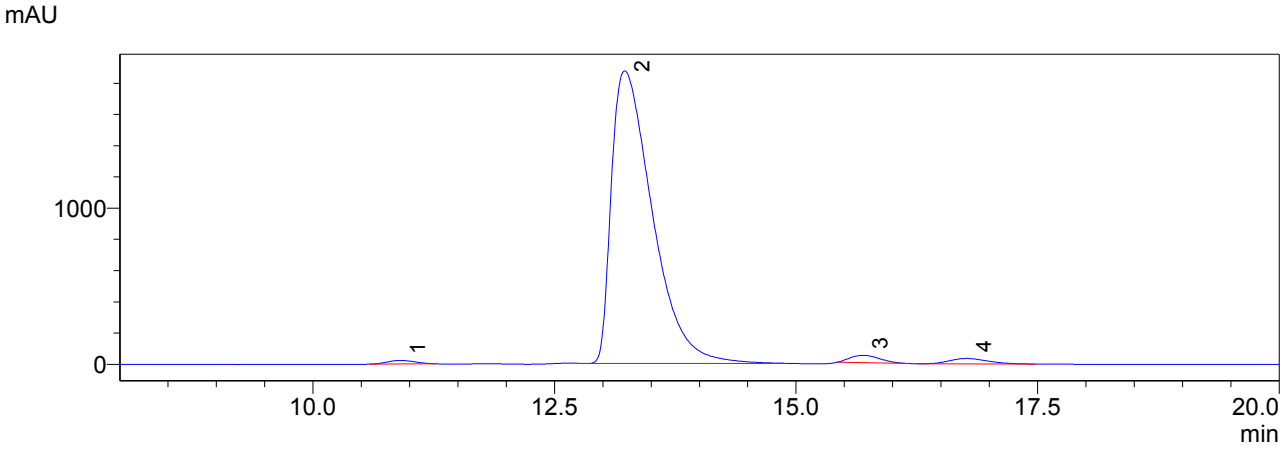
PDA Ch1 254nm

Peak#	Ret. Time	Area%
1	8.11	1.16
2	9.89	82.62
3	11.57	11.87
4	14.35	4.35
Total		100.00



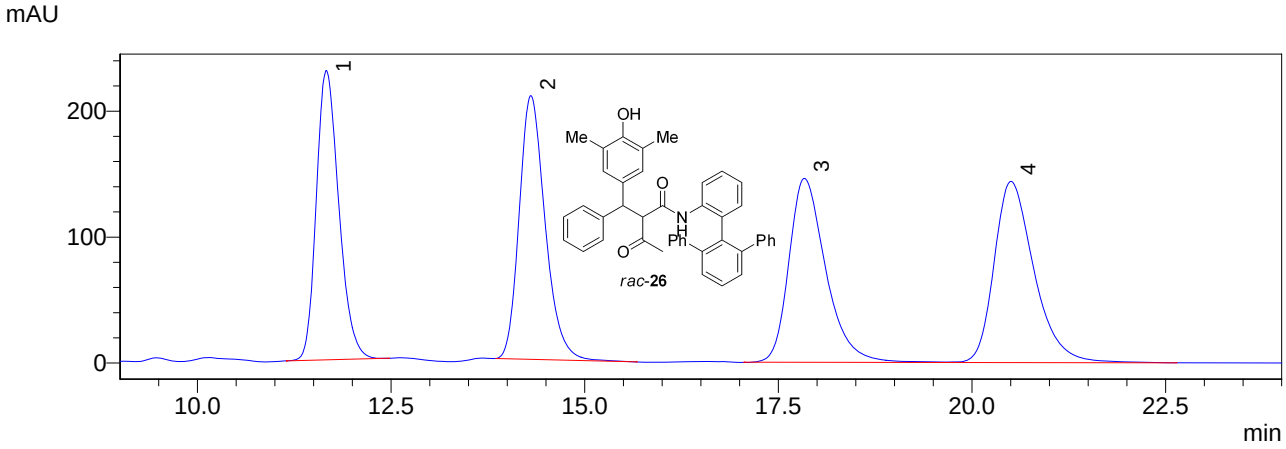
PDA Ch1 254nm

Peak#	Ret. Time	Area%
1	11.06	17.41
2	13.69	17.48
3	15.95	32.14
4	17.04	32.96
Total		100.00



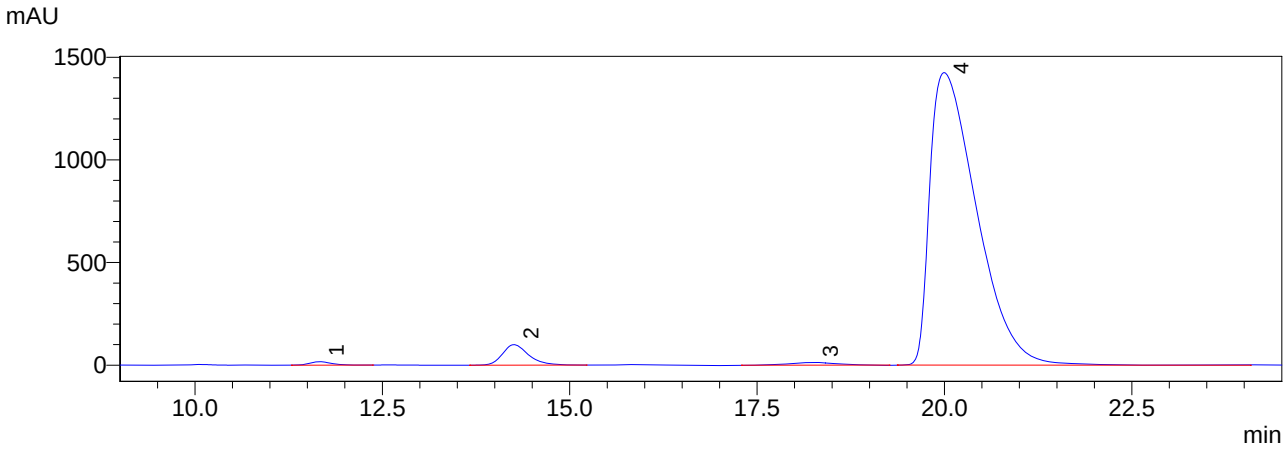
PDA Ch1 254nm

Peak#	Ret. Time	Area%
1	10.91	0.79
2	13.23	95.78
3	15.69	1.77
4	16.76	1.65
Total		100.00



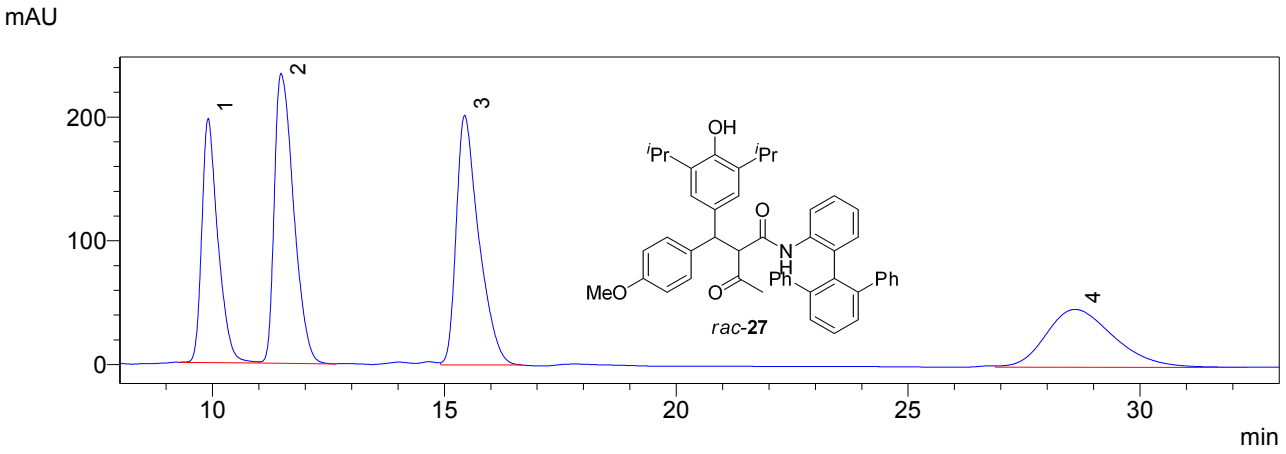
PDA Ch1 254nm

Peak#	Ret. Time	Area%
1	11.66	24.22
2	14.30	25.64
3	17.84	24.31
4	20.50	25.83
Total		100.00



