Stereocontrolled Synthesis of 3-(*trans*-2-Aminocyclopropyl)alanine, A Key Component of Belactosin A

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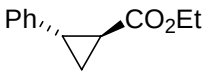
(*S, S*)-*trans*-2-phenyl-cyclopropyl carboxylic acid ethyl ester



6

To a suspension of sodium hydride (30 mg, 0.75 mmol, 60% in mineral oil) in xylenes, (5 ml), was added triethylphosphonoacetate (0.12 ml, 0.62 mmol) dropwise at room temperature. After stirring for 15 min at room temperature *R*-styrene oxide **5** (68 μl, 0.59 mmol) was added dropwise. The mixture was then heated at reflux for 3 hours, followed by cooling to room temperature and removal of solvents *in vacuo*. The crude material was purified *via* flash chromatography (3 petrol : 1 ether, base-washed with 2% triethylamine), to yield the desired cyclopropane **6** (61 mg, 51% yield) as a colourless oil; δ_H (250 MHz, $CDCl_3$) 7.33-7.07 (5H, m, Ar*H*), 4.17 (2H, q, *J*7.0, CH_3CH_2O), 2.52 (1H, ddd, *J*9.2, 6.4, 4.3, C*H*CO_2Et), 1.90 (1H, ddd, *J*8.2, 5.2, 4.3, ArC*H*), 1.60 (1H, ddd, *J*9.2, 5.2, 4.6, CH_2), 1.28-1.22 (4H, m, CH_2, OCH_2CH_3); $[\alpha]^{22}_D$ 240 (*c* 1.05, $CHCl_3$), > 95% e.e. (95.5 : 0.05 hexane : isopropanol, 2ml/min, OD column).

(*R, R*)-*O*-(benzyl)-cyclopropyl carboxylic acid ethyl ester methanol

ent-**3**

To a suspension of sodium hydride (55 mg, 1.39 mmol, 60% in mineral oil) in toluene (2 ml) was added triethylphosphonoacetate (0.26 ml, 1.31 mmol) dropwise over 5 min. After stirring at room temperature for 10 min *S*-benzylglycidyl ether *ent*-**4** (0.10 ml, 0.66 mmol) was added dropwise, followed by heating at reflux for 14 hours. The solution was cooled to room temperature, diluted with ethyl acetate (50 ml), then washed with saturated aqueous ammonium chloride (25 ml). After drying over magnesium sulfate and concentration *in vacuo*, the crude material was purified by flash chromatography (4 petrol : 1 ether), to yield the desired cyclopropane *ent*-**3** (96 mg, 63%) as a colourless oil; ν_{max}/cm^{-1}(film) 2982, 2860, 1724, 1643, 1454, 1368, 1321, 1203, 1181, 1093, 738, 698;

δ_H (250 MHz, $CDCl_3$) 7.38-7.26 (5H, m, Ar*H*), 4.52 (2H, s, PhCH_2O), 4.12 (2H, q, *J*7.1, OCH_2CH$_3$), 3.45 (1H, dd, *J*10.4, 6.1, BnOCH_2), 3.36 (1H, dd, *J*10.4, 6.4, BnOCH_2), 1.81-1.68 (1H, m, H_3), 1.60-1.53 (1H, m, H_6), 1.29-1.18 (4H, m, OCH$_2$CH_3, H_5), 0.86 (1H, ddd, *J*10.4, 6.3, 4.3, H_4); δ_C (62 MHz, $CDCl_3$) 173.8 (C), 138.1 (C), 128.4 (CH), 127.7 (CH), 71.5 (CH_2), 72.7 (CH_2), 60.5 (CH_2), 21.6 (CH), 18.5 (CH), 14.2 (CH_3), 12.9 (CH_2); m/z (CI, NH_3) 235 $[M+H]^+$, found : $[M+H]^+$, 235.1325. $C_{14}H_{19}O_3$ requires $[M+H]^+$, 235.1334; $[\alpha]^{22}_D$ -77 (*c* 0.44, $CHCl_3$), > 95% e.e. (35 mol% Eu(hfc)$_3$).

(*R*, *R*)-*O*-(benzyl)-cyclopropanecarboxylic acid methanol

5

To a solution of cyclopropane *ent*-**3** (0.27 g, 1.17 mmol) in ethanol (11 ml), was added aqueous sodium hydroxide (98 mg, 2.45 mmol) in water (6 ml) over 5 min. The mixture was then stirred at room temperature overnight, diluted with water (100 ml), acidified to pH 4 with concentrated HCl, then extracted with ethylacetate (3 x 50 ml). Organic extracts were combined, dried over magnesium sulfate then concentrated *in vacuo* to afford the desired cyclopropyl acid **5** (0.23 g, 96%) as a colourless oil; ν_{max}/cm^{-1}(film) 3429, 3031, 2928, 2864, 1693, 1454, 1229, 1085, 739, 699; δ_H (250 MHz, $CDCl_3$) 7.37-7.26 (5H, m, Ar*H*), 4.53 (2H, s, PhCH_2O), 3.48 (1H, dd, *J*10.4, 6.1, BnOCH_2), 3.36 (1H, dd, *J*10.4, 6.7, BnOCH_2), 1.87-1.75 (m, 1H, H_3), 1.61-1.54 (1H, m, H_6), 1.29 (1H, app q, *J*4.3, H_5), 0.95 (1H, ddd, *J*10.8, 6.5, 4.3, H_4); δ_C (62 MHz, $CDCl_3$) 180.1 (C), 138.0 (C), 128.4 (CH), 127.7 (CH), 72.7 (CH_2), 71.2 (CH_2), 22.5 (CH), 18.4 (CH), 13.7 (CH_2); m/z (CI, NH_3) 224 $[M+NH_4]^+$, found : $[M+NH_4]^+$, 224.1280. $C_{12}H_{18}NO_3$ requires $[M+NH_4]^+$, 224.1270; $[\alpha]^{22}_D$ -152 (*c* 0.51, $CHCl_3$).

(*R*, *R*)-*O*-(benzyl)-*N*-(boc)-aminocyclopropylmethanol

6

To a solution of cyclopropyl acid **5** (0.24 g, 1.12 mmol) in *tert*-butyl alcohol (14 ml) was added triethylamine (0.19 ml, 1.35 mmol) then diphenylphosphoryl azide (0.27 mmol, 1.24 mmol) dropwise. The mixture was heated at reflux for 20 hours, cooled to room temperature and diluted with ethyl acetate (100 ml). Organics were washed with water (2 x 25 ml), dried over magnesium sulfate and finally concentrated *in vacuo*. The crude product was purified by flash chromatography (1 petrol : 1 ether), to afford the desired amine **6** (0.17 g, 53%) as a colourless oil; ν_{max}/cm^{-1}(film) 3334, 2977,

1706, 1513, 1366, 1252, 1169, 1099, 739, 698; δ_H (250 MHz, $CDCl_3$) 7.37-7.26 (5H, m, Ar*H*), 4.72 (1H, br s, N*H*Boc), 4.52 (2H, s, PhCH_2O), 3.46 (1H, dd, *J*10.2, 6.6, H_2), 3.29 (1H, dd, *J*10.2, 6.8, H_1), 2.41 (1H, br s, H_6), 1.43 (9H, s, Boc), 1.29-1.16 (1H, m, H_3), 0.79-0.67 (m, 2H, H_4, H_5); δ_C (62 MHz, $CDCl_3$) 156.4 (C), 138.3 (C), 128.4 (CH), 127.7 (CH), 79.4 (C), 72.7 (CH_2), 71.8 (CH_2), 28.4 (CH_3), 28.1 (CH), 20.1 (CH), 12.1 (CH_2); m/z (CI, NH_3) 278 $[M+H]^+$, found : $[M+H]^+$, 278.1759. $C_{16}H_{24}NO_3$ requires $[M+H]^+$, 278.1756; $[\alpha]^{22}_D$ -30 (*c* 0.40, $CHCl_3$).

