Supporting Information

Revisiting the Maitland-Japp Reaction: One Pot, Multi-Component Construction of Highly Substituted Tetrahydropyan-4-ones.

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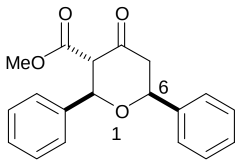
1. General procedure for the $TiCl_4$ promoted Maitland-Japp reaction.
2. General procedure for the $Yb(OTf)_3$ promoted Maitland-Japp reaction.
3. Representative characterisation data, **5b**, **6b**, **5c**, **6c**, **8i** and **9b**.
4. Determination of the enantiomeric excess **8i** and **9b**.
5. X-ray data. CIF files of **5b** and **6b**.
6. Chiral shift ^{1}H NMR of **8i** and **9b**.

General procedure for the $TiCl_4$ promoted Maitland-Japp reaction

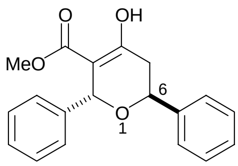
To a solution of aldehyde (1.00 mmol) in CH_2Cl_2 (10 mL) at –78 °C was added titanium tetrachloride (111 μL, 1.00 mmol). The black solution was stirred for 2 min and then Chan's diene (570 μL, 2.00 mmol) was added over a 1 min period. The black solution was stirred at –78 °C for 1 h and then trifluoroacetic acid (308 μL 4 mmol) was added. After 2 min the second aldehyde (1.20 mmol) was added and the solution was allowed to warm to room temperature over a 5 min period. The black solution was stirred at room temperature for 2 h and was then diluted with EtOAc (40 mL) and washed with 5% $NaHCO_3$ (3 × 30 mL), 5% sodium metabisulfite (3 × 30 mL) and brine (2 × 30 mL), dried ($MgSO_4$), and concentrated *in vacuo*. Purification by flash column chromatography (1:19 EtOAc-petroleum. ether) gave pyran products **5** and **6**.

General procedure for the $Yb(OTf)_3$ promoted Maitland-Japp reaction

To a suspension of ytterbium (III) triflate (620 mg, 1.00 mmol) in CH_2Cl_2 (10 mL) at –78 °C was added aldehyde (1 mmol) followed by Chan's diene (570 μL, 2.00 mmol). The white mixture was stirred at –78 °C for 40 min and then trifluoroacetic acid (308 μL, 4 mmol) was added followed by the second aldehyde (1.2 mmol). The mixture was warmed to room temperature over 5 min and then stirred at room temperature for 2 h. The mixture was then diluted with EtOAc (40 mL) and washed with 5% $NaHCO_3$ (3 × 30 mL) and brine (2 × 30 mL), dried ($MgSO_4$), and concentrated *in vacuo*. Purification by flash column chromatography (1:19 EtOAc-petroleum. ether) gave pyran products 5 and 6, which were spectroscopically identical to those made *via* the $TiCl_4$ method.

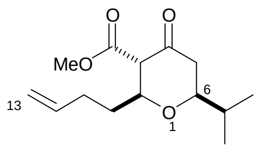


5b. white solid mp. 133-135 °C; ν_{max} (film)/cm^{-1}: 2953, 2921, 1747, 1717, 1496, 1455, 1274, 1067, 757, 699; ^{1}H NMR (400 MHz; $CDCl_3$) δ 7.50-7.30 (10H, m, Ph), 5.13 (1H, d, *J* = 10.6 Hz, H-2), 4.95 (1H, dd, *J* = 11.3, 3.0 Hz, H-6), 3.77 (1H, dd, *J* = 10.6, 0.8 Hz, H-3), 3.70 (3H, s, OMe), 2.86 (1H, dd, *J* = 14.3, 3.0 Hz, H-5), 2.79 (1H, ddd, *J* = 14.3, 11.2, 0.8 Hz, H-5) ppm; ^{13}C NMR (67.8 MHz; $CDCl_3$) δ 201.1 (s), 167.8 (s), 139.9 (s), 138.6 (s), 128.8 (d), 128.8 (d), 128.6 (d), 128.1 (d), 126.8 (d), 125.6 (d), 81.0 (d), 78.9 (d), 64.6 (d), 52.1 (q), 48.9 (t) ppm; m/z (CI+) 310 (62 %, M^+), 293 (100 %, M^+-OH); HRMS: found (M^+), 310.1195. $C_{19}H_{18}O_4$ requires (M^+) 310.1205; Anal. Calcd. for $C_{19}H_{18}O_4$: C, 73.53; H, 5.85. Found C, 73.22; H 5.95 %.