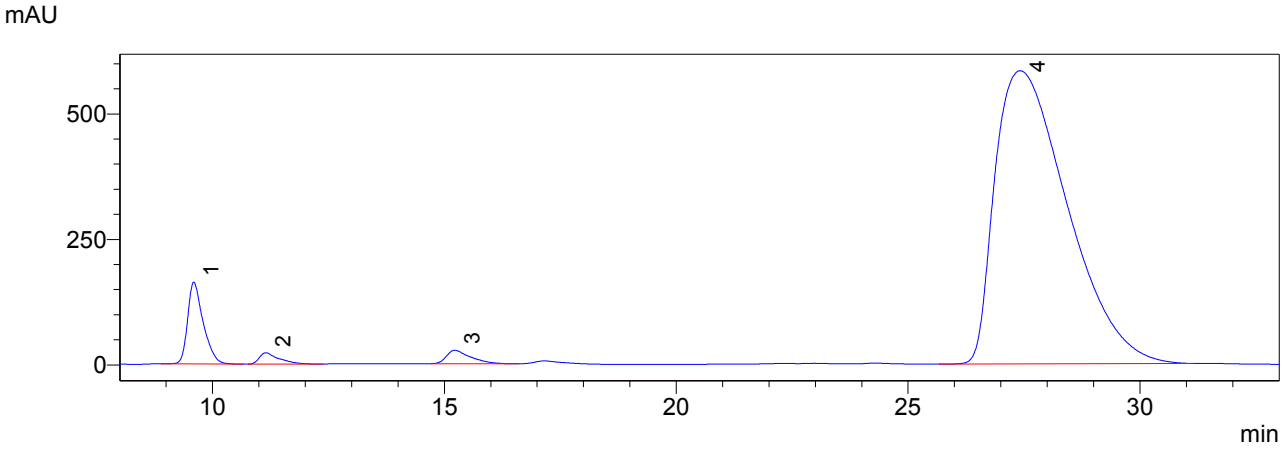
PDA Ch1 254nm

Peak#	Ret. Time	Area%
1	11.66	0.52
2	14.26	3.75
3	18.25	0.88
4	20.00	94.85
Total		100.00



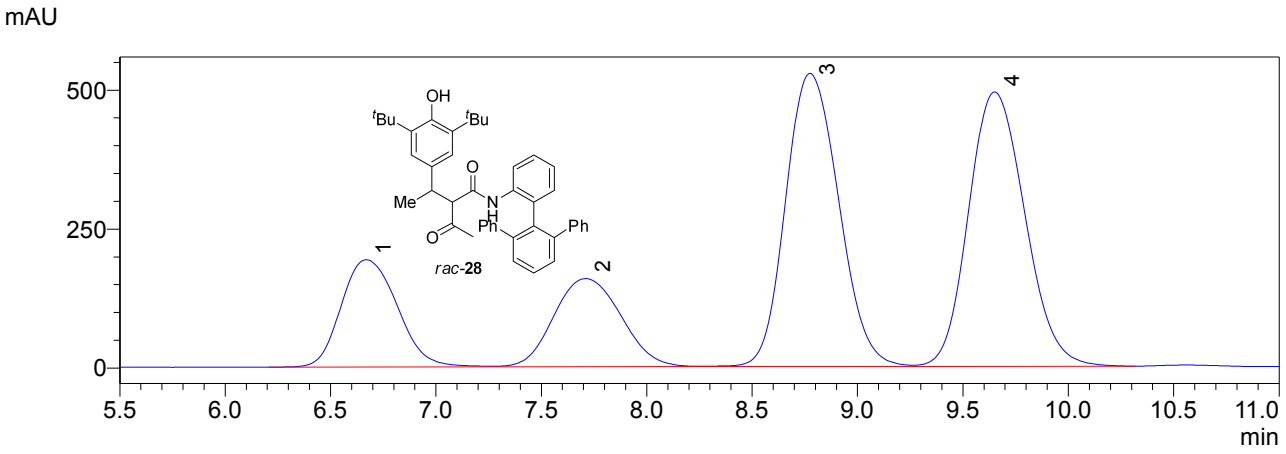
PDA Ch1 254nm

Peak#	Ret. Time	Area%
1	9.90	20.58
2	11.48	29.36
3	15.44	29.45
4	28.61	20.61
Total		100.00



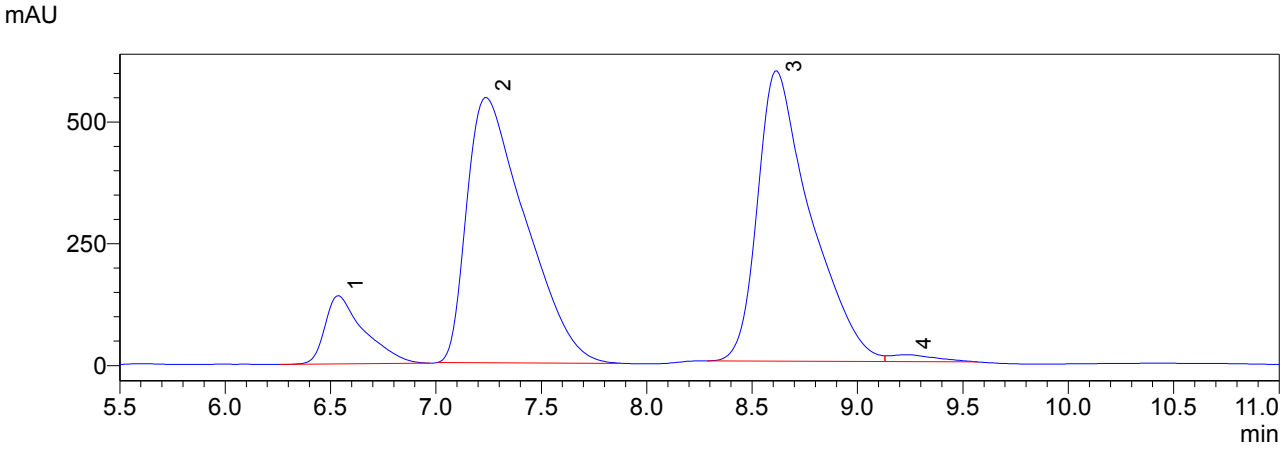
PDA Ch1 220nm

Peak#	Ret. Time	Area%
1	9.59	5.53
2	11.15	0.97
3	15.22	1.39
4	27.42	92.11
Total		100.00



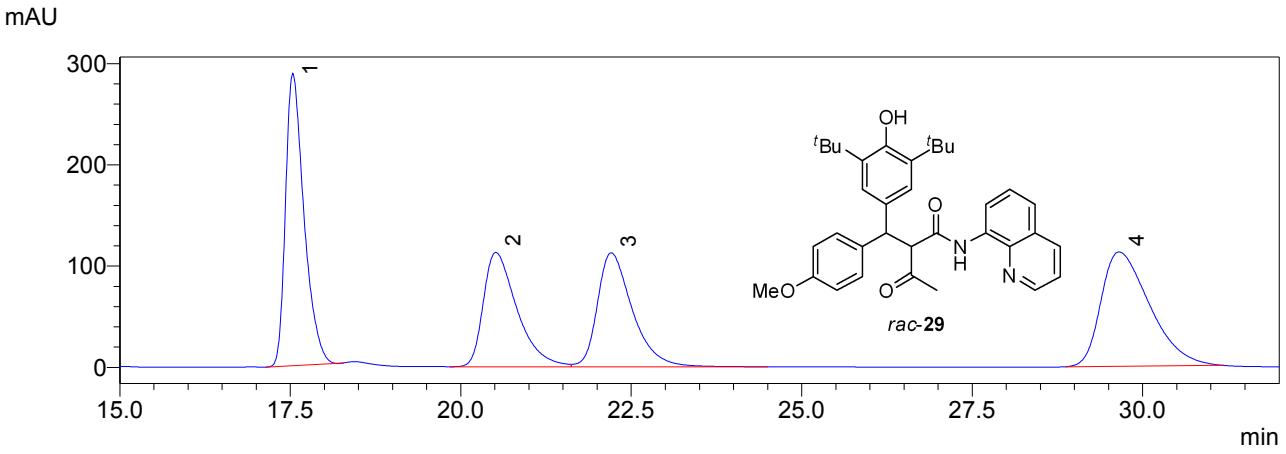
PDA Ch1 254nm

Peak#	Ret. Time	Area%
1	6.67	14.00
2	7.71	13.78
3	8.77	36.26
4	9.65	35.96
Total		100.00