(*R*, *R*)-*O*-(benzyl)-*N*-(bis-boc)-aminocyclopropyl methanol

7

To a solution of cyclopropylamine **6** (0.17 g, 0.60 mmol) in acetonitrile (5 ml) was added Boc-anhydride (0.39 g, 1.80 mmol) as a solution in acetonitrile (3 ml), then *N*,*N*-dimethylaminopyridine (0.02 g, 0.18 mmol) in one portion. The mixture was then stirred at room temperature for 48 hours, followed by removal of solvents *in vacuo*, drying over magnesium sulfate, and purification of the crude material *via* flash chromotography (2 petrol :1 ether) to afford the bis-protected amine **7** (0.21 g, 95%) as a white solid, m.p. 88-89 °C; ν_{max}/cm^{-1}(film) 3064, 2979, 1787, 1743, 1712, 1367, 1285, 1253, 1164, 1116, 855, 739, 698; δ_H (250 MHz, $CDCl_3$) 7.33-7.23 (5H, m, Ar*H*), 4.51 (2H, s, PhCH_2O), 3.82 (1H, dd, *J*10.1, 4.6, H_2), 3.12 (1H, dd, *J*10.1, 7.8, H_1), 2.49-2.43 (1H, m, H_6), 1.48 (18H, s, Boc_2), 1.40-1.27 (1H, m, H_3), 0.98 (1H, app q, *J*6.6, H_4) 0.90-0.83 (1H, m, H_5); δ_C (62 MHz, $CDCl_3$) 152.9 (C), 138.3 (C), 128.4 (CH), 127.7 (CH), 82.2 (C), 72.7 (CH_2), 71.0 (CH_2), 32.12 (CH), 28.05 (CH_3), 22.5 (CH), 14.8 (CH_2); m/z (CI, NH_3) 378 $[M+H]^+$, found: $[M+H]^+$, 378.2291. $C_{21}H_{32}NO_5$ requires $[M+H]^+$, 378.2280; $[\alpha]^{22}_D$ -44 (*c* 0.37, $CHCl_3$).

(*R*, *R*)-*N*-(bis-boc)-aminocyclopropyl methanol

8

To a mixture of bis-protected amine **7** (0.59 g, 1.55 mmol), and 10 mol% palladium (on carbon) (70 mg) was added THF (5 ml) then glacial acetic acid (0.05 ml) under an atmosphere of hydrogen and stirred at room temperature for 4 days. The suspension was diluted with ethyl acetate (100 ml), neutralised with solid potassium carbonate (5.00 g), then passed through a short pad of celite and

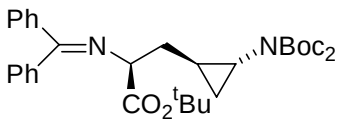
further washed with ethyl acetate (2 x 50 ml). Solvents were removed *in vacuo* and the crude product was purified by flash chromatography (2 ether : 1 petrol) to yield the desired alcohol **8** (0.44 g, 98%) as a colourless oil; ν_{max}/cm^{-1}(film) 3487, 2980, 1741, 1710, 1368, 1285, 1163, 1118, 1035, 853, 782; δ_H (250 MHz, $CDCl_3$) 3.87 (1H, dd, *J*10.8, 5.0, BnOCH_2), 3.10 (1H, dd, *J*10.8, 9.6, BnOCH_2), 2.80 (1H, br s, OH), 2.44 (1H, ddd, *J*6.1, 5.8, 3.3, H_6), 1.49 (18H, s, Boc_2), 1.22-1.35 (1H, m, H_3), 0.89-0.94 (2H, m, H_4, H_5); δ_C (62 MHz, $CDCl_3$) 153.43 (C), 82.9 (C), 65.00 (CH_2), 32.70 (CH), 28.02 (CH_3), 24.84 (CH), 13.64 (CH_2); m/z (CI, NH_3) 288 $[M+H]^+$, found : $[M+H]^+$, 288.1817. $C_{14}H_{26}NO_5$ requires $[M+H]^+$, 288.1811; $[\alpha]^{22}_D$ –3.0 (*c* 1.99, $CHCl_3$).

(*R*, *R*)-*N*-(bis-boc)-aminocyclopropyl-iodomethane

9

To a solution of 2,3-dichloro-5,6-dicyano-p-benzoquinone (79 mg, 0.35 mmol) in chloroform (4.5 ml), was added triphenylphosphine (91 mg, 0.35 mmol) followed by stirring at room temperature for 10 min. Tetrabutylammonium iodide (0.13 g, 0.35 mmol), was then added in one portion and the slurry stirred for a further 5 min. To this mixture was added a solution of alcohol **8** (50 mg, 0.17 mmol) in chloroform (2.0 ml) over 10 min. Petrol (100 ml) was then added with vigorous stirring for 5 min, and the resulting suspension was then passed through a short pad of celite and further washed with petrol (2 x 50 ml). Solvents were removed *in vacuo*, followed by final addition of petrol (5 x 5ml) and removal of triphenylphosphine oxide by filtration. Subsequent concentration of the filtrate *in vacuo* afforded the crude iodide **9** in high purity, which was used directly in subsequent alkylation reactions. Overall yields of the alkylation products for the two steps from alcohol **8** are are quoted below.

(2*S*, 1'*S*, 2'*R*)-(*N*-(bis-Boc)-*N*-(diphenylmethylene)-3-(2-aminocyclopropyl)) alanine *tert*-butyl ester

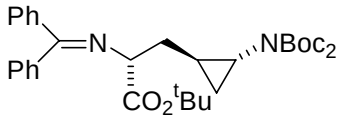


12

To a mixture of cesium hydroxide monohydrate (0.29 g, 1.74 mmol), *N*-(diphenylmethylene)glycine *tert*-butyl ester (0.10 g, 0.35 mmol), *O*(9)-allyl-*N*-(9-anthracenylmethyl)-cinchonidinium bromide (21 mg, 0.04 mmol), and activated 4Å molecular sieves (0.35 g) at –40°C was added a solution of crude iodide **9** (0.17 mmol) as a solution in 1 toluene : 1 CH_2Cl_2 (0.8 ml). The resultant slurry was then stirred rapidly at –40°C for 40 hours. The mixture was then diluted with further dichloromethane (10

ml) and quickly passed through a short pad of celite, followed by further washing with dichloromethane (3 x 50 ml). Solvents were then removed *in vacuo*, and the crude product was purified *via* flash chromotography (4 petrol : 1 ether, base-washed with 5% triethylamine), to afford the desired amino acid **12** (65 mg, 66% from alcohol) as a colourless oil; ν_{max}/cm^{-1}(film) 3059, 2978, 1787, 1733, 1368, 1286, 1160, 1159, 1160, 698; δ_H (500 MHz, d^8-tol) 7.83-7.81 (2H, m, Ar*H*), 7.15-6.98 (8H, m, Ar*H*), 4.21 (1H, dd, *J*8.6, 4.8, Ph_2C=NC*H*), 2.61 (1H, ddd, *J*13.8, 8.6, 4.5, Ph_2C=NCHCH_2), 2.32-2.29 (1H, m,C*H*$NBoc_2$), 1.55 (1H, ddd, *J*13.8, 10.0, 4.8, Ph_2C=NCHCH_2), 1.40 (18H, s, Boc_2), 1.33 (9H, s, $CO_2{}^tBu$), 1.17-1.11 (1H, m, C*H*(CH_2)CH$NBoc_2$), 0.71-0.67 (1H, m, (CH_2)CH$NBoc_2$), 0.50 (1H, app q, *J*6.6, (CH_2)CH$NBoc_2$); δ_C (125 MHz, $CDCl_3$) 171.0 (C), 170.1 (C), 152.8 (C), 139.5 (C), 136.6 (C), 130.1 (CH), 130.0 (CH), 128.7 (CH), 128.4 (CH), 128.3 (CH), 128.2 (CH), 128.0 (CH), 127.9 (CH), 82.1 (C), 80.9 (C), 65.5 (CH), 35.9 (CH_2), 34.6 (CH), 28.1 (CH_3), 28.0 (CH_3), 20.4 (CH), 16.3 (CH_2); m/z (CI, NH_3) 565 $[M+H]^+$, found : $[M+H]^+$, 565.3296. $C_{33}H_{45}N_2O_6$ requires $[M+H]^+$, 565.3278; $[\alpha]^{22}_D$ –52 (*c* 0.12, $CHCl_3$).

