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Supporting Information

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Chiral 2-Trifluoromethyl-4-phenyloxazolidine: A Novel Highly Performing Chiral Auxiliary for Amides Alkylation

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General information:

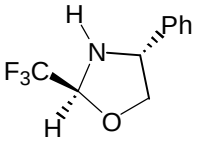
Commercial reagents were purchased from ALDRICH, ACROS, or AVOCADO and used as received. Trifluoroacetaldehyde-methylhemiacetal was generously offered by Central Glass Company. All alkylation reactions were performed under argon atmosphere with oven-dried glassware fitted with rubber septa. Ether and THF were distilled under nitrogen from sodium/benzophenone prior to use. CH_2Cl_2 was distilled under nitrogen from CaH_2 prior to use. Flash chromatography was performed on SDS 60A, (40-63 μm.) silica gel. Thin layer chromatography was performed on precoated aluminium sheets (MACHEREY-NAGEL ALUGRAM SIL/G 0.2mm). They were visualized under a 254-nm UV light. ^{1}H NMR spectra, ^{19}F NMR spectra and ^{13}C NMR spectra were recorded on a BRÜKER ADVANCE 250 DPX (250 MHz ^{1}H, 235.6 MHz ^{19}F, 69.2 MHz ^{13}C) or a JEOL ECX-400 (400 MHz ^{1}H, 376.2 MHz ^{19}F, 100.5 MHz ^{13}C). Chemical shift values (δ) are reported in ppm downfield from Me_4Si (δ 0.0 ppm) , $CFCl_3$ (δ 0.0 ppm) or $CDCl_3$ as internal standard (δ 77.0 ppm). Data are reported as follows: chemical shift (δ ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, m = multiplet), integration, coupling constant (Hz). Infrared (IR) spectra were performed on a BRÜCKER TENSOR 27 (liquids: NaCl pellets deposit; solids: KBr pellets). GC and low resolution mass spectra were performed on a HEWLETT PACKARD GC 6890 coupled with a HEWLETT PACKARD MSD 5973 apparatus (capillary column HP-5MS, 30 m × 250 μm, He as vector gas, method: 70°C during 2min, 20°C/min climb rate and 250°C during 15 min). Specific rotations were measured on a JASCO DIP-370 polarimeter.

(4*R*)-2-Trifluoromethyl-4-phenyloxazolidines (1)

To a solution of *(R)*-phenylglycinol (6.00 g, 43.8 mmol) in toluene at room temperature (130 mL) was slowly added trifluoroacetaldehyde methylhemiacetal (5.99 g, 46.0 mmol) and PPTS (1.1 g,

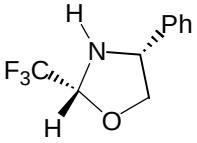
4.38 mmol). The flask was equipped with a Dean-Stark apparatus and the solution was warmed to reflux for 20 h. The solution was cooled down to 0°C and the resulting PPTS precipitate was filtered off. The flask and the precipitate were washed with Et_2O (30 mL) and the combined organic layers were concentrated under reduced pressure. The brown crude mixture was purified by filtration through a short pad of silica gel (25g, cyclohexane/ethyl acetate : 80/20) to afford oxazolidines (2*S*,4*R*)-**1** and (2*R*,4*R*)-**1** (8.85g, 93%) as a 62/38 mixture of two diastereomers. An analytical sample of each diastereomer was isolated.

(2*S*,4*R*)-2-Trifluoromethyl-4-phenyloxazolidine ((2*S*,4*R*)-1)



Colorless oil; $[a]_D^{23}$ = -43.0 (c = 1.08; $CHCl_3$); TLC R_f = 0.63 (cyclohexane / ethyl acetate: 90/10); ^{1}H NMR (250 MHz, $CDCl_3$) **:** δ 2.61 (m, 1H), 3.70 (t, 1H, ^3J = 7.4 Hz), 4.35 (t, 1H, ^3J = 7.4 Hz), 4.47 (t, 1H, ^3J = 7.4 Hz), 5.17 (q, 1H, $^3J_{H\text{-}F}$ = 5.7 Hz), 7.20-7.40 (m, 5H); ^{19}F NMR (235.35 MHz, $CDCl_3$) **:** δ -81.7 (d, 3 F, $^3J_{H\text{-}F}$ = 5.7 Hz); ^{13}C NMR (62.9 MHz, $CDCl_3$) **:** δ 60.8, 73.2, 87.9 (q, CH, $^2J_{C\text{-}F}$ = 34.5 Hz), 123.5 (q, C, $^1J_{C\text{-}F}$ = 238.5 Hz), 126.8, 128.5,129.1, 138.0; IR **:** $\bar{u}$ (cm^{-1}) 2938, 1289, 1147, 1117, 699; MS **:** 216 $(M\text{-}1)^+$: 2), 186 (100), 166 (6), 148 (66), 120 (42), 118 (29), 103 (24), 91 (21), 77(11); GC R_t = 7.04 min.

(2*R*,4*R*)-2-trifluoromethyl-4-phenyloxazolidine ((2*R*,4*R*)-1)



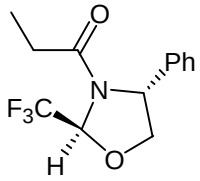
Yellow oil; $[a]_D^{23}$ = -56.4 (c = 1.17; $CHCl_3$); R_f = 0.50 (cyclohexane / ethyl acetate: 90/10); ^{1}H NMR (250 MHz, $CDCl_3$) **:** δ 2.85 (m, 1H), 3.77 (dd, 1H, ^3J = 8.0 Hz, ^3J = 6.9 Hz), 4.35 (dd, 1H, ^3J = 8.0, ^3J = 6.9 Hz), 4.62 (t, 1H, ^3J = 6.9 Hz), 5.11 (p, 1H, $^3J_{H\text{-}F}$ = 5.0 Hz, $^3J_{H\text{-}H}$ = 5.0 Hz), 7.20-7.40 (m, 5H); ^{19}F NMR (235.35 MHz, $CDCl_3$) **:** δ -82.0 (d, 3 F, $^3J_{H\text{-}F}$ = 5.0 Hz); ^{13}C NMR (62.9 MHz, $CDCl_3$) **:** δ 61.1, 73.8, 87.0 (q, CH, $^2J_{C\text{-}F}$ = 34.5 Hz), 123.6 (q, C, $^1J_{C\text{-}F}$ = 238.5 Hz), 126.7, 128.0, 128.6, 138.4; IR : $\bar{u}$ (cm^{-1}) 3364, 2896, 1458, 1291, 1152; MS **:** 216 (M^+-1, 1), 186 (100),

166 (7), 148 (40), 120 (26), 118 (27), 103 (17), 91 (18), 77(9) ; GC R_t = 7.12 min; Anal**.** Calc. for $C_{10}H_{10}F_3NO$: C, 55.30; H, 4.64; N, 6.45. Found : C, 55.67; H, 4.72; N, 6.11.

(4*R*)-2-trifluoromethyl-4-phenyl-3-propanoyloxazolidine (2a,3a)

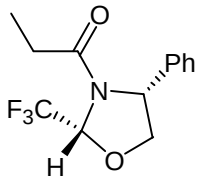
The mixture of diastereomers **1** (4.05 g, 18.6 mmol) was dissolved in pyridine (50 mL) and propanoyl chloride (2.90 mL, 33.3 mmol) was rapidly added at room temperature. The solution was stirred for 20h at 50°C and concentrated under reduced pressure. A solution of diethyl ether and dichloromethane (100 mL, Et_2O/CH_2Cl_2: 8/2) and a saturated solution of sodium chloride (75 mL) were added to the residue. The aqueous layer was extracted with diethyl ether (2x100 mL) and the combined organic layers were dried over $MgSO_4$. The resulting crude mixture was purified by flash column chromatography (cyclohexane/ethyl acetate: 90/10 to 80/20) affording pure **2a** (2.75 g, 54%) and pure **3a** (1.62 g, 32%) (Combined yield: 86%).

(2*S*,4*R*)-2-trifluoromethyl-4-phenyl-3-propanoyloxazolidine (2a)



White solid; $[a]_D^{23}$ =-60.5 (c =2.46 ; $CHCl_3$); mp = 51°C; R_f = 0.55 (cyclohexane/ethyl acetate: 80/20); ^{1}H NMR (250 MHz, $CDCl_3$) **:** δ 0.77 (t, 3H, ^3J = 7.5 Hz), 1.72 (dq, 1H, ^2J = 16.4 Hz, ^3J = 7.5 Hz), 2.10 (dq, 1H, ^2J = 16.4 Hz, ^3J = 7.5 Hz), 3.93 (d, 1H, ^2J = 8.1 Hz), 4.57 (dd, 1H, ^2J = 8.1 Hz, ^3J = 6.5 Hz), 4.91 (d, 1H, ^3J = 6.5 Hz), 6.06 (q, 1H, $^3J_{H\text{-}F}$ = 5.1 Hz), 7.10-7.30 (m, 5H); ^{19}F NMR (235.35 MHz, $CDCl_3$) **:** δ -77.91 (d, 3 F, $^3J_{H\text{-}F}$ = 5.1 Hz); ^{13}C NMR (62.9 MHz, $CDCl_3$) **:** δ 8.8, 29.5, 60.9, 73.6, 85.4 (q, CH, $^2J_{C\text{-}F}$ = 35.0 Hz), 123.6 (q, C, $^1J_{C\text{-}F}$ = 289.0 Hz), 125.8, 128.6, 129.7, 141.6, 174.3; IR : $\bar{u}$ (cm^{-1}) 3070-3037, 2975-2798, 1664, 1401, 1285, 703; MS **:** 273 (M^+,15), 244 (1), 217 (4), 204 (69), 186 (16), 148 (100), 120 (43), 57 (36); GC R_t = 8.87 min; Anal. Calc. for $C_{13}H_{14}F_3NO_2$: C, 57.14; H, 5.16; N, 5.13. Found : C, 57.23; H, 5.15; N, 5.05.

(2*R*,4*R*)-2-trifluoromethyl-4-phenyl-3-propanoyloxazolidine (3a)

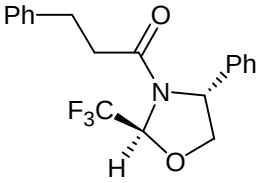


Yellow solid; $[a]_D^{23}$ = -80.8 (c = 2.06; $CHCl_3$); mp = 33°C; R_f = 0.37 (cyclohexane /ethyl acetate : 80/20); ^{1}H NMR (250 MHz, $CDCl_3$) **:** δ 1.03 (t, 3H, ^3J = 7.3 Hz), 2.02 (m, 1H), 2.22 (m, 1H), 4.11 (t, 1H, ^2J = 9.0 Hz), 4.62 (t, 1H, ^2J = 9.0 Hz), 5.06 (t, 1H, ^3J = 9.0 Hz), 5.96 (bs, 1H), 7.26-7.38 (m, 5H); ^{19}F NMR (235.35 MHz, $CDCl_3$) **:** δ -77.91 (d, 3 F, $^3J_{H\text{-}F}$ = 5.6 Hz); ^{13}C NMR (62.9 MHz, $CDCl_3$) **:** δ 8.6, 28.3, 61.6, 76.1, 85.9 (q, CH, $^2J_{C\text{-}F}$ = 35.4 Hz, C-2), 123.7 (q, C, $^1J_{C\text{-}F}$ = 287.4 Hz, CF_3), 126.2, 128.7, 129.6, 137.8, 175.4; IR : $\bar{u}$ (cm^{-1}) 3070-3030, 2983-2913, 1685, 1383, 1288, 1148, 701; MS **:** 273 (M^+, 92), 244 (1), 217 (34), 204 (5), 175 (79), 160 (100), 120 (84), 91 (32), 57 (66); GC R_t = 9.11 min; Anal. Calc. for $C_{13}H_{14}F_3NO_2$: C, 57.14; H, 5.16; N, 5.13. Found: C, 57.11; H, 5.15; N, 5.11.

(4*R*)-2-trifluoromethyl-4-phenyl-3-(3-phenylpropanoyl)-oxazolidine (2b,3b)

The mixture of diastereomers **1** (0.5 g, 2.3 mmol) was dissolved in pyridine (12 mL) and 3-phenylpropionyl chloride (0.615 mL, 4.14 mmol) was rapidly added at room temperature. The solution was stirred for 24h at 50°C and concentrated under reduced pressure. A solution of diethyl ether and dichloromethane (50 mL, Et_2O/CH_2Cl_2: 8/2) and a saturated solution of sodium chloride were added to the residue. The aqueous layer was extracted with diethyl ether (2x50 mL) and the combined organic layers were dried over $MgSO_4$. The resulting crude mixture was purified by flash column chromatography (cyclohexane/ethyl acetate: 90/10) affording pure **2b** (361 mg, 45%) and pure **3b** (312 mg, 39%) (Combined yield: 84%).

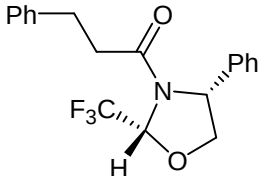
(2*S*,4*R*)-2-trifluoromethyl-4-phenyl-3-(3-phenylpropanoyl)-oxazolidine (2b)



White solid; $[a]_D^{23}$ = -76.81 (c = 2.02 ; $CHCl_3$); mp = 85°C; R_f = 0.35 (cyclohexane / ethyl acetate: 90/10); ^{1}H NMR (250 MHz, $CDCl_3$) **:** δ 2.05 (m, 1H), 2.28 (m, 1H), 2.34 (m, 1H), 2.68 (m, 1H),

3.89 (d, 1H, ^{2}J = 8.6 Hz, H-5), 4.48 (dd, 1H, ^{2}J = 8.6 Hz, ^{3}J = 6.6 Hz), 4.68 (d, 1H, ^{3}J = 6.6 Hz), 6.00 (q, 1H, $^{3}J_{H\text{-}F}$ = 5.1 Hz), 6.77-7.22 (m, 10H); ^{19}F NMR (235.35 MHz, $CDCl_3$) **:** δ -77.84 (d, 3 F, $^{3}J_{H\text{-}F}$ = 5.1 Hz); ^{13}C NMR (62.9 MHz, $CDCl_3$) **:** δ 30.9, 37.8, 60.7, 76.5, 85.2 (q, CH, $^{2}J_{C\text{-}F}$ = 34.5 Hz), 123.4 (q, C, $^{1}J_{C\text{-}F}$ = 290.0 Hz), 125.7, 126.3, 128.4, 128.5, 128.7, 129.6, 140.6, 141.5, 172.5; IR : $\bar{u}$ (cm^{-1}) 3065-3032, 2961-2919, 1654, 1400, 1282, 1147, 700; MS : 349 (M^{+},95), 280 (3), 258 (4), 217 (6), 148 (61), 131 (12), 120 (38), 104 (100), 91 (98); GC R_t = 12.33 min.

(2*R*,4*R*)-2-trifluoromethyl-4-phenyl-3-(3-phenylpropanoyl)-oxazolidine (3b)

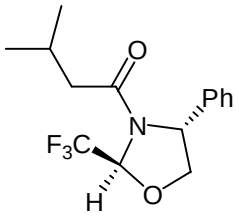


White solid; mp = 91°C; $[a]_D^{23}$ = -67.33 (c = 1.72; $CHCl_3$); R_f = 0.22 (cyclohexane/ethyl acetate : 90/10); ^{1}H NMR (250 MHz, $CDCl_3$) : δ 2.24 (m, 1H), 2.52 (m, 1H), 2.60 (m, 1H), 2.87 (m, 1H), 3.97 (d, 1H, ^{2}J = 9.8 Hz), 4.56 (dd, 1H, ^{2}J = 9.8 Hz, ^{3}J = 6.5 Hz), 4.77 (d, 1H, ^{3}J = 6.5 Hz), 6.09 (q, 1H, $^{3}J_{H\text{-}F}$ = 5.1 Hz), 6.80-7.31 (m, 10H); ^{19}F NMR (235.35 MHz, $CDCl_3$) **:** δ -77.70 (d, 3 F, $^{3}J_{H\text{-}F}$ = 5.1 Hz, CF_3); ^{13}C NMR (62.9 MHz, $CDCl_3$) **:** δ 30.8, 37.7, 60.6, 76.4, 85.1 (q, CH, $^{2}J_{C\text{-}F}$ = 35.2 Hz), 123.3 (q, C, $^{1}J_{C\text{-}F}$ = 289.0 Hz), 126.0, 126.2, 128.3, 128.5, 128.7, 129.5, 140.5, 141.4, 172.5; IR : $\bar{u}$ (cm^{-1}) 3085-3029, 3004-2914, 1681, 1389, 1280, 1145, 1108, 701; MS : 349 (M^{+}, 100), 280 (3), 258 (4), 217 (6), 148 (54), 131 (10), 120 (35), 104 (90), 91 (89); GC R_t = 12.33 min.

(4*R*)-2-trifluoromethyl-3-(3-methylbutanoyl)-4-phenyloxazolidine (2c,3c)

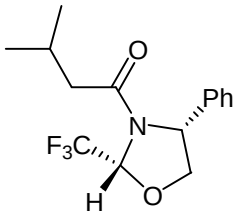
The mixture of diastereomers **1** (1 g, 4.6 mmol) was dissolved in pyridine (24 mL) and 3-methylbutanoyl chloride (1.02 mL, 8.29 mmol) was rapidly added at room temperature. The solution was stirred for 24h at 40°C and concentrated under reduced pressure. A solution of diethyl ether and dichloromethane (100 mL, Et_2O/CH_2Cl_2: 8/2) and a saturated solution of sodium chloride were added to the residue. The aqueous layer was extracted with diethyl ether (2x100 mL) and the combined organic layers were dried over $MgSO_4$. The resulting crude mixture was purified by flash column chromatography (cyclohexane/ethyl acetate : 90/10) affording pure **2c** (877 mg, 63%) and pure **3c** (524 mg, 36%) (Combined yield: 99%).

(2*S*,4*R*)-2-trifluoromethyl-3-(3-methylbutanoyl)-4-phenyloxazolidine (2c)



White solid; mp = 62°C; $[a]_D^{23}$ = -63.8 (c = 2.55; $CHCl_3$); R_f = 0.32 (cyclohexane/ethyl acetate : 90/10); ^{1}H NMR (400 MHz, $CDCl_3$) **:** δ 0.69 (d, 3H, ^3J = 6.4 Hz), 0.86 (d, 3H, ^3J = 6.4 Hz), 1.73 (dd, 1H, ^2J = 14.9 Hz, ^3J = 6.4 Hz), 1.85 (dd, 1H, ^2J = 14.9 Hz, ^3J = 7.8 Hz), 2.05 (m, 1H), 4.07 (d, 1H, ^2J = 8.7 Hz), 4.70 (dd, 1H, ^2J = 8.7 Hz, ^3J = 6.4 Hz), 5.00 (d, 1H, ^3J = 6.4 Hz), 6.16 (q, 1H, $^3J_{H\text{-}F}$ = 5.0 Hz), 7.18-7.39 (m, 5H); ^{19}F NMR (376.2 MHz, $CDCl_3$) : δ -80.82 (d, 3 F, $^3J_{H\text{-}F}$ = 5.0 Hz); ^{13}C NMR (100.5 MHz, $CDCl_3$) : δ 22.2, 22.4, 25.7, 45.0, 60.8, 76.6, 85.1 (q, CH, $^2J_{C\text{-}F}$ = 35.5 Hz), 123.5 (q, C, $^1J_{C\text{-}F}$ = 288.5 Hz), 125.7, 128.6, 129.5, 141.6, 173.0; IR : $\bar{u}$ (cm^{-1}) 2958, 2907, 2873, 1664, 1406, 1175, 1141, 702; MS : 301 (M^+, 4), 259 (30), 217 (4), 188 (6), 148 (100), 120(34), 104(81), 57(77); GC R_t = 9.21 min.

(2*R*,4*R*)-2-trifluoromethyl-3-(3-methylbutanoyl)-4-phenyloxazolidine (3c)

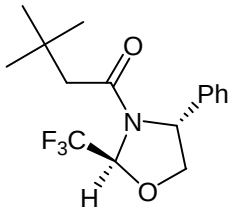


Yellow oil; $[a]_D^{23}$ = -91.4 (c = 3.35; $CHCl_3$); R_f = 0.12 (cyclohexane/ethyl acetate : 90/10); ^{1}H NMR (400 MHz, $CDCl_3$) **:** δ 0.72 (sl, 3H), 0.85 (sl, 3H), 1.92 (m, 1H), 2.11 (m, 2H), 4.12 (t, 1H, ^2J = 9.2 Hz), 4.63 (dd, 1H, ^2J = 9.2 Hz, ^3J = 8.2 Hz), 5.06 (m, 1H), 6.03 (m, 1H), 7.26-7.41 (m, 5H); ^{19}F NMR (376.2 MHz, $CDCl_3$) : δ -80.67 (sl, 3 F); ^{13}C NMR (100.5 MHz, $CDCl_3$) : δ 22.5, 23.3, 25.2, 43.3, 61.4, 76.2, 85.5 (q, CH, $^2J_{C\text{-}F}$ = 35.5 Hz), 123.4 (q, C, $^1J_{C\text{-}F}$ = 287.5 Hz), 126.1, 128.6, 129.4, 137.8, 174.3; IR : $\bar{u}$ (cm^{-1}) 2961, 2873, 1677, 1174, 1146, 1130, 701; MS : 301 (M^+, 67), 259 (14), 217 (71), 188 (86), 148 (63), 120(64), 104(49), 57(100); GC R_t = 9.36 min.

(4*R*)-2-trifluoromethyl-3-(3,3-dimethylbutanoyl)-4-phenyloxazolidine (2d,3d)

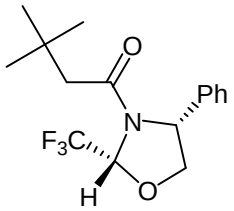
The mixture of diastereomers **1** (1 g, 4.6 mmol) was dissolved in pyridine (24 mL) and 3,3-dimethylbutanoyl chloride (1.16 mL, 8.29 mmol) was rapidly added at room temperature. The solution was stirred for 24h at 40°C and concentrated under reduced pressure. A solution of diethyl ether and dichloromethane (100 mL, Et_2O/CH_2Cl_2: 8/2) and a saturated solution of sodium chloride were added to the residue. The aqueous layer was extracted with diethyl ether (2x100 mL) and the combined organic layers were dried over $MgSO_4$. The resulting crude mixture was purified by flash column chromatography (cyclohexane/ethyl acetate : 92.5/7.5) affording pure **2d** (793 mg, 55%) and pure **3d** (486 mg, 33%) (Combined yield: 88%).

(2*S*,4*R*)-2-trifluoromethyl-3-(3,3-dimethylbutanoyl)-4-phenyloxazolidine (2d)



White solid; mp = 91°C; $[a]_D^{23}$ = -49.3 (c = 3.80; $CHCl_3$); R_f = 0.49 (cyclohexane/ethyl acetate : 90/10); ^{1}H NMR (400 MHz, $CDCl_3$) **:** δ 0.95 (s, 9H), 1.69 (d, 1H, ^2J = 14.0 Hz), 2.06 (d, 1H, ^2J = 14.0 Hz), 4.06 (d, 1H, ^2J = 8.7 Hz), 4.70 (dd, 1H, ^2J = 8.7 Hz, ^3J = 6.4 Hz), 4.99 (d, 1H, ^3J = 6.4 Hz), 6.18 (q, 1H, $^3J_{H\text{-}F}$ = 5.0 Hz), 7.17-7.39 (m, 5H); ^{19}F NMR (376.2 MHz, $CDCl_3$) : δ -80.79 (d, 3 F, $^3J_{H\text{-}F}$ = 5.0 Hz); ^{13}C NMR (100.5 MHz, $CDCl_3$) : δ 29.7, 31.8, 48.6, 61.3, 76.7, 84.9 (q, CH, $^2J_{C\text{-}F}$ = 34.5 Hz), 123.5 (q, C, $^1J_{C\text{-}F}$ = 289.5 Hz), 125.7, 128.6, 129.5, 141.7, 172.5; IR : $\bar{u}$ (cm^{-1}) 2969, 2908, 2872, 1654, 1399, 1381, 1171, 1146, 700; MS : 315 (M^+, 5), 300(12), 259 (100), 246 (5), 201(10), 173 (11), 148 (49), 120(17), 99(39), 57(55); GC R_t = 9.30 min.

(2*R*,4*R*)-2-trifluoromethyl-3-(3,3-dimethylbutanoyl)-4-phenyloxazolidine (3d)



Yellow oil; $[a]_D^{23}$ = -86.22 (c = 3.00; $CHCl_3$); R_f = 0.26 (cyclohexane/ethyl acetate: 90/10); ^1H NMR (400 MHz, $CDCl_3$) **:** δ 0.91 (s, 9H), 2.05 (m, 2H), 4.12 (t, 1H, *J* = 9.2 Hz), 4.62 (t, 1H, *J* = 9.2 Hz), 4.97 (m, 1H), 5.94 (m, 1H), 7.24-7.31 (m, 5H); ^{19}F NMR (376.2 MHz, $CDCl_3$) : δ -80.41 (s, 3 F); ^{13}C NMR (100.5 MHz, $CDCl_3$) : δ 29.6, 31.3, 46.1, 61.6, 76.0, 85.4 (q, CH, $^2J_{C\text{-}F}$ = 35.5 Hz), 123.4 (q, C, $^1J_{C\text{-}F}$ = 287.5 Hz), 126.3, 128.6, 129.3, 137.9, 173.8; IR : $\bar{u}$ (cm^{-1}) 2955, 2907, 2870, 1677, 1363, 1269, 1176, 1144, 701; MS : 315 (M^+, 54), 300(21), 259 (53), 217 (76), 201(13), 173 (17), 148 (40), 120(31), 99(81), 57(100); GC R_t = 9.43 min.

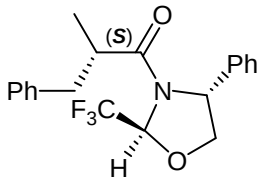
General procedure for alkylation reactions:

The oxazolidine (**2a**,**2b**,**2c**,**3a**,**3b**: 1.19 mmol) was dissolved in THF (10 mL) under argon atmosphere. The solution was cooled down to -78°C and NaHMDS was added dropwise (1.12 mL, 2M in THF, 2.24 mmol). The reaction mixture was stirred for 1.5h at this temperature and the electrophile (2.24 mmol) was added slowly. The reaction mixture was stirred for 2 additional hours at -78°C, quenched with a saturated NH_4Cl solution (15 mL) extracted with diethyl ether (2x30 mL) and dichloromethane (30 ml). The combined organic layers were dried over $MgSO_4$, evaporated under reduced pressure and the resulting crude mixture was purified by filtration through a short pad of silica gel (20g).

General procedure for the epimerization of alkylated compounds

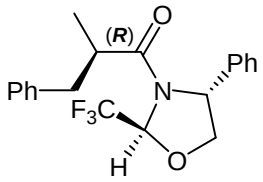
Sodium (47 mg, 2.06 mmol) was added at 0°C to methanol (6 mL) under argon atmosphere. After complete reaction of the metal, the solvent was evaporated under reduced pressure, the residue was taken up with toluene (4 mL), the oxazolidine (**4a**, **5a**, **6a, 8a, 9a**) was added (0.41 mmol) and the reaction mixture was stirred at reflux for 19 h. The solvent was evaporated to dryness and the residue taken up with diethyl ether (15 mL). A saturated NH_4Cl solution was added (10 mL) and the reaction mixture extracted with diethyl ether (2x20 mL). The combined organic layers were dried over $MgSO_4$ and evaporated under reduced pressure. The resulting crude mixture was purified by filtration through a short pad of silica gel (16g) affording the two diastereomers (78%-97%).

(2*S*,4*R*)-2-trifluoromethyl-3-[(*S*)-2-methyl-3-phenylpropanoyl]-4-phenyloxazolidine ((*S*)-4a)



Obtained following the general procedure from the sodium enolate of **2a** and benzyl bromide after filtration through a short pad of silica gel (cyclohexane/ethyl acetate: 90/10) as a white solid (368 mg, 85%); mp = 89°C; $[a]_D^{23}$ = -73.3 (c = 2.08; $CHCl_3$); R_f = 0.17 (cyclohexane/ethyl acetate : 95/5); ^{1}H NMR (250 MHz, $CDCl_3$) **:** δ 0.59 (d, 3H, ^3J = 6.5 Hz), 2.52 (ddq, 1H, ^3J = 9.8 Hz, ^3J = 6.5 Hz, ^3J = 5.0 Hz), 2.63 (dd, 1H, ^2J = 13.1 Hz, ^3J = 5.0 Hz), 2.84 (dd, 1H, ^2J = 13.1 Hz, ^3J = 9.8 Hz), 3.87 (d, 1H, ^2J = 8.1 Hz), 4.31 (dd, 1H, ^2J = 8.1 Hz, ^3J = 6.4 Hz), 4.31 (d, 1H, ^3J = 6.4 Hz), 6.04 (q, 1H, $^3J_{H\text{-}F}$ = 5.2 Hz), 7.10-7.36 (m, 10H); ^{19}F NMR (235.35 MHz, $CDCl_3$) : δ -77.39 (d, 3 F, $^3J_{H\text{-}F}$ = 5.2 Hz); ^{13}C NMR (62.9 MHz, $CDCl_3$) : δ 16.5, 42.4, 43.0, 60.6, 76.4, 85.1 (q, CH, $^2J_{C\text{-}F}$ = 35.0 Hz), 123.4 (q, C, $^1J_{C\text{-}F}$ = 290.0 Hz), 125.8, 126.8, 128.7, 129.1, 129.6, 139.5, 142.1, 176.6; IR : $\bar{u}$ (cm^{-1}) 3084-3030, 2979-2907, 1660, 1453, 1403, 1282, 1180, 700; MS : 363 (M^+, 30), 348 (5), 148 (20), 119 (63), 104 (40), 91 (100); GC R_t = 12.10 min; Anal. **:** Calc. for $C_{20}H_{20}F_3NO_2$ C, 66.11; H, 5.55; N, 3.85. Found: C, 65.97; H, 5.50; N, 3.96.

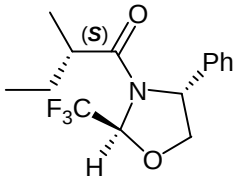
(2*S*,4*R*)-2-trifluoromethyl-3-[(*R*)-2-methyl-3-phenylpropanoyl]-4-phenyloxazolidine ((*R*)-4a)



Obtained following the general procedure from the sodium enolate of **2b** and methyl iodide after filtration through a short pad of silica gel (cyclohexane/ethyl acetate : 95/5) as a yellow oil (337 mg, 78%); $[a]_D^{23}$ = -111.7 (c = 2.00 ; $CHCl_3$); R_f = 0.17 (Cyclohexane / Ethyl acetate: 95/5); ^{1}H NMR (250 MHz, $CDCl_3$) : δ 1.14 (d, 3H, ^3J = 6.6 Hz), 2.47 (m, 3H, H-9), 4.08 (d, 1H, ^2J = 8.6 Hz), 4.70 (dd, 1H, ^2J = 8.6 Hz, ^3J = 6.6 Hz), 5.01 (d, 1H, ^3J = 6.6 Hz), 6.19 (q, 1H, $^3J_{H\text{-}F}$ = 5.1 Hz), 6.55 (d, 2H), 7.08-7.40 (m, 8H); ^{19}F NMR (235.35 MHz, $CDCl_3$) **:** δ -77.89 (d, 3 F, $^3J_{H\text{-}F}$ = 5.1 Hz); ^{13}C NMR (62.9 MHz, $CDCl_3$) : δ 17.8, 37.8, 41.6, 60.6, 77.2, 85.3 (q, CH, $^2J_{C\text{-}F}$ = 35.1 Hz), 123.5 (q, C, $^1J_{C\text{-}F}$ = 289.0 Hz), 125.6, 126.0, 128.2, 128.7, 129.1, 129.7, 139.3, 142.1, 176.9; IR : $\bar{u}$ (cm^{-1}) 3063-3029, 2972-2878, 1675, 1395, 1280, 1206, 1179, 1148, 701; MS : 363 (M^+,

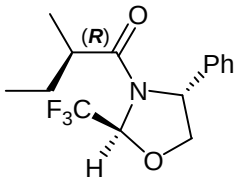
50), 348 (15), 148 (19), 119 (60), 104 (37), 91 (100); GC R_t = 12.27 min; Anal. Calc. for $C_{20}H_{20}F_3NO_2$: C, 66.11; H, 5.55; N, 3.85. Found: C, 66.12; H, 5.51; N, 3.89.

(2*S*,4*R*)-2-trifluoromethyl-3-[(*S*)-2-methylbutanoyl]-4-phenyloxazolidine ((*S*)-5a)



Obtained following the general procedure from the sodium enolate of **2a** and ethyl iodide after filtration through a short pad of silica gel (cyclohexane/ethyl acetate : 90/10) as a yellow solid (279 mg, 78%); mp = 57°C; $[a]_D^{23} = -48.2$ (c = 0.8; $CHCl_3$); R_f = 0.36 (cyclohexane/ethyl acetate : 95/5); ^{1}H NMR (250 MHz, $CDCl_3$) **:** δ 0.45 (d, 3H, ^3J = 6.6 Hz), 0.91 (t, 3H, ^3J = 7.4 Hz), 1.43 (dqd, 1H, ^2J = 14.3 Hz, ^3J = 7.4 Hz, ^3J = 5.8 Hz), 1.61 (ddq, 1H, ^2J = 14.3 Hz, ^3J = 8.1 Hz, ^3J = 7.4 Hz), 2.22 (dqd, 1H, ^3J = 8.1 Hz, ^3J = 6.6 Hz, ^3J = 5.8 Hz), 4.09 (d, 1H, ^2J = 8.4 Hz), 4.70 (dd, 1H, ^2J = 8.6 Hz, ^3J = 8.4 Hz), 5.03 (d, 1H, ^3J = 8.4 Hz), 6.18 (q, 1H, $^3J_{H\text{-}F}$ = 5.2 Hz), 7.15-7.40 (m, 5H); ^{19}F NMR (235.35 MHz, $CDCl_3$) : δ -78.06 (d, 3 F, $^3J_{H\text{-}F}$ = 5.2 Hz); ^{13}C NMR (62.9 MHz, $CDCl_3$) **:** δ 11.5, 15.5, 28.9, 41.7, 60.9, 76.5, 84.9 (q, CH, $^2J_{C\text{-}F}$ = 35.0 Hz), 123.5 (q, C, $^1J_{C\text{-}F}$ = 289.0 Hz), 125.6, 128.6, 129.4, 141.9, 177.5; IR **:** $\bar{u}$ (cm^{-1}) 3068-3034, 2971-2879, 1661, 1461, 1404, 1274, 1147, 700; MS **:** 301 (M^+, 14), 273 (79), 232 (52), 186 (15), 148 (100), 120 (25), 104 (27), 85 (41), 57 (77); GC R_t = 9.43 min; Anal. Calc. for $C_{15}H_{18}F_3NO_2$**:** C, 59.79; H, N, 6.02, 4.65. Found: C, 59.90; H, 6.06, N, 4.64.