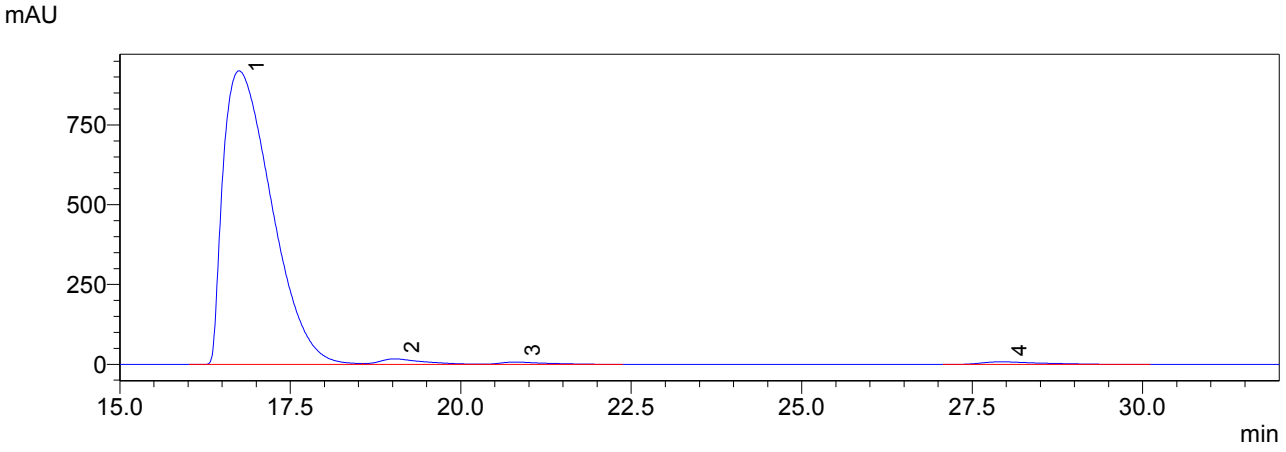
PDA Ch1 254nm

Peak#	Ret. Time	Area%
1	6.54	7.81
2	7.24	45.82
3	8.61	45.45
4	9.23	0.92
Total		100.00



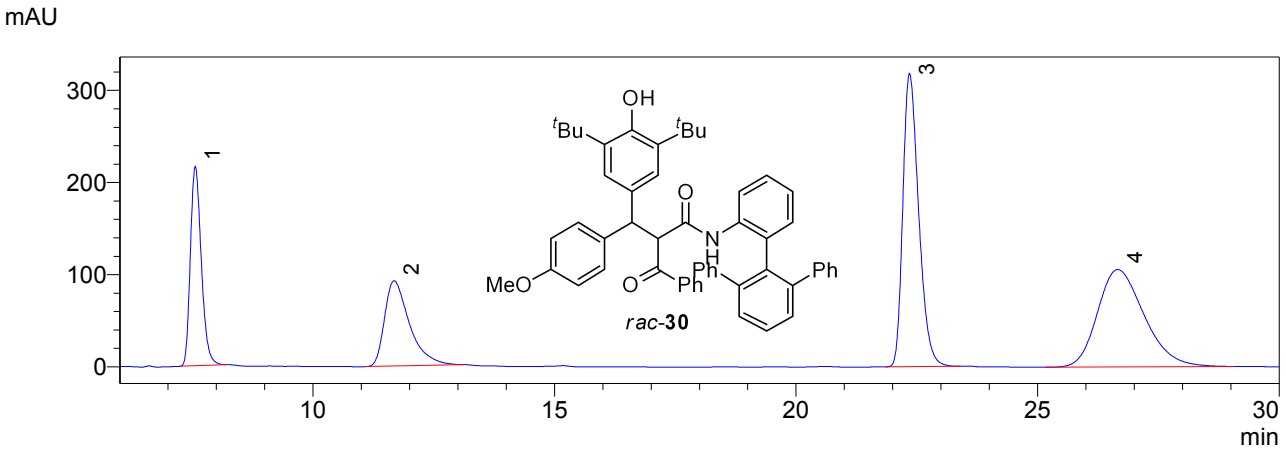
PDA Ch1 254nm

Peak#	Ret. Time	Area%
1	17.54	28.74
2	20.51	20.48
3	22.21	21.19
4	29.65	29.58
Total		100.00



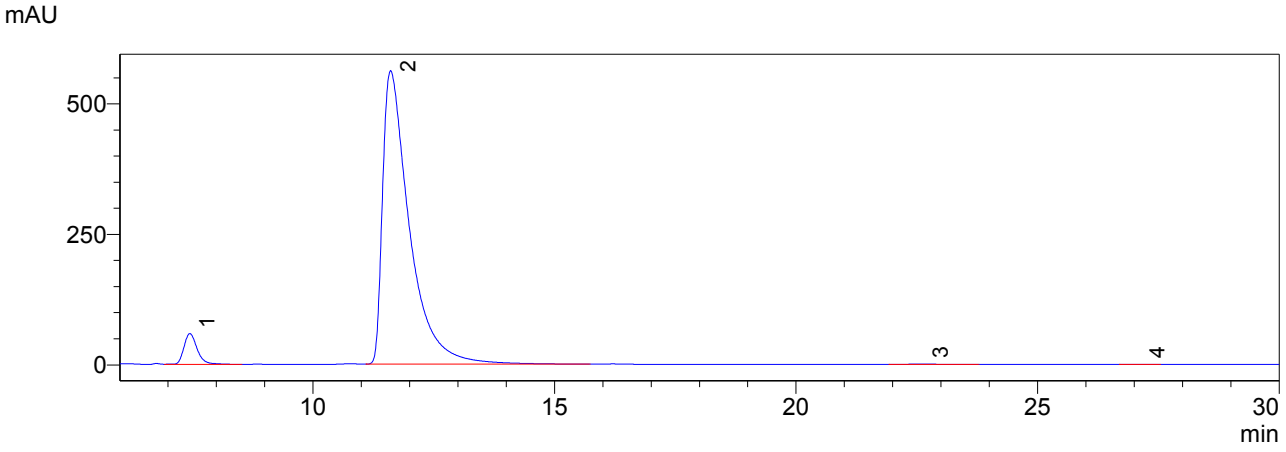
PDA Ch1 254nm

Peak#	Ret. Time	Area%
1	16.75	96.45
2	19.03	1.69
3	20.80	0.72
4	27.93	1.14
Total		100.00



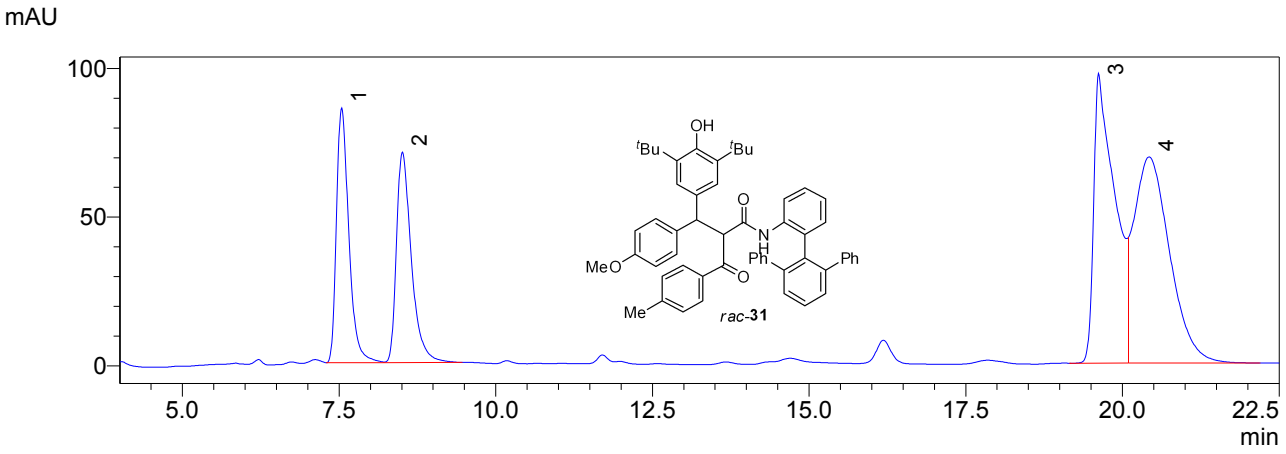
PDA Ch1 254nm

Peak#	Ret. Time	Area%
1	7.56	16.13
2	11.68	15.78
3	22.35	34.37
4	26.66	33.72
Total		100.00