(2*R*, 1'*S*, 2'*R*)- (*N*-(bis-boc)-*N*-(diphenylmethylene)-3-(2-aminocyclopropyl))alanine *tert*-butyl ester

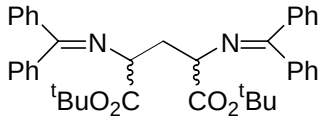


11

To a mixture of cesium hydroxide monohydrate (0.29 g, 1.74 mmol), *N*-(diphenylmethylene)glycine *tert*-butyl ester (0.10 g, 0.35 mmol), *O*(9)-allyl-*N*-(9-anthracenylmethyl)-cinchonium bromide (21 mg, 0.04 mmol), and activated 4Å molecular sieves (0.35 g) at –40°C was added a solution of crude iodide **9** (0.17 mmol) as a solution in 1 toluene : 1 CH_2Cl_2 (0.8 ml). The resultant slurry was then stirred rapidly at –40°C for 40 hours. The mixture was then diluted with further dichloromethane (10 ml) and quickly passed through a short pad of celite, followed by further washing with dichloromethane (3 x 50 ml). Solvents were then removed *in vacuo*, and the crude product was purified *via* flash chromotography (4 petrol : 1 ether, base-washed with 5% triethylamine), to afford the desired amino acid **11** (51 mg, 52% from alcohol) as a white solid, m.p. 127-128 °C; ν_{max}/cm^{-1}(film) 3059, 2978, 1787, 1735, 1368, 1285, 1258, 1160, 1116, 801, 783, 698; δ_H (500 MHz, d^8-tol) 7.82-7.80 (2H, m, Ar*H*), 7.16-6.98 (8H, m, Ar*H*), 4.28 (1H, app t, *J*6.3, Ph_2C=NC*H*), 2.73-2.69 (1H, m, Ph_2C=NCHCH_2), 2.41-2.39 (1H, m, C*H*$NBoc_2$), 1.47-1.28 (29H, m, Ph_2C=NCHCH_2, Boc_2, $CO_2{}^tBu$, C*H*(CH_2)CH$NBoc_2$), 0.85-0.81 (1H, m, (CH_2)CH$NBoc_2$), 0.74 (1H, app q, *J*6.5, (CH_2)CH$NBoc_2$); δ_C (125 MHz, $CDCl_3$) 171.0 (C), 169.7 (C), 153.0 (C), 139.6 (C), 136.7 (C), 132.4 (CH), 130.1 (CH), 130.0 (CH), 128.8 (CH), 128.5 (CH), 128.3 (CH), 128.0 (CH), 127.8 (CH), 82.1 (C), 80.9 (C), 65.0 (CH), 36.2 (CH_2), 33.8 (CH), 28.1 (CH_3), 28.0 (CH_3), 20.4 (CH), 16.7 (CH_2); m/z (CI, NH_3) 565

$[M+H]^+$, found : $[M+H]^+$, 565.3304. $C_{33}H_{45}N_2O_6$ requires $[M+H]^+$, 565.3278; $[\alpha]^{22}_D$ 21 (*c* 0.39, $CHCl_3$).

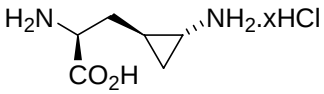
Diaminoester 13



13

87:13 Meso:C_2. ν_{max}/cm^{-1}(film) 2921, 2853, 1734, 1622, 1460, 1376, 1151, 695; δ_H (250 MHz, $CDCl_3$) 7.83-6.74 (20H, m, Ar*H*), 4.18 (2H, t, *J*7.2, Ph_2C=NC*H* minor), 4.06 (2H, t, *J*6.4, Ph_2C=NC*H* major), 2.89 (1H, app dt, *J* 13.7, 6.4, CH_2 major), 2.66 (2H, t, *J*7.2, CH_2 minor), 2.23- 2.17 (1H, m, CH_2 major), 1.37 (18H, Boc, minor), 1.35 (18H, Boc, major); δ_C (62 MHz, $CDCl_3$) 170.7 (C), 170.3 (C), 139.7 (C), 136.4 (C), 130.1 (CH), 128.9 (CH), 128.3 (CH), 127.9 (CH), 127.8 (CH), 127.6 (CH), 80.9 (C), 63.5 (CH), 62.4 (CH), 37.5 (CH_2), 28.0 (CH_3); m/z (CI, NH_3) 603 $[M+H]^+$, found: $[M+H]^+$, 603.3229. $C_{39}H_{43}N_2O_4$ requires $[M+H]^+$, 603.3223.

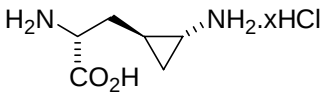
(2*S*, 1'*S*, 2'*R*)-aminocyclopropylalanine .xHCl



16.xHCl

To a solution of amino acid **12** (65 mg, 0.11 mmol) in THF (1ml), was added 1.2 M HCl (2.60 ml), followed by stirring at room temperature for 48 hours. The mixture was dilluted with distilled water (50 ml), then organics were extracted by washing with ether (2 x 25 ml). The aqueous fraction was concentrated *in vacuo*, then freeze-dried to afford **16**.xHCl (22 mg), as a glassy solid; ν_{max}/cm^{-1}(film) 3403, 2992, 2927, 1737, 1603, 1504; δ_H (250 MHz, D_2O) 4.04 (1H, app t, *J*6.3, H_2NCH), 2.58-2.52 (1H, m, C*H*NH_2), 2.07-1.95 (1H, m, H_2NCHCH_2), 1.90-1.78 (1H, m, H_2NCHCH_2), 1.37-1.22 (1H, m, C*H*(CH_2)$CHNH_2$), 1.05 (1H, ddd, *J*9.5, 7.0, 4.3, (CH_2)$CHNH_2$), 0.84 (1H, app q, *J*7.0, (CH_2)$CHNH_2$); δ_C (125 MHz, $CDCl_3$) 175.0 (C), 55.7 (CH), 34.4 (CH_2), 30.7 (CH), 15.6 (CH), 12.7 (CH_2); m/z (CI, NH_3) 145 $[M-xHCl+H]^+$, found : $[M-xHCl+H]^+$, 145.0977. $C_6H_{13}N_2O_2$ requires $[M-xHCl+H]^+$, 145.0981; $[\alpha]^{22}_D$ -10 (*c* 0.41, MeOH).