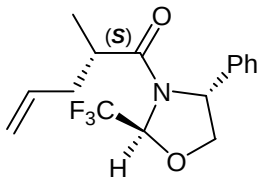
(2*S*,4*R*)-2-trifluoromethyl-3-[(*R*)-2-methylbutanoyl]-4-phenyloxazolidine ((*R*)-5a)



Obtained from epimerization of **(*S*)-5a.** R_f = 0.36 (cyclohexane/ethyl acetate : 95/5); ^{1}H NMR (250 MHz, $CDCl_3$) **:** δ 0.26 (t, 3H, ^3J = 7.4 Hz), 1.15 (d, 3H, ^3J = 7.0 Hz), 1.43 (m, 1H), 1.61 (m, 1H), 2.22 (m, 1H), 4.09 (m, 1H), 4.70 (m, 1H), 4.97 (m, 1H), 6.18 (q, 1H, $^3J_{H\text{-}F}$ = 5.2 Hz, H-2), 7.15-7.40 (m, 5H, H-Ar); ^{19}F NMR (235.35 MHz, $CDCl_3$) **:** δ -78.06 (d, 3 F, $^3J_{H\text{-}F}$ = 5.2 Hz, CF_3);

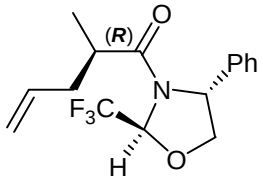
^{13}C NMR (62.9 MHz, $CDCl_3$) **:** δ 11.4, 18.7, 26.9, 41.3, 60.5, 76.5, 85.1 (q, CH, $^2J_{C\text{-}F}$ = 35.0 Hz), 123.5 (q, C, $^1J_{C\text{-}F}$ = 289.0 Hz), 125.6, 128.6, 129.4, 142.2, 177.5; MS : 301 (M^+, 14), 273 (57), 232 (43), 186 (11), 148 (83), 120 (19), 104 (27), 85 (44), 57 (100); GC R_t = 9.38 min;

(2*S*,4*R*)-2-trifluoromethyl-3-[(*S*)-2-methylpent-4-enoyl]-4-phenyloxazolidine ((*S*)-6a)



Obtained following the general procedure from the sodium enolate of **2a** and allyl bromide after filtration through a short pad of silica gel (cyclohexane/ethyl acetate : 90/10) as a colorless oil (328 mg, 88%). $[a]_D^{23}$ = -65.79 (c = 2.15; $CHCl_3$); R_f = 0.43 (cyclohexane/ethyl acetate: 90/10); ^{1}H NMR (250 MHz, $CDCl_3$) **:** δ 0.48 (d, 3H, ^3J = 6.1 Hz) 2.11 (dd, 1H, ^2J = 17.1 Hz, ^3J = 10.2 Hz), 2.32 (dd, 1H, ^2J = 17.1 Hz, ^3J =10.2 Hz), 2.32 (m, 1H), 4.08 (d, 1H, ^2J = 8.7 Hz), 4.69 (dd, 1H, ^2J = 8.7 Hz, ^3J = 6.6 Hz, H-5), 5.05 (m, 2H), 5.05 (d, 1H, ^3J = 6.6 Hz), 5.75 (dtd, 1H, ^3J = 13.9 Hz , ^3J = 10.2 Hz , ^3J = 6.8 Hz), 6.16 (q, 1H, $^3J_{H\text{-}F}$ = 5.2 Hz), 7.18-7.39 (m, 5H); ^{19}F NMR (235.35 MHz, $CDCl_3$) : δ -77.89 (d, 3 F, $^3J_{H\text{-}F}$ = 5.2 Hz); ^{13}C NMR (62.9 MHz, $CDCl_3$) : δ 15.6, 40.1, 40.4, 60.9, 76.9, 85.05 (q, CH, $^2J_{C\text{-}F}$ = 35.0 Hz), 117.6, 123.6 (q, C, $^1J_{C\text{-}F}$ = 289.0 Hz), 125.9, 128.8, 129.6, 134.9, 142.0, 176.9; IR : $\bar{u}$ (cm^{-1}) 3069-3036, 2979-2912, 1676, 1392, 1280, 1179, 1147, 702; MS : 313 (M^+, 35), 298 (3), 271 (42), 244 (9), 148 (57), 120 (19), 104 (45), 91 (18), 69 (100); GC R_t = 9.74 min; Anal. Calc. for $C_{16}H_{18}F_3NO_2$: C, 61.33; H, 5.79; N, 4.47. Found: C, 61.41; H, 5.69; N, 4.59.

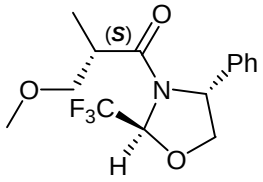
(2*S*,4*R*)-2-trifluoromethyl-3-[(*R*)-2-methylpent-4-enoyl]-4-phenyloxazolidine ((*R*)-6a)



Obtained from epimerization of **(*S*)-6a.** ^{1}H NMR (250 MHz, $CDCl_3$) : δ 1.15 (d, 3H, ^3J = 6.95 Hz), 1.79 (m, 2H), 2.32 (m, 1H), 4.08 (m, 1H), 4.69 (m, 1H), 5.05 (m, 2H), 5.05 (m, 1H), 5.75

(m, 1H), 6.16 (q, 1H, $^{3}J_{H\text{-}F}$ = 5.0 Hz), 7.18-7.39 (m, 5H); ^{19}F NMR (235.35 MHz, $CDCl_3$) **:** δ -78.11 (d, 3 F, $^{3}J_{H\text{-}F}$ = 5.0 Hz); ^{13}C NMR (62.9 MHz, $CDCl_3$) **:** δ 18.3, 36.2, 39.9, 60.7, 76.9, 85.3 (q), 116.8, 123.6 (q), 125.9, 128.8, 129.6, 135.5, 142.0, 177.1; GC R_t = 9.74 min.

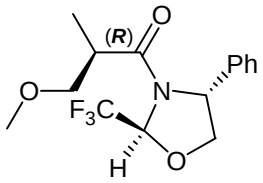
(2*S*,4*R*)-2-trifluoromethyl-3-[(*S*)-3-methoxy-2-methylpropanoyl]-4-phenyloxazolidine ((*S*)-7a)



The oxazolidine **2a** (325 mg, 1.19 mmol) was dissolved in THF (9 mL) under argon atmosphere and DMPU (1 mL) was added. The solution was cooled down to -78°C and NaHMDS was added dropwise (1.12 mL, 2M in THF, 2.24 mmol). The reaction mixture was stirred for 1h at this temperature and methoxymethyl bromide (179 µL, 2.24 mmol) was added slowly. The reaction mixture was stirred for 5 additional hours at -78°C, quenched with a saturated NH_4Cl solution (15 mL) extracted with diethyl ether (2x30 mL) and dichloromethane (30 ml). The combined organic layers were dried over $MgSO_4$, evaporated under reduced pressure and the resulting crude mixture was purified by column chromatography (cyclohexane/ethyl acetate : 95/05) to afford a 95:5 mixture of **(*S*)-7a** and **(*R*)-7a** (186 mg, 50%) as a colorless oil.

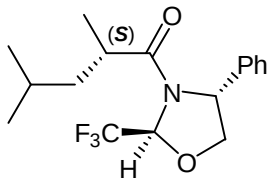
R_f = 0.41 (cyclohexane/ethyl acetate : 90/10); ^{1}H NMR (250 MHz, $CDCl_3$) **:** δ 0.45 (d, 3H, ^{3}J = 6.6 Hz), 2.60 (ddd, 1H, ^{3}J = 9.0 Hz, ^{3}J = 6.6 Hz, ^{3}J = 5.6 Hz), 3.30 (s, 3H), 3.31 (dd, 1H, ^{2}J = 16.0 Hz, ^{3}J = 5.6 Hz), 3.42 (dd, 1H, ^{2}J = 16.0 Hz, ^{3}J = 9.0 Hz), 4.10 (d, 1H, ^{2}J = 8.1 Hz), 4.70 (dd, 1H, ^{2}J = 8.1 Hz, ^{3}J = 6.6 Hz), 5.18 (d, 1H, ^{3}J = 6.6 Hz), 6.15 (q, 1H, $^{3}J_{H\text{-}F}$ = 5.0 Hz), 7.21-7.41 (m, 5H); ^{19}F NMR (235.35 MHz, $CDCl_3$) **:** δ -77.78 (d, 3 F, $^{3}J_{H\text{-}F}$ = 5.0 Hz); ^{13}C NMR (62.9 MHz, $CDCl_3$) **:** δ 12.1, 40.7, 59.0, 60.4, 76.4, 76.5, 85.1 (q, CH, $^{2}J_{C\text{-}F}$ = 35.0 Hz), 125.7 (q, C, $^{1}J_{C\text{-}F}$ = 289.3 Hz), 125.8, 128.5, 129.3, 142.1, 175.5; IR : $\bar{u}$ (cm^{-1}) 3066-3033, 2981-2828, 1666, 1457, 1412, 1279, 1145, 703; MS **:** 317 (M^{+}, 15), 302 (4), 286 (3), 248 (15), 216 (100), 173 (7), 148 (78), 120 (23), 104 (45), 73 (81); GC R_t = 9.71 min.

(2*S*,4*R*)-2-trifluoromethyl-3-[(*R*)-3-methoxy-2-methylpropanoyl]-4-phenyloxazolidine ((*R*)-7a)



Obtained from the sodium enolate of **2a** and methoxymethyl bromide as the minor diastereomer. Purification by column chromatography (cyclohexane/ethyl acetate : 95/05); ^{1}H NMR (250 MHz, $CDCl_3$) : δ 1.05 (d, 3H, ^{3}J = 6.3 Hz), 2.60 (m, 1H), 3.30 (s, 3H), 3.31 (m, 1H), 3.42 (m, 1H), 4.10 (m, 1H), 4.65 (m, 1H), 5.12 (m, 1H), 6.15 (q, 1H, $^{3}J_{H\text{-}F}$ = 4.9 Hz, H-2), 7.21-7.41 (m, 5H); ^{19}F NMR (235.35 MHz, $CDCl_3$) : δ -78.33 (d, 3 F, $^{3}J_{H\text{-}F}$ = 4.9 Hz); ^{13}C NMR (62.9 MHz, $CDCl_3$) **:** δ 13.0, 39.7, 58.6, 60.7, 75.3, 76.8, 85.1 (q), 125.7 (q), 126.2, 127.5, 128.9, 141.2, 173.0; MS **:** 317 (M^+, 5), 302 (54), 286 (24), 248 (6), 216 (39), 173 (8), 148 (59), 120 (20), 104 (70), 73 (100); GC R_t = 9.75 min.

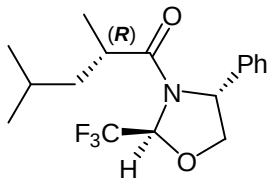
(2*S*,4*R*)-2-trifluoromethyl-3-[(*S*)-2,4-dimethylpentanoyl]-4-phenyloxazolidine ((*S*)-8a)



The oxazolidine **2a** (325 mg, 1.19 mmol) was dissolved in THF (8 mL) under argon atmosphere. The solution was cooled down to -78°C and NaHMDS was added dropwise (1.12 mL, 2M in THF, 2.24 mmol). The reaction mixture was stirred for 2h at this temperature and isobutyl iodide (0.567 ml, 4.76 mmol) was added slowly. The reaction mixture was stirred for 24 hours at -55°C, quenched with a saturated NH_4Cl solution (15 mL) extracted with diethyl ether (2x30 mL) and dichloromethane (30 ml). The combined organic layers were dried over $MgSO_4$, evaporated under reduced pressure and the resulting crude mixture was purified by filtration through a short pad of silica gel (20g, cyclohexane/ethyl acetate: 90/10) to afford **(*S*)-8a** as a yellow solid (290 mg, 74%); mp = 71°C; $[a]_D^{23}$ =-50.55 (c = 2.85; $CHCl_3$); R_f = 0.45 (cyclohexane/ethyl acetate : 90/10); ^{1}H NMR (400 MHz, $CDCl_3$) **:** δ 0.39 (d, 3H, ^{3}J = 6.8 Hz), 0.86 (d, 3H, ^{3}J = 6.0 Hz), 0.94 (d, 3H, ^{3}J = 6.4 Hz), 1.19 (ddd, 1H, ^{2}J = 20.1 Hz, ^{3}J = 13.3 Hz, ^{3}J = 6.8 Hz), 1.51 (ddd, 1H, ^{2}J = 20.1 Hz, ^{3}J = 12.8 Hz, ^{3}J = 6.8 Hz), 2.34 (sext, 1H, ^{3}J = 6.8 Hz), 4.09 (d, 1H, ^{2}J = 8.7 Hz), 4.71

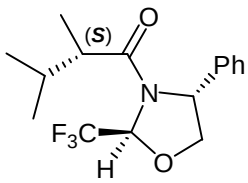
(dd, 1H, ^2J = 8.7 Hz, ^3J = 6.9 Hz), 5.01 (d, 1H, ^3J = 6.9 Hz), 6.18 (q, 1H, $^3J_{H\text{-}F}$ = 5.0 Hz), 7.10-7.33 (m, 5H); ^{19}F NMR (376.2 MHz, $CDCl_3$) : δ -80.91 (d, 3 F, $^3J_{H\text{-}F}$ = 5.0 Hz); ^{13}C NMR (100.5 MHz, $CDCl_3$) : δ 15.6, 22.7, 22.9, 25.5, 37.9, 45.1, 60.9, 76.2, 84.9 (q, CH, $^2J_{C\text{-}F}$ = 34.5 Hz), 123.5 (q, C, $^1J_{C\text{-}F}$ = 289.4 Hz), 125.8, 128.7, 129.5, 142.0, 177.9; IR : $\bar{u}$ (cm^{-1}) 2972, 2960, 2938, 1660, 1389, 1267, 1176, 1146, 1100, 700; MS : 329 (M^+, 1), 314 (3), 286 (3), 273 (100), 260 (4), 204 (4), 173(5), 148 (47), 113 (19), 85 (99); GC R_t = 9.75 min.

(2*S*,4*R*)-2-trifluoromethyl-3-[(*R*)-2,4-dimethylpentanoyl]-4-phenyloxazolidine ((*R*)-8a)



Obtained from epimerization of **(*S*)-8a.** ^{19}F NMR (376.2 MHz, $CDCl_3$) : δ -80.67 (d, 3 F, $^3J_{H\text{-}F}$ = 5.2 Hz); MS : 329 (M^+, 1), 314 (4), 286 (5), 273 (100), 260 (2), 204 (6), 173(4), 148 (31), 113 (12), 85 (88); GC R_t = 9.87 min.

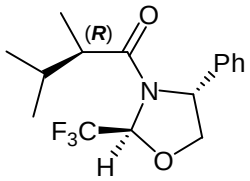
(2*S*,4*R*)-2-trifluoromethyl-3-[(*S*)-2,3-dimethylbutanoyl]-4-phenyloxazolidine ((*S*)-9a)



The oxazolidine **2a** (325 mg, 1.19 mmol) was dissolved in THF (10 mL) under argon atmosphere. The solution was cooled down to -78°C and NaHMDS was added dropwise (1.12 mL, 2M in THF, 2.24 mmol). The reaction mixture was stirred for 2h at this temperature and isopropyl iodide (0.952 ml, 9.52 mmol) was added slowly. The reaction mixture was stirred for 35 hours at -55°C, quenched with a saturated NH_4Cl solution (15 mL) extracted with diethyl ether (2x30 mL) and dichloromethane (30 ml). The combined organic layers were dried over $MgSO_4$, evaporated under reduced pressure and the resulting crude mixture was purified by filtration through a short pad of silica gel (20g, cyclohexane/ethyle acetate: 85/15) to afford **(*S*)-9a** as a white solid (284 mg, 76%); mp = 85°C; $[a]_D^{23}$ =-42.27 (c = 3.10; $CHCl_3$); R_f = 0.55 (cyclohexane/ethyl acetate: 80/20); ^{1}H NMR (400 MHz, $CDCl_3$) **:** δ 0.41 (d, 3H, ^3J = 6.9 Hz),

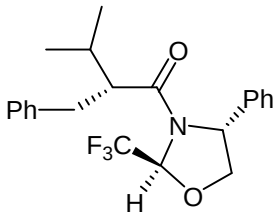
0.88 (d, 3H, ^3J = 6.4 Hz), 0.94 (d, 3H, ^3J = 6.9 Hz), 1.78 (m, 1H), 2.00 (p, 1H, ^3J = 6.9 Hz), 4.09 (d, 1H, ^2J = 8.7 Hz), 4.71 (dd, 1H, ^2J = 8.7 Hz, ^3J = 6.4 Hz), 5.03 (d, 1H, ^3J = 6.4 Hz), 6.18 (q, 1H, $^3J_{H\text{-}F}$ = 5.0 Hz), 7.20-7.39 (m, 5H); ^{19}F NMR (376.2 MHz, $CDCl_3$) : δ -80.55 (d, 3 F, $^3J_{H\text{-}F}$ = 5.0 Hz); ^{13}C NMR (100.5 MHz, $CDCl_3$) : δ 13.0, 19.7, 20.4, 32.8, 46.7, 61.0, 76.5, 84.8 (q, CH, $^2J_{C\text{-}F}$ = 34.5 Hz), 123.5 (q, C, $^1J_{C\text{-}F}$ = 288.5 Hz), 125.9, 128.6, 129.4, 141.9, 177.1; IR : $\bar{u}$ (cm^{-1}) 2973, 2944, 2912, 1656, 1389, 1174, 1144, 700; MS : 315 (M^+, 3), 300 (1), 273 (100), 246 (7), 204(5), 148 (44), 120 (14), 99 (30), 71 (92); GC R_t = 9.52 min.

(2*S*,4*R*)-2-trifluoromethyl-3-[(*R*)-2,3-dimethylbutanoyl]-4-phenyloxazolidine ((*R*)-9a)



Obtained from epimerization of **(*S*)-9a.** ^{1}H NMR (400 MHz, $CDCl_3$) **:** δ 0.14 (d, 3H, ^3J = 6.4 Hz), 0.65 (d, 3H, ^3J = 6.9 Hz), 1.16 (d, 3H, ^3J = 7.3 Hz), 1.65 (m, 1H), 2.00 (m, 1H), 4.09 (m, 1H), 4.68 (m, 1H), 4.91 (d, 1H, ^3J = 6.4 Hz), 6.18 (1H), 7.21-7.39 (m, 5H); ^{19}F NMR (376.2 MHz, $CDCl_3$) : δ -80.34 (d, 3 F, $^3J_{H\text{-}F}$ = 4.8 Hz); ^{13}C NMR (100.5 MHz, $CDCl_3$) : δ 16. 7, 19.0, 21.0, 29.0, 46.3, 60.3, 76.6, 84.8, 123.5, 126.1, 128.5, 129.3, 142.2, 177.2; MS : 315 (M^+, 3), 300 (2), 273 (43), 246 (4), 204(4), 148 (32), 120 (10), 99 (26), 71 (100); GC R_t = 9.50 min.

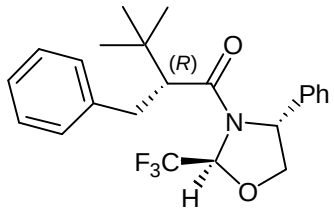
(2*S*,4*R*)-2-trifluoromethyl-3-[(*R*)-2-isopropyl-3-phenylpropanoyl]-4-phenyloxazolidine ((*R*)-4c)



Obtained following the general procedure from the sodium enolate of **2c** and benzyl bromide. Purification by column chromatography (cyclohexane/ethyl acetate : 98/2) affords **(*R*)-4c** as a white solid (331 mg, 71%); mp = 41°C; $[a]_D^{23}$ = -57.2 (c = 2.60; $CHCl_3$); R_f = 0.77 (Cyclohexane / Ethyl acetate: 90/10); ^{1}H NMR (400 MHz, $CDCl_3$) **:** δ 0.22 (d, 3H, ^3J = 6.9 Hz), 0.79 (d, 3H, ^3J =

6.9 Hz), 1.57 (sext, 1H, ^3J = 6.9 Hz), 2.22 (ddd, 1H, ^3J = 11.5 Hz , ^3J = 6.9 Hz, ^3J = 2.8 Hz), 2.67 (dd, 1H, ^2J = 12.8 Hz , ^3J = 11.5 Hz), 2.94 (dd, 1H, ^2J = 12.8 Hz , ^3J = 2.8 Hz), 3.62 (d, 1H, ^3J = 6.4 Hz), 3.77 (d, 1H, ^2J = 8.7 Hz), 4.12 (dd, 1H, ^2J = 8.7 Hz , ^3J = 6.4 Hz), 5.99 (q, 1H, $^3J_{H\text{-}F}$ = 5.5 Hz), 7.06-7.36 (m, 10H); ^{19}F NMR (376.2 MHz, $CDCl_3$) : δ -78.88 (d, 3 F, $^3J_{H\text{-}F}$ = 5.5 Hz); ^{13}C NMR (100.5 MHz, $CDCl_3$) : δ 19.3, 20.9, 29.5, 37.4, 54.4, 59.8, 76.2, 85.2 (q, CH, $^2J_{C\text{-}F}$ = 34.5 Hz), 123.3 (q, C, $^1J_{C\text{-}F}$ = 290.4 Hz), 126.4, 126.6, 128.7, 129.2, 129.3, 140.0, 142.2, 175.6; IR : $\bar{u}$ (cm^{-1}) 2965, 2904, 1658, 1404, 1263, 1141, 849, 700; MS : 391 (M^+, 4), 348 (20), 300 (3), 175 (3), 147 (14), 131 (26), 105 (23), 91(100); GC R_t = 12.49 min.

(2*S*,4*R*)-2-trifluoromethyl-4-phenyl-3-[(*R*)-2-*tert*-butyl-3-phenylpropanoyl]-oxazolidine ((*R*)-4d)



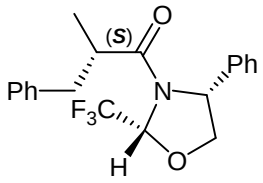
The oxazolidine **2d** (375 mg, 1.19 mmol) was dissolved in THF (10 mL) under argon atmosphere. The solution was cooled down to -78°C and NaHMDS was added dropwise (1.12 mL, 2M in THF, 2.24 mmol). The reaction mixture was stirred for 2h at this temperature and benzyl bromide (0.569 ml, 4.76 mmol) was added slowly. The reaction mixture was stirred for 35 hours at -55°C, quenched with a saturated NH_4Cl solution (15 mL) extracted with diethyl ether (2x30 mL) and dichloromethane (30 ml). The combined organic layers were dried over $MgSO_4$, evaporated under reduced pressure and the resulting crude mixture was purified by filtration through a short pad of silica gel (20g, cyclohexane/ethyl acetate : 98/02) to afford **(*R*)-4d** as a white solid (270 mg, 56%); mp = 126°C; $[a]_D^{23}$ =-38.37 (c = 2.05; $CHCl_3$); R_f = 0.59 (cyclohexane /ethyl acetate: 90/10); ^{1}H NMR (400 MHz, $CDCl_3$) **:** δ 0.62 (s, 9H), 2.33 (dd, 1H, ^3J = 11.45 Hz, ^3J = 1.83 Hz), 2.72 (dd, 1H, ^2J = 12.8 Hz , ^3J = 11.5 Hz), 3.00 (dd, 1H, ^2J = 12.8 Hz , ^3J = 1.8 Hz), 3.23 (d, 1H, ^3J = 6.0 Hz), 3.73 (d, 1H, ^2J = 8.7 Hz), 4.02 (dd, 1H, ^2J = 8.7 Hz , ^3J = 6.0 Hz), 5.98 (q, 1H, $^3J_{H\text{-}F}$ = 5.0 Hz), 7.02-7.38 (m, 10H); ^{19}F NMR (376.2 MHz, $CDCl_3$) : δ -78.07 (d, 3 F, $^3J_{H\text{-}F}$ = 5.0 Hz); ^{13}C NMR (100.5 MHz, $CDCl_3$) : δ 27.4, 33.5, 36.9, 56.4, 59.5, 76.3, 85.2 (q, CH, $^2J_{C\text{-}F}$ = 34.5 Hz), 123.4 (q, C, $^1J_{C\text{-}F}$ = 290.4 Hz), 126.7, 126.9, 128.7, 129.2,

129.3, 140.6, 142.2, 175.3; IR : $\bar{u}$ (cm^{-1}) 2966, 2954, 1672, 1173, 1145, 842, 702; MS : 405 (M^+, 2), 390 (2), 348 (13), 258 (11), 189 (10), 160 (63), 131 (17), 105 (77), 91(100); GC R_t = 12.69 min.

(2*R*,4*R*)-2-trifluoromethyl-3-[(*S*)-2-methyl-3-phenylpropanoyl]-4-phenyloxazolidine (10).

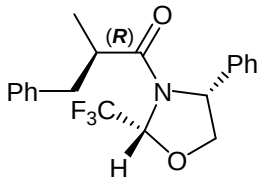
Obtained following the general procedure from the sodium enolate of **3b** and methyl iodide. Purification by column chromatography (cyclohexane/ethyl acetate : 90/10) affords **(*S*)-10** (140 mg, 33%) and **(*S*)-10** (140 mg, 33%). The reaction from the sodium enolate of **3a** and benzyl bromide gave **(*S*)-10** and **(*R*)-10** in 55% yield with a 69:33 diastereomeric ratio.

(2*R*,4*R*)-2-trifluoromethyl-3-[(*S*)-2-methyl-3-phenylpropanoyl]-4-phenyloxazolidine ((*S*)-10).



Yellow solid; ^{1}H NMR (250 MHz, $CDCl_3$) : δ 0.97 (d, 3H, ^3J = 5.7 Hz), 2.57 (m, 1H), 2.57 (m, 1H), 2.93 (m, 1H), 3.83 (dd, 1H, ^2J = 7.8 Hz, ^3J = 7.4 Hz, H-5), 3.95 (dd, 1H, ^2J = 7.8 Hz, ^3J = 7.2 Hz), 4.07 (dd, 1H, ^3J = 7.4 Hz, ^3J = 7.2 Hz), 5.90 (q, 1H, ^3J = 5.4 Hz), 7.12-7.36 (m, 10H); ^{19}F NMR (235.35MHz, $CDCl_3$) : δ -77.75 (d, 3F, $^3J_{H\text{-}F}$ = 5.4 Hz); ^{13}C NMR (62.9 MHz, $CDCl_3$) : δ 18.7, 41.3, 41.8, 60.6, 75.8, 116.5 (q, CH, $^2J_{C\text{-}F}$ = 35.3 Hz), 121.1 (q, C, $^1J_{C\text{-}F}$ = 286.9 Hz), 125.9, 126.9, 128.2, 128.8, 129.3, 129.6, 137.9, 139.8, 178.3; MS : 363 (M^+, 40), 265 (8), 250 (9), 216 (6), 148 (16), 131 (8), 119 (56), 104 (24), 91 (100), 77 (8), 65 (7); GC R_t = 11.77 min.

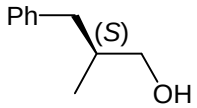
(2*R*,4*R*)-2-trifluoromethyl-3-[(*R*)-2-methyl-3-phenylpropanoyl]-4-phenyloxazolidine ((*R*)-10).



Yellow solid (140 mg, 33%) mp = 51°C; ^{1}H NMR (250 MHz, $CDCl_3$) : δ 1.07 (d, 3H, ^3J = 5.2 Hz), 2.41 (dd, 1H, ^2J = 12.5 Hz, ^3J = 6.9 Hz), 2.60 (m, 1H), 2.85 (dd, 1H, ^2J = 12.5 Hz, ^3J = 5.9

Hz), 4.05 (m, 1H), 4.58 (m, 1H), 5.1 (m, 1H), 5.94 (m, 1H), 6.60-7.30 (m, 10H); ^{19}F NMR (235.35MHz, $CDCl_3$) : δ -77.74 (sl, 3F); ^{13}C NMR (62.9 MHz, $CDCl_3$) : δ 13.6, 40.1, 40.3, 61.2, 75.9, 121.1 (q, CH, $^2J_{C\text{-}F}$ = 35.2 Hz), 123.3 (q, C, $^1J_{C\text{-}F}$ = 286.7 Hz), 125.9, 126.3, 128.3, 129.1, 129.5, 137.9, 139.9, 177.9; IR : $\bar{u}$ (cm^{-1}) 3028, 2979-2912, 1668, 1398, 1288, 1261, 1182, 1143, 697; MS : 363 (M^+, 22), 265 (4), 250 (5), 216 (4), 148 (13), 131 (6), 119 (23), 104 (22), 91 (100), 77 (6), 65 (6); GC R_t = 12.07 min.

Reductive cleavage of (*S*)-4a: (*S*)-2-methyl-3-phenylpropan-1-ol (11).

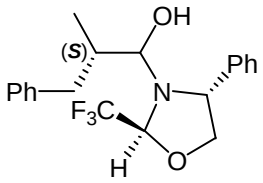


Diisopropylamine (0.85 mL, 6.05 mmol) and *n*-butyllithium (2.17 mL, 2.7 M in hexanes, 5.87 mmol) were added to tetrahydrofuran (5mL) at -78°C under argon atmosphere. The resulting yellow solution was stirred at -78°C for 10 min, then at 0°C for 5 min and finally was cooled down at -78°C. After 5 min, solid 90% borane ammonia complex (364 mg, 1 mmol) was added to the cold reaction solution in one portion. The resulting suspension was warmed to 0°C, stirred at 0°C for 20 min and a solution of **(*S*)-4a** (363 mg, 1mmol) in THF (5 mL) was added. The reaction was stirred for 70 h at 0°C and hydrolyzed with a NH_4Cl saturated solution. The aqueous layer was extracted with diethyl ether (2x20mL) and dichloromethane (20mL). Combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure. The resulting crude material was purified by column chromatography (cyclohexane/ethyl acetate : 90/10 to 80/20) affording **11** as colorless oil (103mg, 69%) and (2*S*,4*R*)-**1a** (106 mg, 49%). Compound **12** resulting from the oxazolidine reduction was also obtained (44 mg, 20%). Spectroscopic data of **11** were in accordance with the literature data.[1] $[a]_D^{18}$ = -12.97 (c = 4.2 ; C_6H_6); Lit. (*R*): $[a]_D^{23}$ = +11.2 (c = 4.2 ; C_6H_6); ^{1}H NMR (250 MHz, $CDCl_3$) : δ 0.90 (d, 3H, ^3J = 6.7 Hz), 1.91 (m, 1H), 2.40 (dd, 1H, ^2J = 13.4 Hz, ^3J = 8.08 Hz), 2.75 (dd, 1H, ^2J = 13.4 Hz, ^3J = 6.3 Hz), 3.44 (dd, 1H, ^2J = 10.6 Hz, ^3J = 6.1 Hz), 3.49 (dd, 1H, ^2J = 10.6 Hz, ^3J = 5.95 Hz), 7.10-7.27 (m, 5H); ^{13}C NMR (62.9 MHz, $CDCl_3$) : δ 16.3, 37.9, 39.8, 67.7, 125.9, 127.9, 129.2, 140.7; MS : 150 (M^+, 26), 132 (26), 117 (68), 104 (5), 91 (100), 77 (8), 65 (13); GC R_t = 6.81 min.

Reductive cleavage of (*S*)-4a: (*S*)-2-methyl-3-phenylpropanal (13).

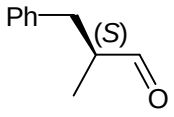
(*S*)-4a (400 mg, 1.1 mmol) was dissolved in anhydrous diethyl ether (10 mL) under argon and the solution was cooled down to -10°C. LAH (167 mg, 4.4 mmol) was added slowly and the mixture was stirred for 1.5 h at -10°C. A NH_4Cl saturated solution (10mL) was added dropwise at -10°C and the solution was vigorously stirred for 2.5 h at ambient temperature. At this stage the intermediate hemiacetal could be detected. The aqueous layer was extracted with diethyl ether (2x20mL) and dichloromethane (20mL). Combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure. The resulting crude material was purified by column chromatography (cyclohexane/diethyl ether : 98/02 to 95/5) affording **13** as colorless oil (116mg, 71%) and (2*S*,4*R*)-**1a** (213 mg, 90%). Spectroscopic data of **13** were identical to those already reported.[1]

Intermediate hemiacetal: (2*R*,4*R*)-2-trifluoromethyl-3-[(2*S*)-1-hydroxy-2-methyl-3-phenylpropyl]-4-phenyloxazolidine



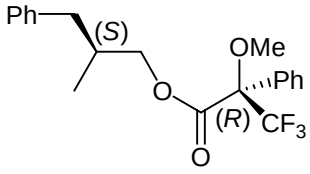
^{1}H NMR (250 MHz, $CDCl_3$) **:** δ 0.78 (d, 3H, ^3J = 6.6 Hz), 1.73 (d, 1H, ^3J = 4.9 Hz), 1.82 (m, 1H), 2.18 (dd, 1H, ^2J = 13.4 Hz, ^3J = 9.1 Hz), 2.86 (dd, 1H, ^2J = 13.4 Hz, ^3J = 4.3 Hz), 3.88 (dd, 1H, ^3J = 9.2 Hz, ^3J = 4.9 Hz), 4.15 (t, 1H, ^2J = 6.8 Hz, ^3J = 6.8 Hz), 4.33 (t, 1H, ^2J = 6.8 Hz, ^3J = 6.8 Hz), 4.59 (t, 1H, ^3J = 6.8 Hz), 5.38 (q, 1H, $^3J_{H\text{-}F}$ = 5.7 Hz), 7.10-7.40 (m, 10H); ^{19}F NMR (235.35 MHz, $CDCl_3$) : δ -79.57 (d, 3 F, $^3J_{H\text{-}F}$ = 5.7 Hz); ^{13}C NMR (62.9 MHz, $CDCl_3$) : δ 15.5, 39.0, 41.1, 64.9, 71.0, 85.4, 85.7 (q, CH, $^2J_{C\text{-}F}$ = 33.8 Hz), 123.7 (q, C, $^1J_{C\text{-}F}$ = 290.0 Hz), 125.9, 126.7, 128.2, 128.3, 128.7, 129.0, 135.7, 140.3.