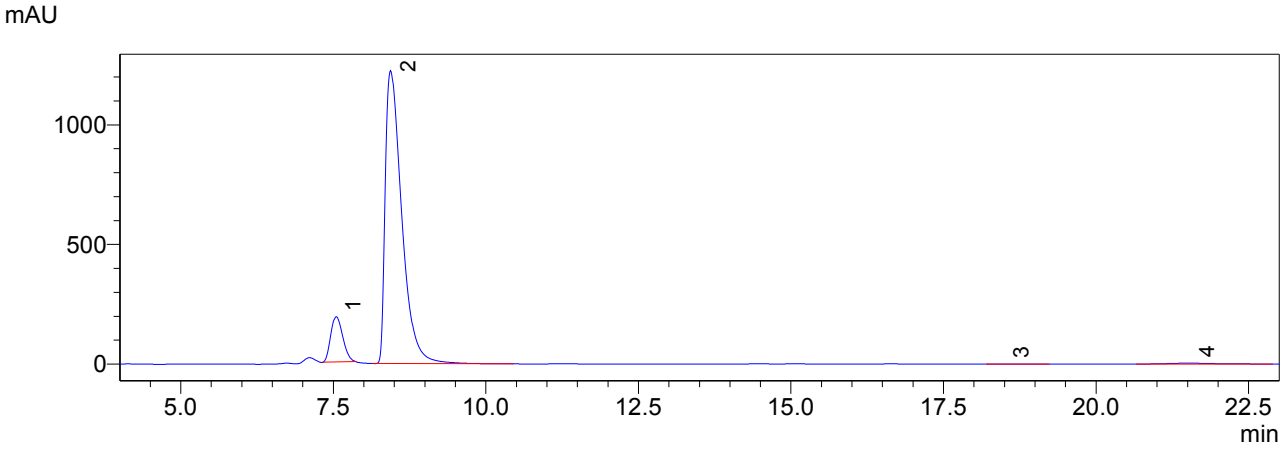
PDA Ch1 254nm

Peak#	Ret. Time	Area%
1	7.45	4.90
2	11.61	94.92
3	22.63	0.18
4	27.12	0.01
Total		100.00



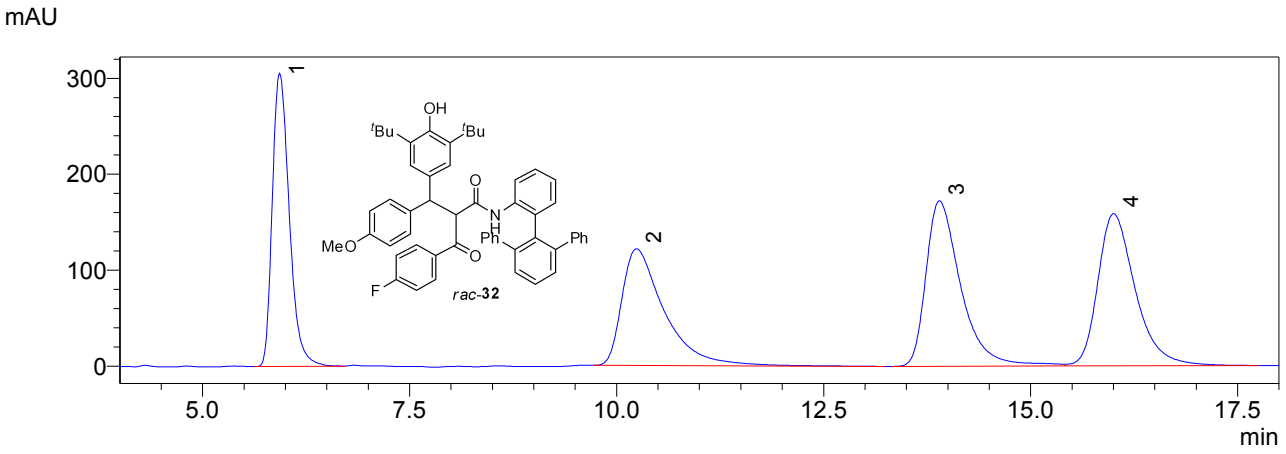
PDA Ch1 280nm

Peak#	Ret. Time	Area%
1	7.54	15.92
2	8.51	15.84
3	19.62	31.46
4	20.43	36.78
Total		100.00



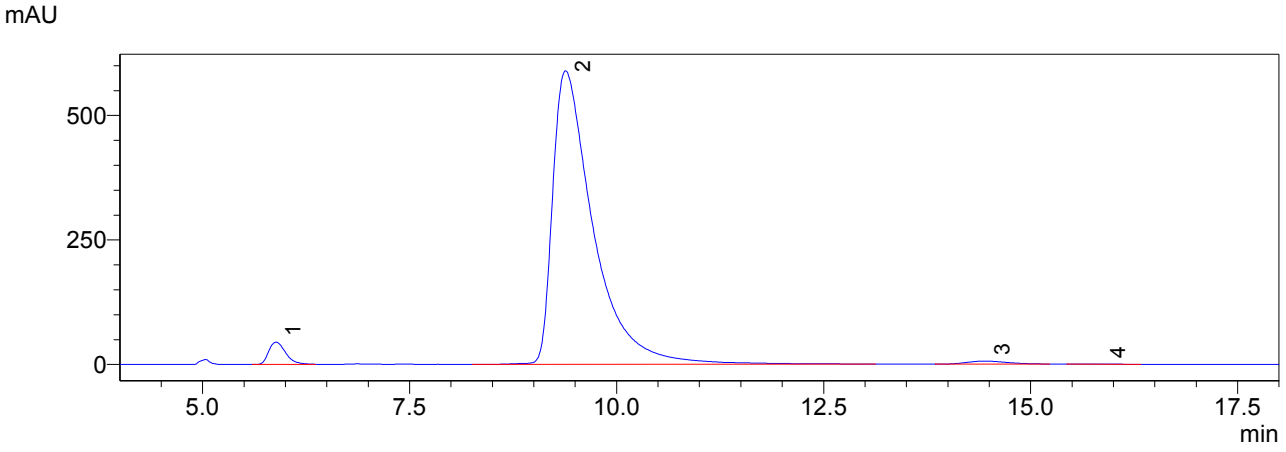
PDA Ch1 280nm

Peak#	Ret. Time	Area%
1	7.55	10.05
2	8.44	89.28
3	18.49	0.01
4	21.53	0.65
Total		100.00



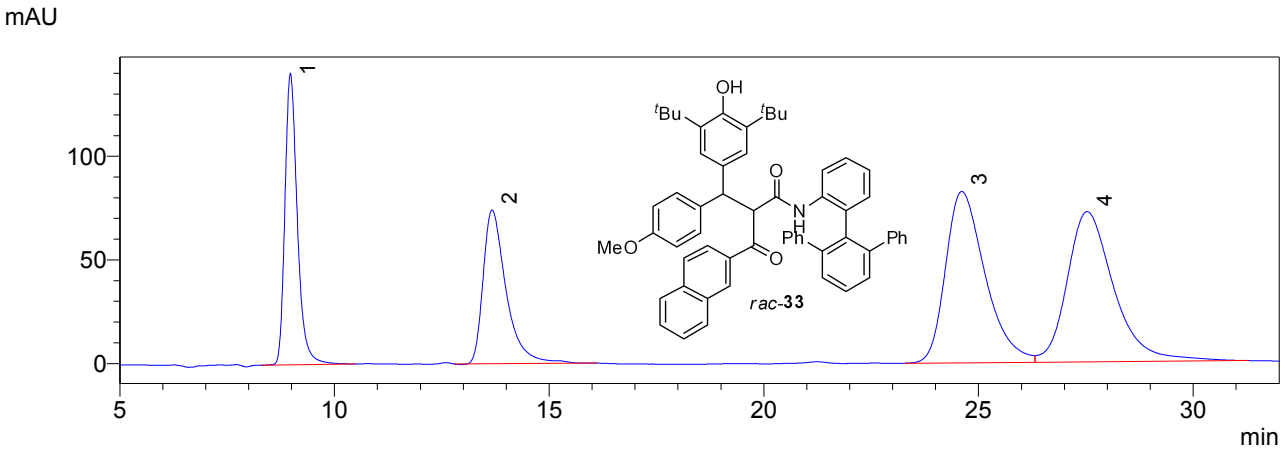
PDA Ch1 254nm

Peak#	Ret. Time	Area%
1	5.93	23.28
2	10.24	23.12
3	13.90	26.98
4	16.00	26.63
Total		100.00