(2*R*, 1'*S*, 2'*R*)-aminocyclopropylalanine .xHCl



ent-**2**.xHCl

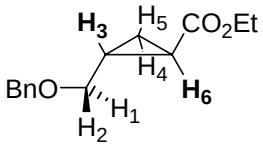
To a solution of amino acid **11** (51 mg, 0.09 mmol) in THF (1ml), was added 1.2 M HCl (2.60 ml), followed by stirring at room temperature for 48 hours. The mixture was dilluted with distilled water (50 ml), then organics were extracted by washing with ether (2 x 25 ml). The aqueous fraction was concentrated *in vacuo*, then freeze-dried to afford *ent*-**2**.xHCl (17 mg), as a glassy solid; ν_{max}/cm^{-1}(film) 3427, 3012, 2934, 1735, 1621, 1509; δ_H (250 MHz, D_2O) 4.00 (1H, app t, *J*6.3, H_2NCH), 2.56-2.50 (1H, m, $CHNH_2$), 2.10 (1H, app dt, *J*15.0, 6.3, H_2NCHCH_2), 1.71 (1H, ddd, *J*15.0, 8.2, 6.3, H_2NCHCH_2), 1.37-1.22 (1H, m, $CH(CH_2)CHNH_2$), 1.04 (1H, ddd, *J*9.8, 6.9, 4.1, $(CH_2)CHNH_2$), 0.82 (1H, app q, *J*6.9, $(CH_2)CHNH_2$); δ_C (125 MHz, $CDCl_3$) 175.4 (C), 55.1 (CH), 34.5 (CH_2), 30.7 (CH), 15.8 (CH), 12.6 (CH_2); m/z (CI, NH_3) 145 $[M\text{-}xHCl+H]^+$, found : $[M\text{-}xHCl+H]^+$, 145.0977. $C_6H_{13}N_2O_2$ requires $[M\text{-}xHCl+H]^+$, 145.0978; $[\alpha]^{22}_D$ -8 (*c* 0.30, MeOH).

Optimisation of the Wadsworth-Emmons cyclopropanation of *ent*-4

Entry	Base	Solvent	Eq. Triethyphosphono acetate	Temp/°C	Time	Yield* (Yield*†)
1	K^{t}BuO	DMF	2.0	70	14h	27 (31)
2		DME	2.0	82	14h	32
3		THF	2.0	65	14h	55
4		THF	2.0	65	24h	25
5		tol	2.0	110	14h	28
6		hex	2.0	68	14h	30
7	NaH	DMF	2.0	70	14h	20 (29)
8		DME	2.0	82	14h	56
9		DME	2.0	82	24h	47
10		THF	2.0	65	14h	49
11		**tol**	**2.0**	**110**	**14h**	**63**
12		**tol**	**3.0**	**110**	**14h**	**64**
13		tol	3.0	110	1h	60
14		xylenes	3.0	135	1h	60
15		tol	2.0	110	24h	54

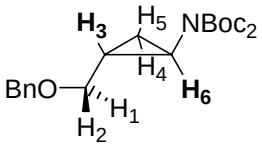
*Isolated yields. †Yield with respect to recovered starting material. All reactions were carried out at a phosphonate concentration of 0.66 M, except entries 13 and 14, which was carried out at 0.31 M.