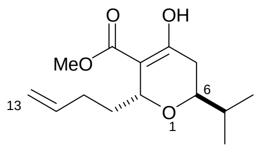


6b. white solid mp: 118-120 °C; ν_{max} (film)/cm^{-1} 2955, 2918, 2849, 1745, 1662, 1443, 1269, 1219, 1063, 698; ^{1}H NMR (400 MHz; $CDCl_3$) δ 12.38 (1H, s, OH), 7.57-7.28 (10H, m, Ph), 5.80 (1H, d, *J* = 1.0 Hz, H2), 4.59 (1H, dd, *J* = 10.8, 3.9 Hz, H-6), 3.67 (3H, s, OMe), 2.73 (1H, ddd, *J* = 18.1, 10.8, 1.0 Hz, H-5), 2.60 (1H, dd, *J* = 18.1, 3.9 Hz, H-5) ppm; ^{13}C NMR (67.8 MHz; $CDCl_3$) δ

171.2, 165.8, 141.0, 140.8, 128.8, 128.4, 128.0, 127.9, 126.9, 126.0, 98.7, 73.7, 68.3, 52.2, 35.6, 29.8 ppm; m/z (CI+) 310 (50 %, M^+), 279 (10 %, M^+-OMe), 233 (77 %, M^+-Ph); HRMS: found (M^+), 310.1205. $C_{19}H_{18}O_4$ requires (M^+), 310.1205; Anal. Calcd. for $C_{19}H_{18}O_4$: C, 73.53; H, 5.85. Found C, 73.32; H 5.75 %.

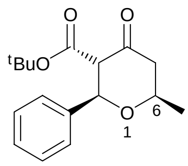


5c. oil ν_{max} (film) 2961, 2876, 1747, 1660, 1344, 1268, 1222, 1130, 1038, 913 cm^{-1}; ^{1}H NMR (400 MHz; $CDCl_3$) δ 5.75 (1H, dddd, *J* = 17.1, 10.3, 7.3, 6.4 Hz, H-12), 4.98 (1H, ddt, *J* = 17.1, 3.4, 2.0 Hz, H-13*trans*), 4.93 (1H, ddt, *J* = 10.3, 3.4, 1.5 Hz, H-13*cis*), 3.80 (1H, ddd, *J* = 10.8, 9.3, 2.9 Hz, H-2), 3.70 (3H, s, OMe), 3.28 (1H, ddd, *J* = 11.7, 6.8, 2.0 Hz, H-6), 3.19 (1H, dd, *J* = 10.8, 1.0 Hz, H-3), 2.45 (1H, dd, *J* = 14.2, 2.0 Hz, H-5*eq*), 2.23 (1H, ddd, *J* = 14.2, 11.7, 1.0 Hz, H-5*ax*), 2.22 (2H, m, H-10), 1.76 (1H, octet, *J* = 6.8 Hz, H-7), 1.62 (2H, m, H-11), 0.99 (3H, d, *J* = 6.8 Hz, H-8 or H-9), 0.90 (3H, d, *J* = 6.8 Hz, H-8 or H-9) ppm; ^{13}C NMR (67.8 MHz; $CDCl_3$) 202.7, 168.6, 137.6, 115.1, 81.7, 77.4, 63.1, 52.0, 44.6, 34.1, 33.4, 29.5, 18.2, 18.1 ppm; ; m/z (ES+) 318 (68 %, M^++Na+CH_3CN), 277 (100 %, M^++Na), 171 (98 %, M^++H-CH_2=CH(CH_2)$_2$CHO); HRMS: found (M^++Na), 277.1425. $C_{14}H_{22}O_4$ requires (M^++Na) 277.1416.

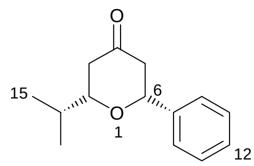


6c. oil ν_{max} (film) 2956, 1748, 1662, 1623, 1443, 1365, 1270, 1221, 1067, cm^{-1}; ^{1}H NMR (400 MHz; $CDCl_3$) δ 12.04 (1H, s, OH), 5.85 (1H, ddt, *J* = 17.2, 10.3, 6.8 Hz, H-12), 5.07 (1H, ddt, *J* = 17.2, 1.5, 1.5 Hz, H-13*cis*), 4.97 (1H, ddt, *J* = 10.3, 1.5, 1.5 Hz, H-13*trans*), 4.46 (1H, d, *J* = 6.8 Hz, H-2), 3.75 (3H, s, OMe), 3.46 (1H, ddd, *J* = 12.7, 7.3, 5.4 Hz, H-6), 2.22 (4H, m, H-5 + H-10), 1.69 (3H, m, H-7 + H-11), 1.00 (3H, d, *J* = 6.8 Hz, H-8 or H-9), 0.92 (3H, d, *J* = 6.8 Hz, H-8 or H-

9) ppm; ^{13}C NMR (67.8 MHz; $CDCl_3$) δ (67.8 MHz; $CDCl_3$) 171.0 (s), 170.1 (s), 138.3 (d), 114.5 (t), 101.1 (s), 70.9 (d), 70.5 (d), 51.4 (q), 33.1 (d), 32.1 (t), 31.8 (t), 30.2 (t), 18.7 (q), 18.2 (q) ppm; m/z (ES+) 318 (48 %, M^++Na+CH_3CN), 277 (100 %, M^++Na), 255 (12 %, M^++H), 171 (98 %, M^++H-CH_2=CH(CH_2)$_2$CHO); HRMS: found (M^++Na+CH_3CN), 318.1681. $C_{14}H_{22}O_4$ requires (M^++Na+CH_3CN) 318.1674.