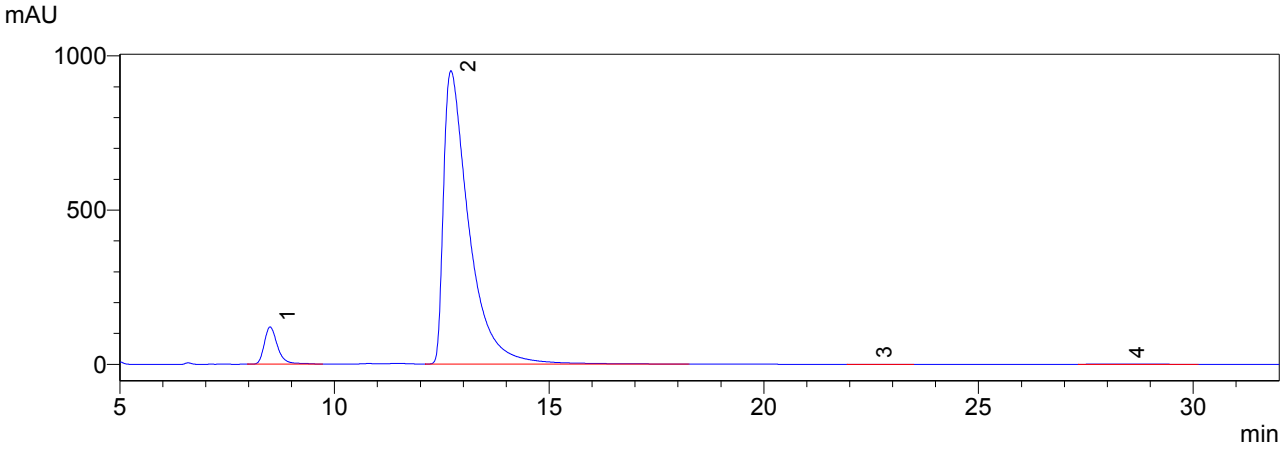
PDA Ch1 254nm

Peak#	Ret. Time	Area%
1	5.89	3.03
2	9.38	95.93
3	14.45	1.00
4	15.85	0.04
Total		100.00



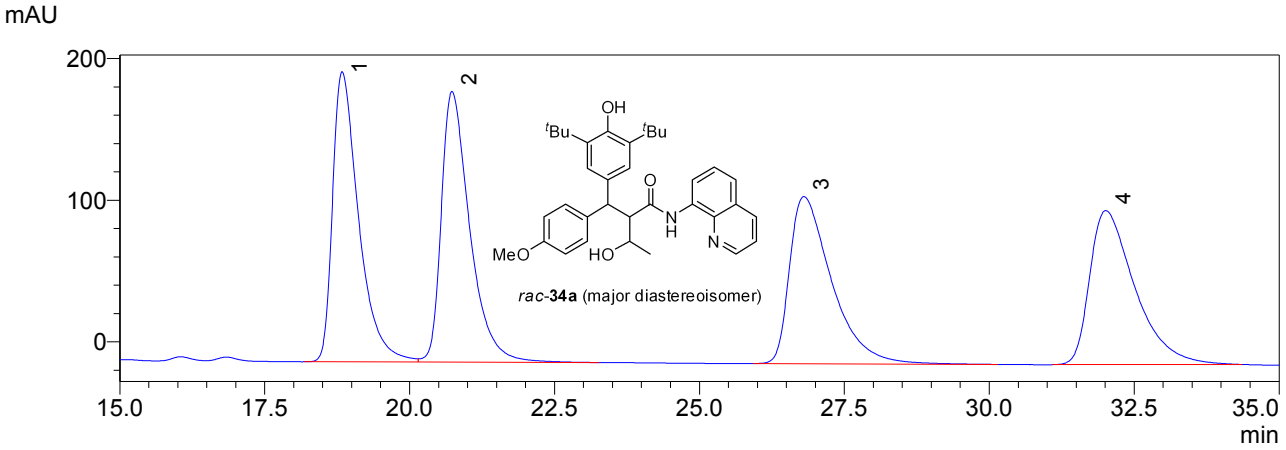
PDA Ch1 254nm

Peak#	Ret. Time	Area%
1	8.97	17.32
2	13.67	16.88
3	24.61	32.34
4	27.53	33.46
Total		100.00



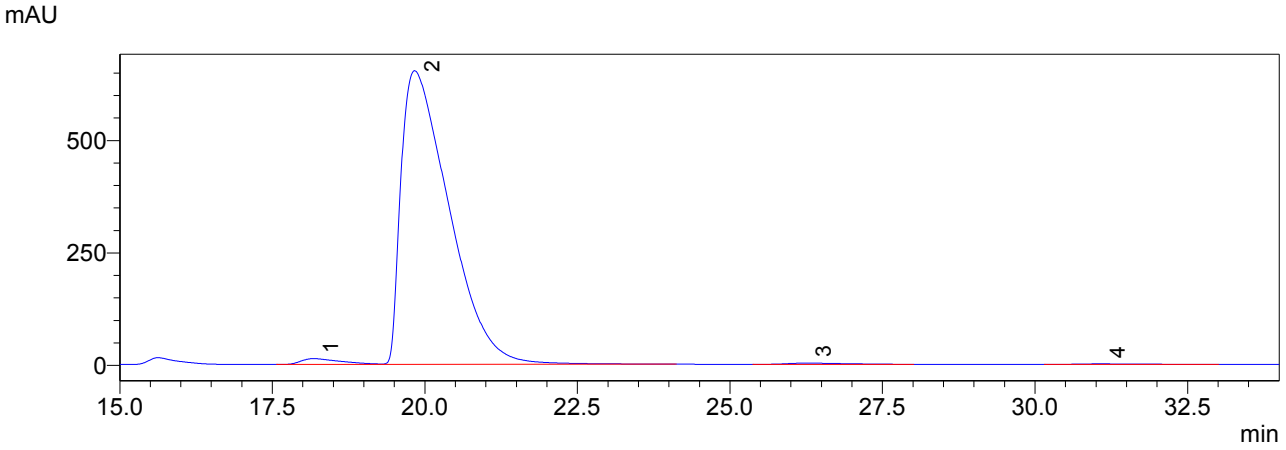
PDA Ch1 254nm

Peak#	Ret. Time	Area%
1	8.50	6.16
2	12.71	93.62
3	22.40	0.01
4	28.28	0.22
Total		100.00