(*S*)-2-methyl-3-phenylpropanal (13).



^{1}H NMR (250 MHz, $CDCl_3$) **:** δ 1.07 (d, 3H, ^3J = 6.8 Hz), 2.59 (dd, 1H, ^2J = 12.6 Hz, ^3J = 8.20 Hz), 2.65 (m, 1H), 3.08 (dd, 1H, ^2J = 12.6 Hz, ^3J = 4.9 Hz), 7.13-7.31 (m, 5H), 9.70 (d, 1H, ^3J = 1.4 Hz); ^{13}C NMR (62.9 MHz, $CDCl_3$) **:** δ 13.2, 36.7, 48.1, 126.5, 128.5, 129.1, 138.9, 204.5.

(2*R*)-[(*S*)-2-methyl-3-phenylpropyl]-3,3,3-trifluoro-2-methoxy-2-phenylpropanoate (Mosher ester).

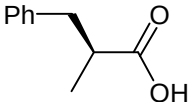


A 10ml round-bottomed flask was charged with (trifluoromethyl)phenylacetic acid (40 mg, 0.17 mmol) and toluene (2 ml). The resulting solution was concentrated under reduced pressure and anhydrous dichloromethane (1 ml) was added under argon. To the resulting solution was added sequentially oxalyl chloride (19µL, 0.22 mmol) and anhydrous DMF (2µL, 0.026 mmol). The latter addition caused bubbling which persists for 10 min. The mixture was stirred for 20 min at room temperature before dichloromethane and excess of oxalyl chloride was removed under vacuum (0.1 mm). The resulting crude preparation of (*S*)-(+)-α-methoxy-α-trifluoromethylphenylacetyl chloride was dissolved in dichloromethane (1 ml) and transferred via cannula to an ice cooled solution of (*S*)-2-methyl-3-phenylpropan-1-ol (9 mg, 0.06 mmol), 4-dimethylaminopyridine (2 mg, 0.016 mmol) and triethylamine (42µL, 0.30 mmol) in dichloromethane (0.5 ml). The yellow solution was stirred for 24 hours at room temperature, transferred in a separatory funnel containing dichloromethane (10 ml) and washed sequentially with saturated ammonium chloride solution (2x10 ml), saturated sodium bicarbonate solution (2x10 ml) and water (10ml). The organic layer was dried over anhydrous sodium sulfate, filtered and concentrated to give yellow oil that was filtered through an half-filled silica gel Pasteur pipette (eluting: cyclohexane/ethyl acetate : 70/30). After concentration of the solvent under reduced pressure, the expected ester was obtained as colorless oil (24 mg, 100%). Only one diastereomer could be detected by ^{1}H or ^{19} F NMR spectra of this product using $CDCl_3$ or C_6D_6. Integration of a pair of doublets of doublets corresponding to the major diastereomer (3.82-3.97 ppm) against those corresponding to the minor diastereomer (3.76-3.83 ppm and 3.98-4.05 ppm) allows accurate determination of original alcohol ee. [1]

^{1}H NMR (250 MHz, $CDCl_3$) **:** δ 0.94 (d, 3H, ^{3}J = 6.8 Hz), 2.15 (m, 1H), 2.44 (dd, 1H, ^{2}J = 13.5 Hz, ^{3}J = 7.7 Hz), 2.66 (dd, 1H, ^{2}J = 13.5 Hz, ^{3}J = 6.8 Hz), 3.57 (q, 3H, $^{5}J_{H\text{-}F}$ = 1.15 Hz), 4.11 (dd, 1H, ^{2}J = 10.8 Hz, ^{3}J = 5.5 Hz), 4.16 (dd, 1H, ^{2}J = 10.8 Hz, ^{3}J = 5.8 Hz), 7.06-7.55 (m, 10H).^{19}F

NMR (235.35 MHz, $CDCl_3$) **:** δ -71.84 (s, 3F).^{13}C NMR (62.9 MHz, $CDCl_3$) **:** δ 16.8, 34.7, 39.5, 55.6, 70.3, 85.00 (q, C, $^2J_{C\text{-}F}$ = 27.8 Hz), 123.5 (q, C, $^1J_{C\text{-}F}$ = 289.0 Hz), 126.3, 127.5, 128.5, 128.6, 129.2, 129.8, 132.5, 139.6, 166.8; MS **:** 77 (8), 91 (100), 105 (15), 117 (18), 132 (67), 189 (79); GC R_t = 11.74 min; ^{1}H NMR (250 MHz, C_6D_6) **:** δ 0.66 (d, 3H, ^3J = 6.8 Hz), 1.81 (m, 1H), 2.09 (dd, 1H, ^2J = 13.4 Hz, ^3J = 7.9 Hz), 2.43 (dd, 1H, ^2J = 13.4 Hz, ^3J = 6.7 Hz), 3.40 (q, 3H, $^5J_{H\text{-}F}$ = 1.15 Hz), 3.85 (dd, 1H, ^2J = 10.8 Hz, ^3J = 5.5 Hz), 3.93 (dd, 1H, ^2J = 10.8 Hz, ^3J = 5.9 Hz), 6.87-7.70 (m, 10H); ^{19}F NMR (235.35 MHz, C_6D_6) **:** δ -71.78 (s, 3F); ^{13}C NMR (62.9 MHz, C_6D_6) **:** δ 15.1, 33.2, 38.1, 54.0, 68.7, 85.01 (q, C, $^2J_{C\text{-}F}$ = 27.5 Hz), 122.9 (q, C, $^1J_{C\text{-}F}$ = 288.0 Hz), 125.0, 126.2, 126.6, 127.2, 127.9, 128.3, 131.7, 138.4, 165.2.

(*S*)-2-methyl-3-phenylpropanoic acid (14).

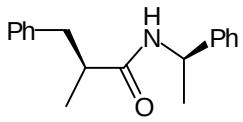


To a solution of amide (*S*)-**4a** (340 mg, 0.94 mmol) in anhydrous diethyl ether (8 mL) was slowly added LAH (142 mg, 3.74 mmol) at -10°C. The mixture was stirred for 30 min at this temperature and gently hydrolysed at -10°C by dropwise addition of a saturated NaCl solution (10mL). The resulting emulsion was stirred vigorously for 2 hours at room temperature, extracted with diethyl ether (2x20mL) and dichloromethane (20 ml). Organic layers were washed with a saturated NH_4Cl solution (20 ml), dried over $MgSO_4$, and concentrated under reduced pressure. The crude product (400 mg) was engaged without purification in the oxidation step.

To a solution of crude product (aldehyde and oxazolidine, 400 mg, 0.94 mmol) in *tert*-butanol (16 mL) was added 2-methyl-2-butene (2M in THF, 5 ml, 10 mmol), sodium chlorite (858 mg, 9.5 mmol) and dihydrogenophosphate monohydrate (1180 mg, 7.5 mmol) in water (10 ml). The biphasic mixture was stirred for 1.2h at room temperature. The crude was concentrated under reduced pressure to evaporate 2-methyl-2-butene and *tert*-butanol. The residue was taken up with water (50 ml) and a saturated $NaHCO_3$ solution (6 ml) and extracted with a cyclohexane / ethyl acetate mixture (9/1, 2x30 ml). The organic layers were dried over $MgSO_4$, concentrated under reduced pressure to afford oxazolidine (2*S*,4*R*)-**1a** (197 mg, 97 %). The aqueous layers were acidified (HCl 1M), extracted with ethyl acetate (3x30 ml), dried over Na_2SO_4, evaporated under reduced pressure to afford acid **12** (143 mg, 93%) as a colorless oil.

^{1}H NMR (250 MHz, $CDCl_3$) **:** δ 1.17 (d, 3H, ^{3}J = 6.9 Hz), 2.66 (dd, 1H, ^{2}J = 13.3 Hz, ^{3}J = 8.2 Hz), 2.76 (m, 1H), 3.07 (dd, 1H, ^{2}J = 13.3 Hz, ^{3}J = 5.9 Hz), 7.17-7.27 (m, 5H, H-Ar), 8.93 (s, 1H); ^{13}C NMR (62.9 MHz, $CDCl_3$) **:** δ 16.6, 39.4, 41.4, 126.6, 128.5, 129.1, 139.1, 182.7.

(2*S*)-2-benzyl-*N*-((*R*)-1-phenylethyl)propanamide



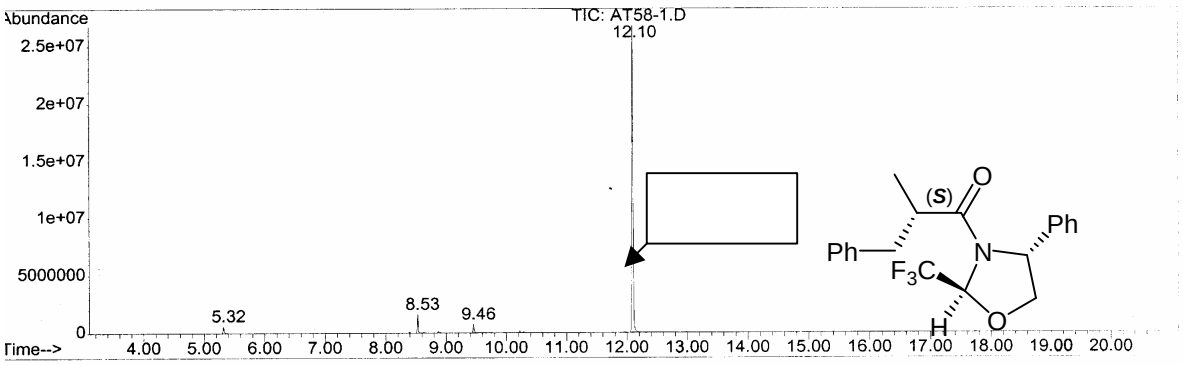
To a solution of acid **14** (25 mg, 15 mmol) in anhydrous DMF (0.5 mL) under argon atmosphere, was added 1-hydroxybenzotriazole (31 mg, 0.23 mmol) and 1-(3-diméthylamino)propyl-3-éthylcarbodiimide hydrochloride (44 mg, 0.23 mmol). This solution was stirred for 10 min at room temperature. (*R*)-1-phenylethylamine (24 µL, 0.19 mmol) and triethylamine (86 µL, 0.62 mmol) were added at 0°C. The solution was stirred for 1 hour at this temperature and for 20 hours at room temperature. The crude mixture was taken up with dichloromethane (10 ml), washed with an aqueous hydrochloric solution (1M, 4x10 ml), a saturated $NaHCO_3$ solution (10 mL) and water (10 ml). The organic layer was concentrated under reduced pressure to give the expected amide (33 mg, 100%) as a yellow solid.

^{1}H NMR (250 MHz, $CDCl_3$) : δ 1.17 (d, 3H, ^{3}J = 6.8 Hz), 1.22 (d, 3H, ^{3}J = 6.9 Hz), 2.41 (m, 1H), 2.70 (dd, 1H, ^{2}J = 13.4 Hz, ^{3}J = 6.0 Hz), 2.93 (dd, 1H, ^{2}J = 13.4 Hz, ^{3}J = 9.0 Hz), 5.01 (dq, 1H, ^{3}J = 7.3 Hz, ^{3}J = 6.8 Hz), 5.45 (d, 1H, ^{3}J = 7.3 Hz), 7.12-7.29 (m, 10H); ^{13}C NMR (62.9 MHz, $CDCl_3$) **:** δ 17.8, 21.5, 40.8, 44.0, 48.5, 126.2, 126.4, 127.3, 128.4, 128.7, 129.1, 140.0, 143.3, 174.6; MS **:** 267 (M^+, 82), 252 (14), 176 (39), 148 (23), 120 (27), 105 (100), 91 (99), 77(20); GC R_t = 12.06 min.

Reference

[1] A. G. Myers, B. H. Yang, H. Chen, *Org. Synth.* **2000,** *77*, 29-44.

Benzylation reaction of 2a : crude mixture



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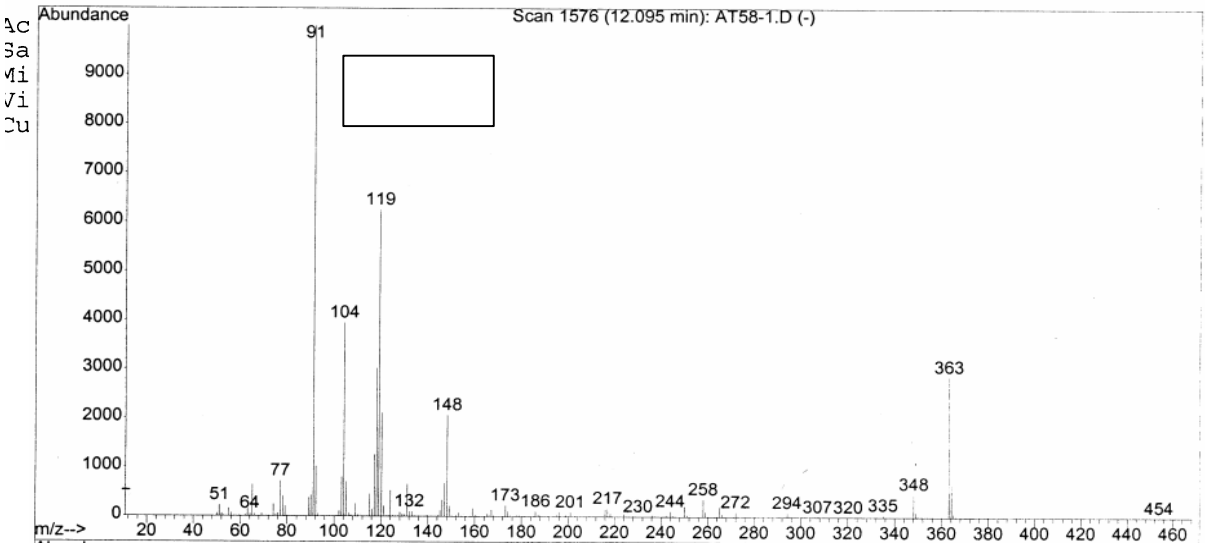
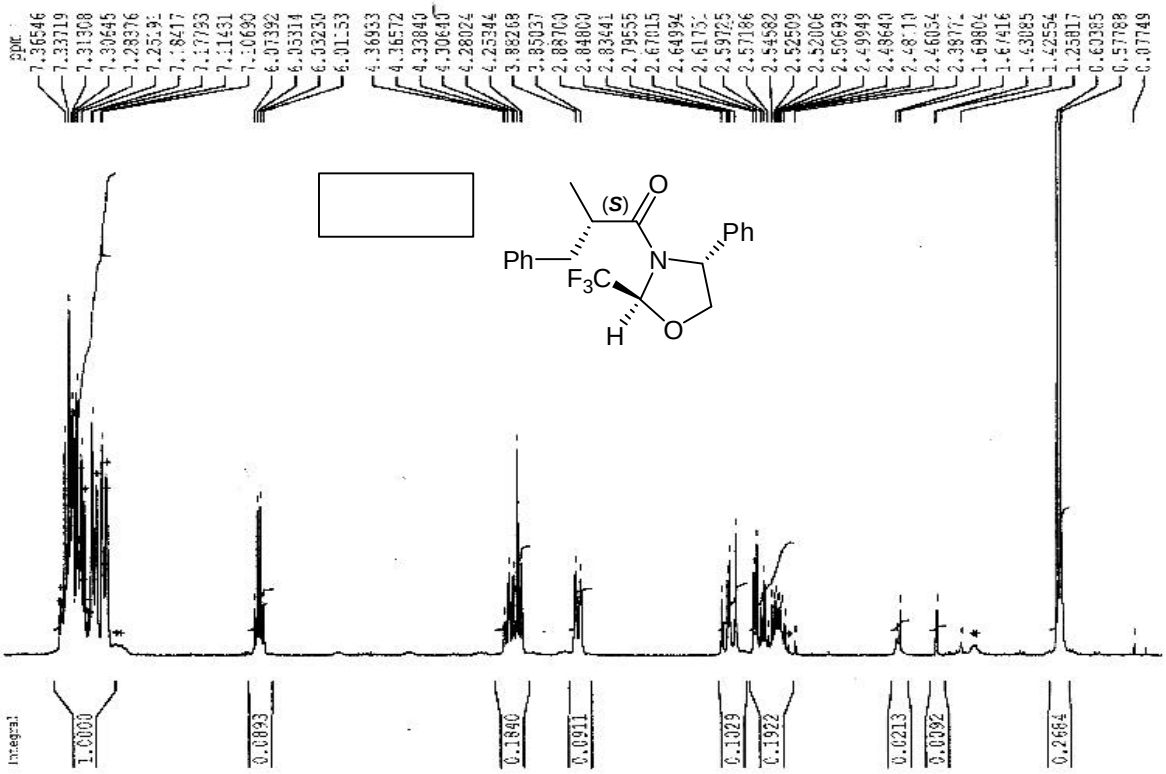
8.531	15138232	3.592	3.881
9.456	8764101	2.080	2.247
12.097	390020026	92.554	100.000

4	12.10	92.55	C:\DATABASE\NIST98.L		
			Benzene, (1-ethylpropyl)-	38055	001196-58-3 3
			4-Aminostyrene	53513	001520-21-4 3
			Benzeneacetaldehyde, .alpha.-ethyl	38054	002439-43-2 2

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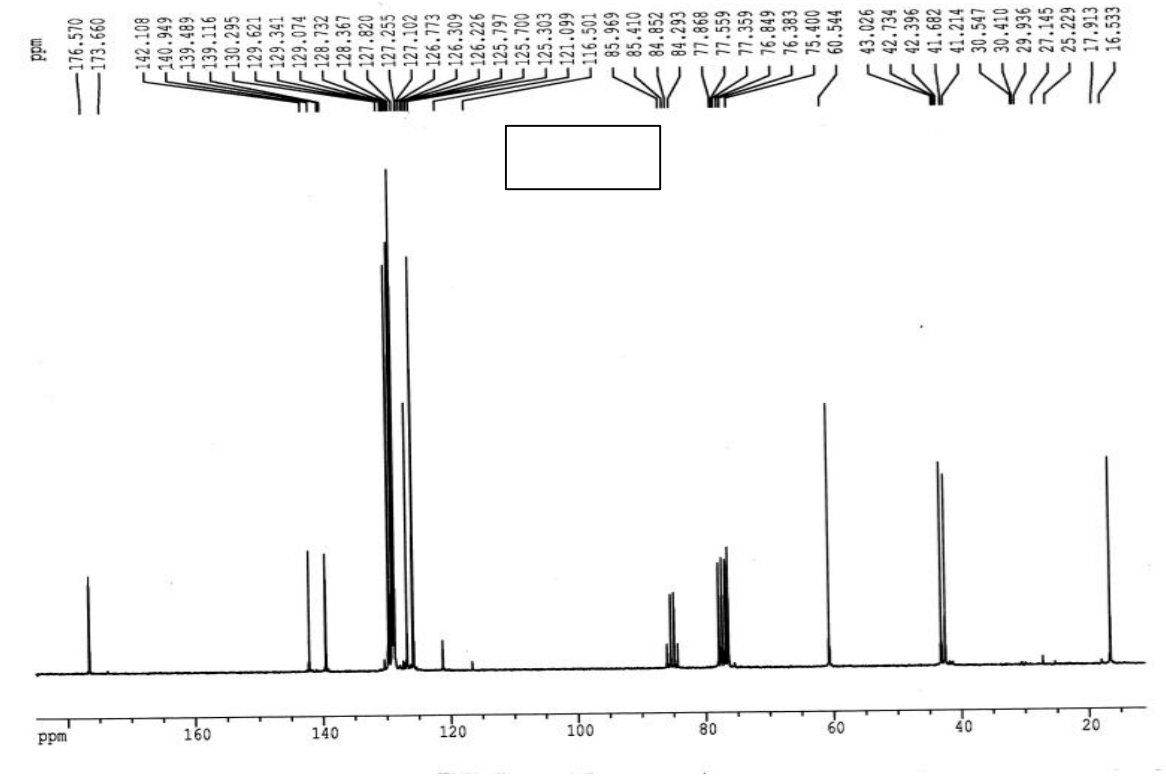
O
Ph
N
Ph
F3C
H
O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127.255
127.102
126.773
126.309
126.226
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125.303
121.099
116.501
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84.852
84.293
77.868
77.559
77.359
76.849
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75.400
60.544
43.026
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42.396
41.682
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30.547
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29.936
27.145
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17.913
16.533
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120
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80
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40
20

Epimerisation reaction of (*S*)-4a : crude mixture

```
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Acquired   : 25 Feb 2004    3:43 pm using AcqMethod METHODE1
Sample Name:
Misc Info  :
Vial Number: 4
CurrentMeth: C:\HPCHEM\1\METHODS\METHODE1.M
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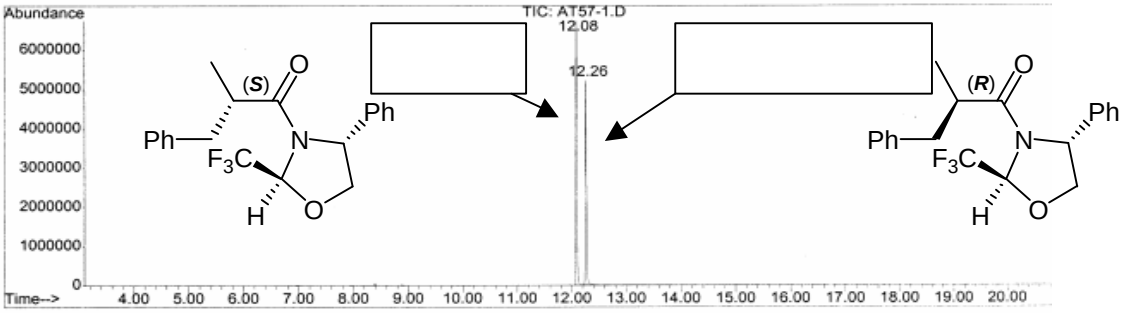

Retention Time	Area	Area %	Ratio %
Total Ion Chromatogram			
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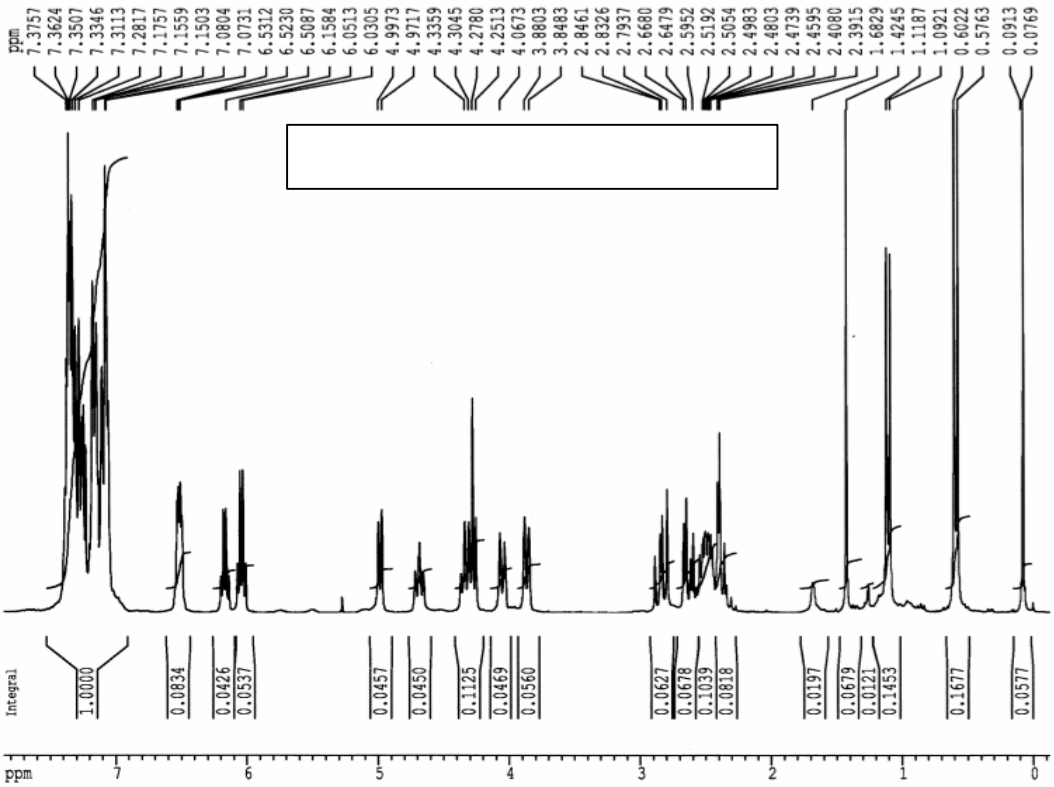

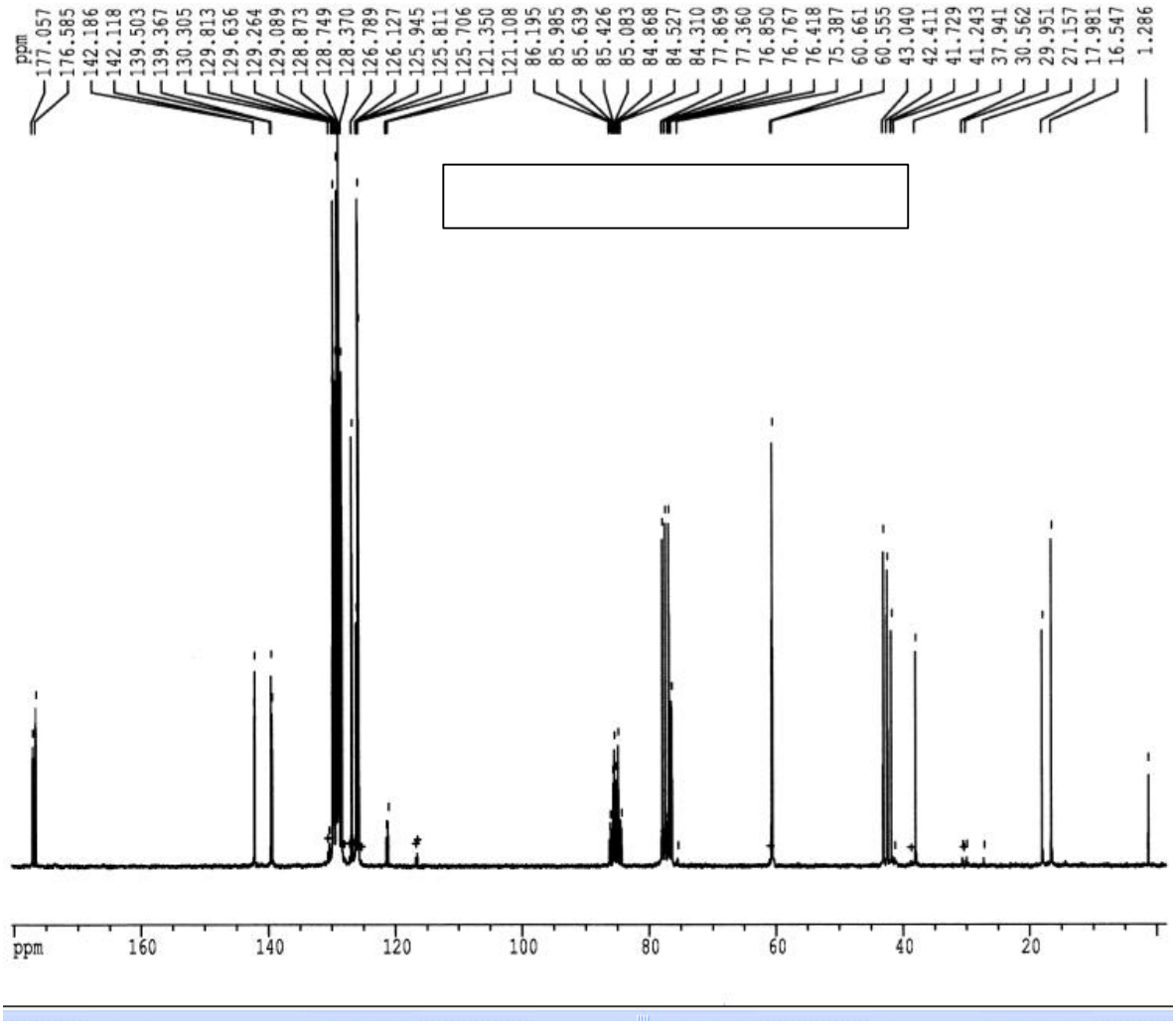
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128.749
128.370
126.789
126.127
125.945
125.811
125.706
121.350
121.108
86.195
85.985
85.639
85.426
85.083
84.868
84.527
84.310
77.869
77.360
76.850
76.767
76.418
75.387
60.661
60.555
43.040
42.411
41.729
41.243
37.941
30.562
29.951
27.157
17.981
16.547
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ppm
160
140
120
100
80
60
40
20

Ethylation reaction of 2a : crude mixture

```
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Operator   :
Acquired   :  2 Jun 2004    3:53 pm using AcqMethod METHODE1
Sample Name:
Misc Info  :
Vial Number: 5
CurrentMeth: C:\HPCHEM\1\METHODS\METHODE1.M
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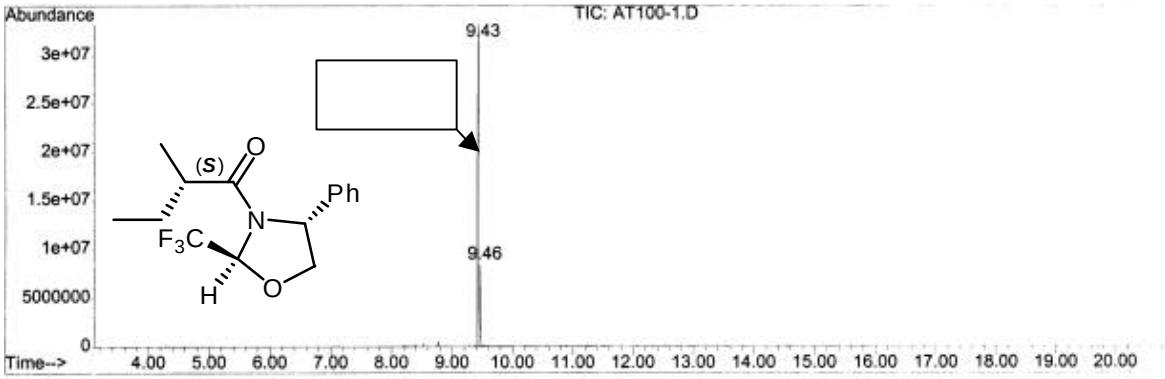

Retention Time	Area	Area %	Ratio %
Total Ion Chromatogram			
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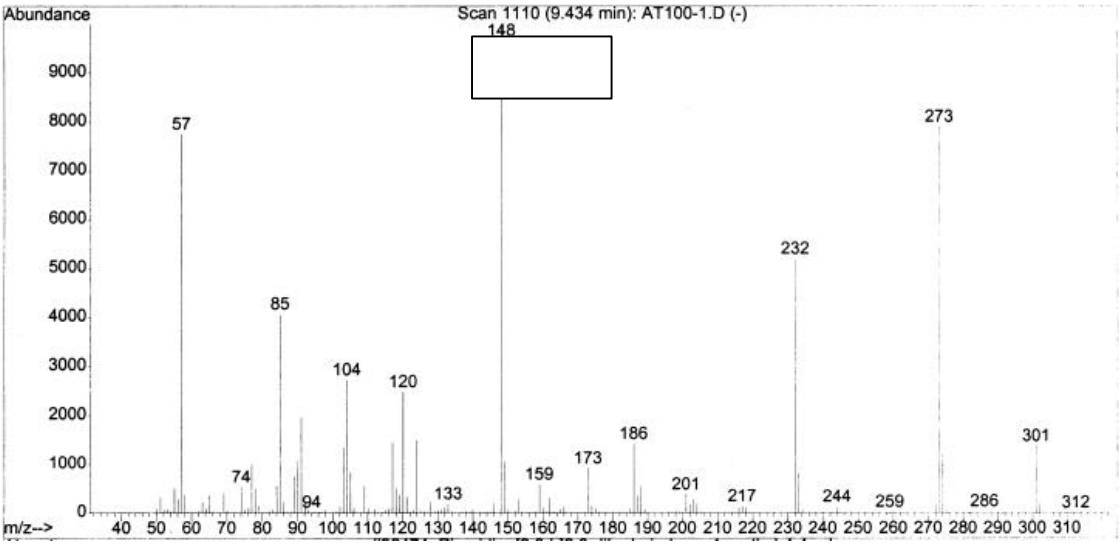
9.459	77571056	14.097	16.411

Pk#	RT	Area%	Library/ID	Ref#	CAS#	Qual
1	9.43	85.90	C:\DATABASE\NIST98.L			
			Piperidino[2,3-b]2,3-dihydroindene	96474	1000128-54-2	18
			7(1H)-Pteridinone	66500	002432-27-1	14
			Furan, 2,2'-methylenebis-	123381	001197-40-6	14



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6.19079
6.17036
5.07368
5.04850
4.75957
4.72735
4.69925
4.39085
4.12434
4.08975
2.27636
2.25091
2.24375
2.22573
2.21880
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1.43342
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1.37245
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0.91101
0.48038
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0.10015
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0.1900
0.1894
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0.2173
0.5385
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0.5149
ppm
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128.908
128.597
127.830
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126.219
125.842
125.574
121.210
116.617
85.772
85.215
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84.103
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77.157
76.648
76.513
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41.679
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28.938
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1.740
ppm
160
140
120
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80
60
40
20