NOE results for *ent*-3 and 7



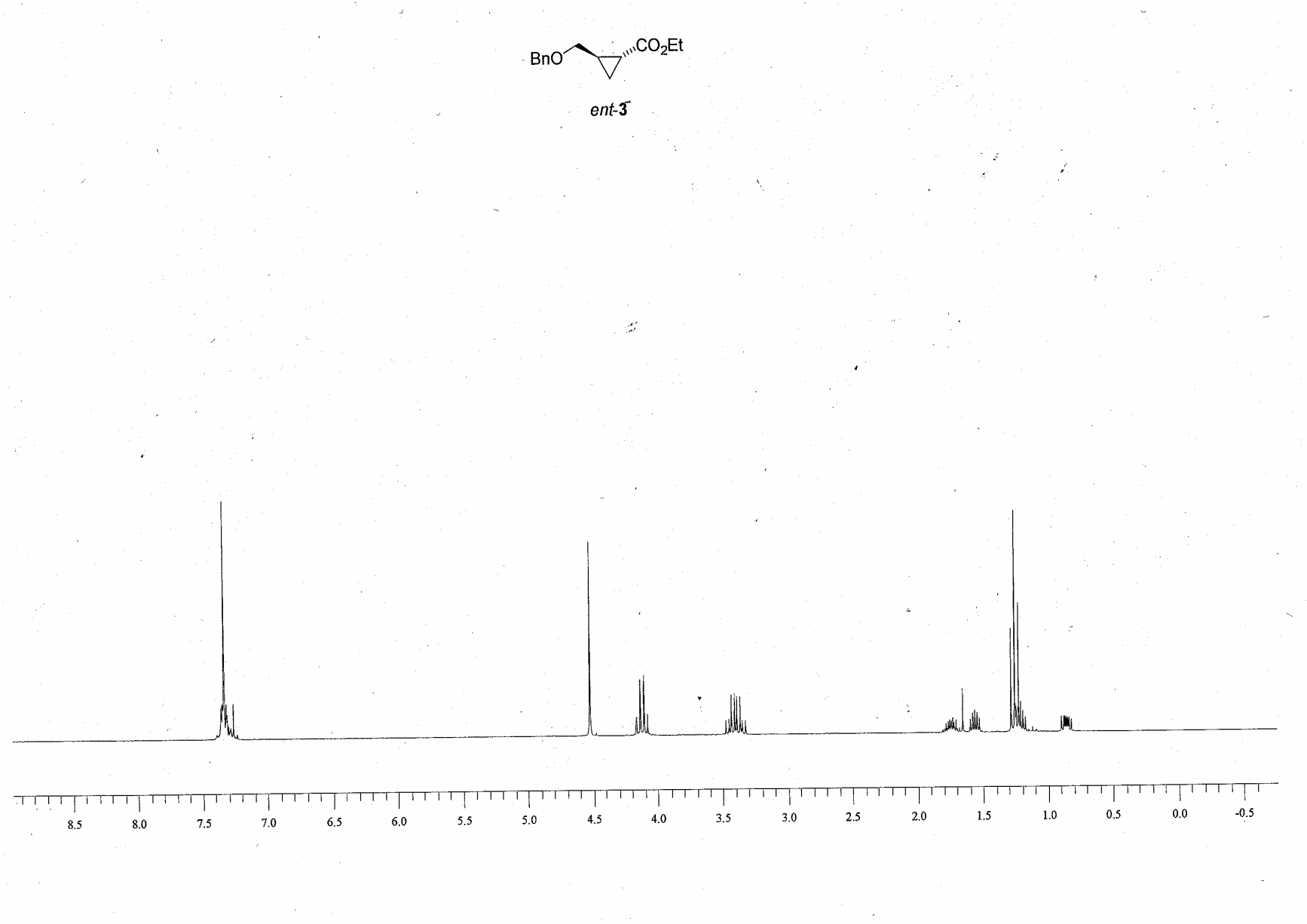
ent-**3**

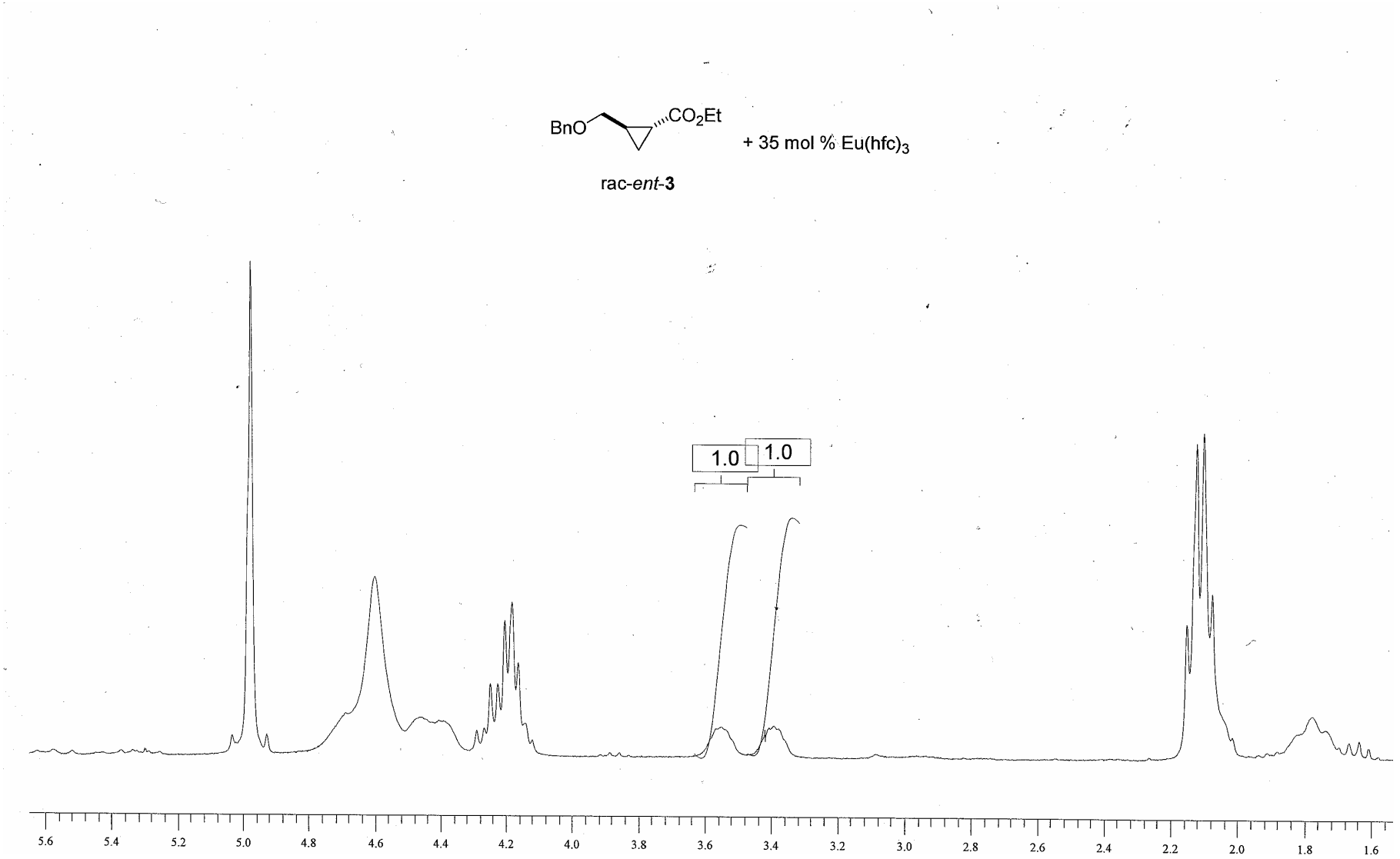
$H_3 \rightarrow H_5$ = 2.50%
$H_3 \rightarrow H_1$, H_2 = 2.65%
$H_6 \rightarrow H_4$ = 3.21%
$H_6 \rightarrow H_1$, H_2 = 1.90%