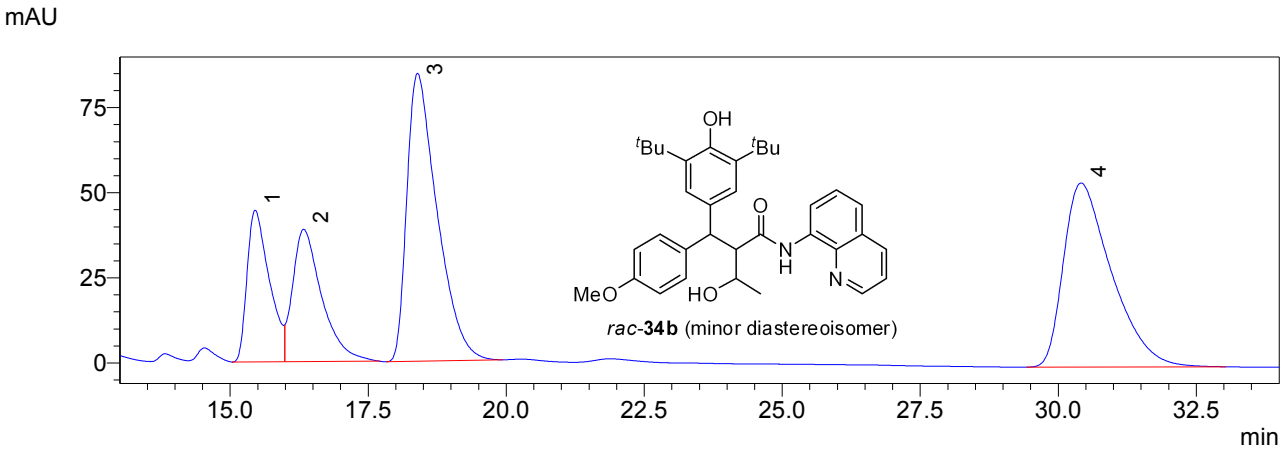
PDA Ch1 254nm

Peak#	Ret. Time	Area%
1	18.84	25.85
2	20.73	26.35
3	26.80	24.05
4	32.01	23.76
Total		100.00



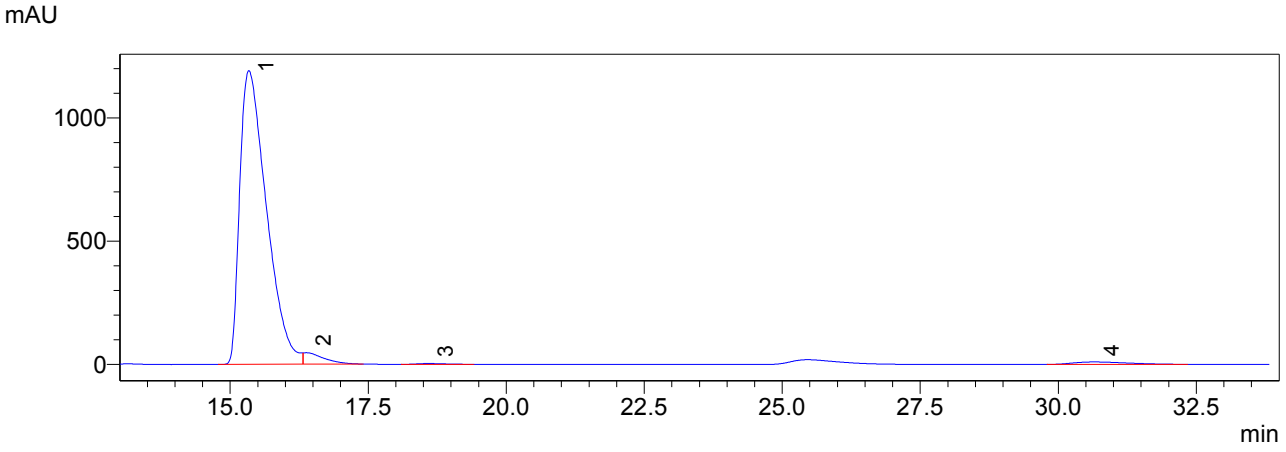
PDA Ch1 254nm

Peak#	Ret. Time	Area%
1	18.18	1.64
2	19.83	97.59
3	26.25	0.50
4	31.07	0.27
Total		100.00



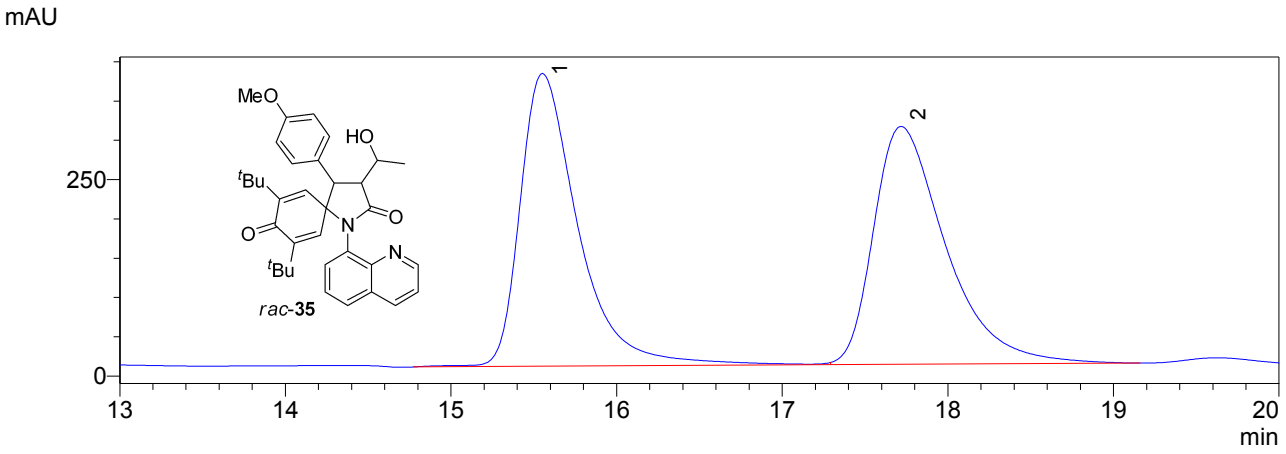
PDA Ch1 254nm

Peak#	Ret. Time	Area%
1	15.45	13.72
2	16.33	15.48
3	18.39	35.14
4	30.41	35.66
Total		100.00



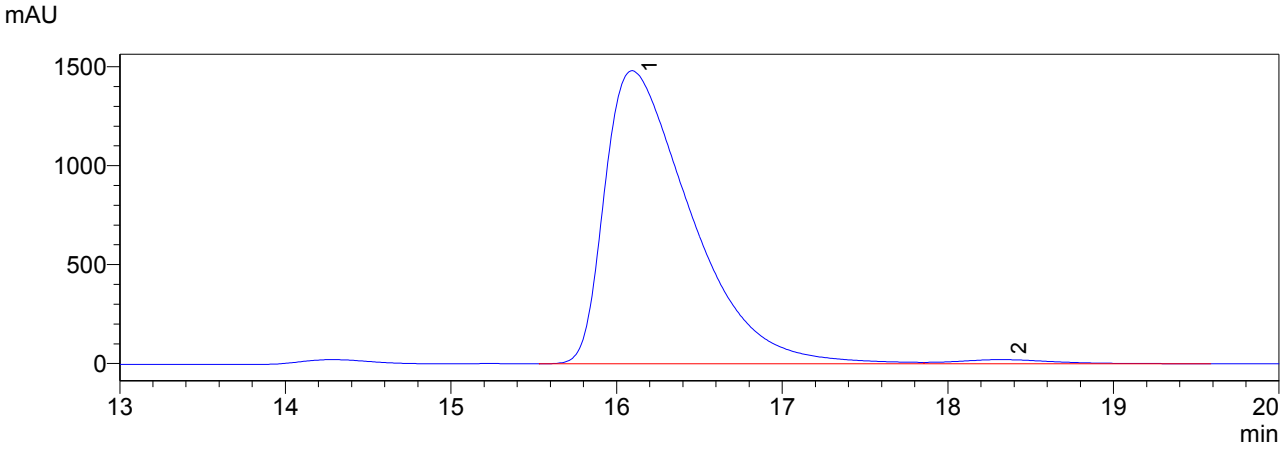
PDA Ch1 254nm

Peak#	Ret. Time	Area%
1	15.34	95.27
2	16.38	2.79
3	18.59	0.29
4	30.65	1.65
Total		100.00