8i. white solid mp. 88-90 °C; $[\alpha]_D$ ($CHCl_3$, c = 1) + 4.5; ν_{max} (film) 2978, 2932, 1740, 1714, 1369, 1288, 1127, cm^{-1}; ^1H NMR (500 MHz; $CDCl_3$) δ 7.43-7.27 (5H, m, Ph), 4.84 (1H, d, *J* = 10.8 Hz, H-2), 4.00 (1H, ddq, *J* = 10.8, 5.9, 2.9 Hz, H-6), 3.47 (1H, dd, *J* = 10.8, 1.0 Hz, H-3), 2.53 (1H, dd, *J* = 14.6, 2.9 Hz, H-5*eq*), 2.40 (1H, ddd, *J* = 14.6, 10.8, 1.0 Hz, H-5*ax*), 1.29 (9H, s, ^{t}Bu), 1.38 (3H, d, *J* = 5.9 Hz, H-7) ppm; ^{13}C NMR (125 MHz; $CDCl_3$) δ 202.3 (s), 166.6 (s), 138.7 (s), 128.7 (d), 128.6 (d), 127.2 (d), 82.0 (s), 81.1 (d), 73.8 (d), 64.9 (d), 48.7 (t), 27.9 (q), 22.2 (q) ppm; m/z (ES+) 354 (100 %, M^++Na+CH_3CN), 313 (82 %, M^++Na); HRMS: found (M^++Na), 313.1428. $C_{17}H_{22}O_4$ requires (M^++Na) 313.1416.



9b. white solid mp. $[\alpha]_D$ ($CHCl_3$, c = 1) – 46.8; ν_{max} (film) 3031, 2963, 1717, 1347, 1252, 1153, 1065 5.72, cm^{-1}; ^1H NMR (400 MHz; $CDCl_3$) δ 7.31-7.16 (5H, m, Ph), 4.51 (1H, dd, *J* = 11.5, 2.6 Hz, H-6), 3.39 (1H, ddd, *J* = 11.5, 6.0, 2.6 Hz, H-2), 2.53 (1H, ddd, *J* = 14.5, 2.6, 2.1 Hz, H-5*eq*), 2.40 (1H, dd, *J* = 14.5, 11.5 Hz, H-5*ax*), 2.35 (1H, ddd, *J* = 14.1, 2.6, 2.1 Hz, H-2*eq*), 2.28 (1H, dd, *J* = 14.1, 11.5 Hz, H-2*ax*), 1.81 (1H, octet, *J* = 6.8 Hz, H-13), 0.92 (3H, d, *J* = 6.8 Hz, H-14 or H-15), 0.88 (3H, d, *J* = 6.8 Hz, H-14 or H-15) ppm; ^{13}C NMR (100 MHz; $CDCl_3$) δ 207.6 (s), 141.1

(s), 128.5 (d), 127.8 (d), 125.4 (d), 81.9 (d), 78.2 (t), 49.7 (t), 44.6 (t), 33.2 (d), 18.2 (q), 17.9 (q) ppm; m/z (CI+) 218 (59 %, M^+), 175 (16 %, M^+-C_3H_7), 77 (31 %, Ph); HRMS: found (M^+), 218.1307. $C_{14}H_{18}O_2$ requires (M^+) 218.1307.