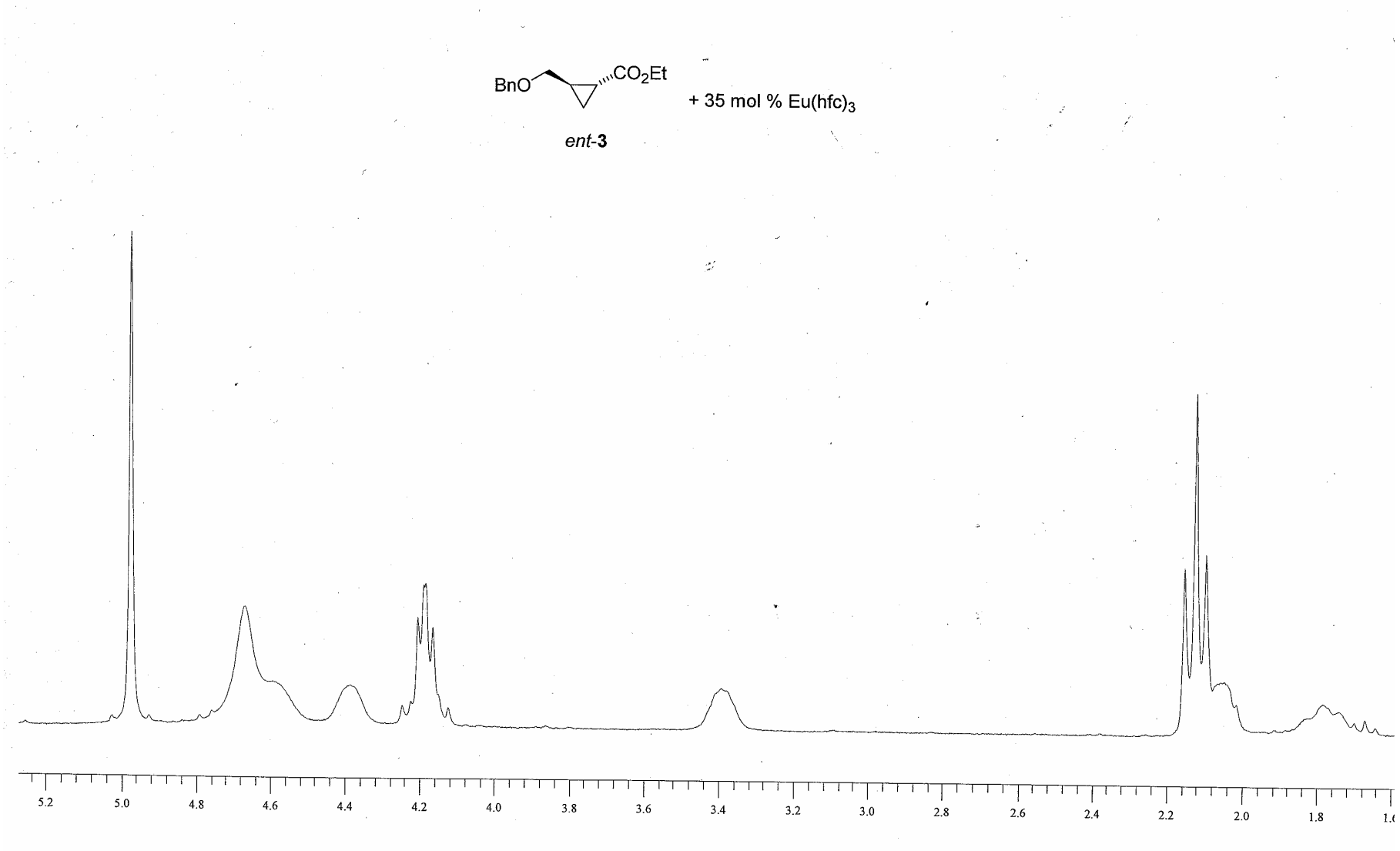


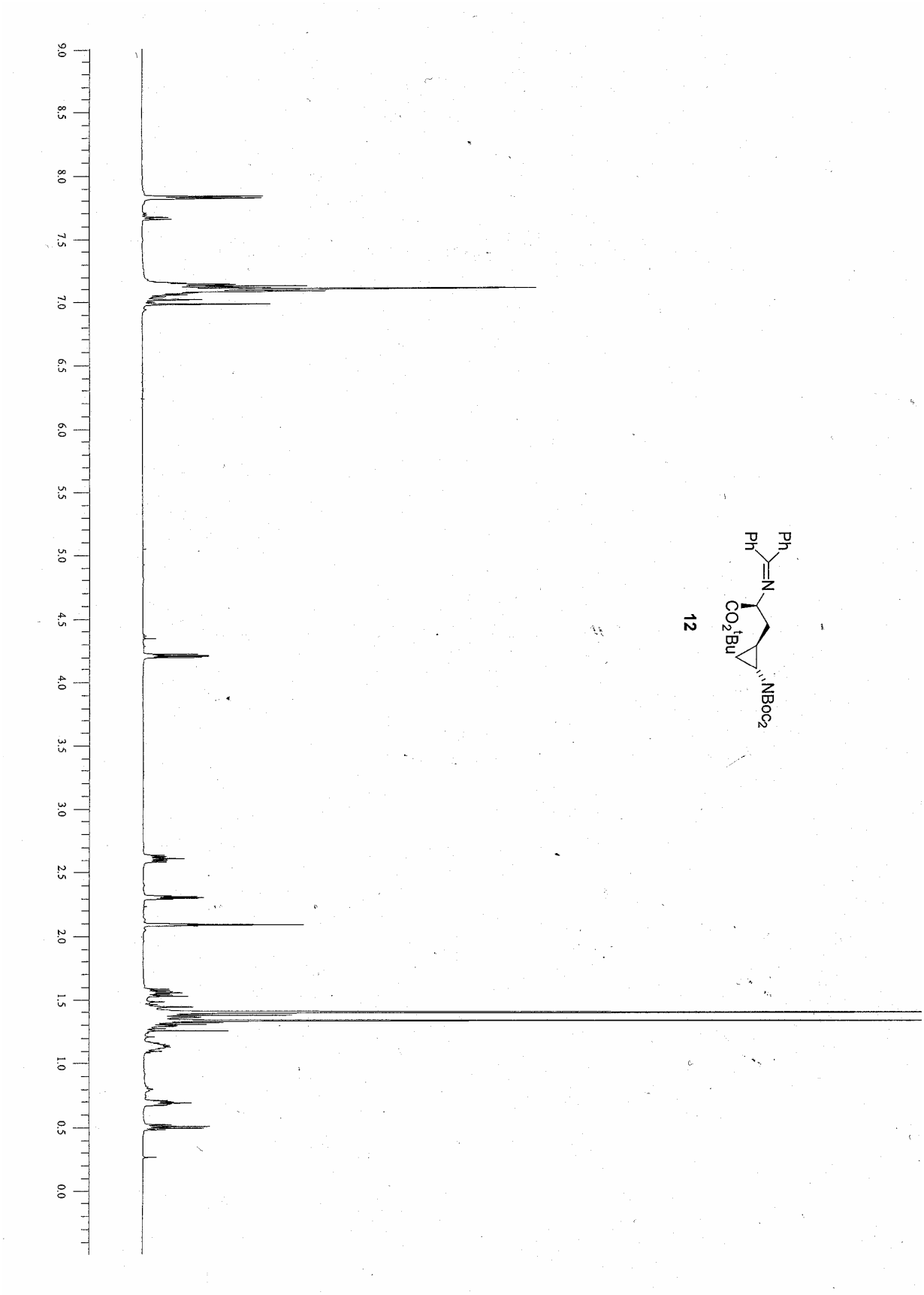
7

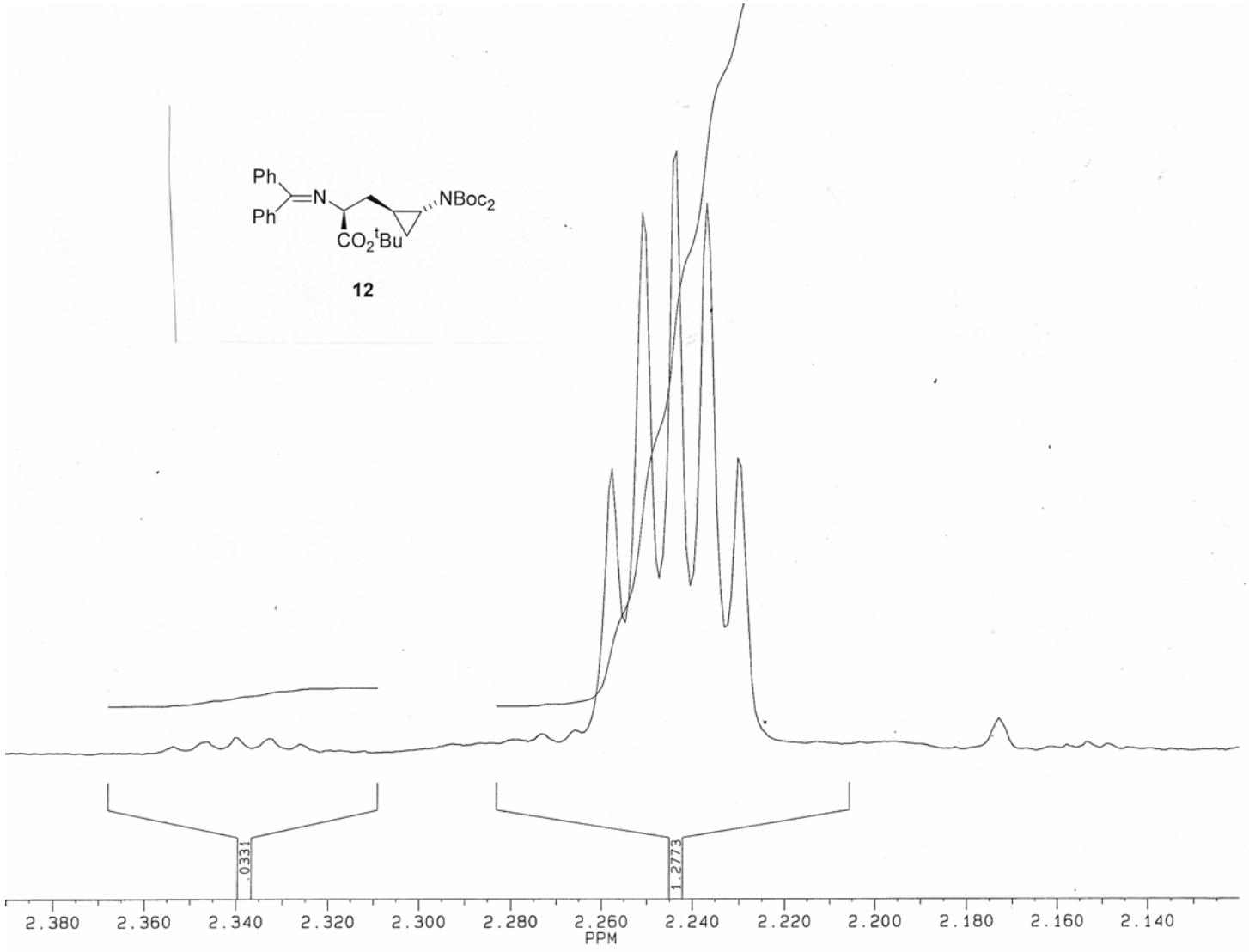
$H_3 \rightarrow H_5$ = 4.90%
$H_3 \rightarrow H_2$ (or H_1) = 3.83%
$H_6 \rightarrow H_4$ = 4.70%
$H_6 \rightarrow H_1$ (or H_2) = 4.30%


BnO
CO2Et
ent-3
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5


BnO
CO2Et
+ 35 mol % Eu(hfc)3
rac-ent-3
1.0
1.0
5.6
5.4
5.2
5.0
4.8
4.6
4.4
4.2
4.0
3.8
3.6
3.4
3.2
3.0
2.8
2.6
2.4
2.2
2.0
1.8
1.6


BnO
CO2Et
+ 35 mol % Eu(hfc)3
ent-3
5.2
5.0
4.8
4.6
4.4
4.2
4.0
3.8
3.6
3.4
3.2
3.0
2.8
2.6
2.4
2.2
2.0
1.8