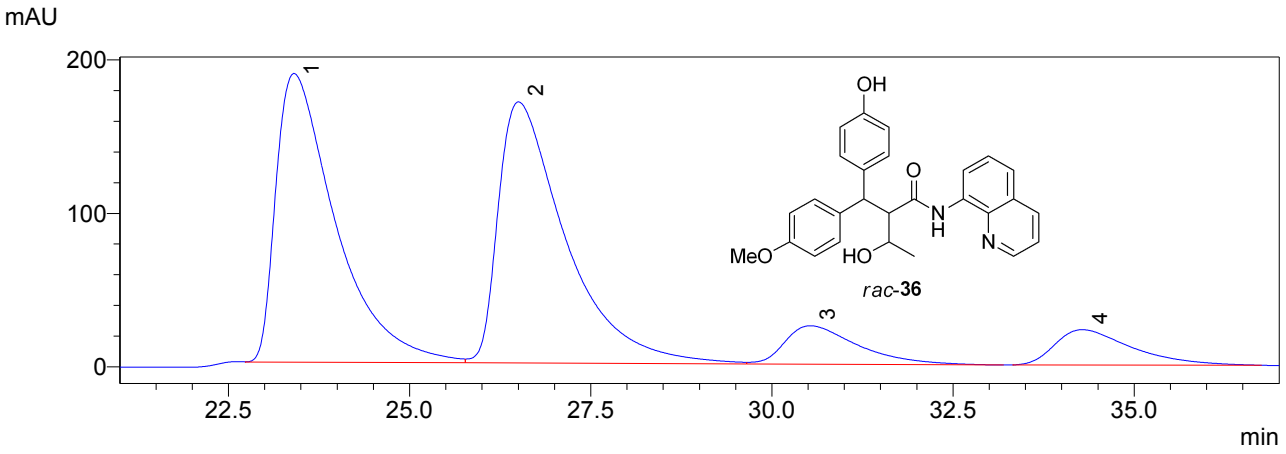
PDA Ch1 220nm

Peak#	Ret. Time	Area%
1	15.55	49.75
2	17.72	50.25
Total		100.00



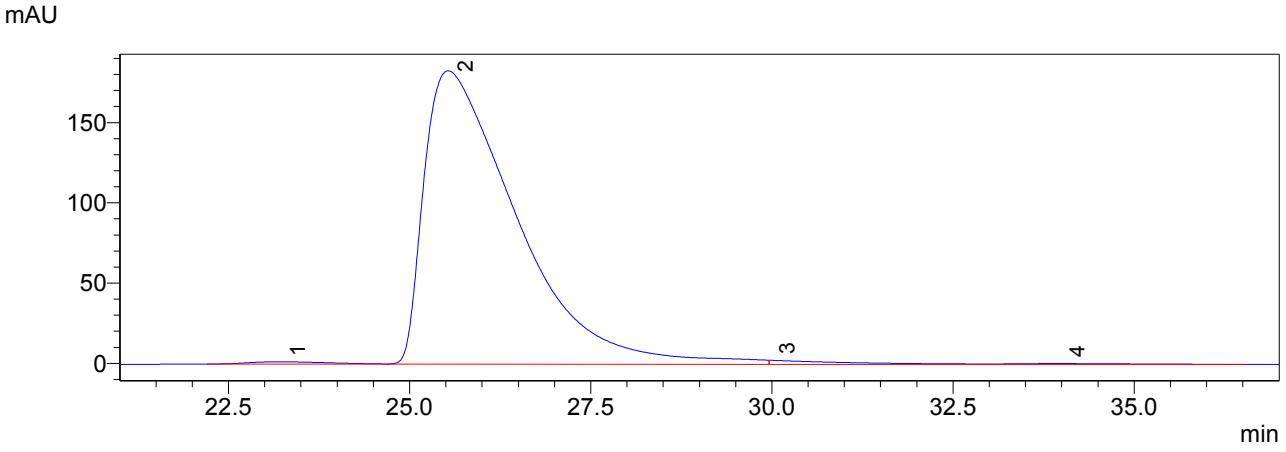
PDA Ch1 220nm

Peak#	Ret. Time	Area%
1	16.09	98.45
2	18.32	1.55
Total		100.00



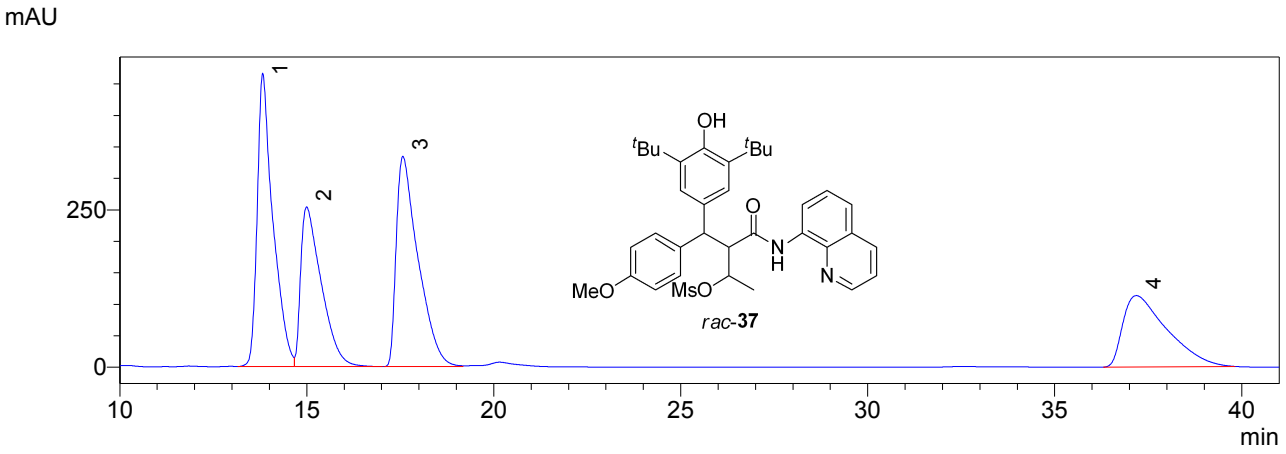
PDA Ch1 254nm

Peak#	Ret. Time	Area%
1	23.40	42.68
2	26.50	43.62
3	30.53	7.00
4	34.28	6.70
Total		100.00



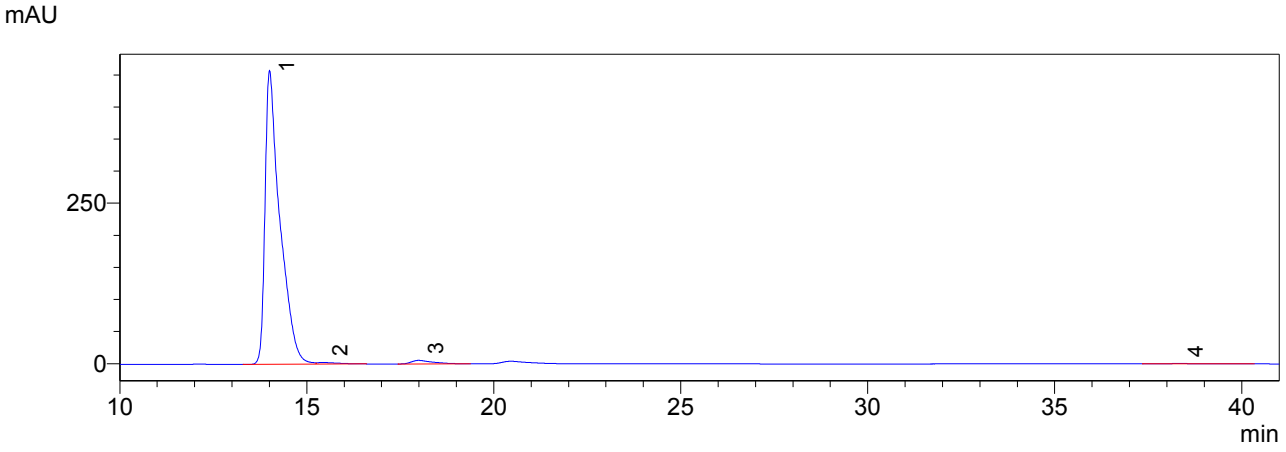
PDA Ch1 254nm

Peak#	Ret. Time	Area%
1	23.22	0.64
2	25.53	97.98
3	29.97	1.02
4	33.98	0.36
Total		100.00