Epimerisation reaction of (*S*)-5a : crude mixture

```
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Operator   :
Acquired   :  7 Jun 2004    5:11 pm using AcqMethod METHODE1
Sample Name:
Misc Info  :
Vial Number: 5
CurrentMeth: C:\HPCHEM\1\METHODS\METHODE1.M
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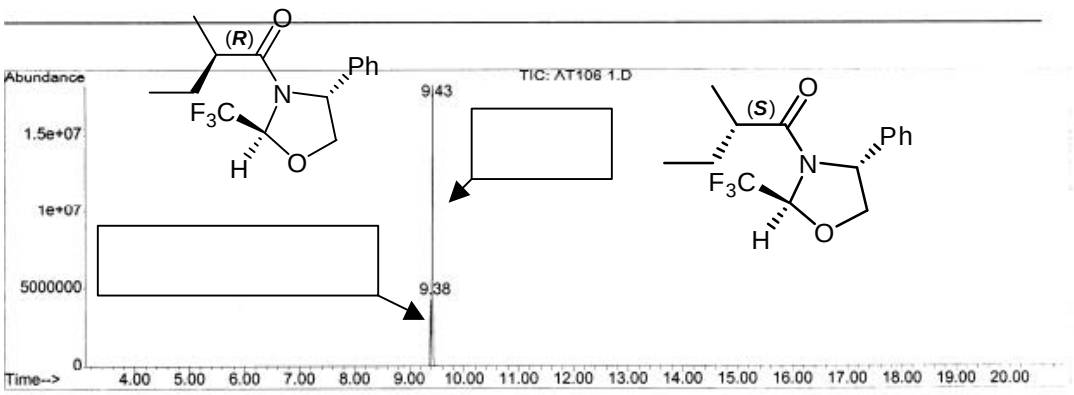

Retention Time	Area	Area %	Ratio %
Total Ion Chromatogram			
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Pk#	RT	Area%	Library/ID	Ref#	CAS#	Qual
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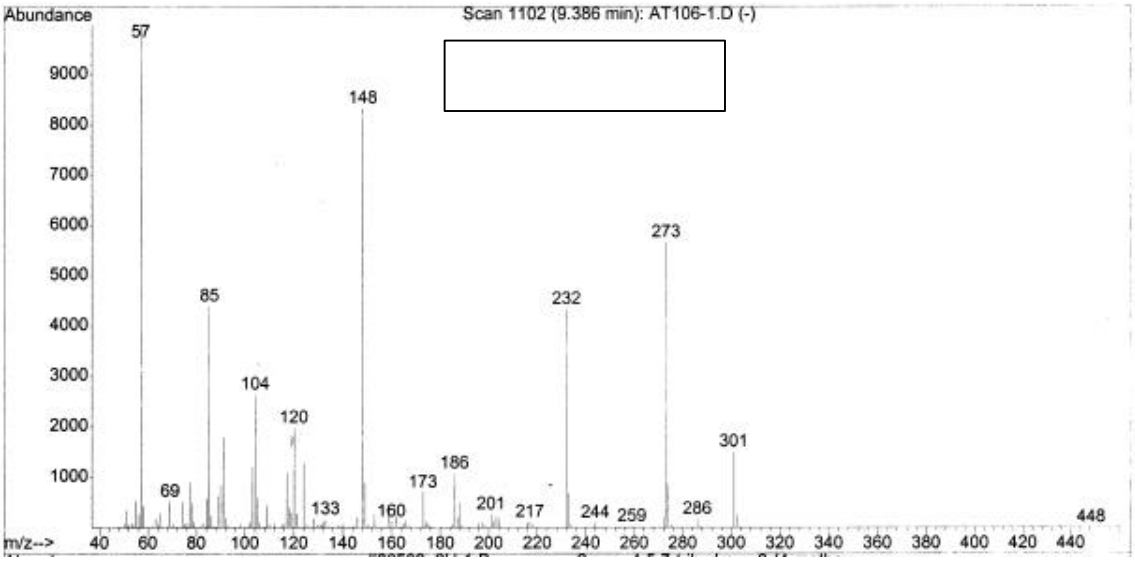
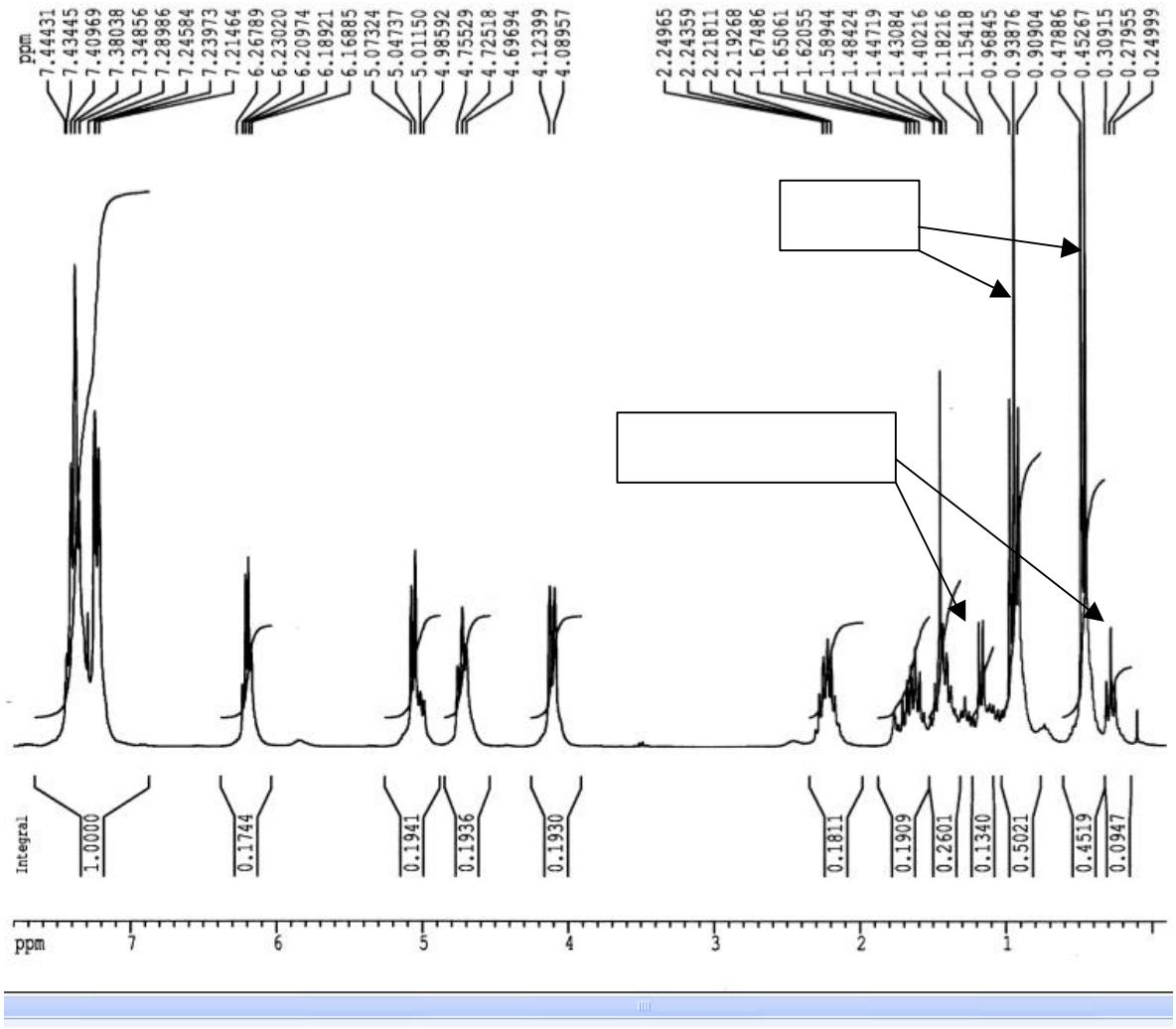
			2H-1-Benzopyran-2-one, 4,5,7-trihy	66502	004376-81-2	25
			Furan, 2,2'-methylenebis-	123381	001197-40-6	22
			7(1H)-Pteridinone	66500	002432-27-1	22

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3
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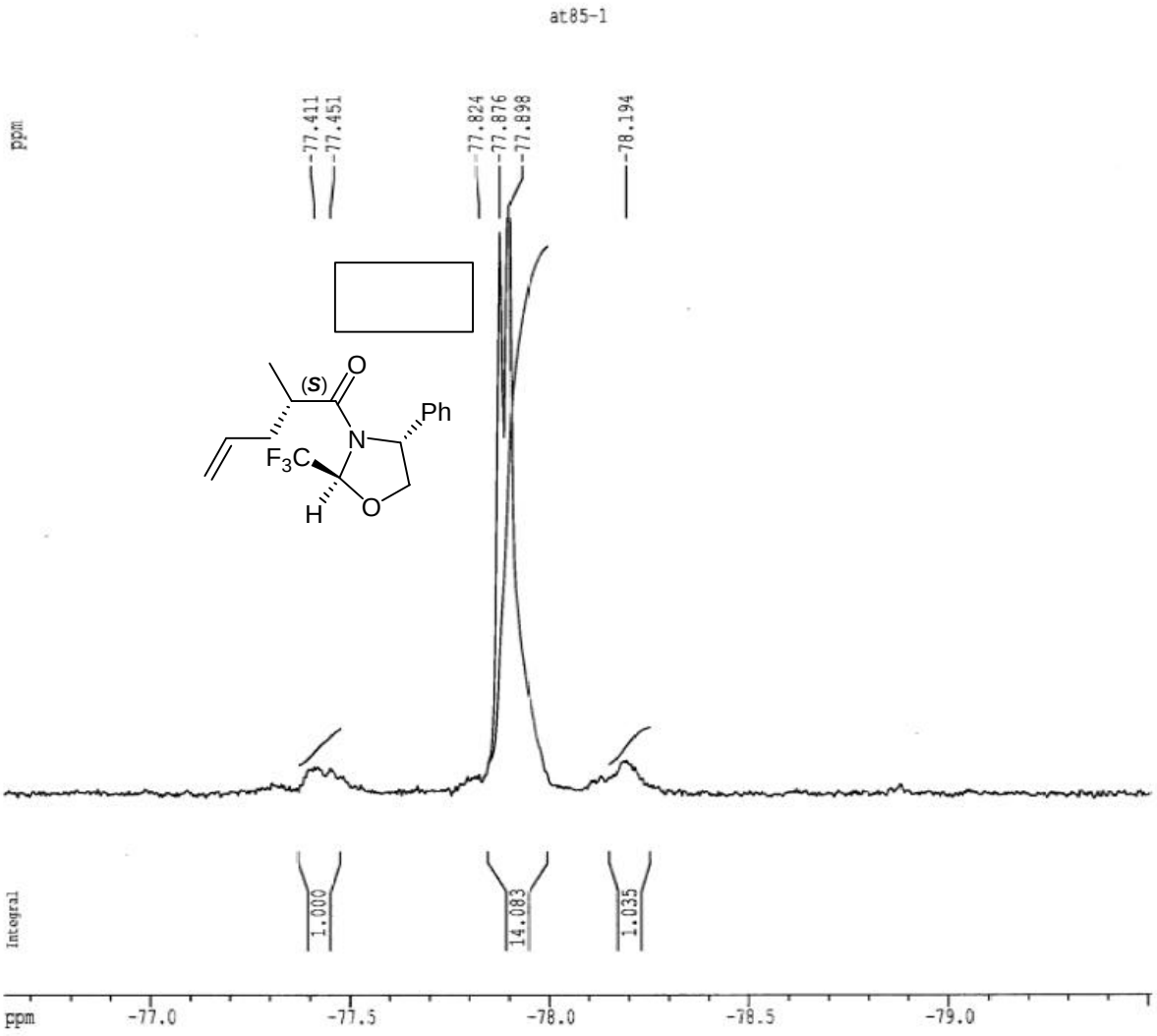
1

Allylation reaction of 2a : crude mixture



AT85-1

```
Information from Data File:
File       : C:\HPCHEM\1\DATA\AB-1.D
Operator   :
Acquired   :  8 Apr 2004  12:04 pm using AcqMethod METHODE1
Sample Name:
Misc Info  :
Vial Number: 1
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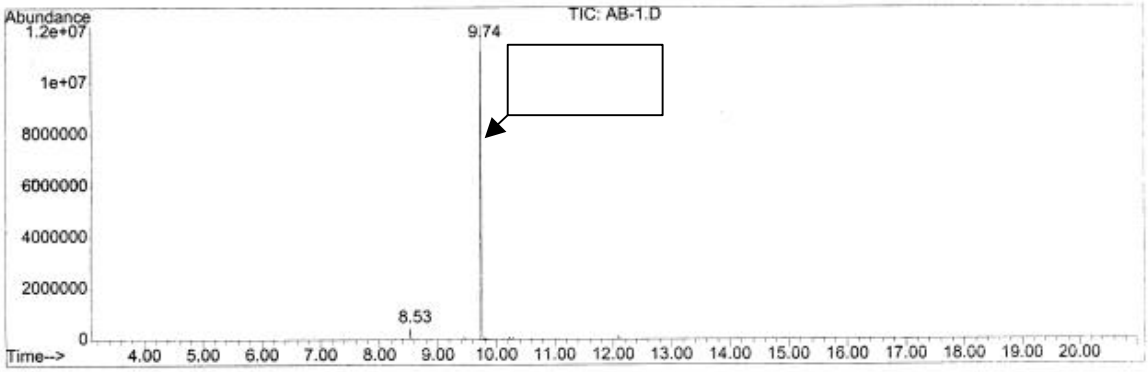

Retention Time	Area	Area %	Ratio %
Total Ion Chromatogram			
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Pk#	RT	Area%	Library/ID	Ref#	CAS#	Qual
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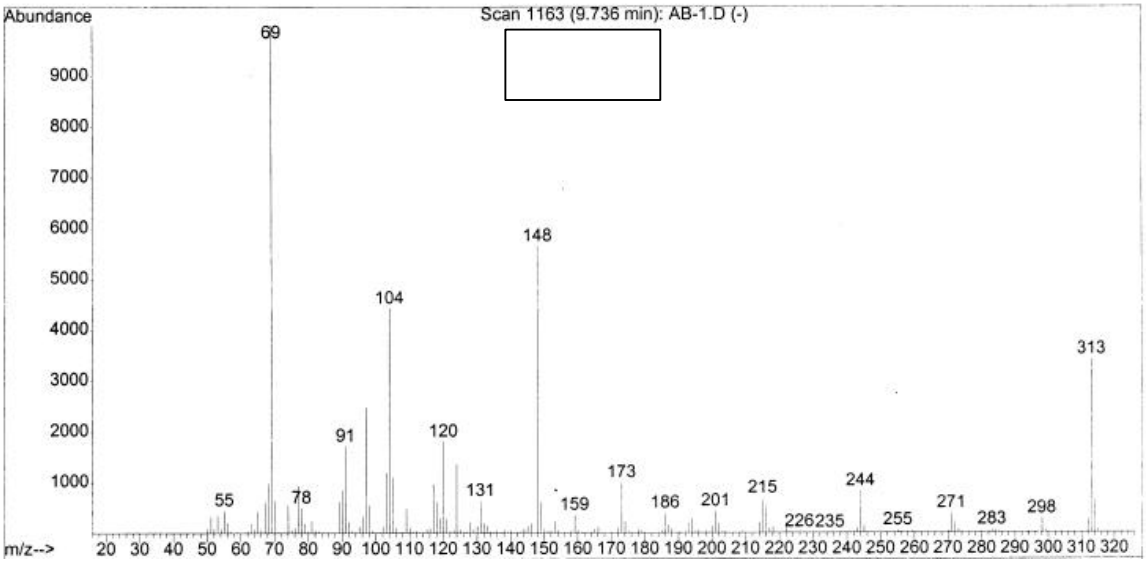
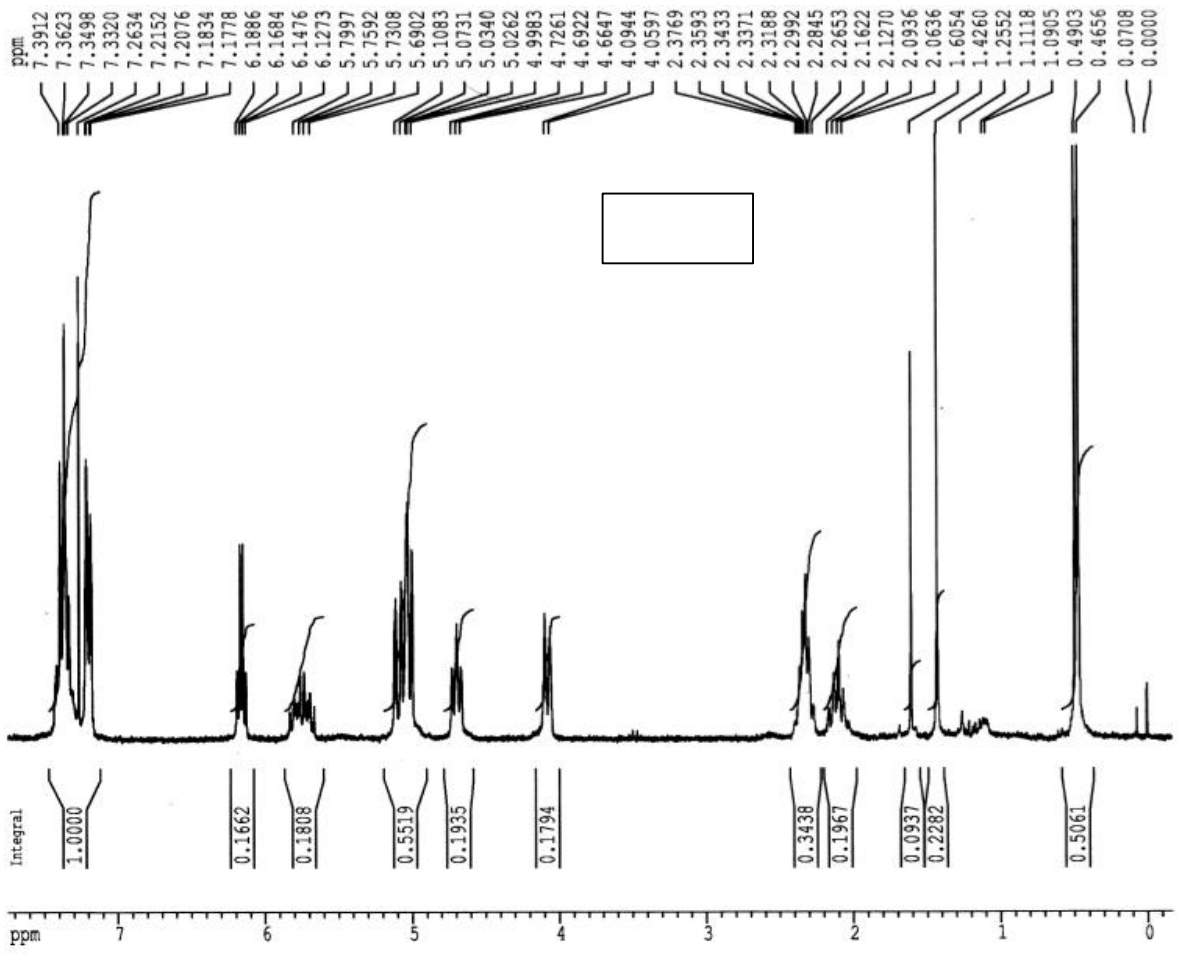
			2-Butene, 1-chloro-3-methyl-	114165	000503-60-6	38
			2,6-Octadiene, 4,5-dimethyl-	22330	018476-57-8	22
			Cyclopentanecarboxylic acid, ethen	22474	016523-06-1	16

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0.4903
0.4656
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Integral
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0.1935
0.1794
0.3438
0.1967
0.0937
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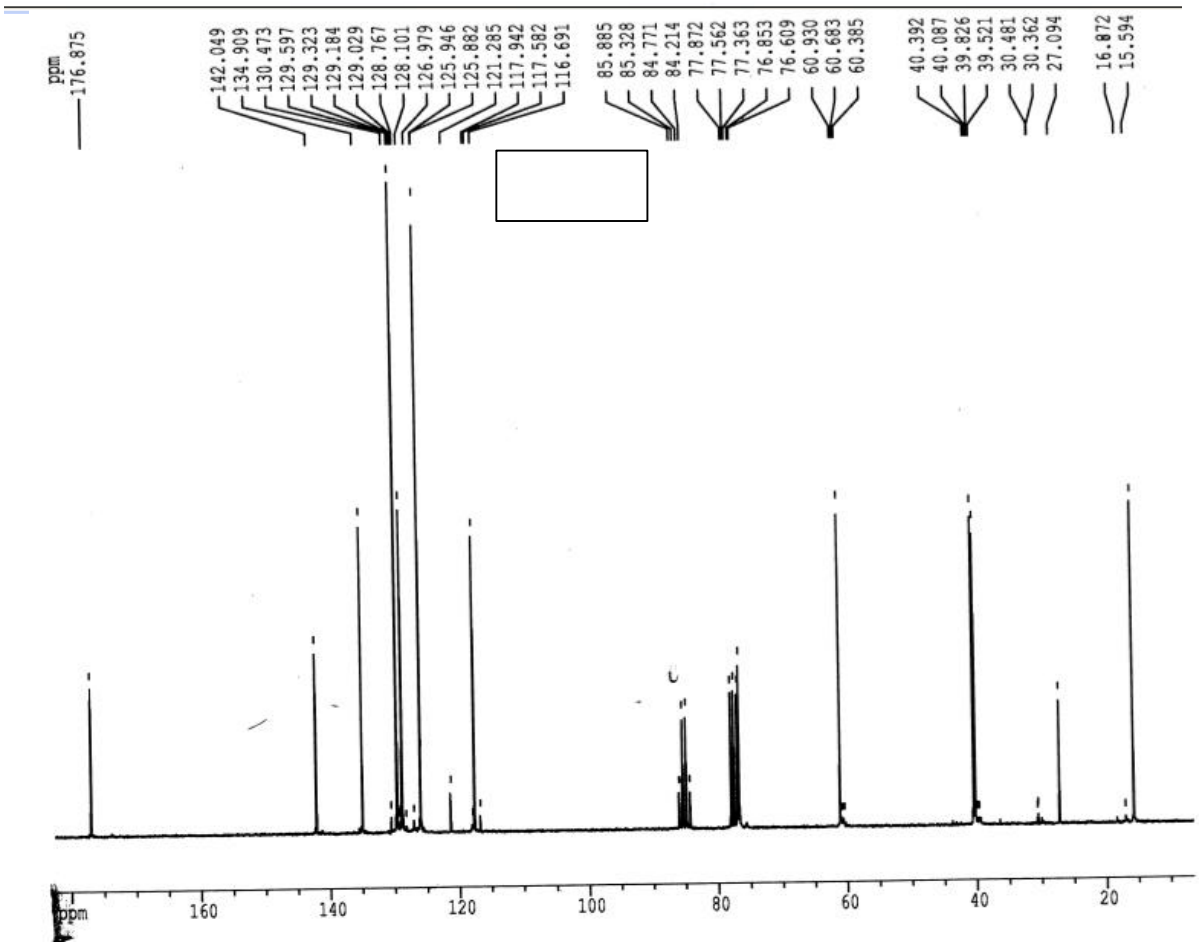
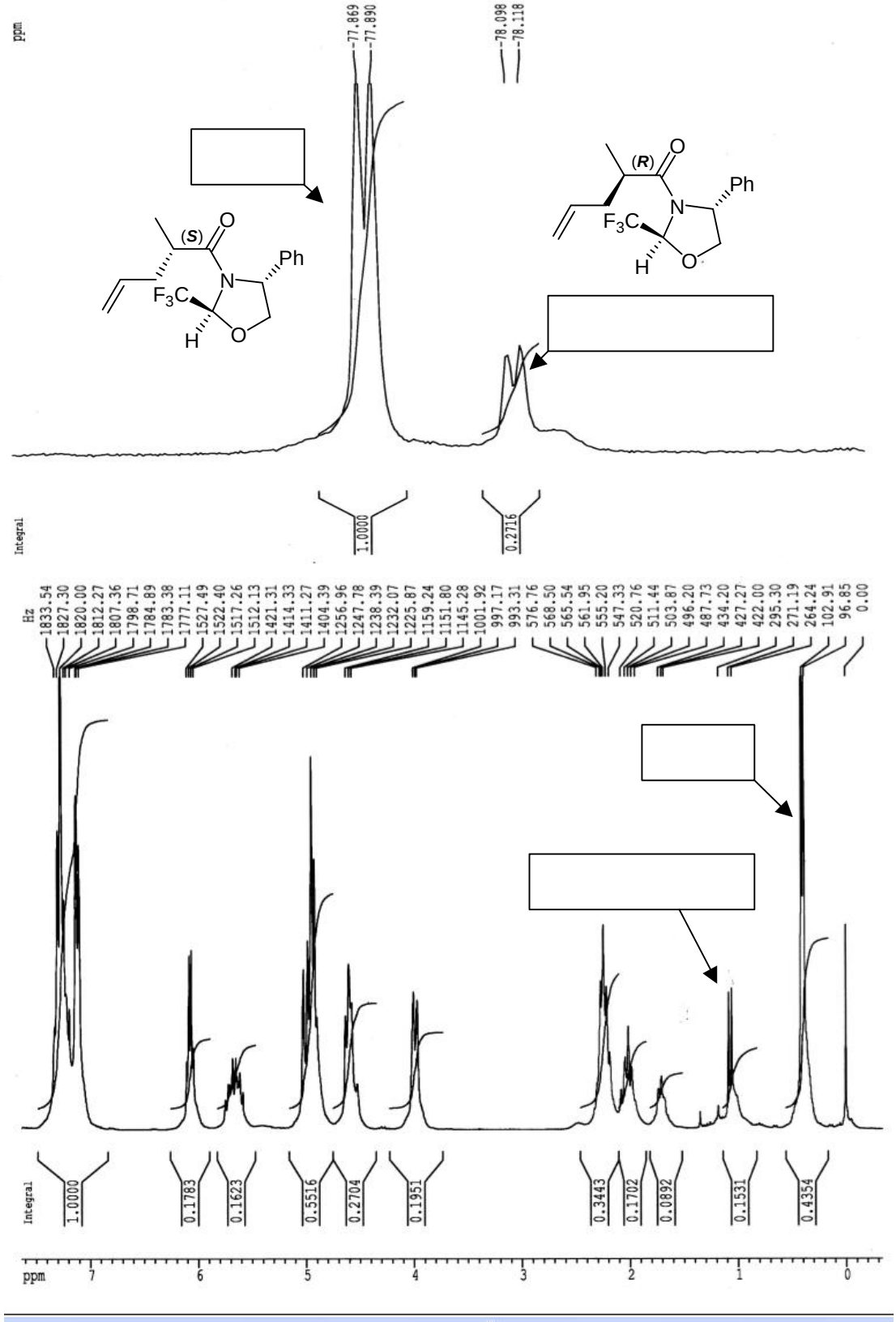
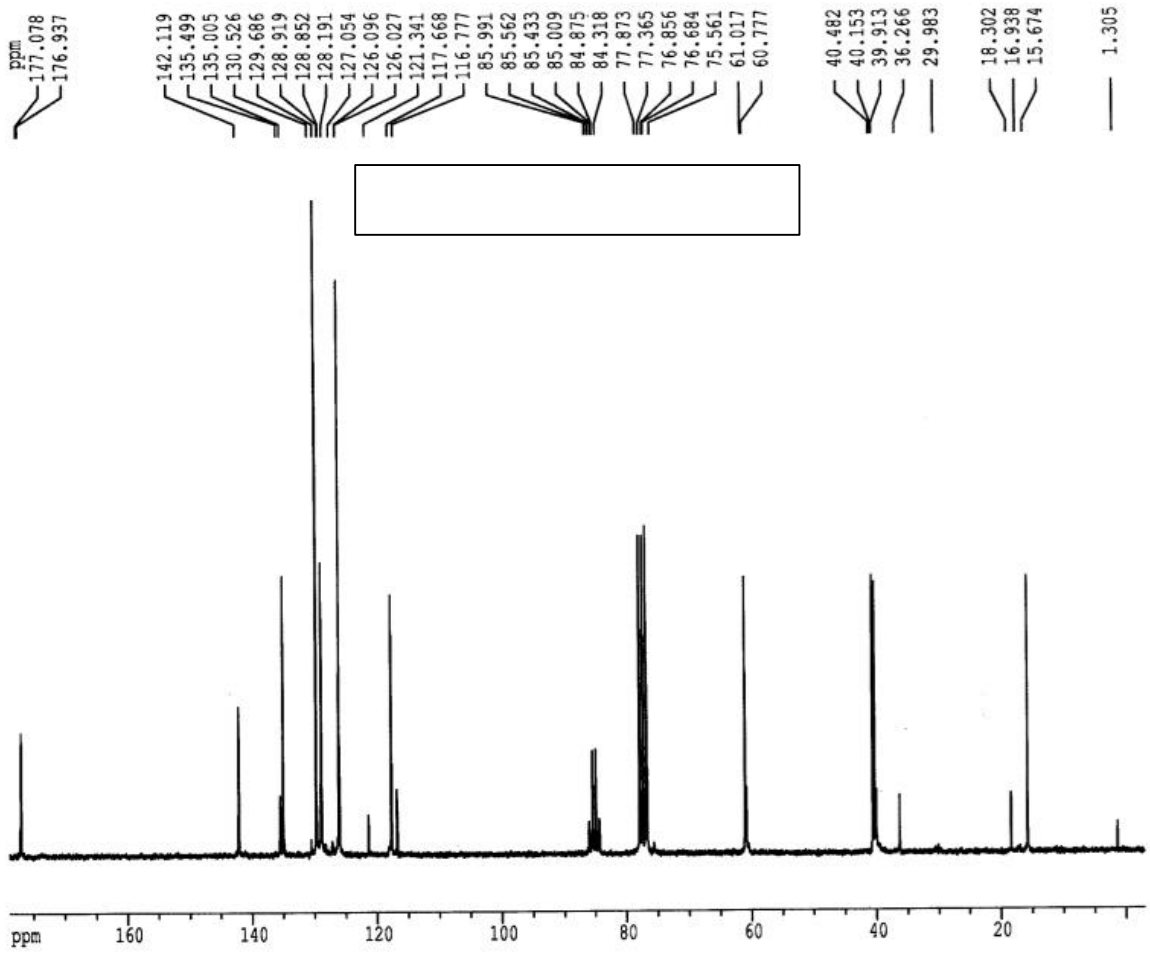
3
2
1
0


ppm
176.875
142.049
134.909
130.473
129.597
129.323
129.184
129.029
128.767
128.101
126.979
125.946
125.882
121.285
117.942
117.582
116.691
85.885
85.328
84.771
84.214
77.872
77.562
77.363
76.853
76.609
60.930
60.683
60.385
40.392
40.087
39.826
39.521
30.481
30.362
27.094
16.872
15.594
ppm
160
140
120
100
80
60
40
20

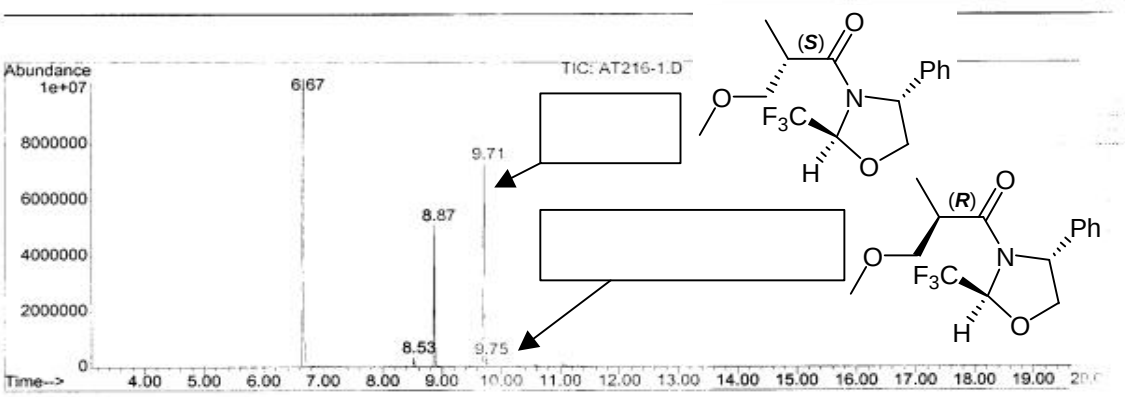
Epimerisation reaction of (*S*)-6a : crude mixture




ppm
177.078
176.937
142.119
135.499
135.005
130.526
129.686
128.919
128.852
128.191
127.054
126.096
126.027
121.341
117.668
116.777
85.991
85.562
85.433
85.009
84.875
84.318
77.873
77.365
76.856
76.684
75.561
61.017
60.777
40.482
40.153
39.913
36.266
29.983
18.302
16.938
15.674
1.305
ppm
160
140
120
100
80
60
40
20

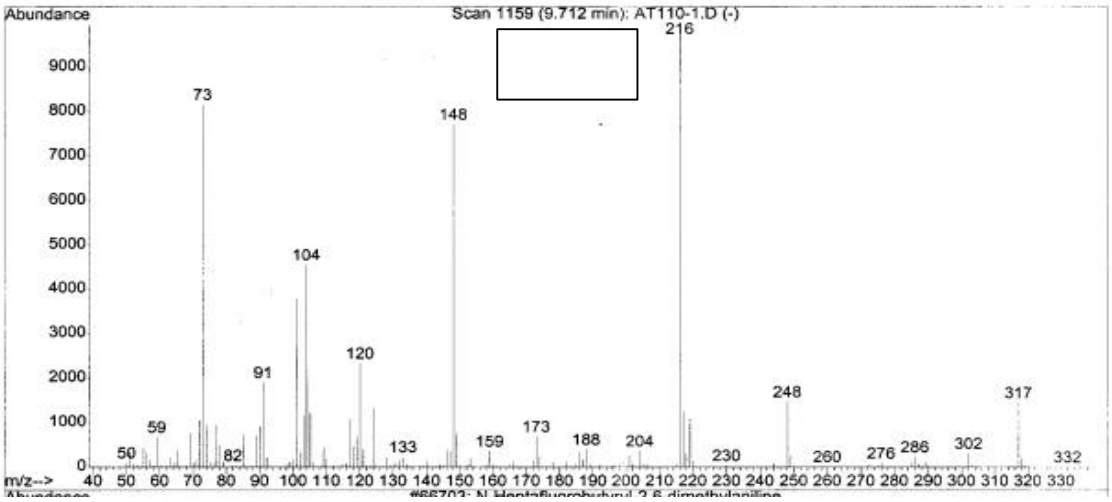
MOM reaction of 2a : crude mixture

```
Information from Data File:
File       : C:\HPCHEM\1\DATA\AT216-1.D
Operator   :
Acquired   : 18 May 2005    6:33 pm using AcqMethod METHODE1
Sample Name:
Misc Info  :
Vial Number: 4
CurrentMeth: C:\HPCHEM\1\METHODS\METHODE1.M
```