Ph
Ph
N
CO2tBu
NBoc2
12



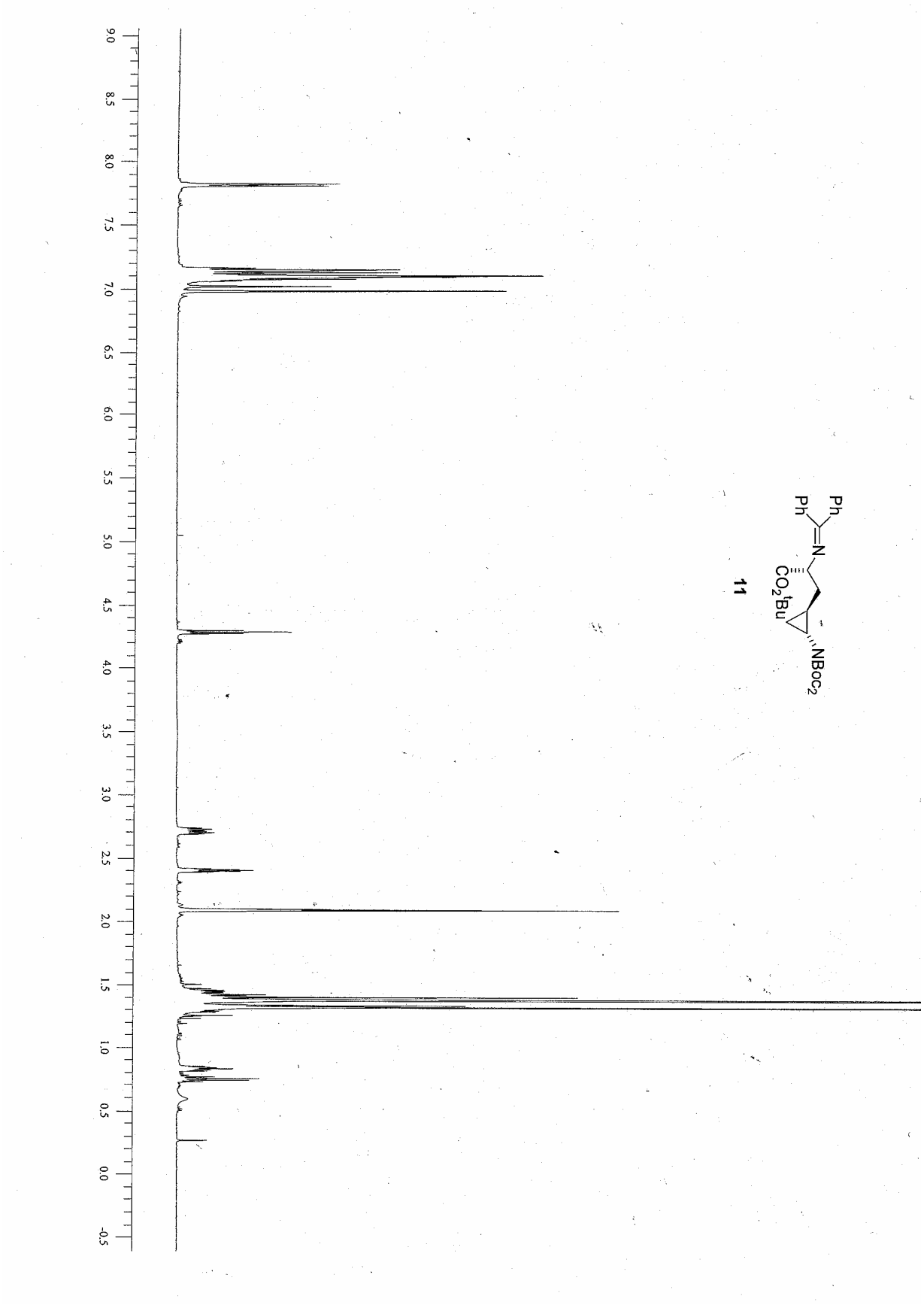
JS140303.001
DATE 14-3-3

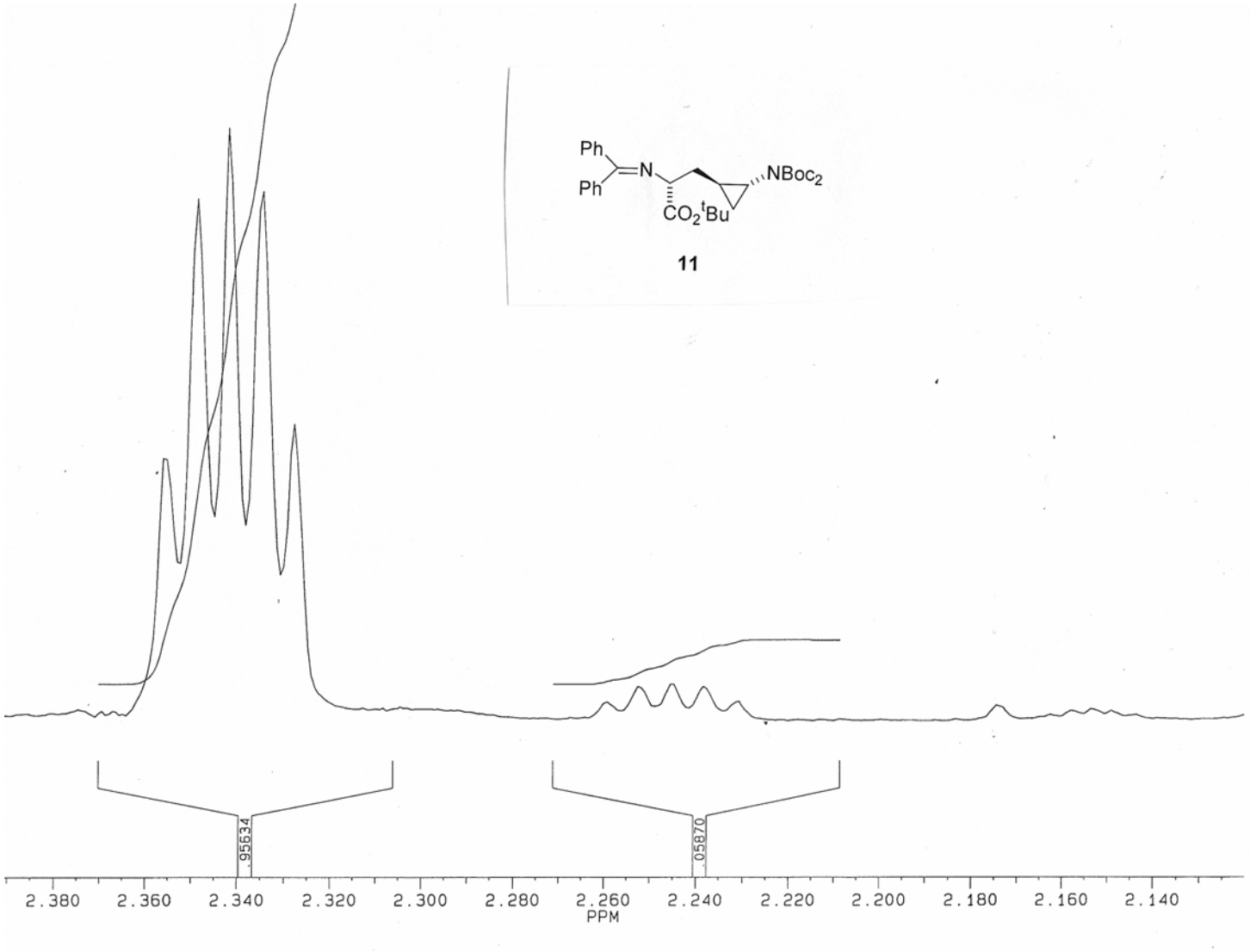
SF 500.13
SY 83.0
O1 8000.00
SI 32768
TD 32768
SW 6097.56
HZ/PT .37