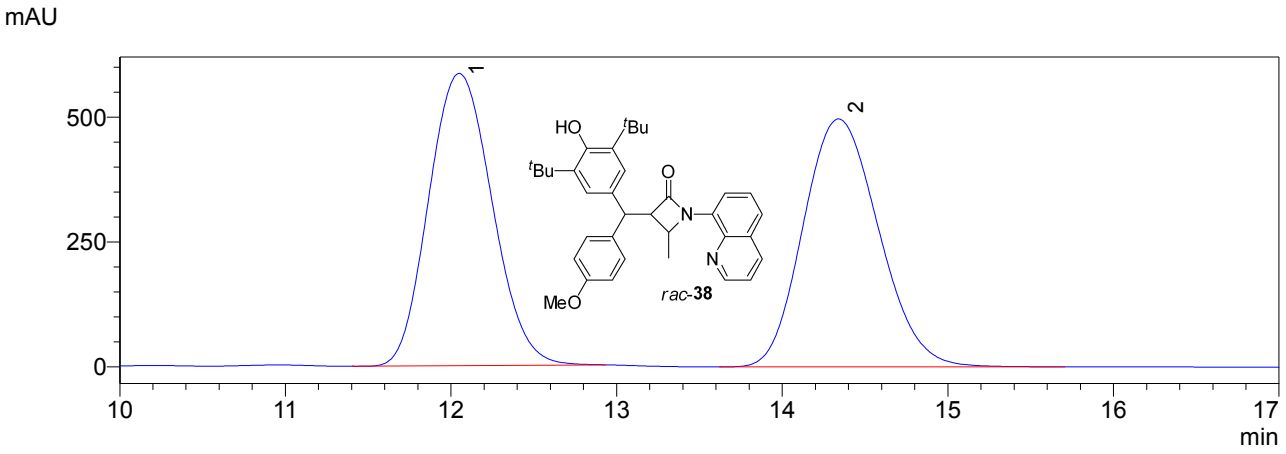
PDA Ch1 254nm

Peak#	Ret. Time	Area%
1	13.82	29.47
2	15.00	21.02
3	17.57	29.39
4	37.18	20.12
Total		100.00



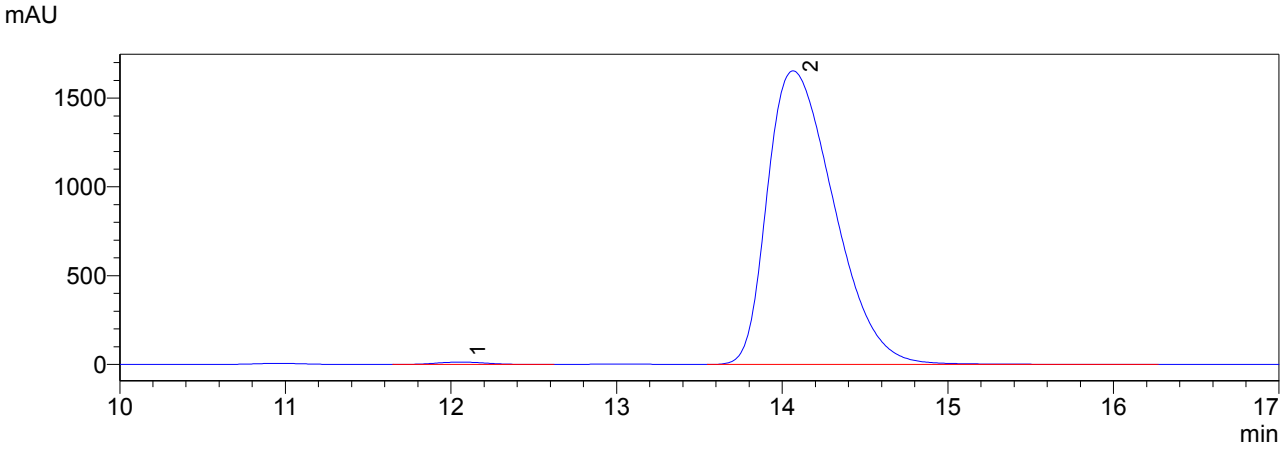
PDA Ch1 254nm

Peak#	Ret. Time	Area%
1	14.01	97.31
2	15.43	0.73
3	17.99	1.71
4	38.30	0.26
Total		100.00



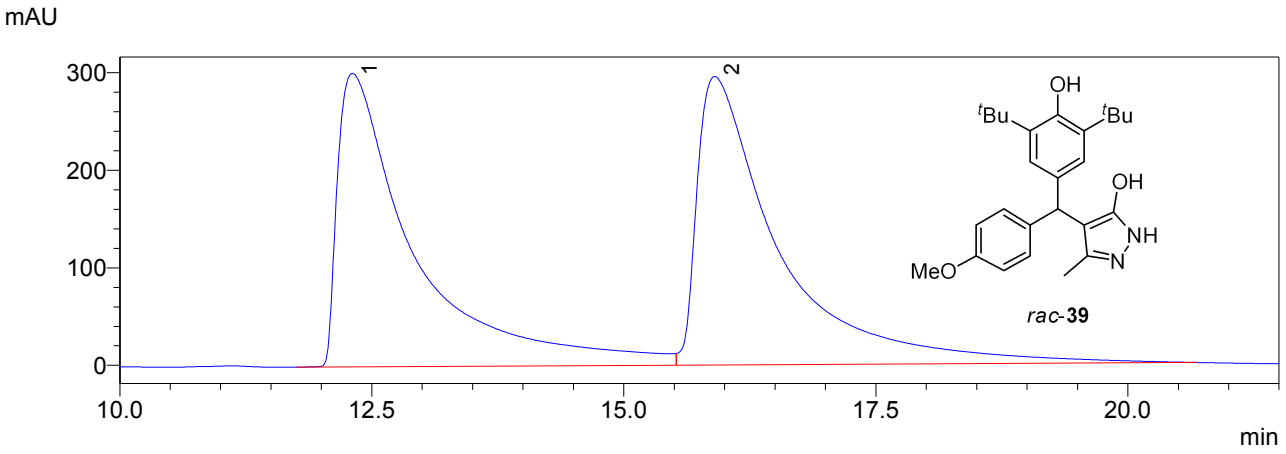
PDA Ch1 254nm

Peak#	Ret. Time	Area%
1	12.05	49.77
2	14.34	50.23
Total		100.00



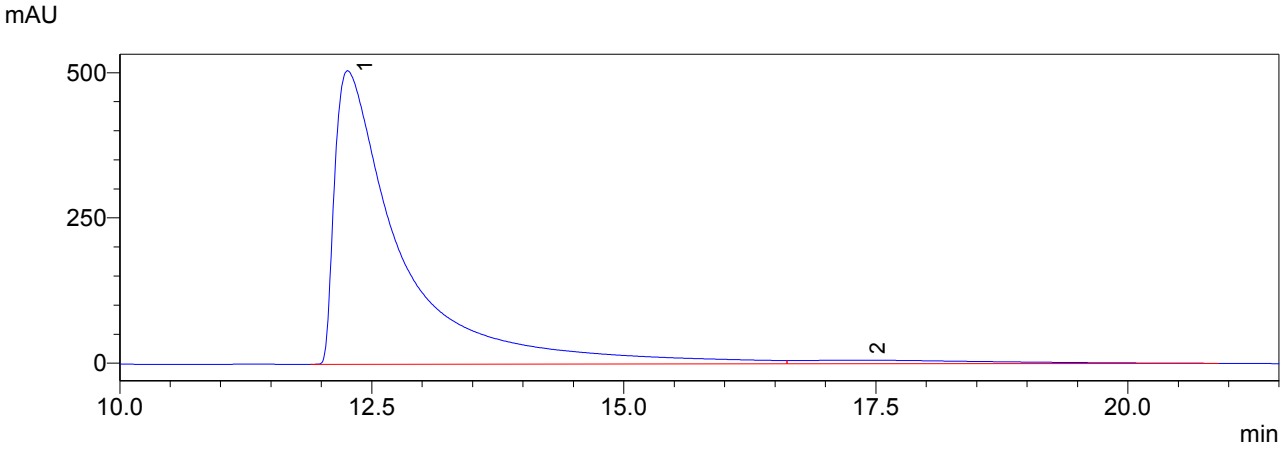
PDA Ch1 254nm

Peak#	Ret. Time	Area%
1	12.06	0.64
2	14.06	99.36
Total		100.00



PDA Ch1 220nm

Peak#	Ret. Time	Area%
1	12.31	49.11
2	15.90	50.89
Total		100.00



PDA Ch1 220nm

Peak#	Ret. Time	Area%
1	12.26	96.59
2	17.34	3.41
Total		100.00