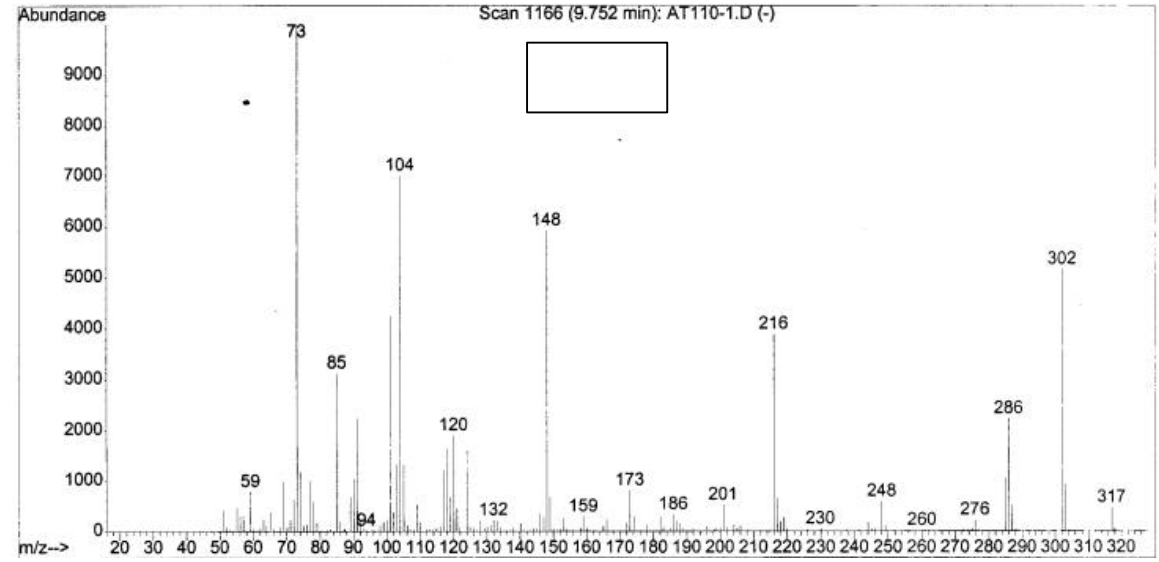


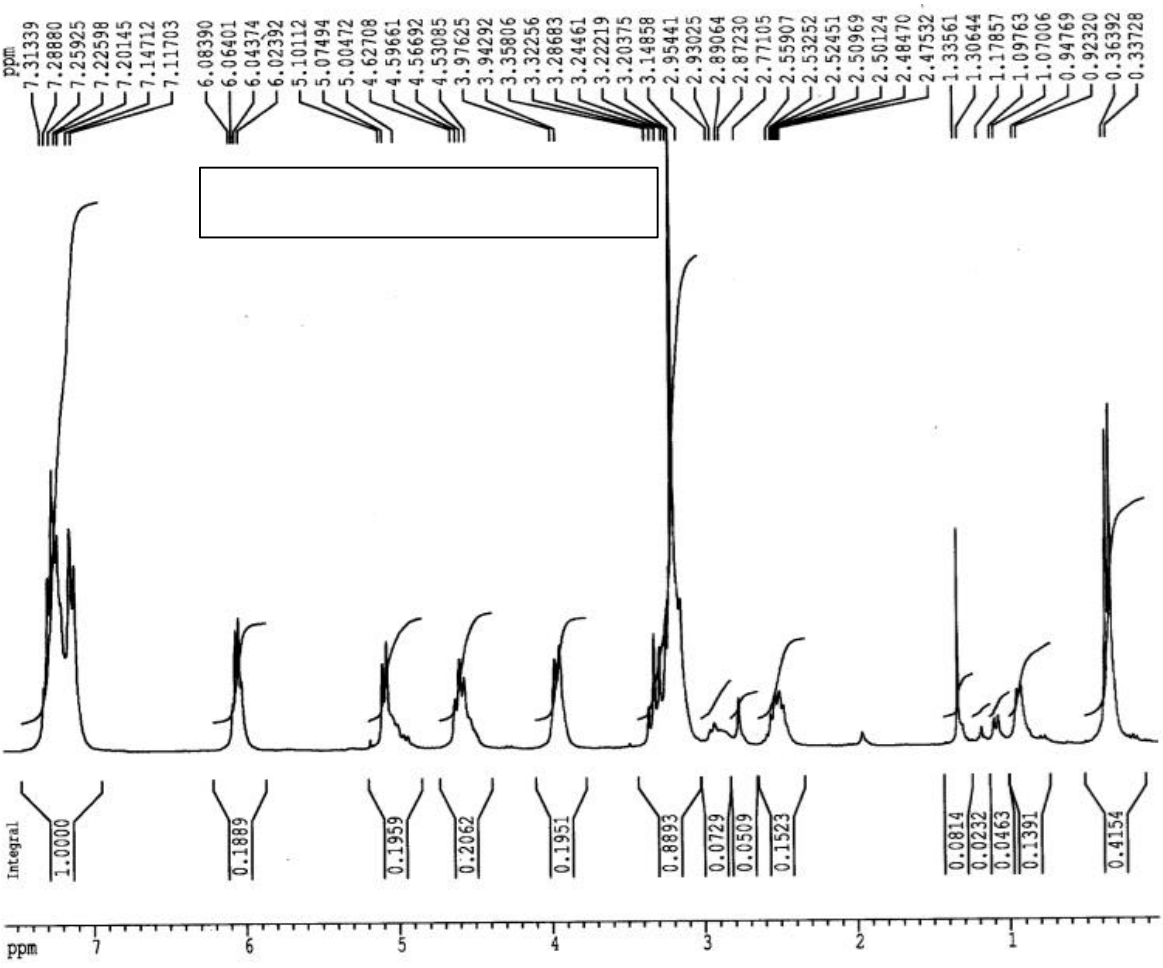
Retention Time	Area	Area %	Ratio %
Total Ion Chromatogram			
6.668	191722792	59.742	100.000
8.526	3404342	1.061	1.776
8.869	49529910	15.434	25.834
9.709	72115953	22.472	37.615
9.751	4147214	1.292	2.163

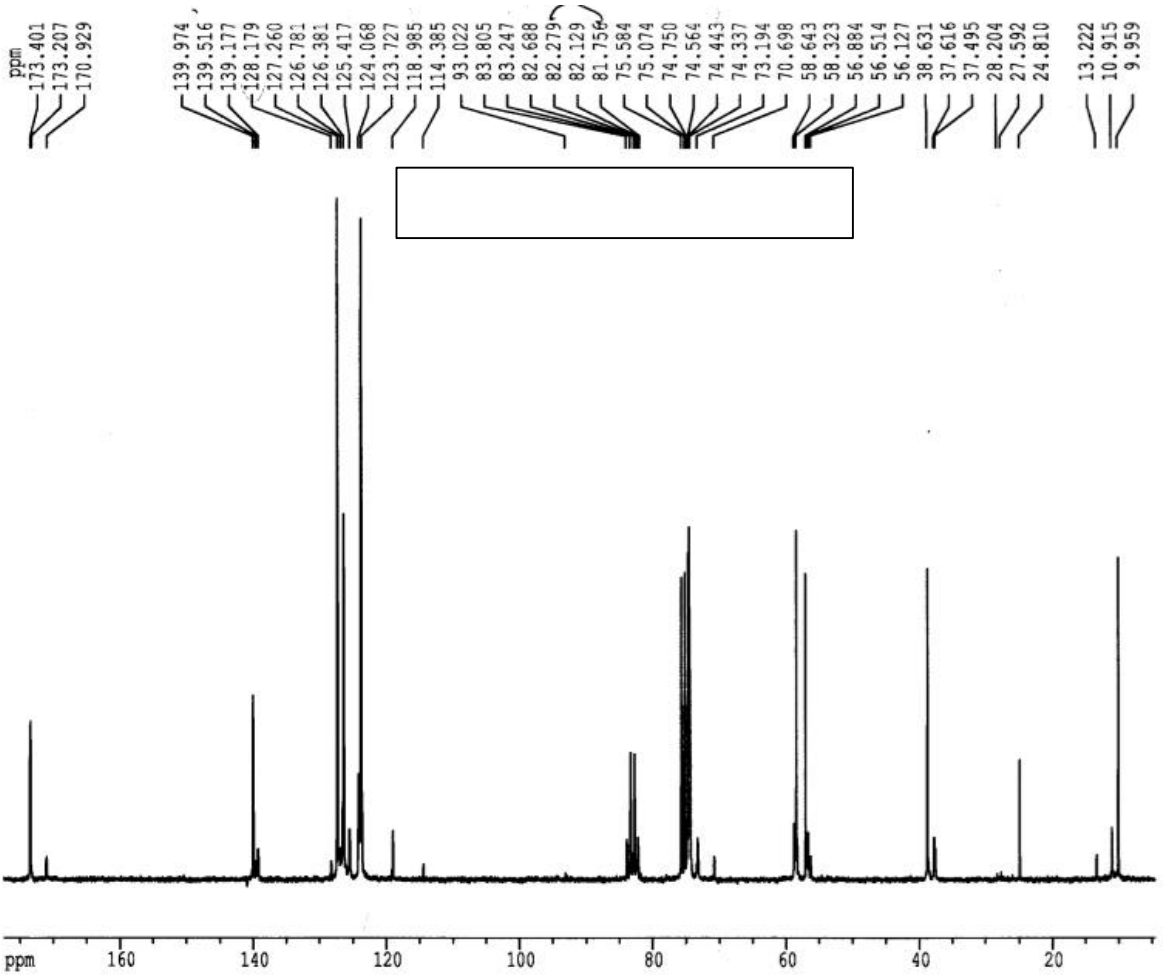
Pk#	RT	Area%	Library/ID	Ref#	CAS#	Qual
3	9.71	66.62	C:\DATABASE\NIST98.L			
			N-Heptafluorobutyryl-2,6-dimethyla	66703	101948-89-4	22
			Propanenitrile, 3-[ethyl(3-methylp	66497	000148-69-6	14
			6(5H)-Pteridinone	66490	002432-26-0	14



Pk#	RT	Area%	Library/ID	Ref#	CAS#	Qual
4	9.75	10.47	C:\DATABASE\NIST98.L			
			2-Acetyl-8-methyl-4-oxa-bicyclo[9.	4514	1000193-49-3	12
			3-Pyridinecarbonitrile, 1,2-dihydr	66486	000769-28-8	11
			3-Butenal, 3,4,4-trichloro-	25438	108562-62-5	10

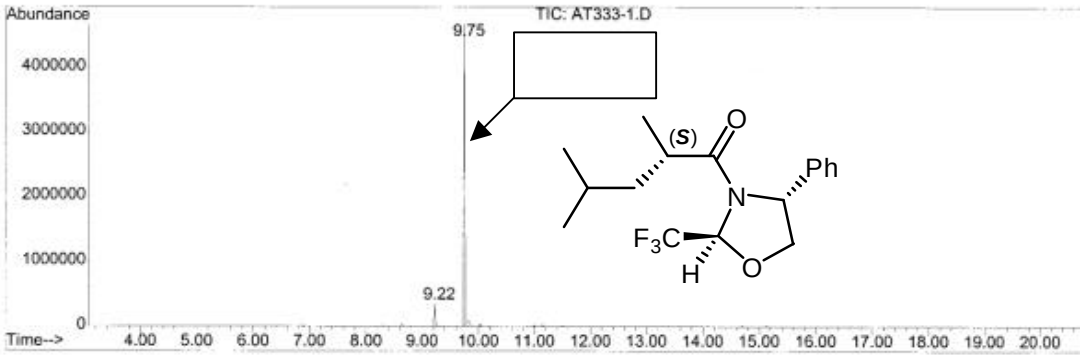




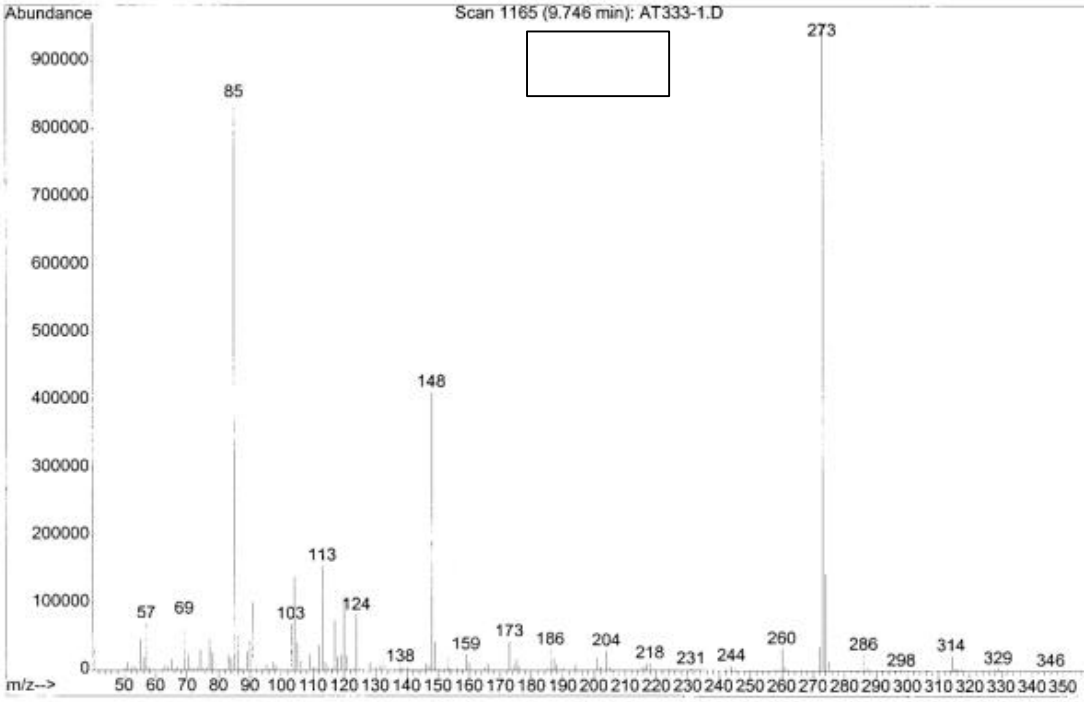

ppm
173.401
173.207
170.929
139.974
139.516
139.177
128.179
127.260
126.781
126.381
125.417
124.068
123.727
118.985
114.385
93.022
83.805
83.247
82.688
82.279
82.129
81.756
75.584
75.074
74.750
74.564
74.443
74.337
73.194
70.698
58.643
58.323
56.884
56.514
56.127
38.631
37.616
37.495
28.204
27.592
24.810
13.222
10.915
9.959
ppm
160
140
120
100
80
60
40
20

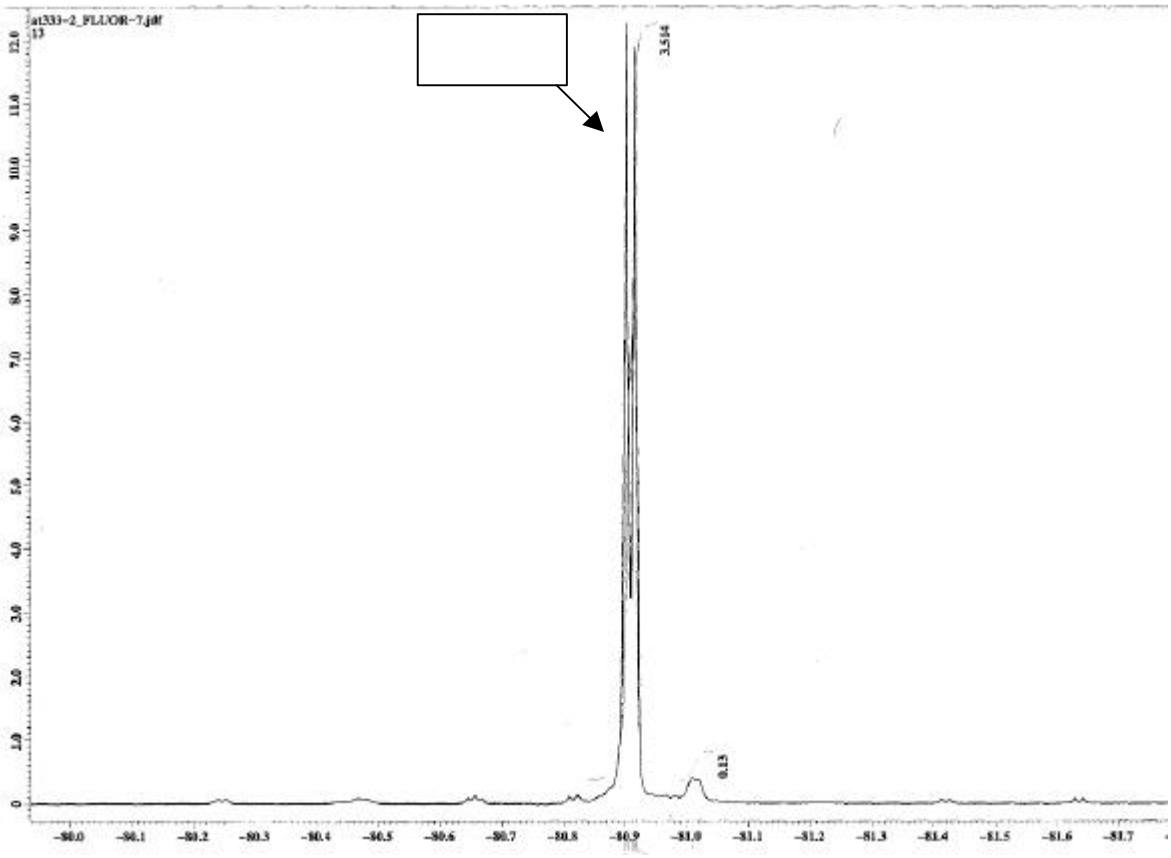
Reaction of 2a with *i*-BuI : crude mixture

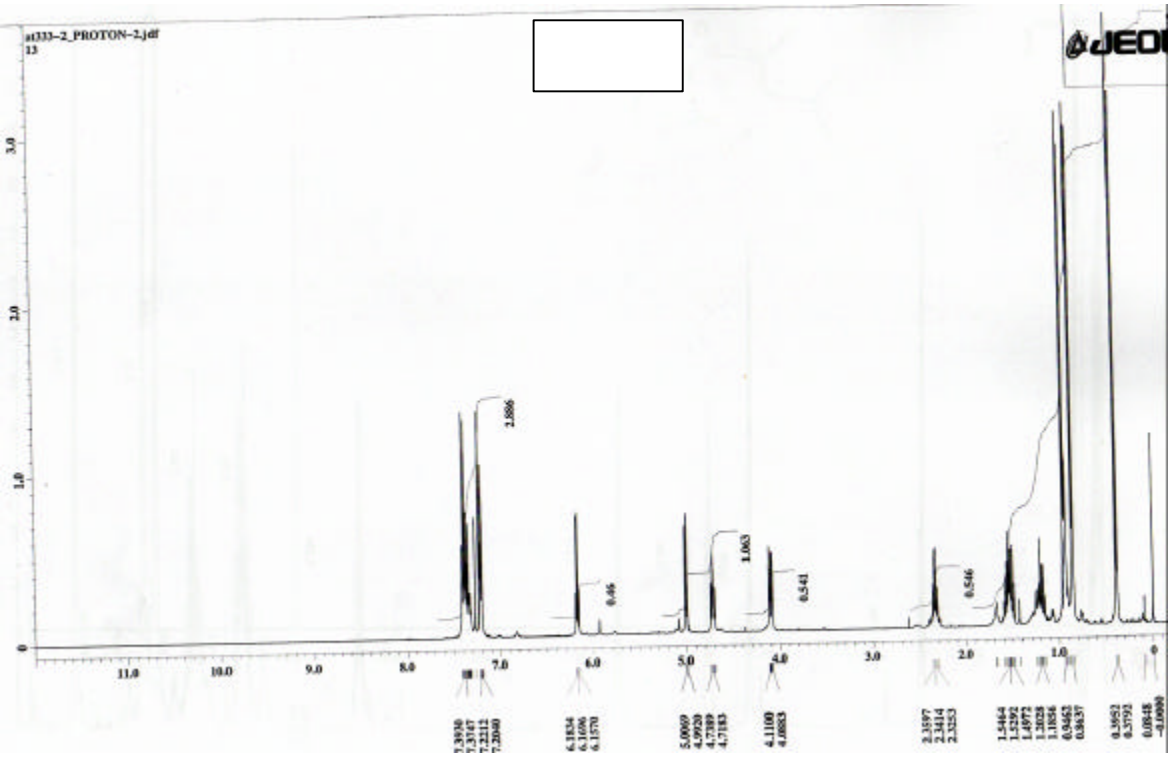
```
Information from Data File:
File       : C:\HPCHEM\1\DATA\AT333-1.D
Operator   : arno
Acquired   :  3 Feb 2006    9:44 am using AcqMethod M1
Sample Name: at333-1
Misc Info  :
Vial Number: 1
CurrentMeth: C:\HPCHEM\1\METHODS\M1.M
```

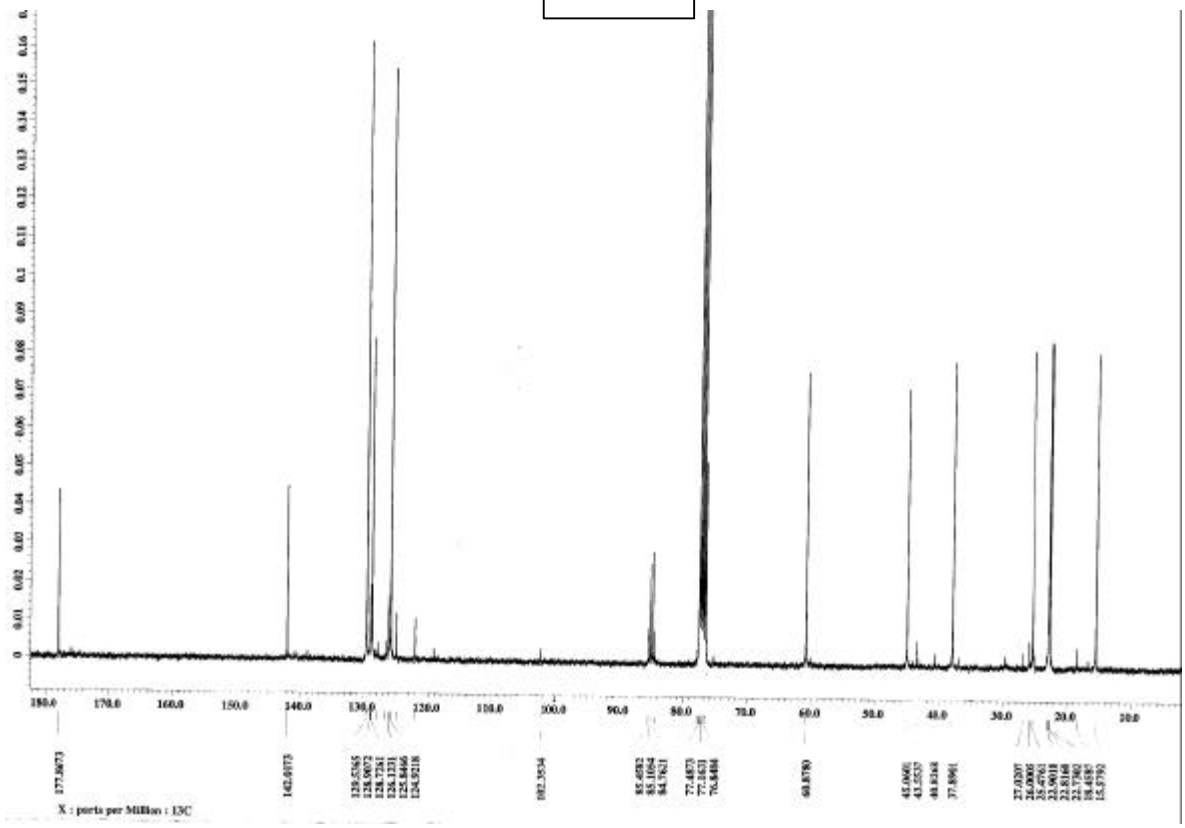


Retention Time	Area	Area %	Ratio %
Total Ion Chromatogram			
9.220	3658146	7.662	8.298
9.747	44086460	92.338	100.000

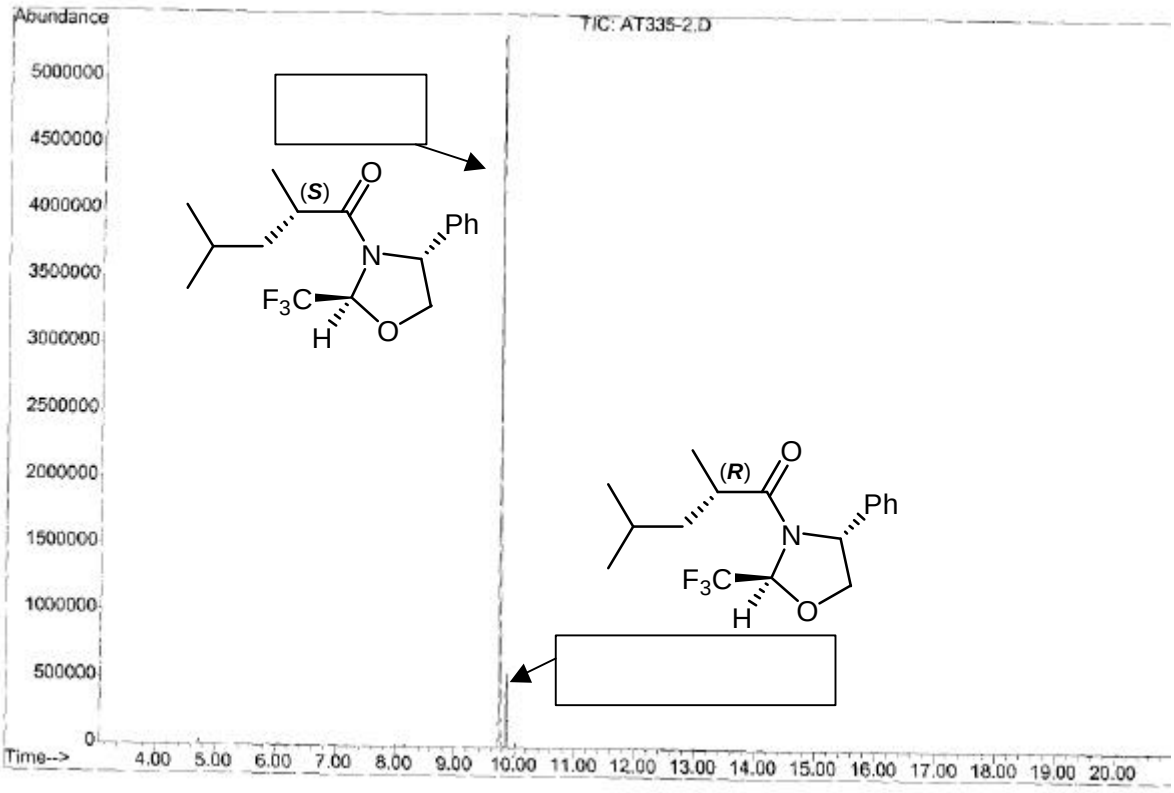



at333-2_FLUOR-7.jdf
13
3.544
0.13


at333-2_PROTON-2.jdf
13
2.886
0.46
1.063
0.541
0.546

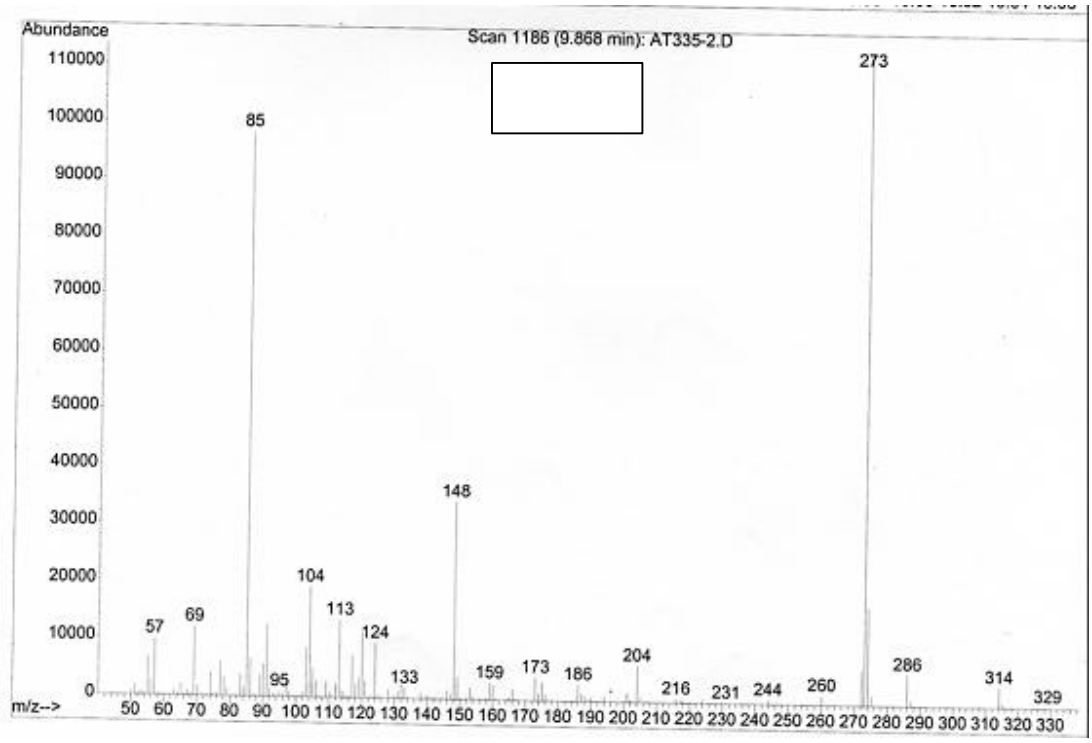

X : parts per Million : 13C

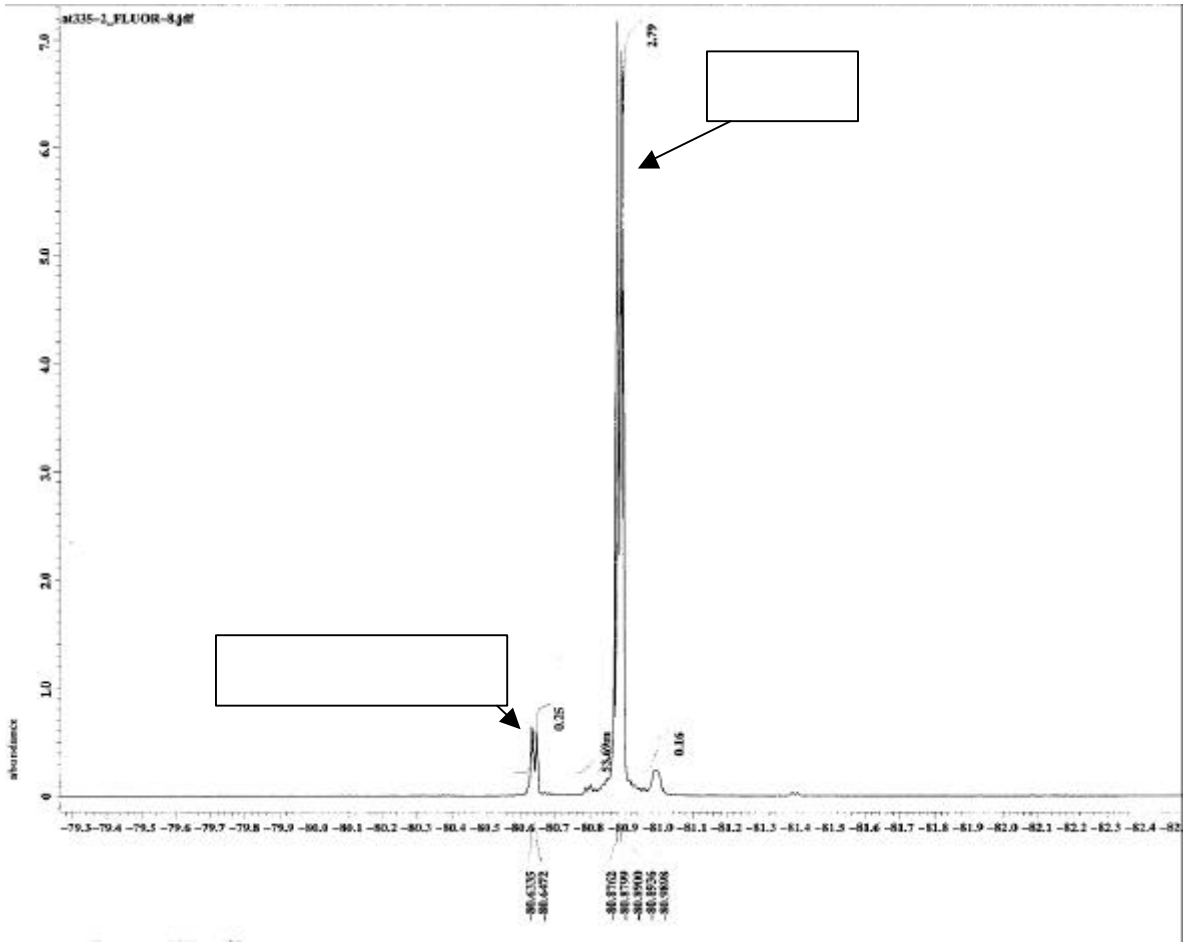
Epimerisation reaction of (*S*)-8a: crude mixture




```
Information from Data File:
File        : C:\HPCHEM\1\DATA\AT335-2.D
Operator    : arno
Acquired    :  8 Feb 2006    3:20 pm using AcqMethod M1
Sample Name: at335-2
Misc Info   :
Vial Number: 1
CurrentMeth: C:\HPCHEM\1\METHODS\M1.M
```