PW 9.0
RD 1.00
AQ 2.68
RG 16
NS 346
TE 297

FW 7700
O2 1.00
DP 63L PO

LB 0.0
GB .40
CX 23.00
CY 11.00
F1 2.40
F2 2.12
HZ/CM 6.08
PPM/CM .01
SR 5507.23


Ph
Ph
N
CO2tBu
NBoc2
11
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5

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JS140303.002
DATE 14-3-3

SF     500.13
SY   83.0
O1    8000.00
SI   32768
TD   32768
SW    6097.56
HZ/PT     .37

PW        9.0
RD        1.00
AQ        2.68
RG       20
NS      314
TE      297

FW    7700
O2       1.00
DP   63L PO

LB        0.0
GB         .40
CX       23.00
CY       11.00
F1        2.40
F2        2.12
HZ/CM     6.08
PPM/CM     .01
SR     5506.86
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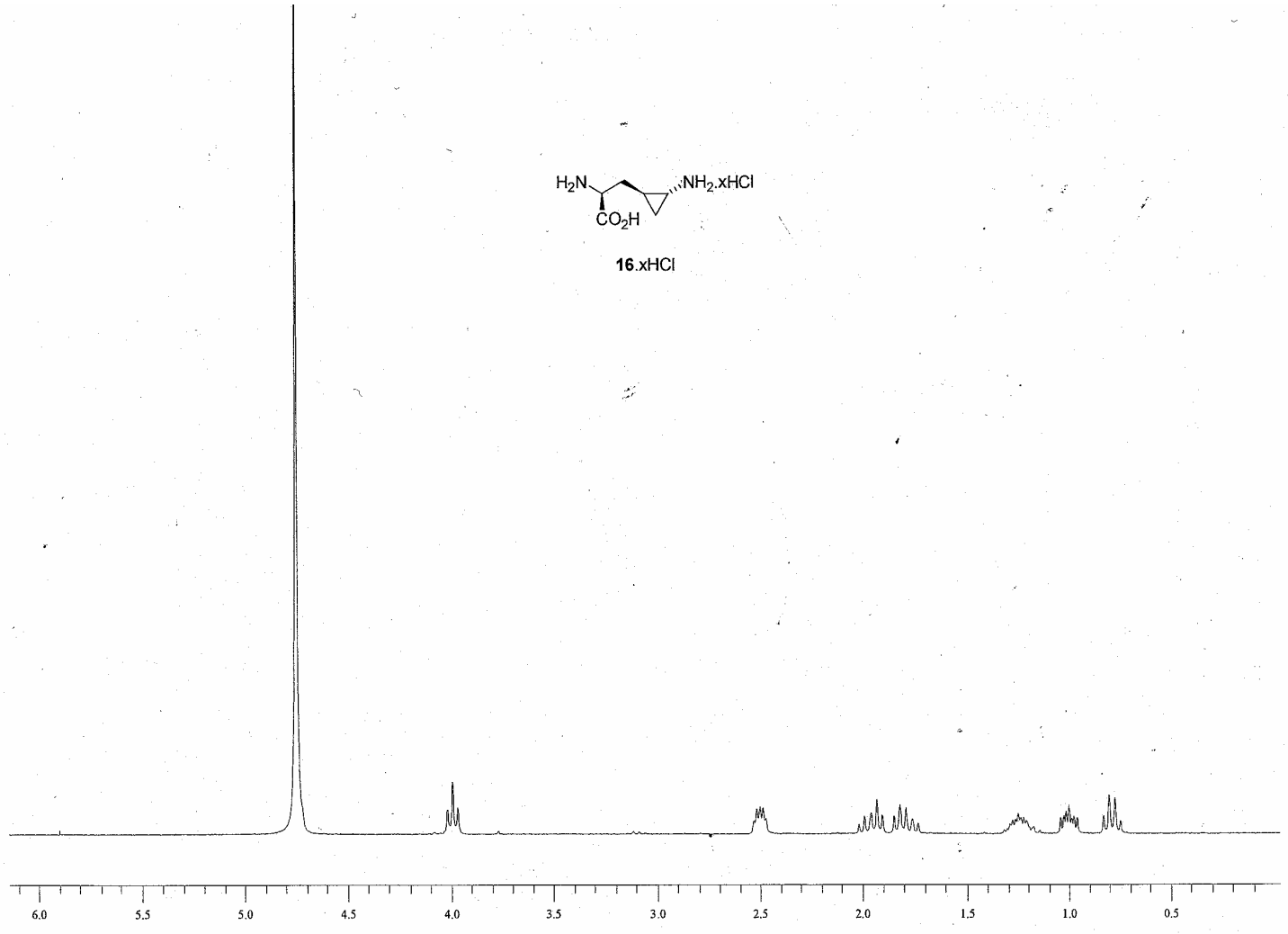
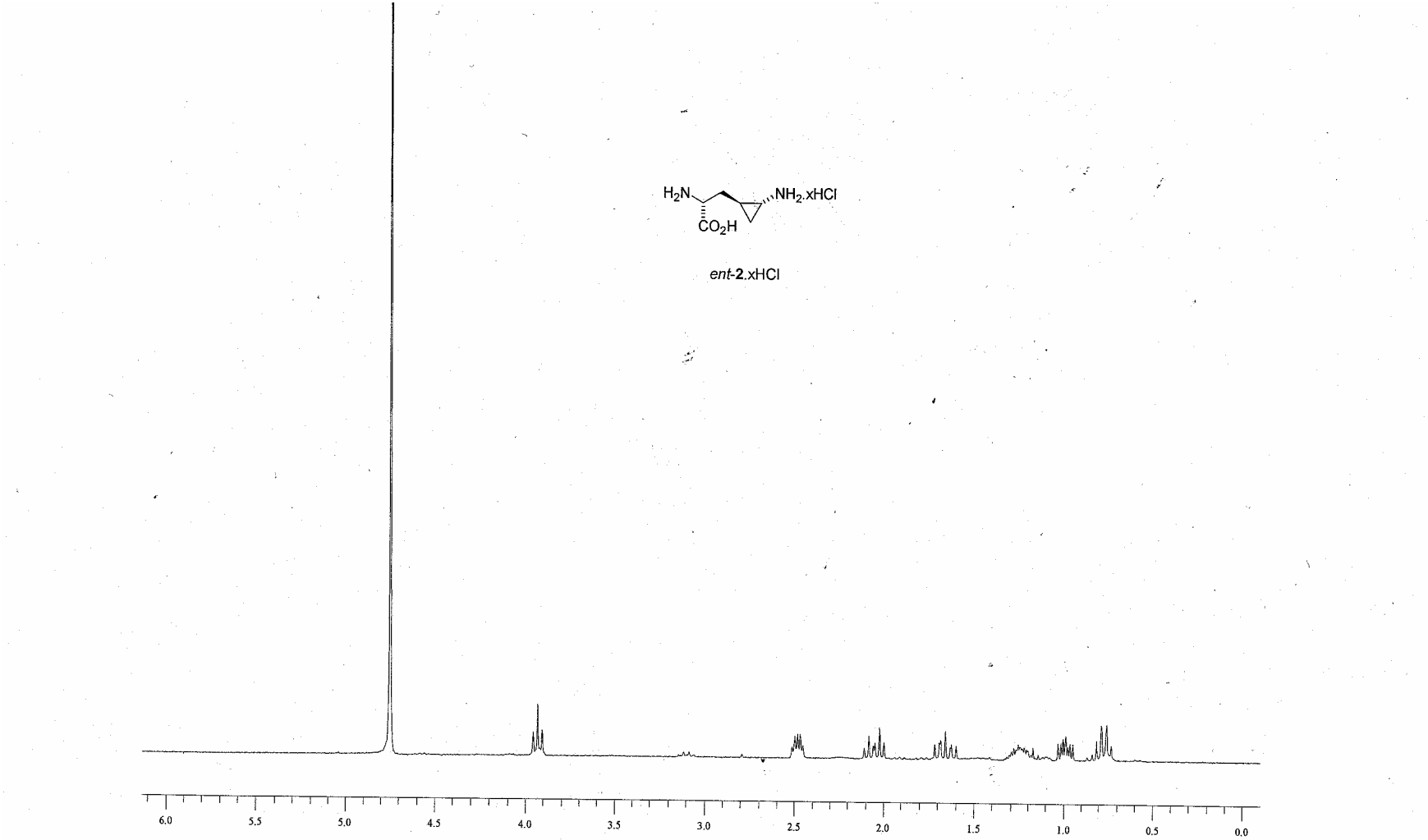

H2N
NH2.xHCl
CO2H
16.xHCl
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5


H2N
NH2.xHCl
CO2H
ent-2.xHCl
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0