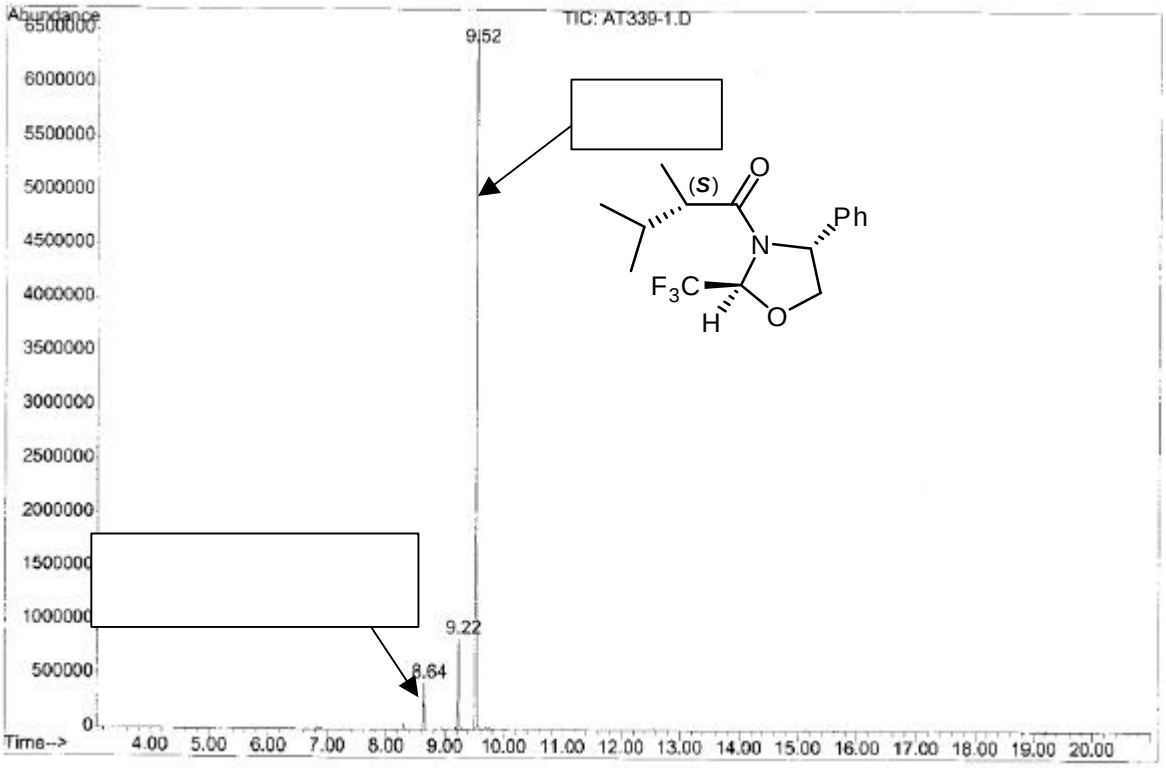
Retention Time	Area	Area %	Ratio %
Total Ion Chromatogram			
9.753	55120728	91.902	100.000
9.871	4857252	8.098	8.812


Abundance
Scan 1186 (9.868 min): AT335-2.D
110000
100000
90000
80000
70000
60000
50000
40000
30000
20000
10000
0
m/z-->
85
273
148
104
113
124
57
69
95
133
159
173
186
204
216
231
244
260
286
314
329
50 60 70 80 90 100 110 120 130 140 150 160 170 180 190 200 210 220 230 240 250 260 270 280 290 300 310 320 330


2.79
0.25
0.16
Abundance

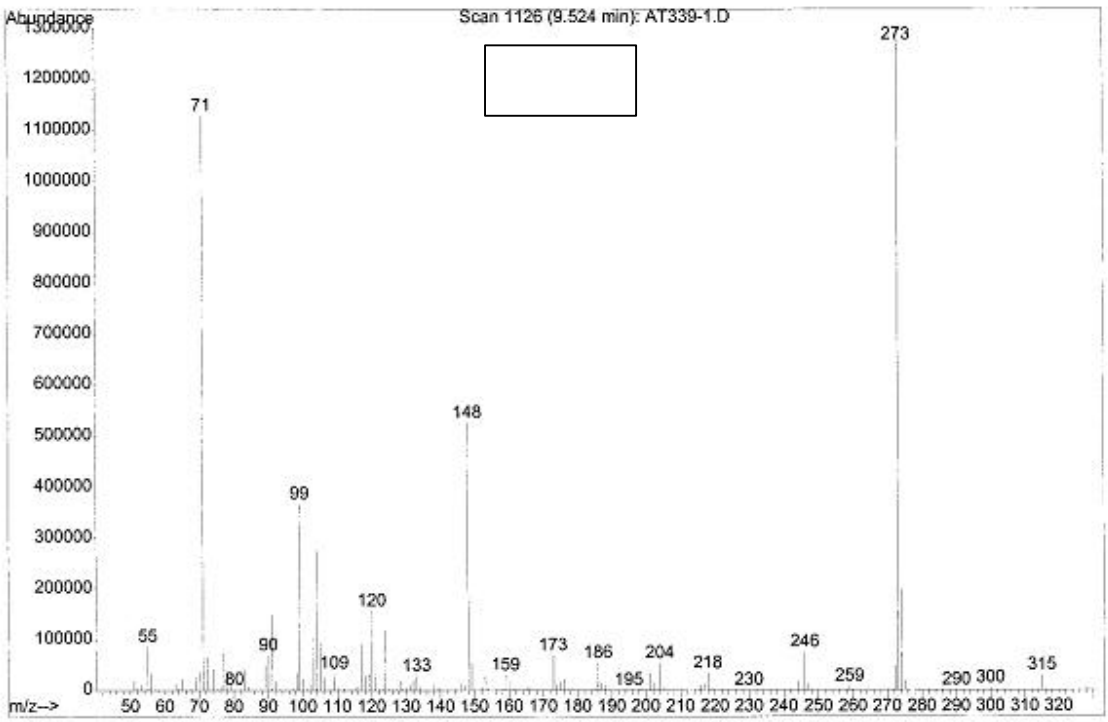
Reaction of 2a with *i*-PrI : crude mixture

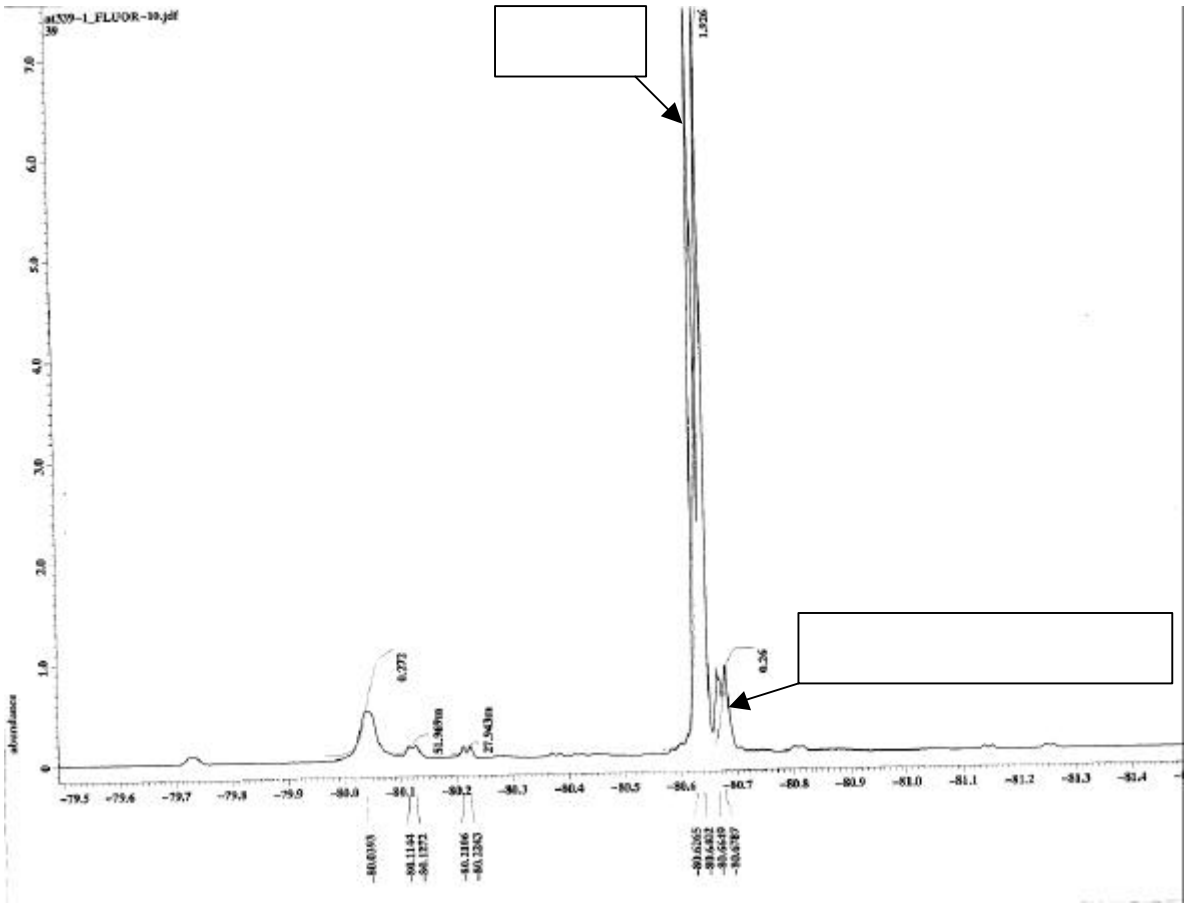
```
Information from Data File:
File       : C:\HPCHEM\1\DATA\AT339-1.D
Operator   : arno
Acquired   :  8 Feb 2006   5:55 pm using AcqMethod M1
Sample Name: at339-1
Misc Info  :
Vial Number: 1
CurrentMeth: C:\HPCHEM\1\METHODS\M1.M
```

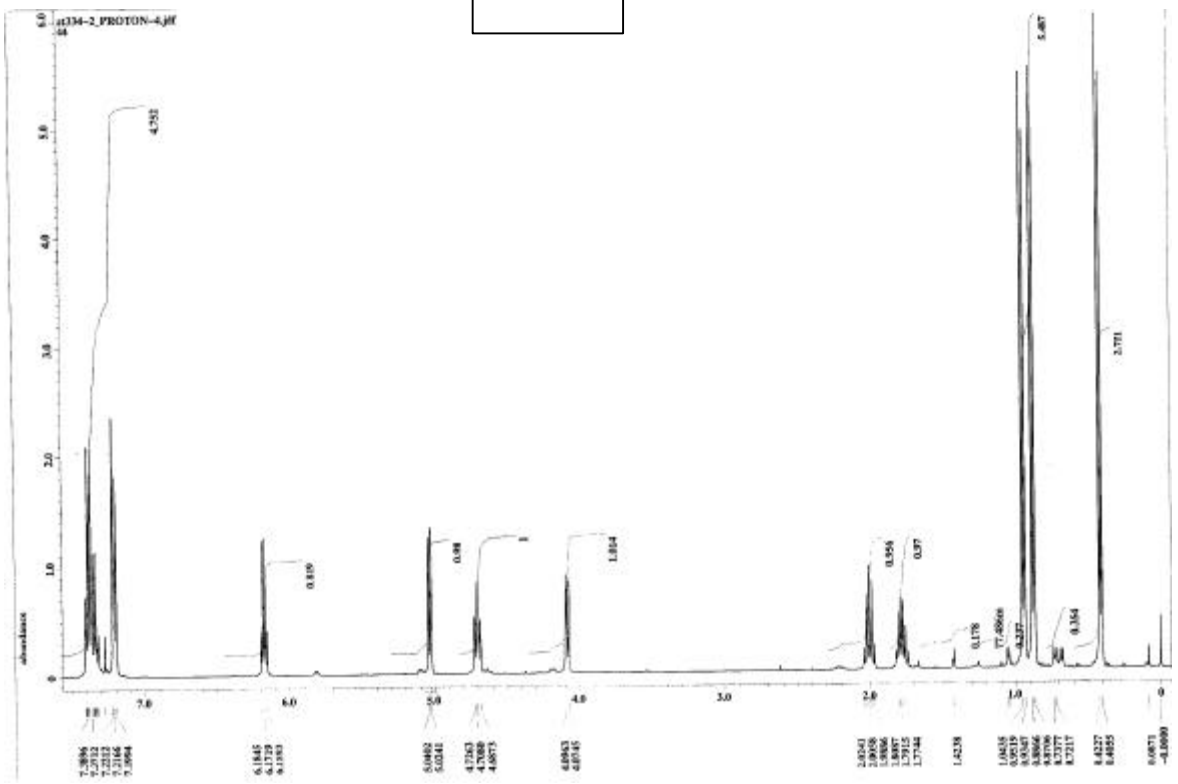


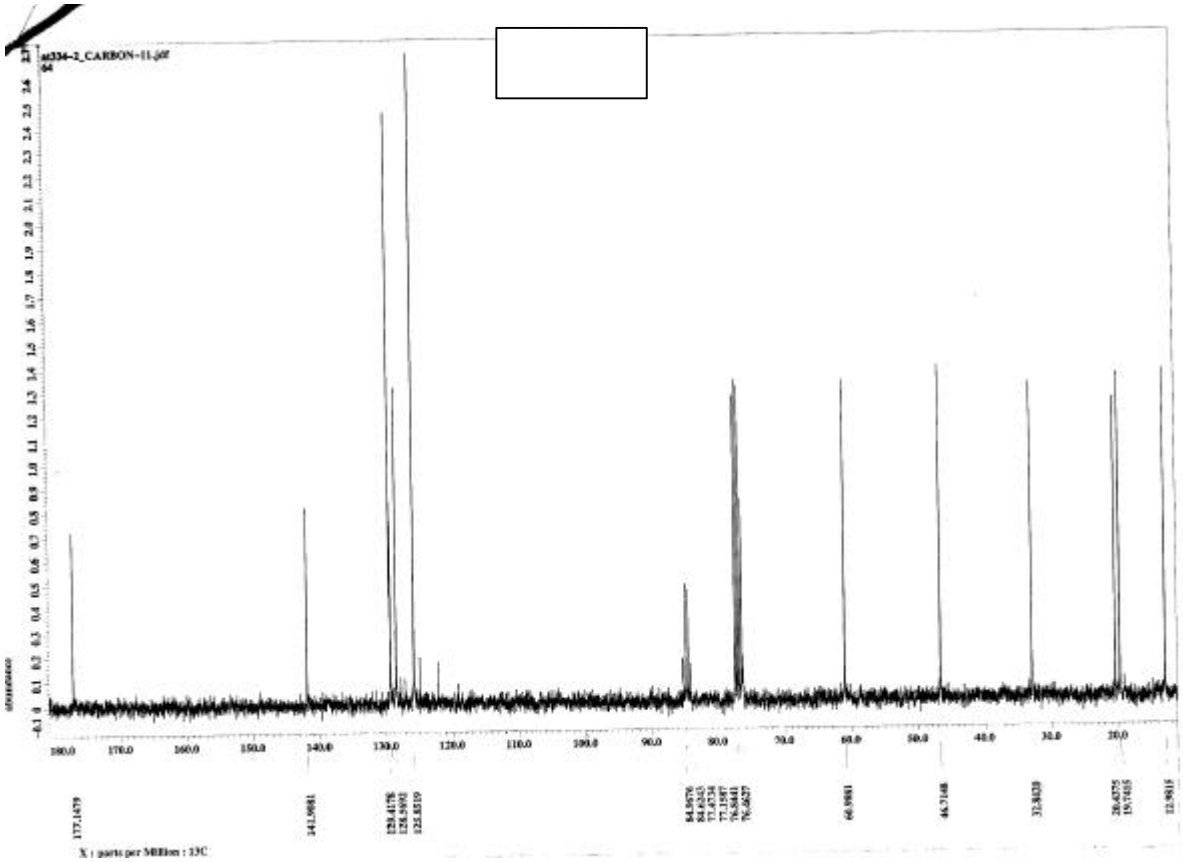
Retention Time	Area	Area %	Ratio %
Total Ion Chromatogram			
8.641	3874182	4.780	5.651
9.222	8623210	10.639	12.579
9.523	68551978	84.581	100.000

Thu Feb 09 15:06:15 2006


Abundance
Scan 1126 (9.524 min): AT339-1.D
m/z-->
273
71
148
99
120
55
90
109
133
159
173
186
204
218
246
195
230
259
290 300
315

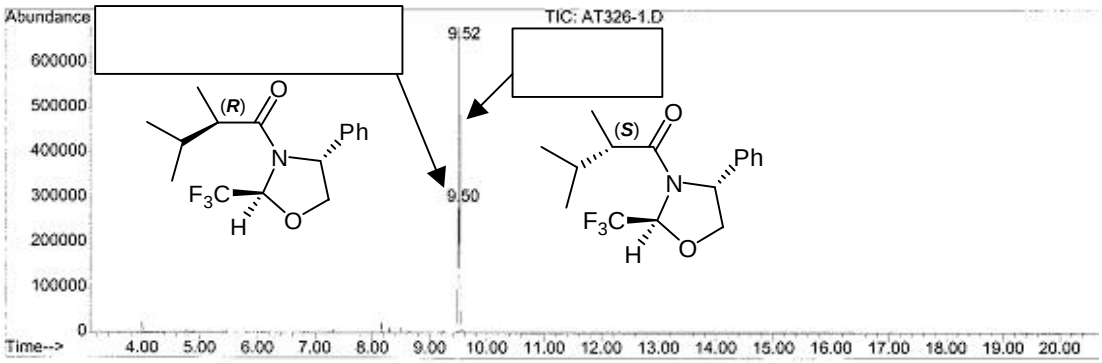

abundance
6.272
6.56
51.969m
27.543m



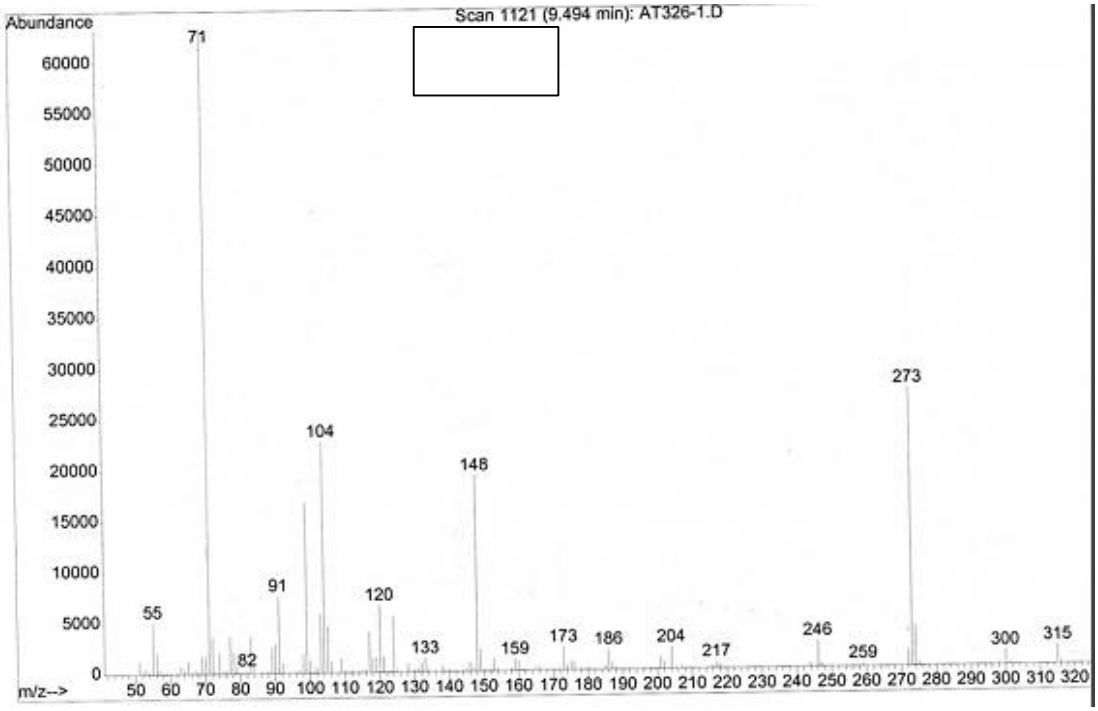


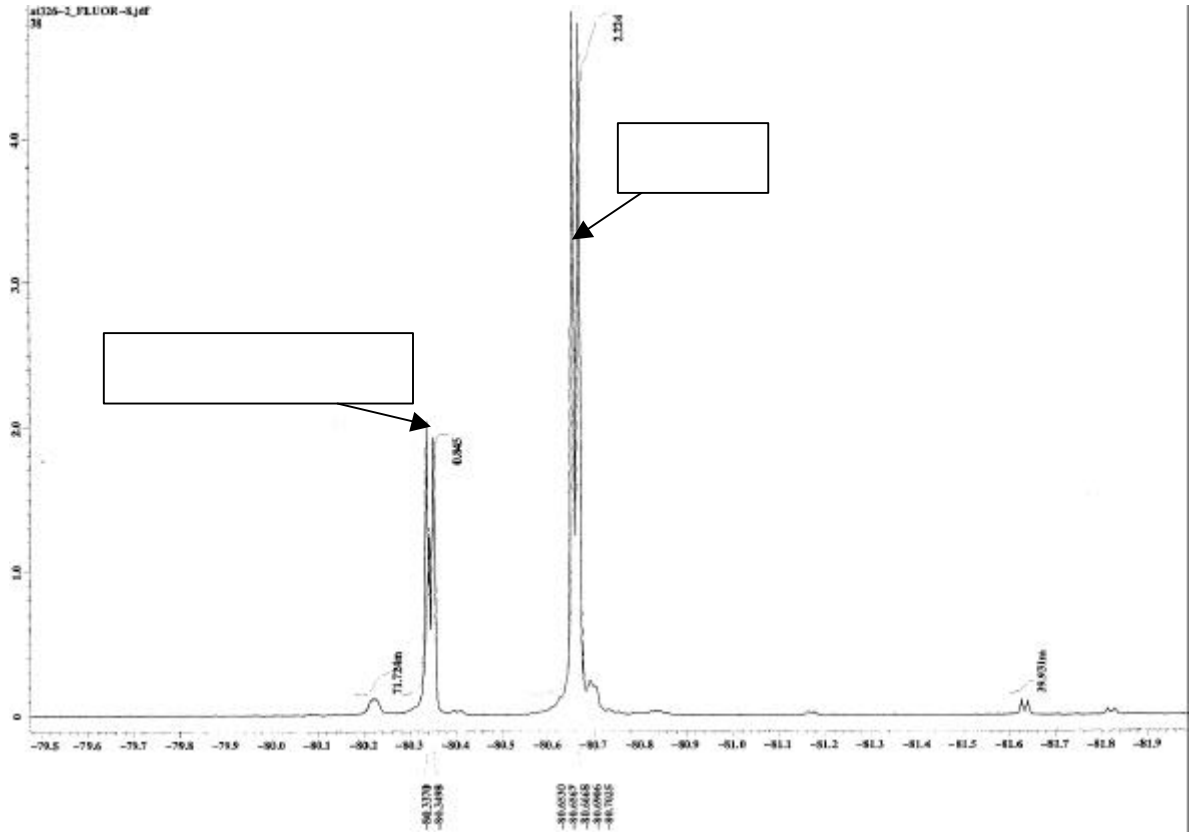
Epimerisation reaction of (*S*)-9a: crude mixture

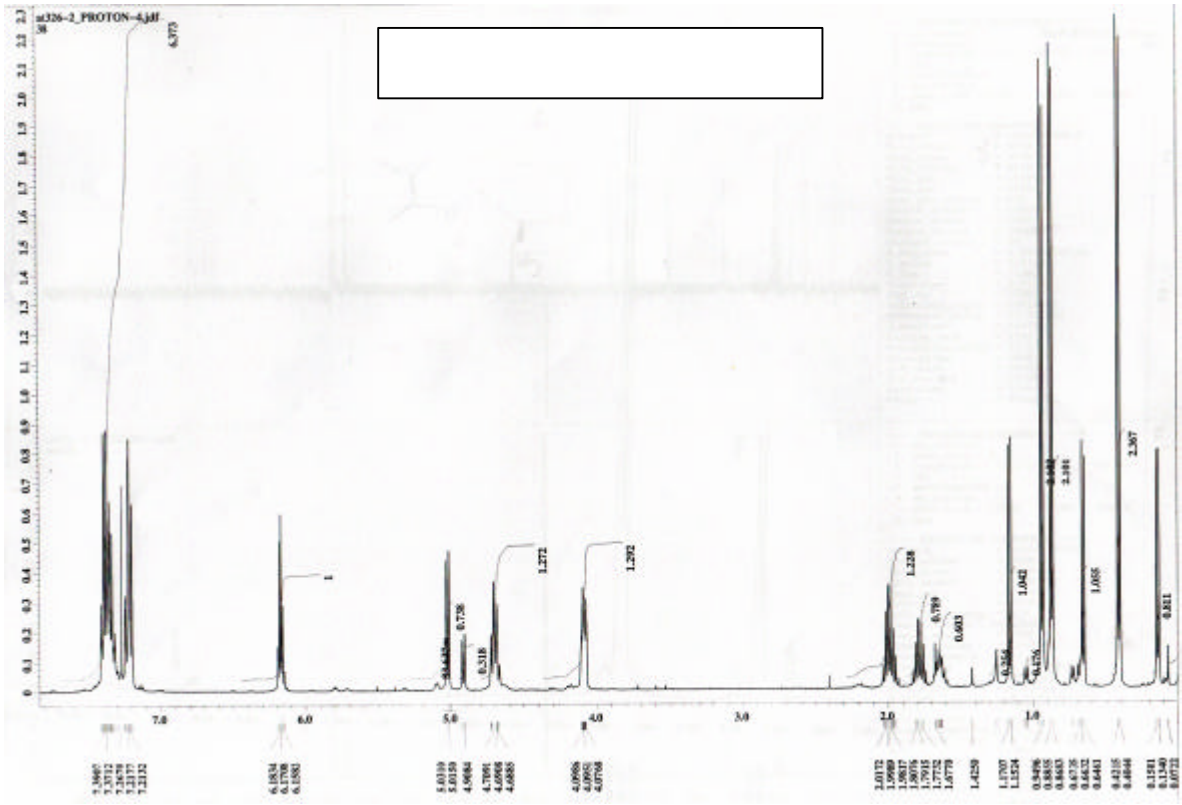
```
Information from Data File:
File       : C:\HPCHEM\1\DATA\AT326-1.D
Operator   : arno
Acquired   : 27 Jan 2006   9:04 am using AcqMethod M1
Sample Name:
Misc Info  :
Vial Number: 1
CurrentMeth: C:\HPCHEM\1\METHODS\M1.M
```

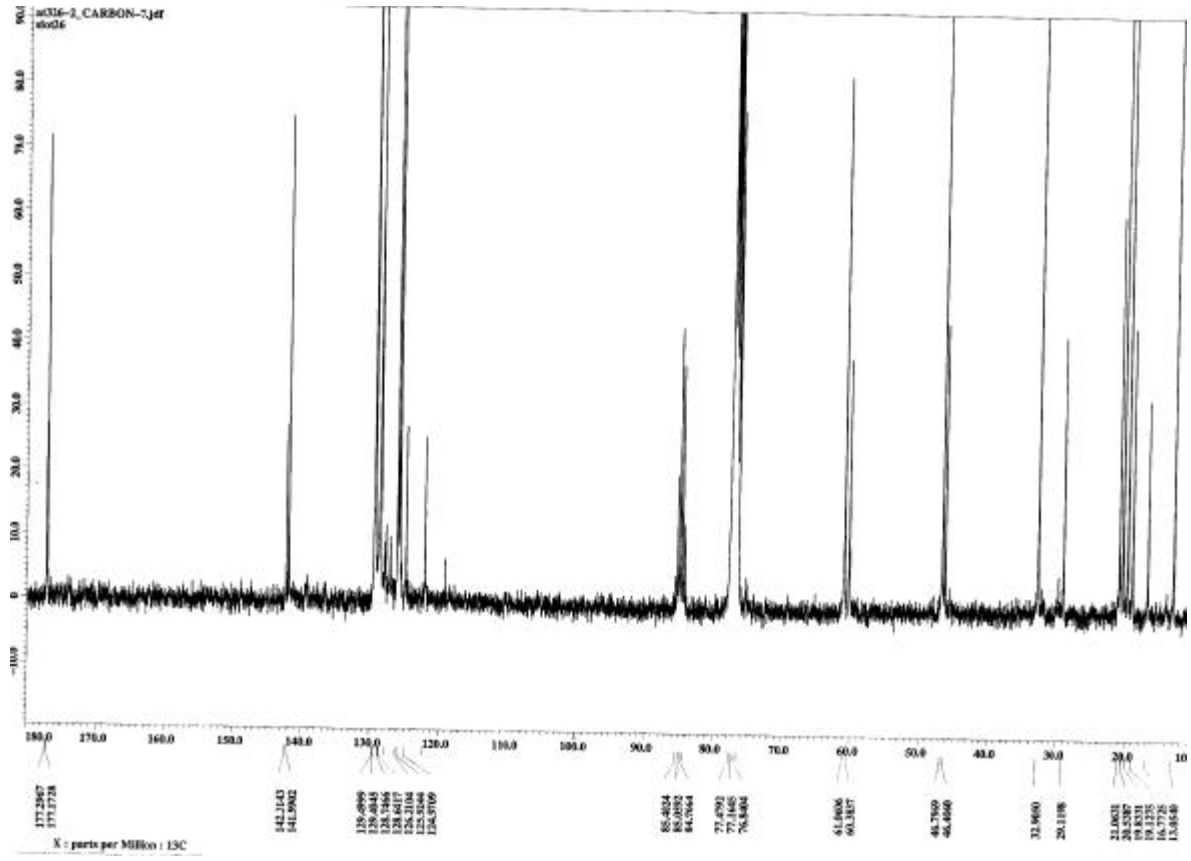


Retention Time	Area	Area %	Ratio %
Total Ion Chromatogram			
9.498	2452145	26.129	35.372
9.522	6932508	73.871	100.000



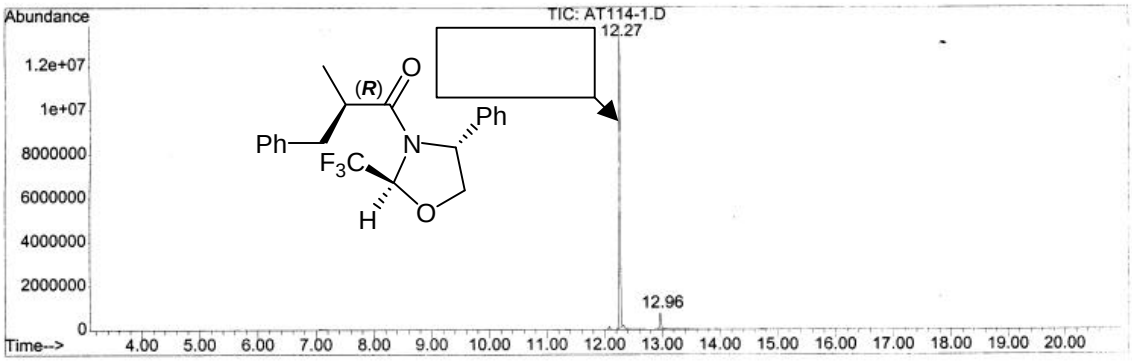





ac316-2_CARBON-7.jdf
X : parts per Million : 13C

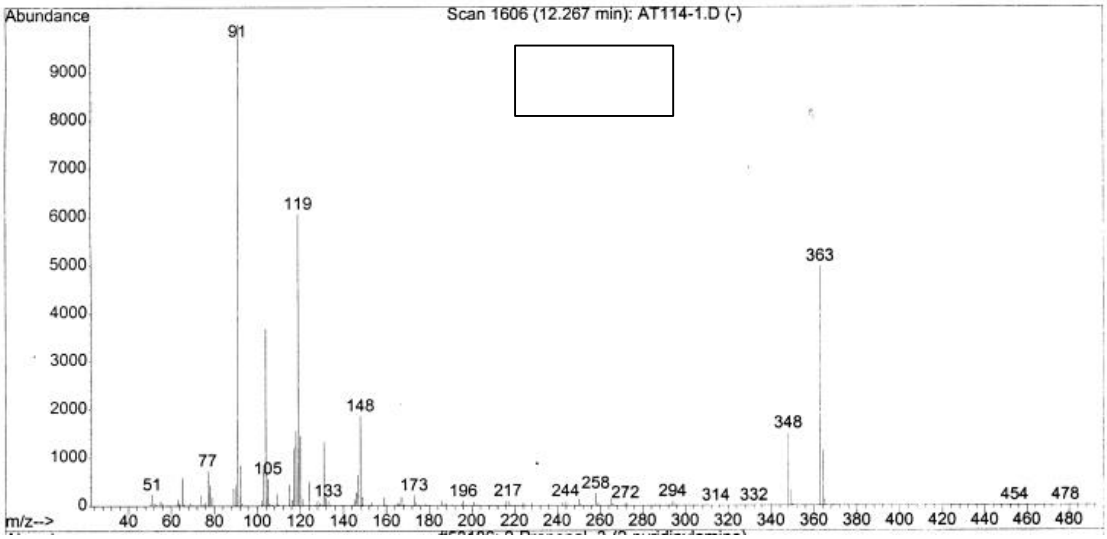
Methylation reaction of 2b : crude mixture

```
Information from Data File:
File        : C:\HPCHEM\1\DATA\AT114-1.D
Operator    :
Acquired    : 28 Jun 2004  12:49 pm using AcqMethod METHODE1
Sample Name:
Misc Info   :
Vial Number: 4
CurrentMeth: C:\HPCHEM\1\METHODS\METHODE1.M
```

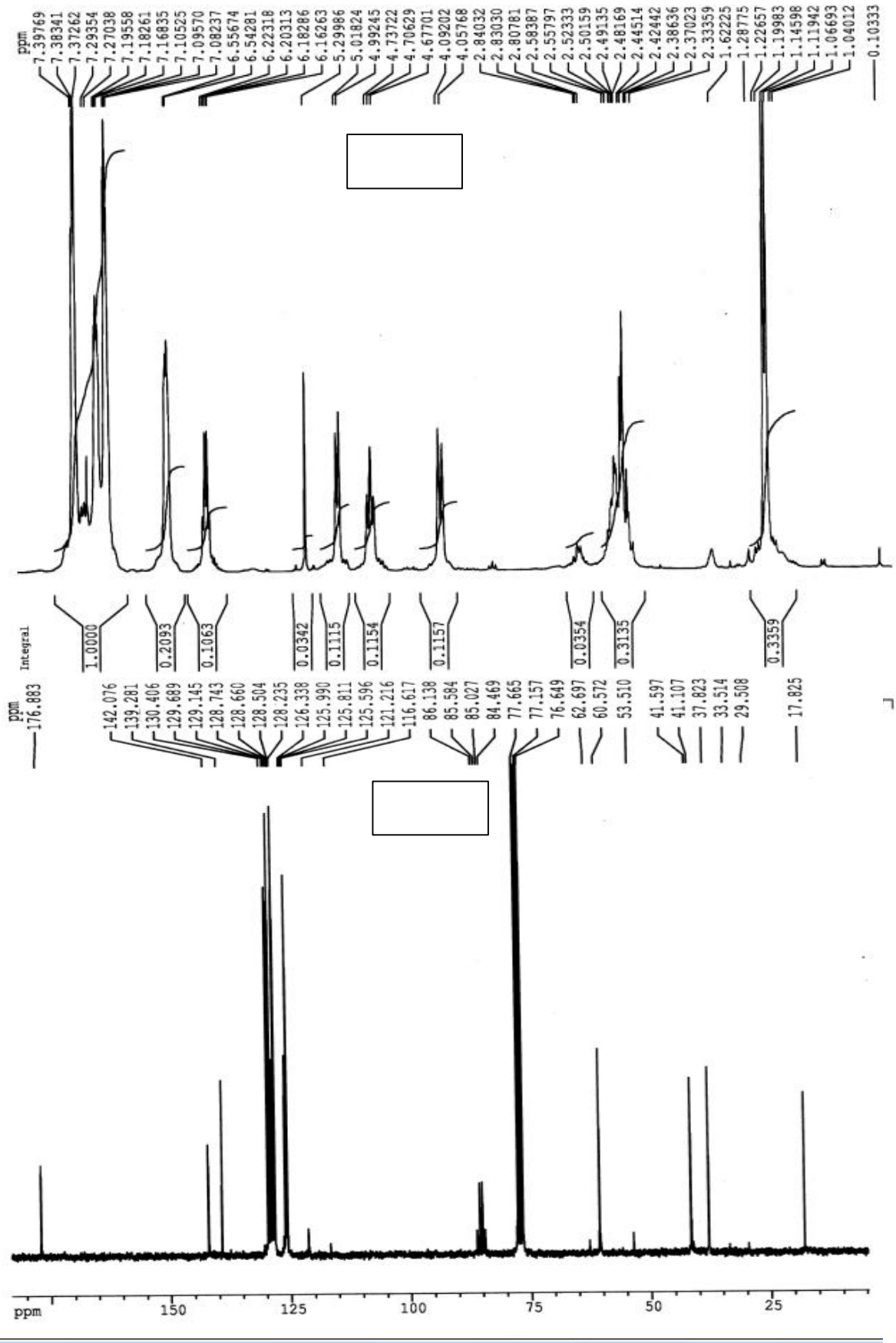


Retention Time	Area	Area %	Ratio %
Total Ion Chromatogram			
12.268	199681880	92.987	100.000
12.964	15060418	7.013	7.542

Pk#	RT	Area%	Library/ID	Ref#	CAS#	Qual
1	12.27	92.99	C:\DATABASE\NIST98.L			
			2-Propenal, 3-(2-pyridinylamino)-	53186	1000221-37-3	27
			Benzene, (1-ethylpropyl)-	117456	001196-58-3	25
			Cedren-13-ol, 8-	53090	018319-35-2	22

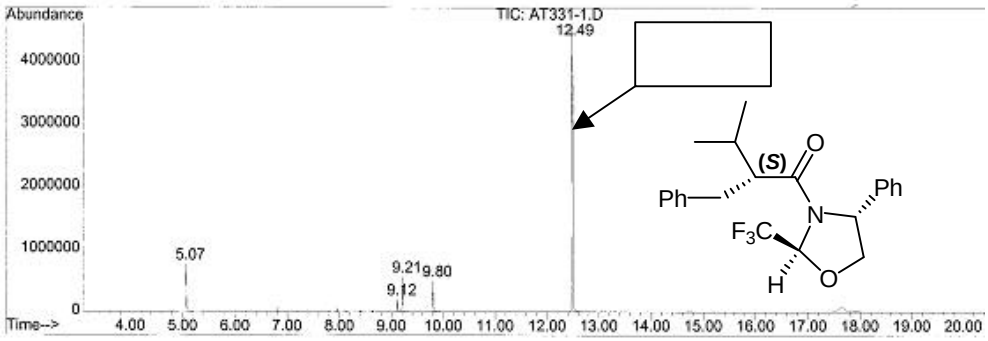


at114-2

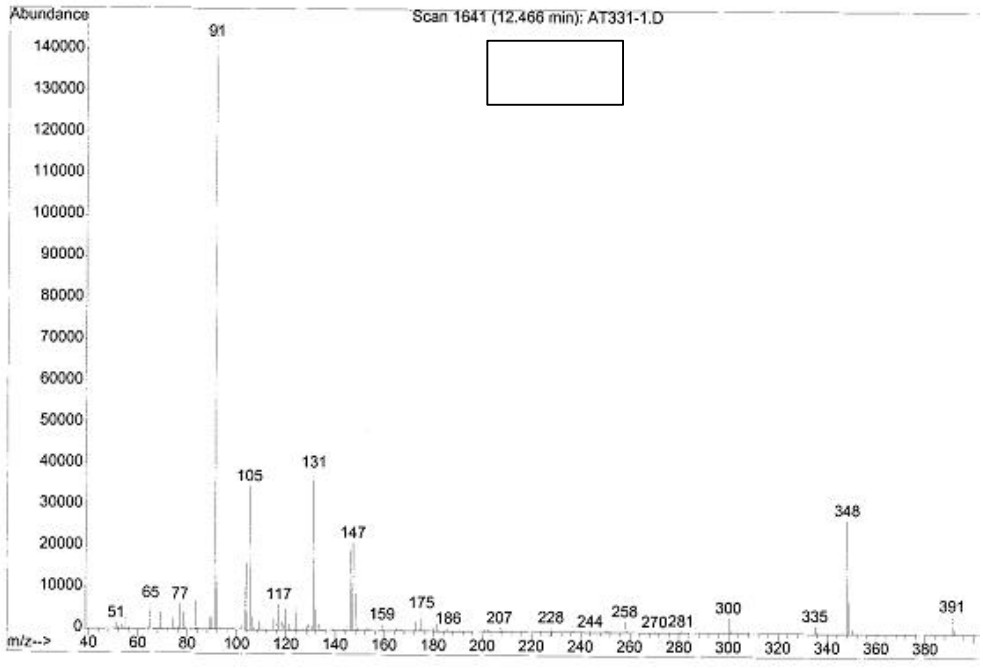

ppm
7.39769
7.38341
7.37262
7.29354
7.27038
7.19558
7.18261
7.16835
7.10525
7.09570
7.08237
6.55674
6.54281
6.22318
6.20313
6.18286
6.16263
5.29986
5.01824
4.99245
4.73722
4.70629
4.67701
4.09202
4.05768
2.84032
2.83030
2.80781
2.58387
2.55797
2.52333
2.50159
2.49135
2.48169
2.44514
2.42442
2.38636
2.37023
2.33359
1.62225
1.28775
1.22657
1.19983
1.14598
1.11942
1.06693
1.04012
0.10333
Integral
1.0000
0.2093
0.1063
0.0342
0.1115
0.1154
0.1157
0.0354
0.3135
0.3359
ppm
176.883
142.076
139.281
130.406
129.689
129.145
128.743
128.660
128.504
128.235
126.338
125.990
125.811
125.596
121.216
116.617
86.138
85.584
85.027
84.469
77.665
77.157
76.649
62.697
60.572
53.510
41.597
41.107
37.823
33.514
29.508
17.825
ppm
150
125
100
75
50
25

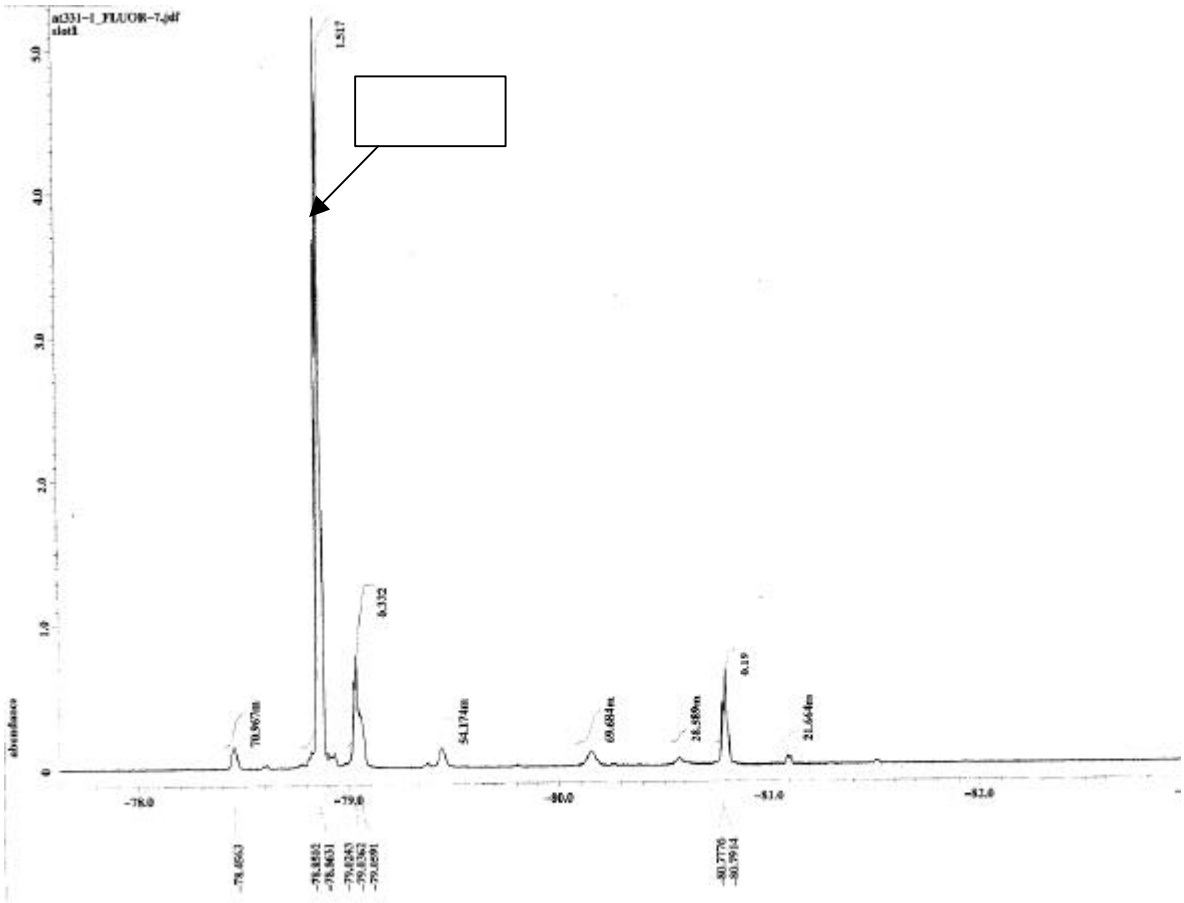
Benzylation reaction of 2c : crude mixture

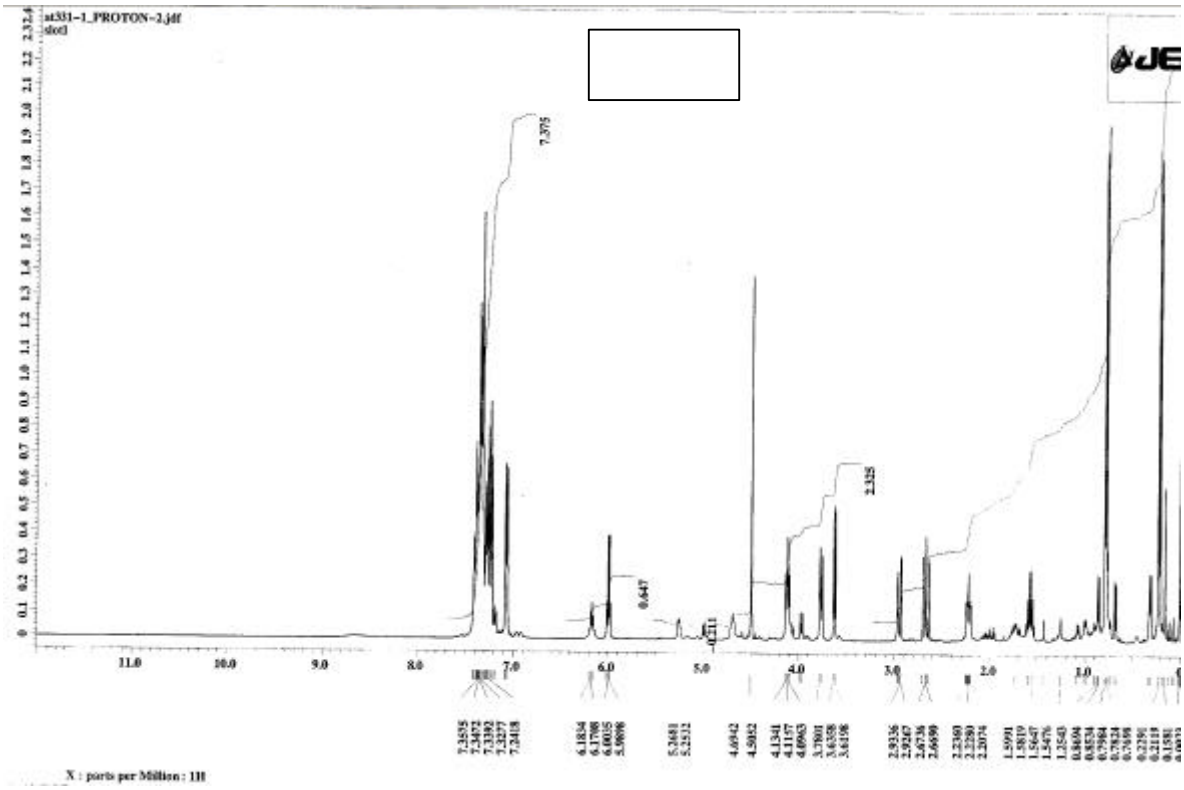
```
Information from Data File:
File       : C:\HPCHEM\1\DATA\AT331-1.D
Operator   :
Acquired   : 31 Jan 2006  10:10 am using AcqMethod M1
Sample Name: at331-1
Misc Info  :
Vial Number: 1
CurrentMeth: C:\HPCHEM\1\METHODS\M1.M
```

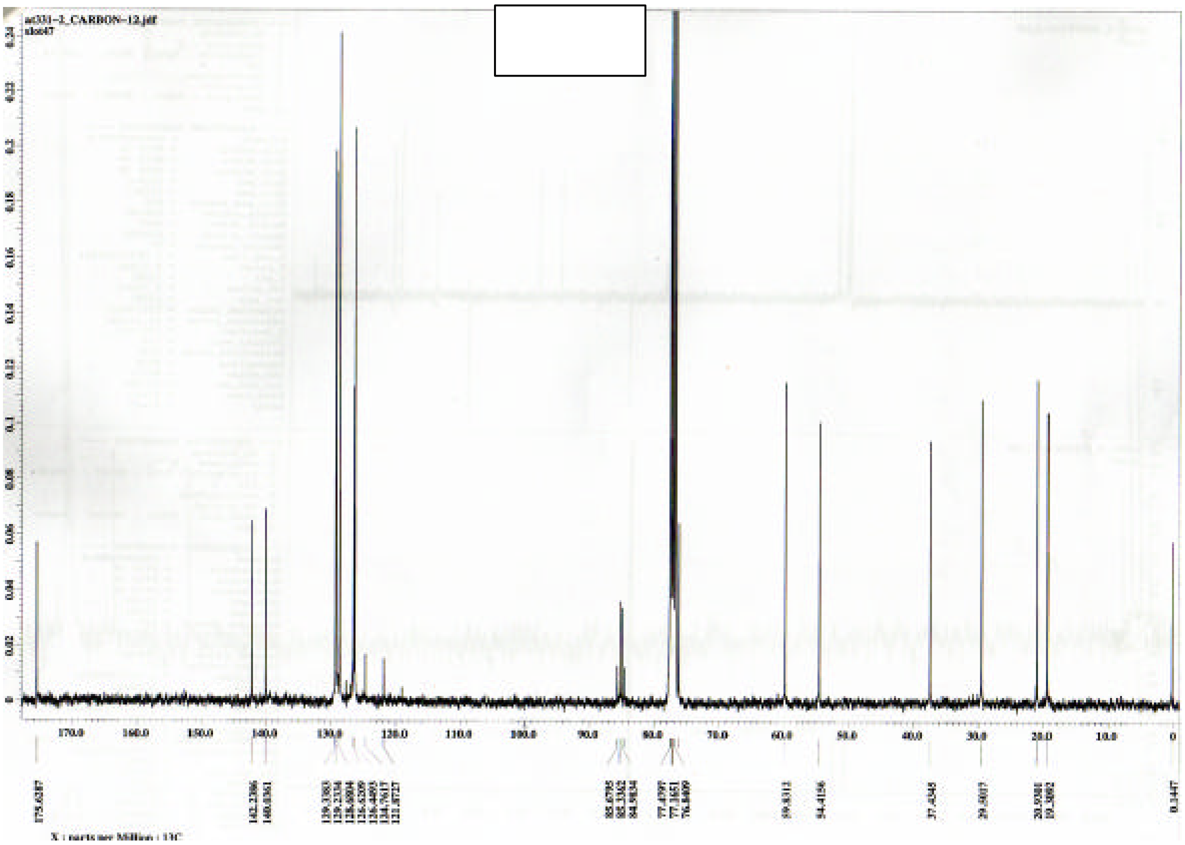


Retention Time	Area	Area %	Ratio %
Total Ion Chromatogram			
5.068	8214422	9.634	12.572
9.115	1801513	2.113	2.757
9.212	5155430	6.046	7.890
9.804	4756018	5.578	7.279
12.491	65338635	76.629	100.000



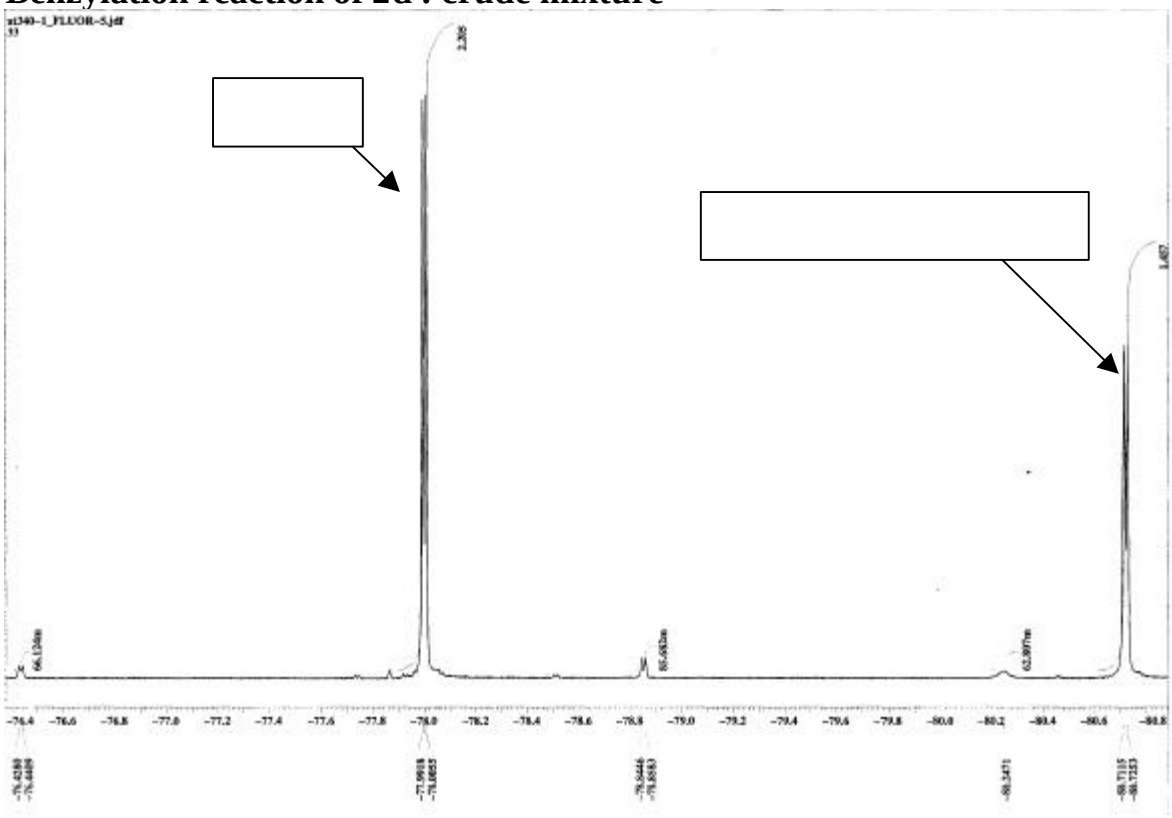

st331-1_FLUOR-7.jdf
slot1
1.517
0.352
0.19
70.967m
54.174m
69.684m
28.589m
21.664m
abundance
-78.0
-79.0
-80.0
-81.0
-82.0

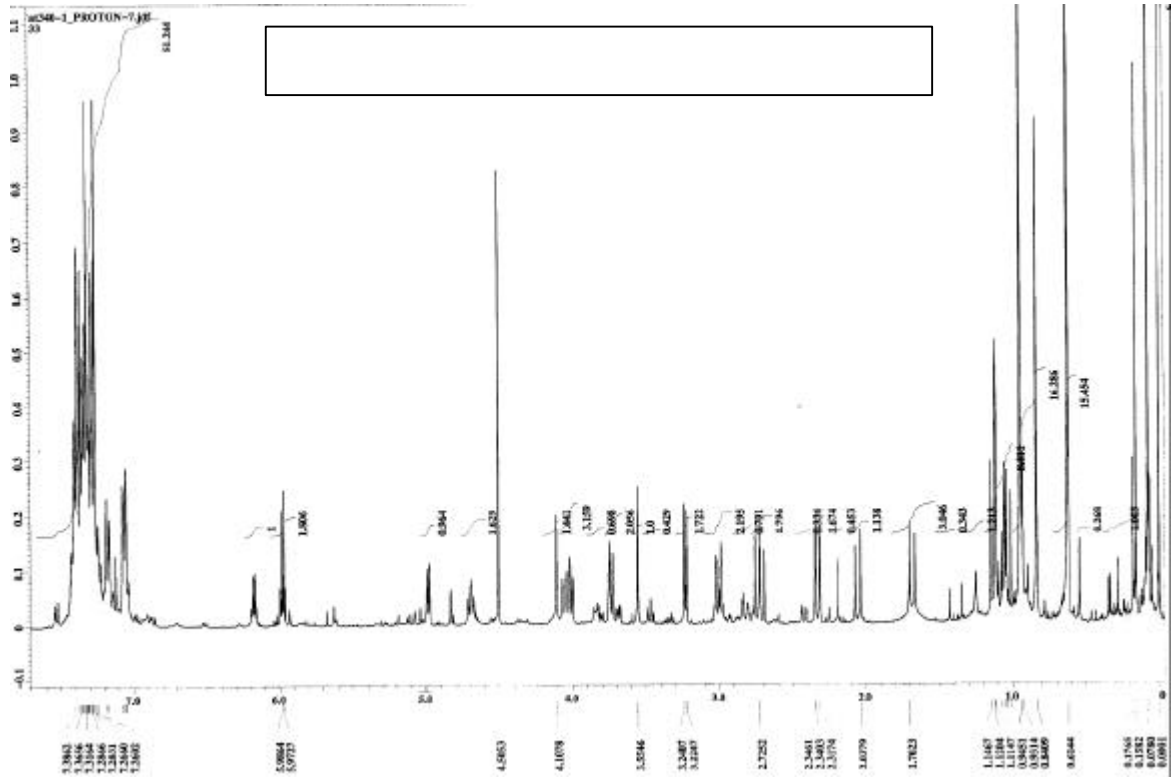

st331-1_PROTON-2.jdf
slot1
7.375
2.325
0.647
X : parts per Million : 1H



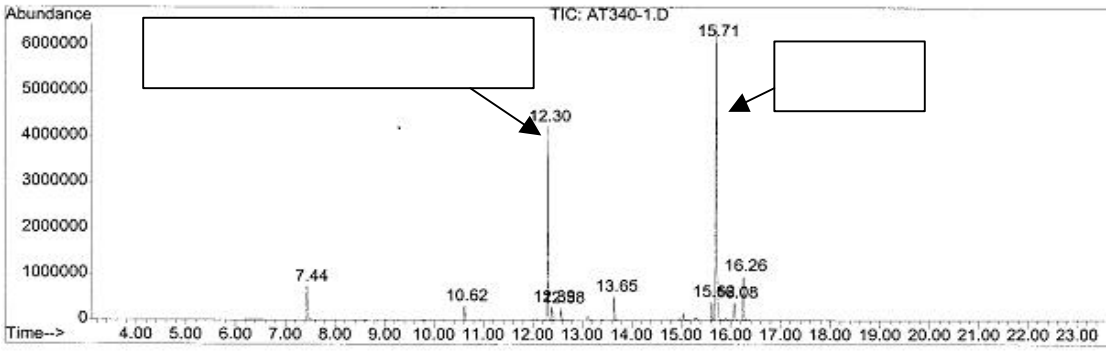
175.6287
142.2386
140.0361
129.3383
129.2334
128.6804
126.6209
126.4693
124.7617
121.8727
85.6795
85.3342
84.9834
77.4797
77.1651
76.8409
59.8312
54.4156
37.4348
29.5017
20.9381
19.3892
0.3447
X : parts per Million : 13C

Benzylation reaction of 2d : crude mixture

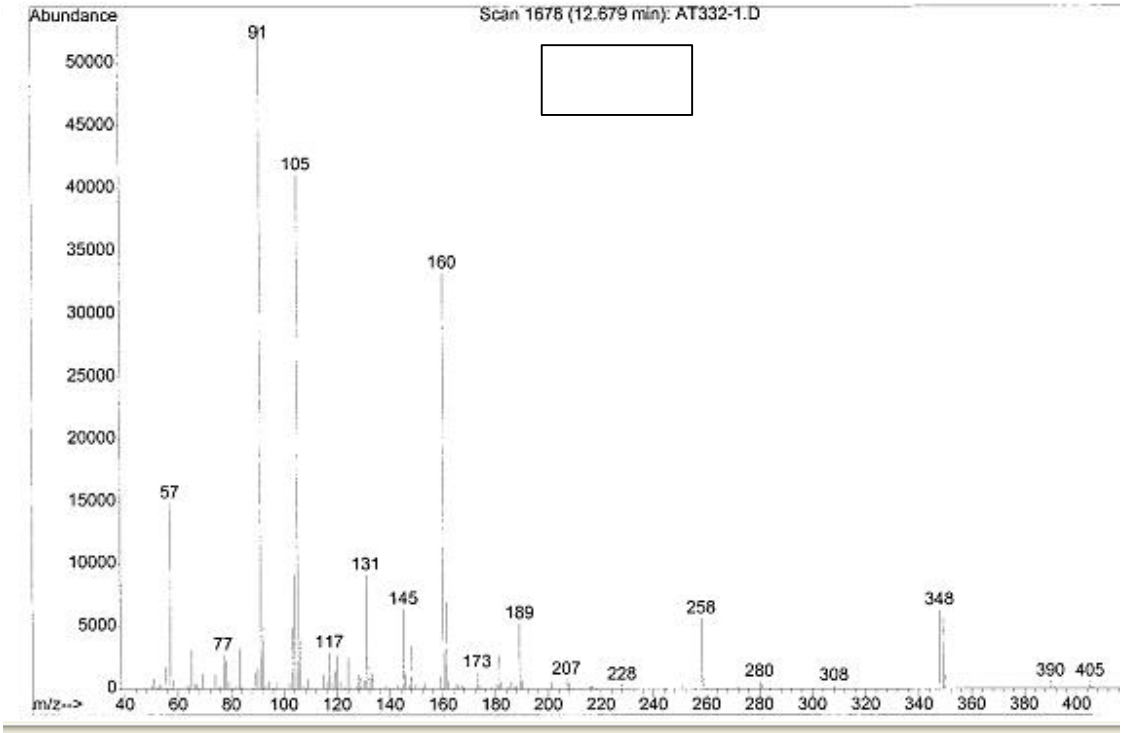


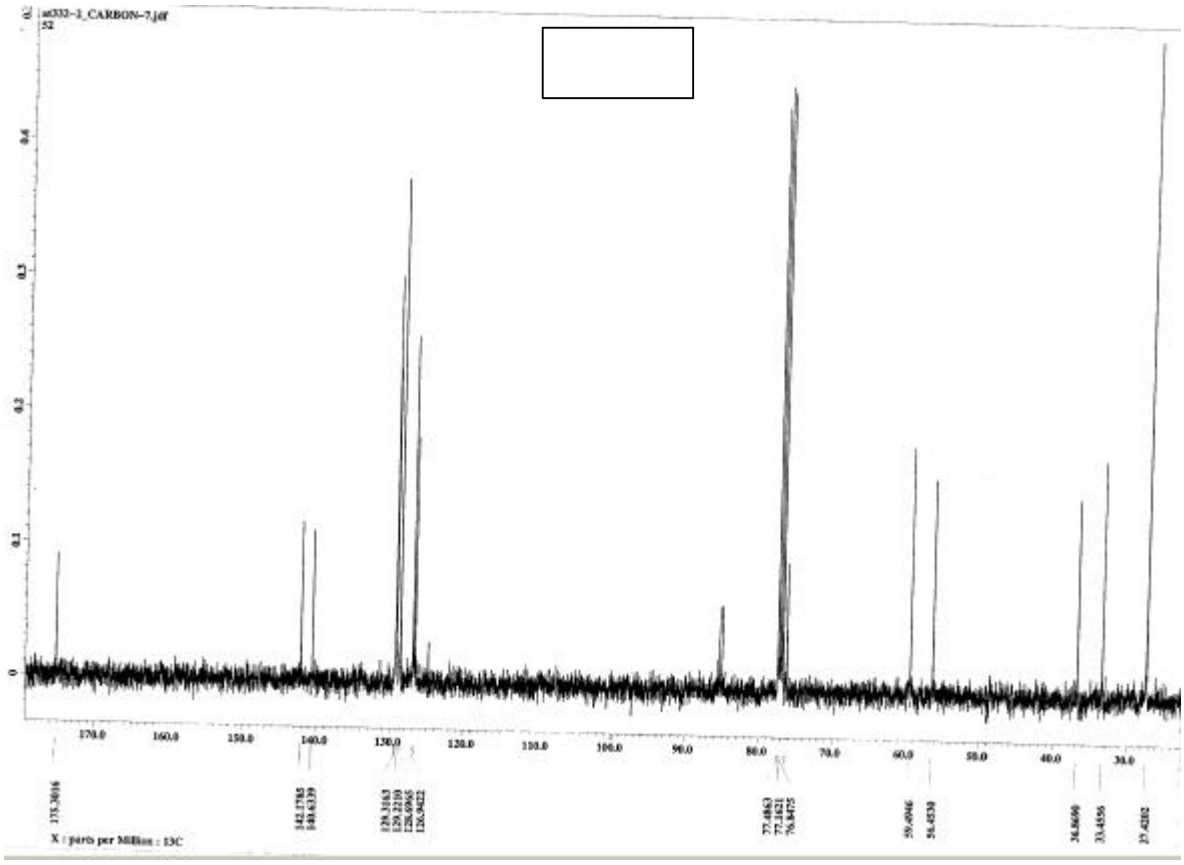


```
Information from Data File:
File       : C:\HPCHEM\1\DATA\AT340-1.D
Operator   : arno
Acquired   :  9 Feb 2006   3:17 pm using AcqMethod M1
Sample Name: at340-1
Misc Info  :
Vial Number: 1
CurrentMeth: C:\HPCHEM\1\METHODS\M1.M
```

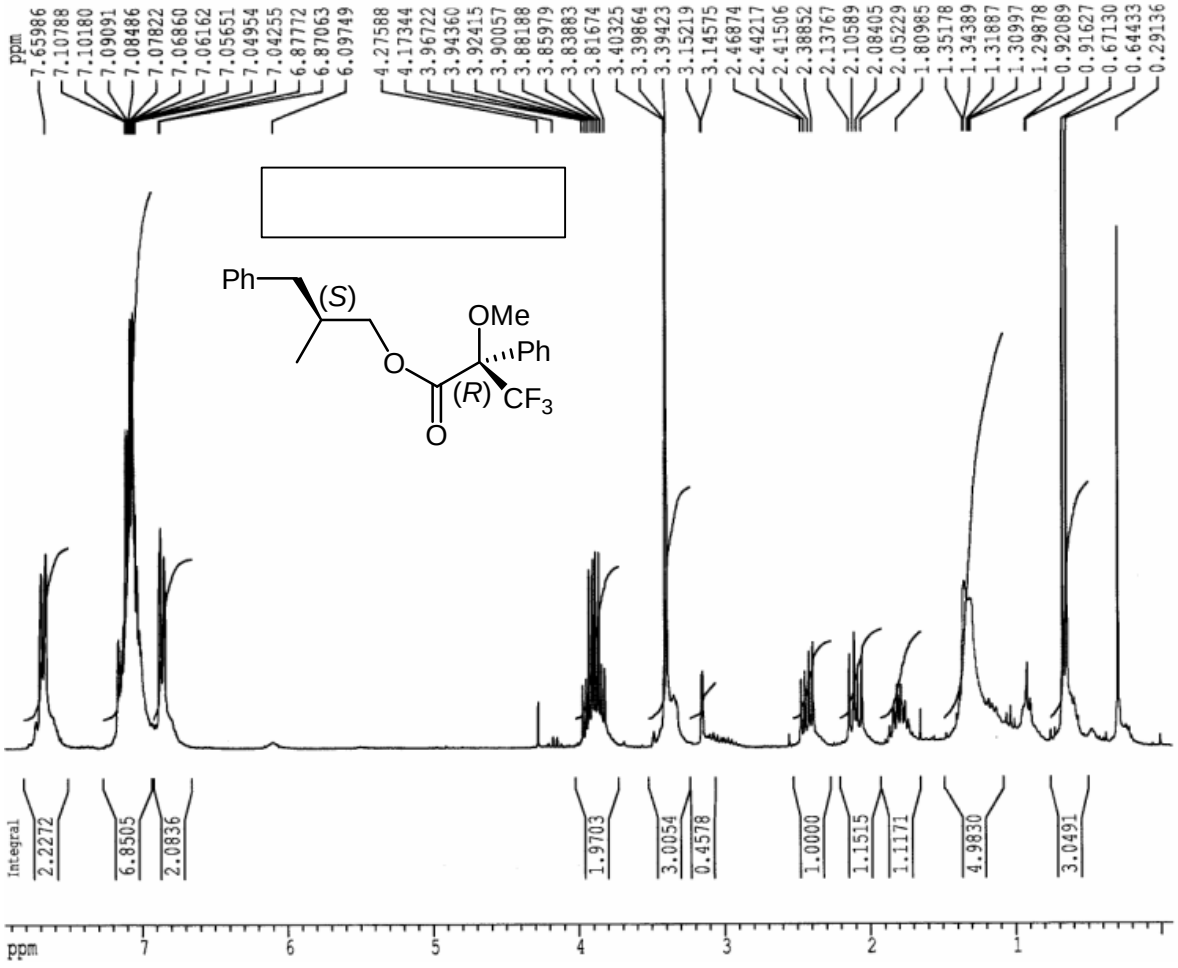


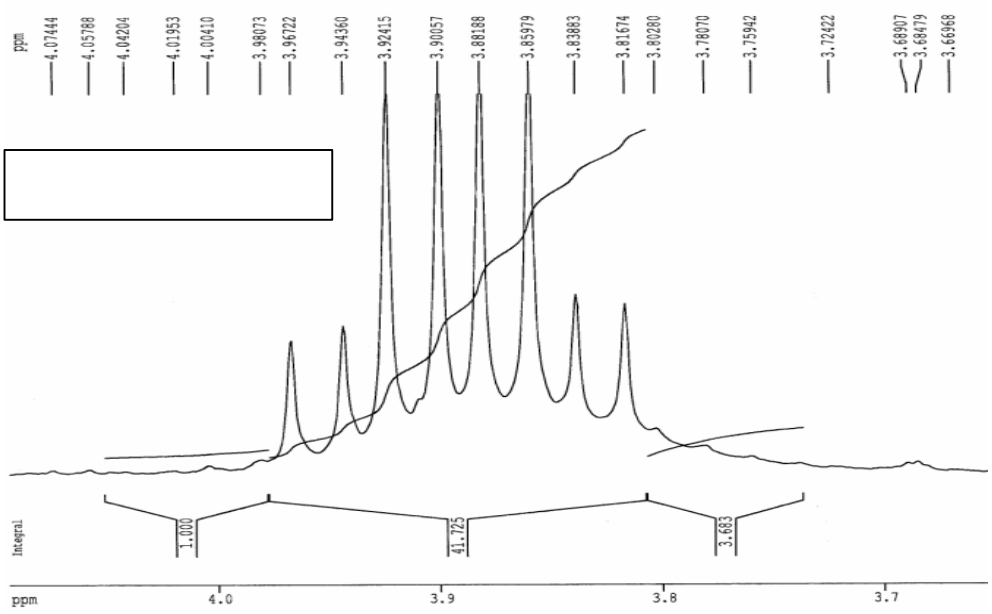
Retention Time	Area	Area %	Ratio %
Total Ion Chromatogram			
7.441	10520203	5.238	10.003
10.619	3144875	1.566	2.990
12.302	39205058	19.519	37.277
12.391	4620965	2.301	4.394
12.577	3260364	1.623	3.100
13.650	4921279	2.450	4.679
15.619	6466710	3.220	6.149
15.714	105172543	52.363	100.000
16.078	6911277	3.441	6.571
16.258	16630044	8.280	15.812

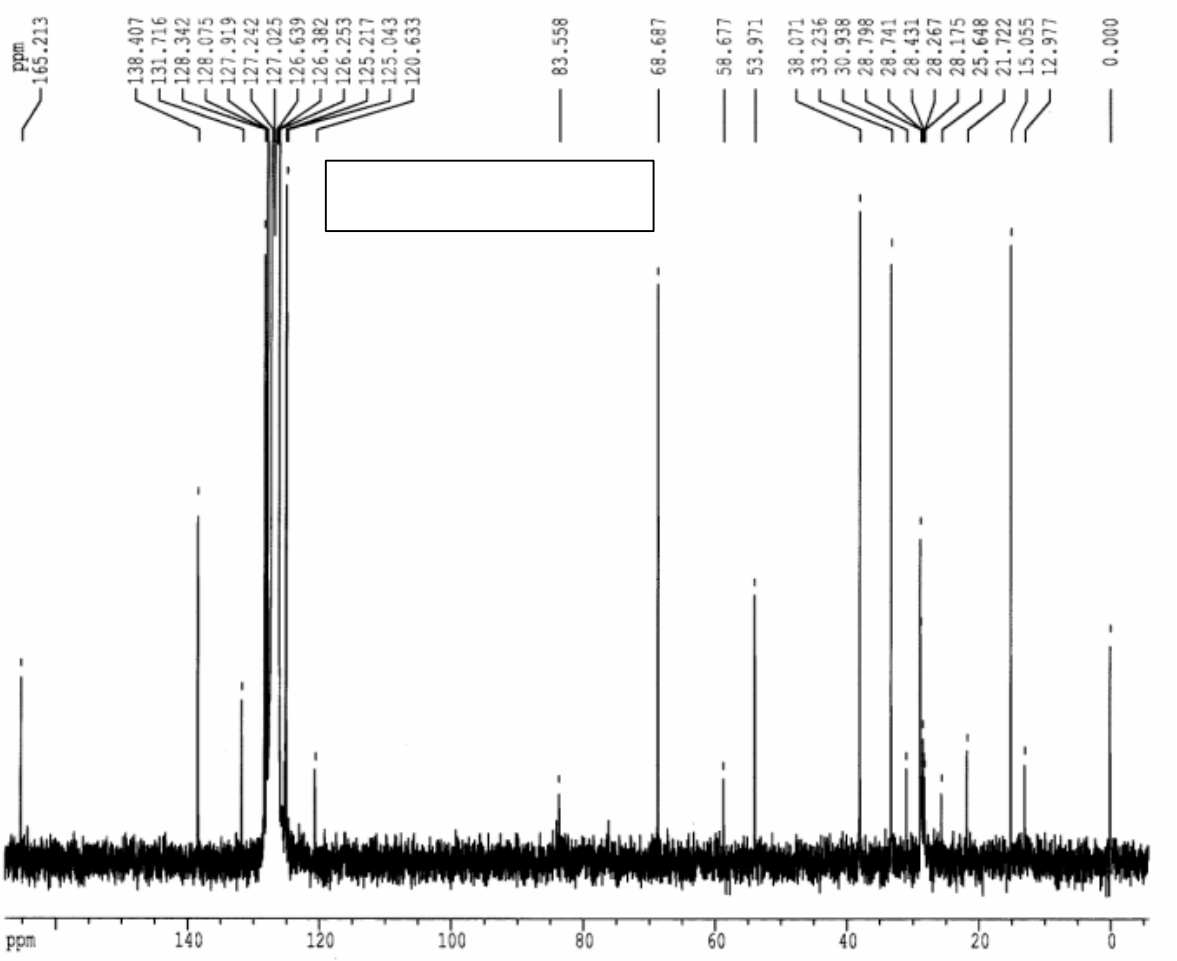



ai332-2_CARBON-7.jdf
52
0.5
0.4
0.3
0.2
0.1
0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
175.3016
142.1785
140.6339
129.3163
129.2210
128.4955
126.9422
77.4863
77.1621
76.8475
59.4046
56.4530
36.8690
33.4556
27.4202
X : parts per Million : 13C

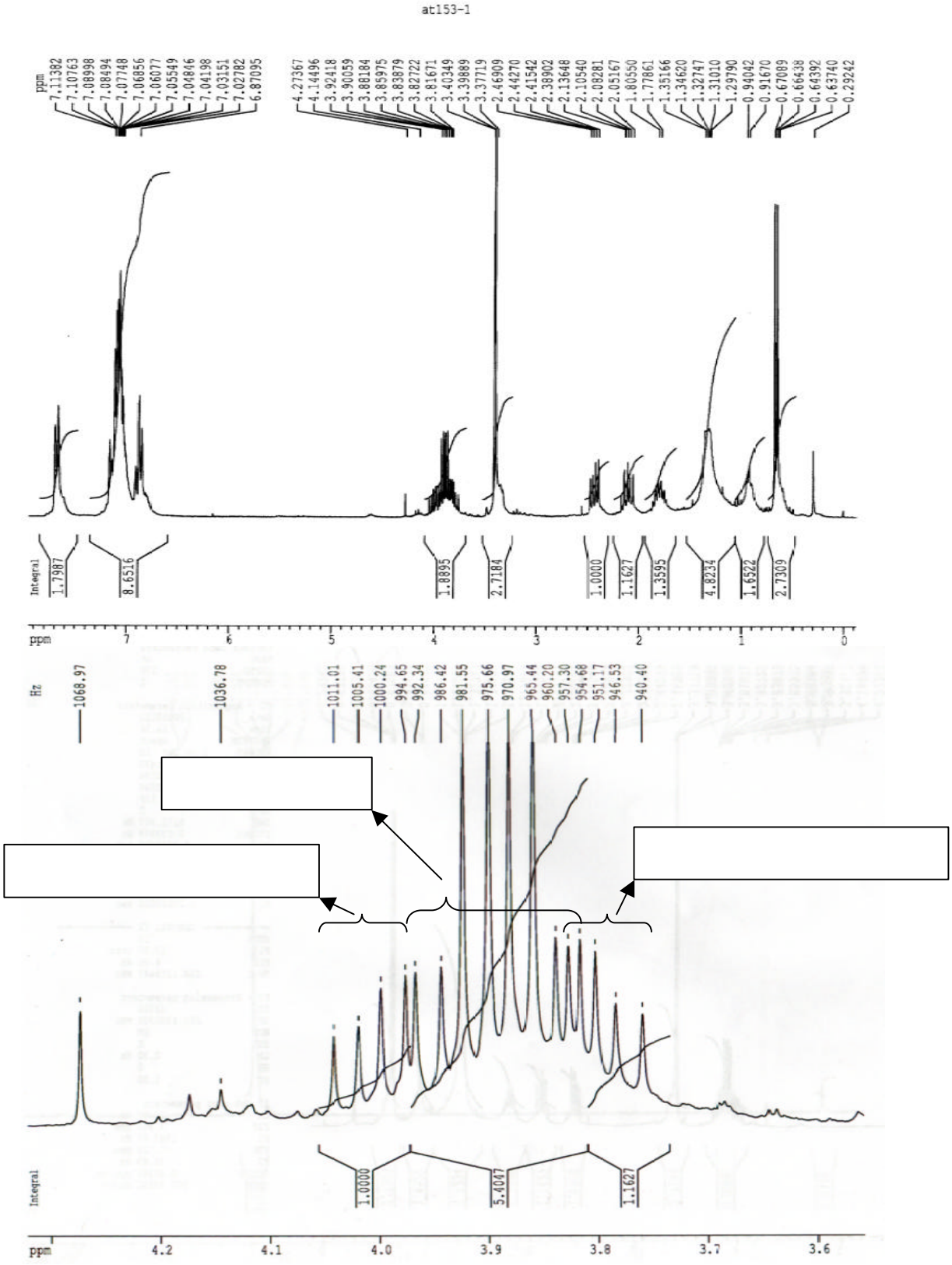
Mosher ester of 11: (S)-MTPA Ester

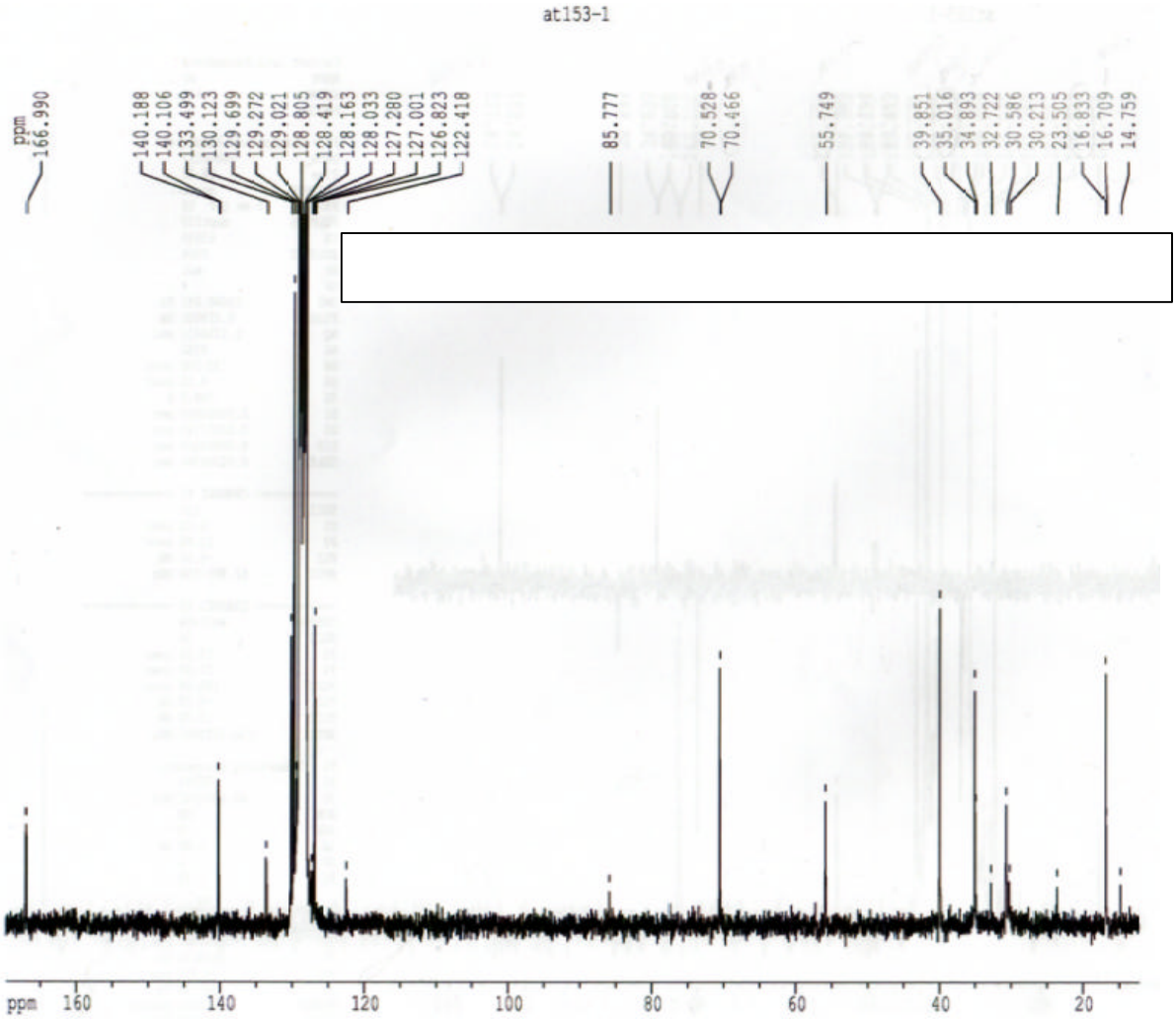





ppm
165.213
138.407
131.716
128.342
128.075
127.919
127.242
127.025
126.639
126.382
126.253
125.217
125.043
120.633
83.558
68.687
58.677
53.971
38.071
33.236
30.938
28.798
28.741
28.431
28.267
28.175
25.648
21.722
15.055
12.977
0.000
ppm
140
120
100
80
60
40
20
0

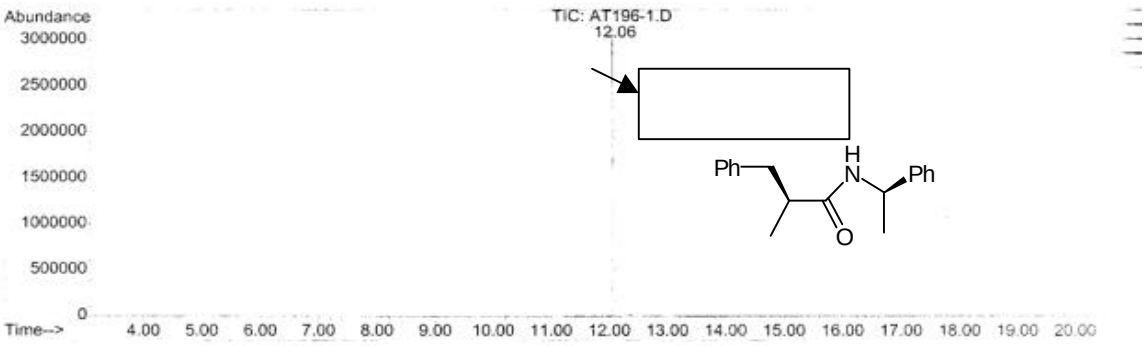
Mosher ester of 11 partially epimerized




at153-1
ppm
166.990
140.188
140.106
133.499
130.123
129.699
129.272
129.021
128.805
128.419
128.163
128.033
127.280
127.001
126.823
122.418
85.777
70.528
70.466
55.749
39.851
35.016
34.893
32.722
30.586
30.213
23.505
16.833
16.709
14.759
ppm
160
140
120
100
80
60
40
20

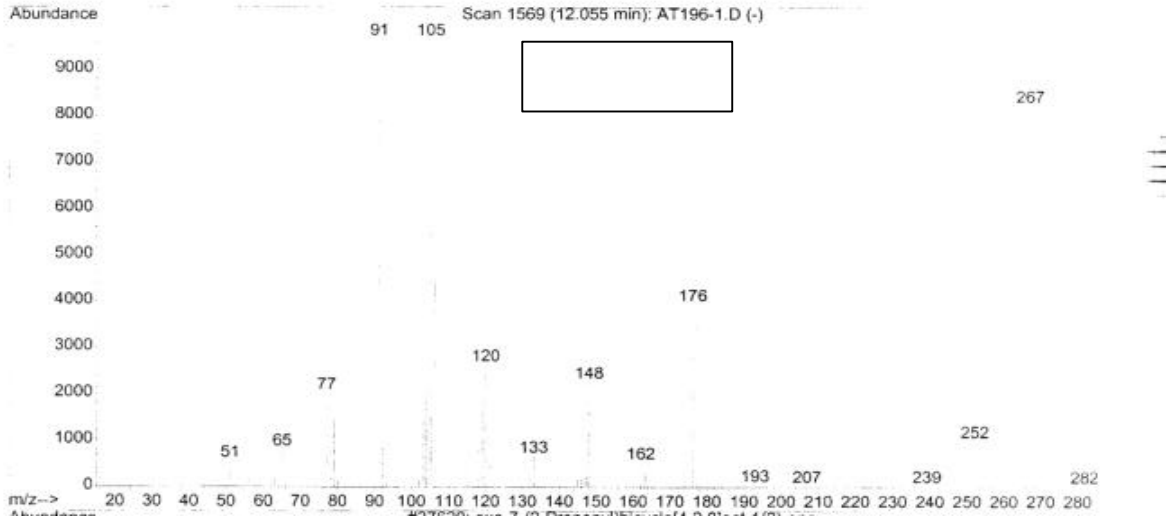
(2*S*)-2-benzyl-N-((*R*)-1-phenylethyl)propanamide of 14

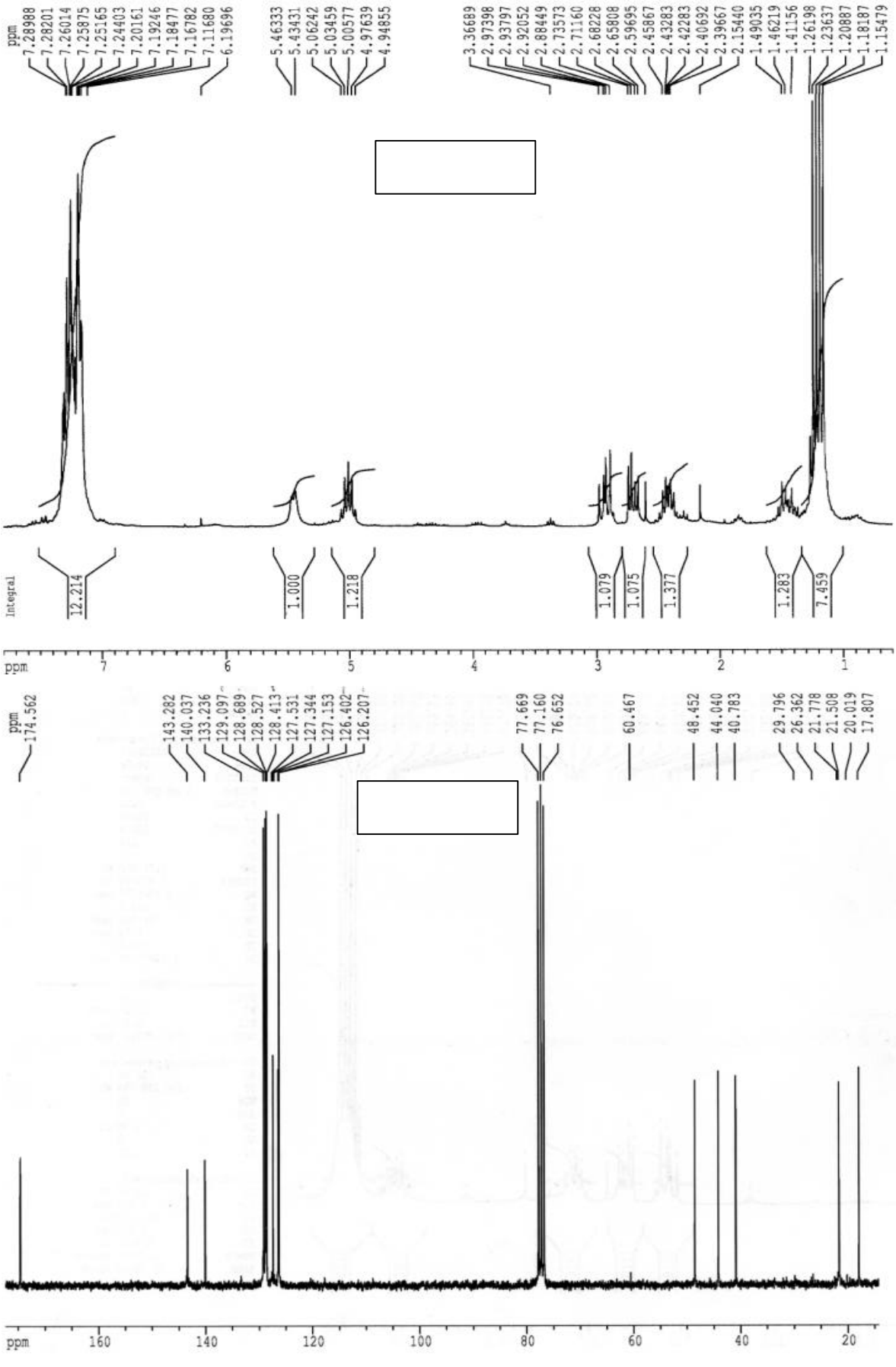
```
Information from Data File:
File       : C:\HPCHEM\1\DATA\AT196-1.D
Operator   :
Acquired   : 22 Mar 2005   2:03 pm using AcqMethod M1
Sample Name:
Misc Info  :
Vial Number: 4
CurrentMeth: C:\HPCHEM\1\METHODS\M1.M
```



Retention Time	Area	Area %	Ratio %
Total Ion Chromatogram			
12.057	61669826	100.000	100.000

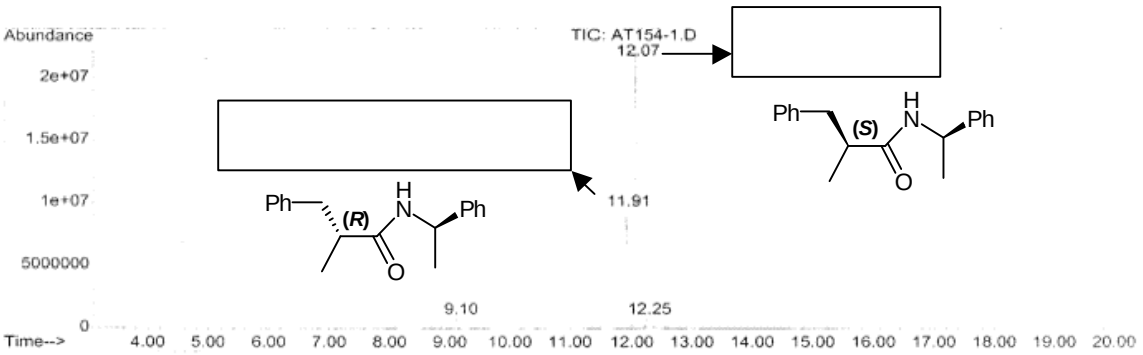
Pk#	RT	Area%	Library/ID	Ref#	CAS#	Qual
1	12.06	100.00	C:\DATABASE\NIST98.L			
			exo-7-(2-Propenyl)bicyclo[4.2.0]oc	37620	1000200-97-5	27
			1-(4-Nitrophenyl)-3-phenyl-2-pyraz	95450	1000148-39-2	22
			5H-Naphtho[2,3-b]carbazole	95521	000248-96-4	22




ppm
7.28988
7.28201
7.26014
7.25875
7.25165
7.24403
7.20161
7.19246
7.18477
7.16782
7.11680
6.19696
5.46333
5.43431
5.06242
5.03459
5.00577
4.97639
4.94855
3.36689
2.97398
2.93797
2.92052
2.88449
2.73573
2.71160
2.68228
2.65808
2.59695
2.45867
2.43283
2.42283
2.40692
2.39667
2.15440
1.49035
1.46219
1.41156
1.26198
1.23637
1.20887
1.18187
1.15479
Integral
12.214
1.000
1.218
1.079
1.075
1.377
1.283
7.459
ppm
7
6
5
4
3
2
1
ppm
174.562
143.282
140.037
133.236
129.097
128.689
128.527
128.413
127.531
127.344
127.153
126.402
126.207
77.669
77.160
76.652
60.467
48.452
44.040
40.783
29.796
26.362
21.778
21.508
20.019
17.807
ppm
160
140
120
100
80
60
40
20

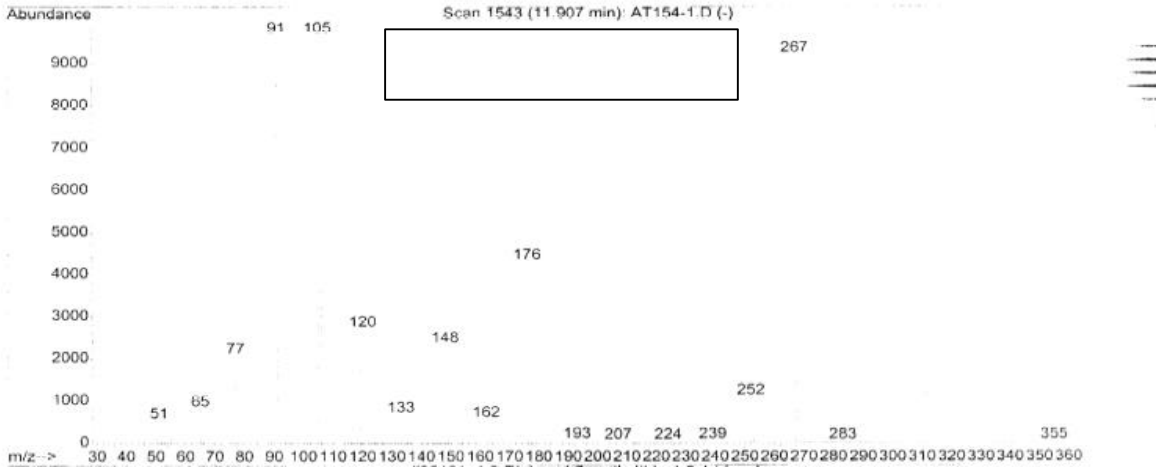
2-benzyl-N-((*R*)-1-phenylethyl)propanamide of 14 partially epimerized

```
Information from Data File:
File       : C:\HPCHEM\1\DATA\AT154-1.D
Operator   :
Acquired   :  3 Mar 2005    4:06 pm using AcqMethod METHODE1
Sample Name:
Misc Info  :
Vial Number: 6
CurrentMeth: C:\HPCHEM\1\METHODS\METHODE1.M
```

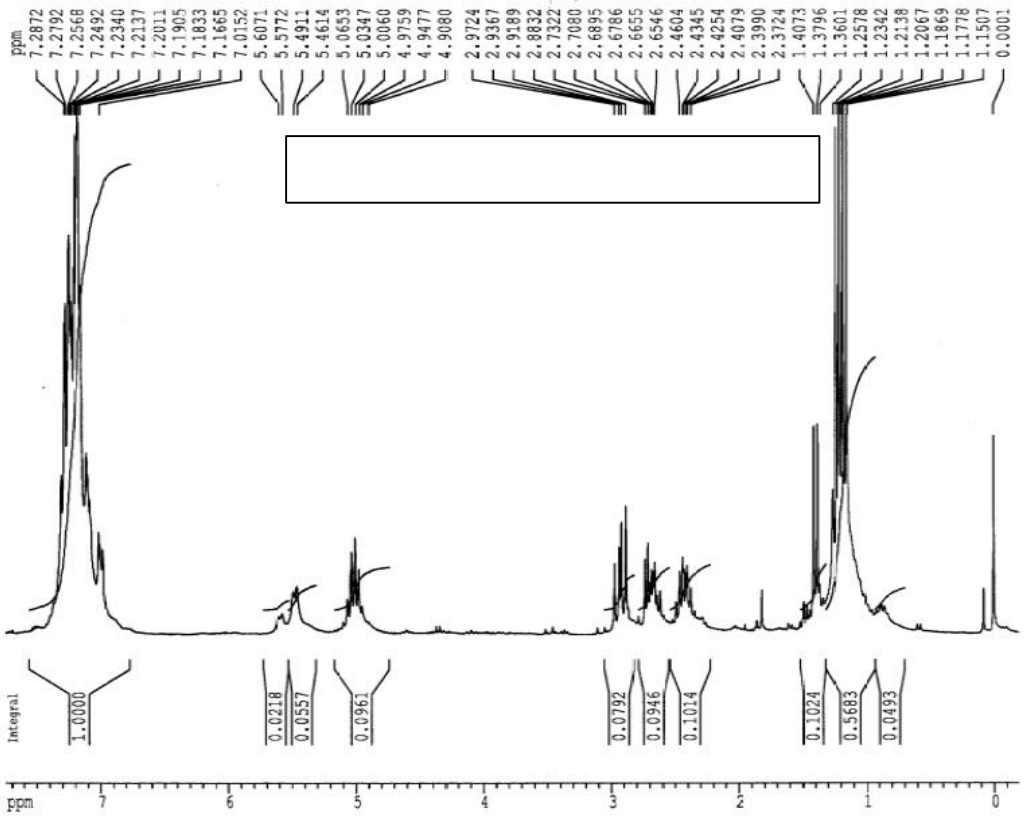


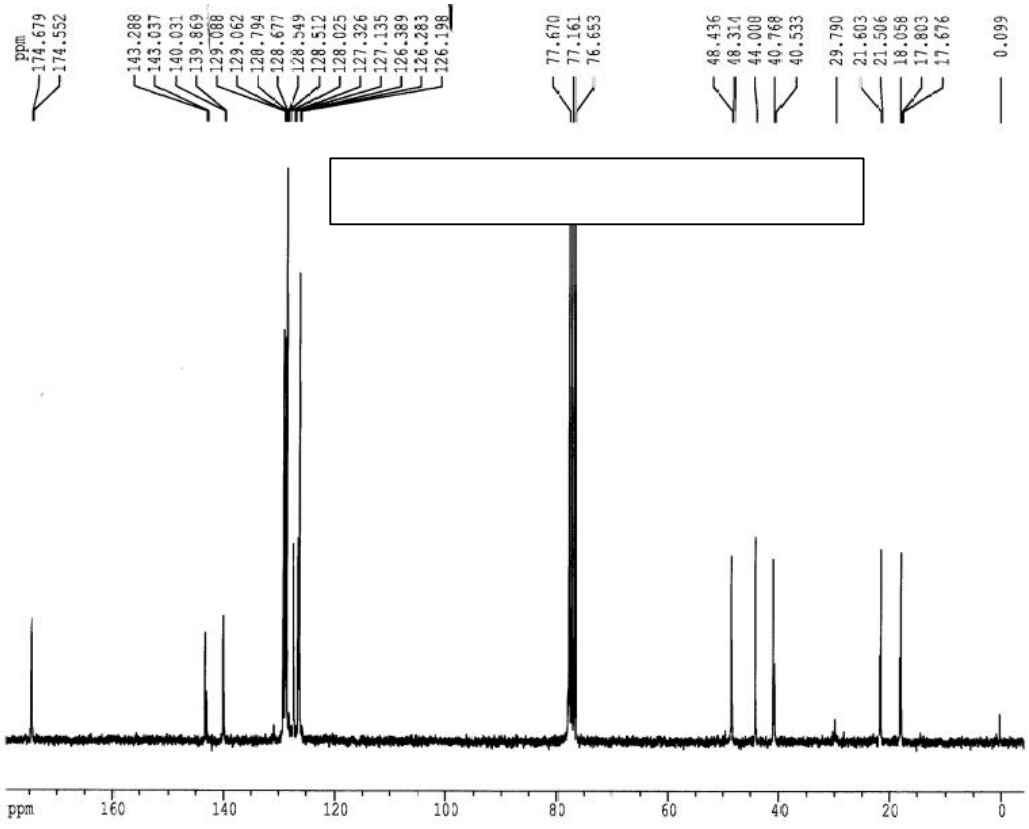
Retention Time	Area	Area %	Ratio %
Total Ion Chromatogram			
9.104	7909876	1.395	1.985
11.907	144571998	25.497	36.279
12.068	398500794	70.280	100.000
12.253	16038463	2.829	4.025

Pk#	RT	Area%	Library/ID	Ref#	CAS#	Qual
2	11.91	25.50	C:\DATABASE\NIST98.L			
			1,3-Diphenyl-5-methylthio-1,2,4-tr	95461	051384-17-9	22
			exo-7-(2-Propenyl)bicyclo[4.2.0]oc	37620	1000200-97-5	22
			1-(4-Nitrophenyl)-3-phenyl-2-pyraz	95450	1000148-39-2	22



at154-1


ppm
7.2872
7.2792
7.2568
7.2492
7.2340
7.2137
7.2011
7.1905
7.1833
7.1665
7.0152
5.6071
5.5772
5.4911
5.4614
5.0653
5.0347
5.0060
4.9759
4.9477
4.9080
2.9724
2.9367
2.9189
2.8832
2.7322
2.7080
2.6895
2.6786
2.6655
2.6546
2.4604
2.4345
2.4254
2.4079
2.3990
2.3724
1.4073
1.3796
1.3601
1.2578
1.2342
1.2138
1.2067
1.1869
1.1778
1.1507
0.0001
Integral
1.0000
0.0218
0.0557
0.0961
0.0792
0.0946
0.1014
0.1024
0.5683
0.0493
ppm
7
6
5
4
3
2
1
0


ppm
174.679
174.552
143.288
143.037
140.031
139.869
129.088
129.062
128.794
128.677
128.549
128.512
128.025
127.326
127.135
126.389
126.283
126.198
77.670
77.161
76.653
48.436
48.314
44.000
40.768
40.533
29.790
21.603
21.506
18.058
17.803
17.676
0.099
ppm
160
140
120
100
80
60
40
20
0