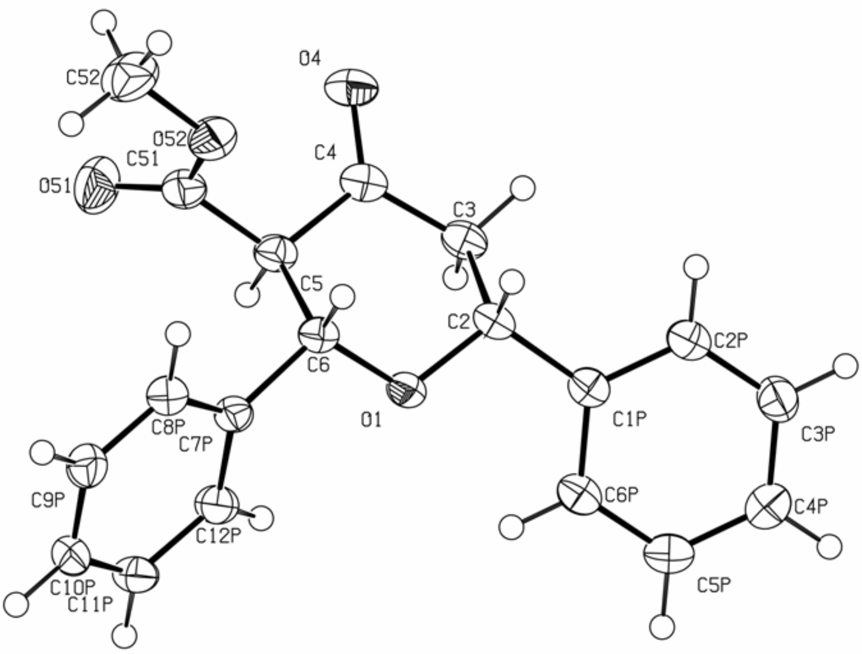
Determination of the enantiomeric excess 8i and 9b

^{1}H NMR shift reagent experiment: **8i** (1 mg) in $CDCl_3$ (0.45 ml) with 50 mol% (-) $Eu(hfc)_3$ at 500 MHz. ^{1}H NMR shift reagent experiment: **9b** (1 mg) in $CDCl_3$ (0.45 ml) with 15 mol% (-) $Eu(hfc)_3$ at 400 MHz. See following spectra.

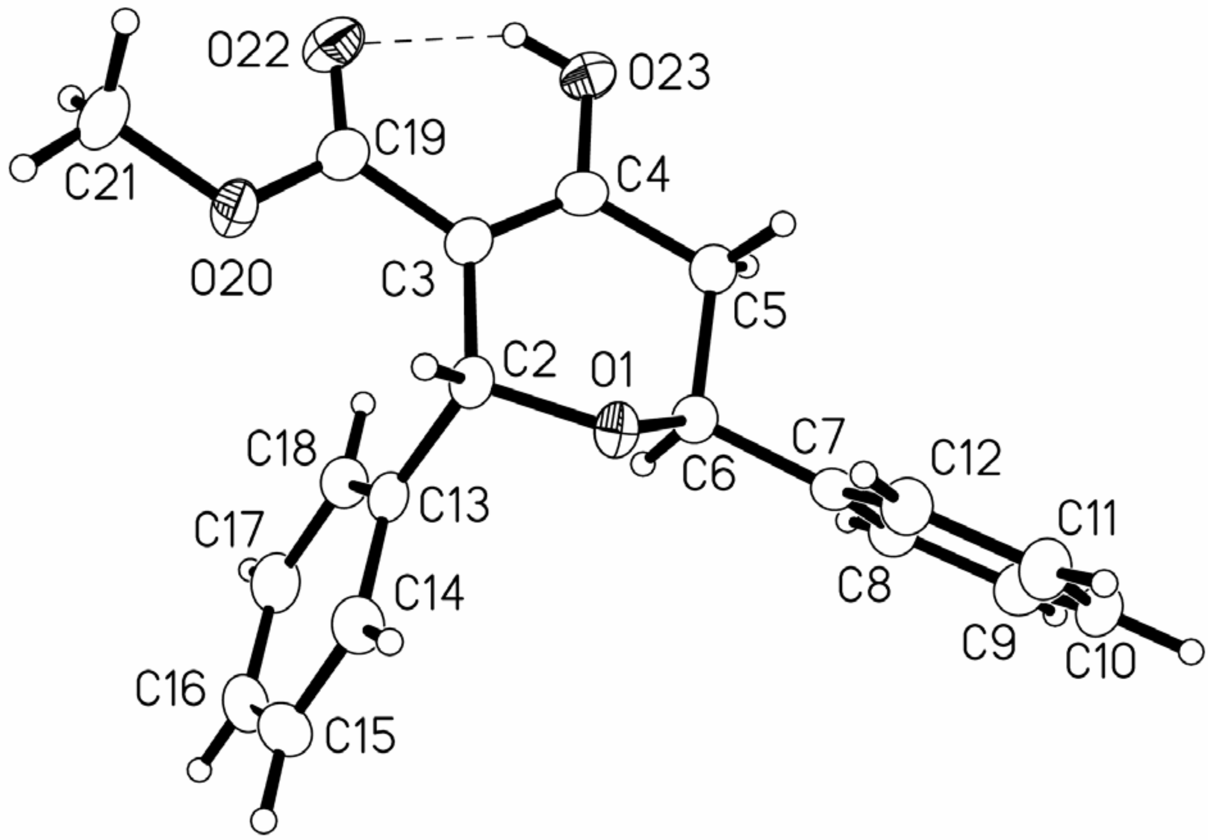
Notes on X-ray crystal data

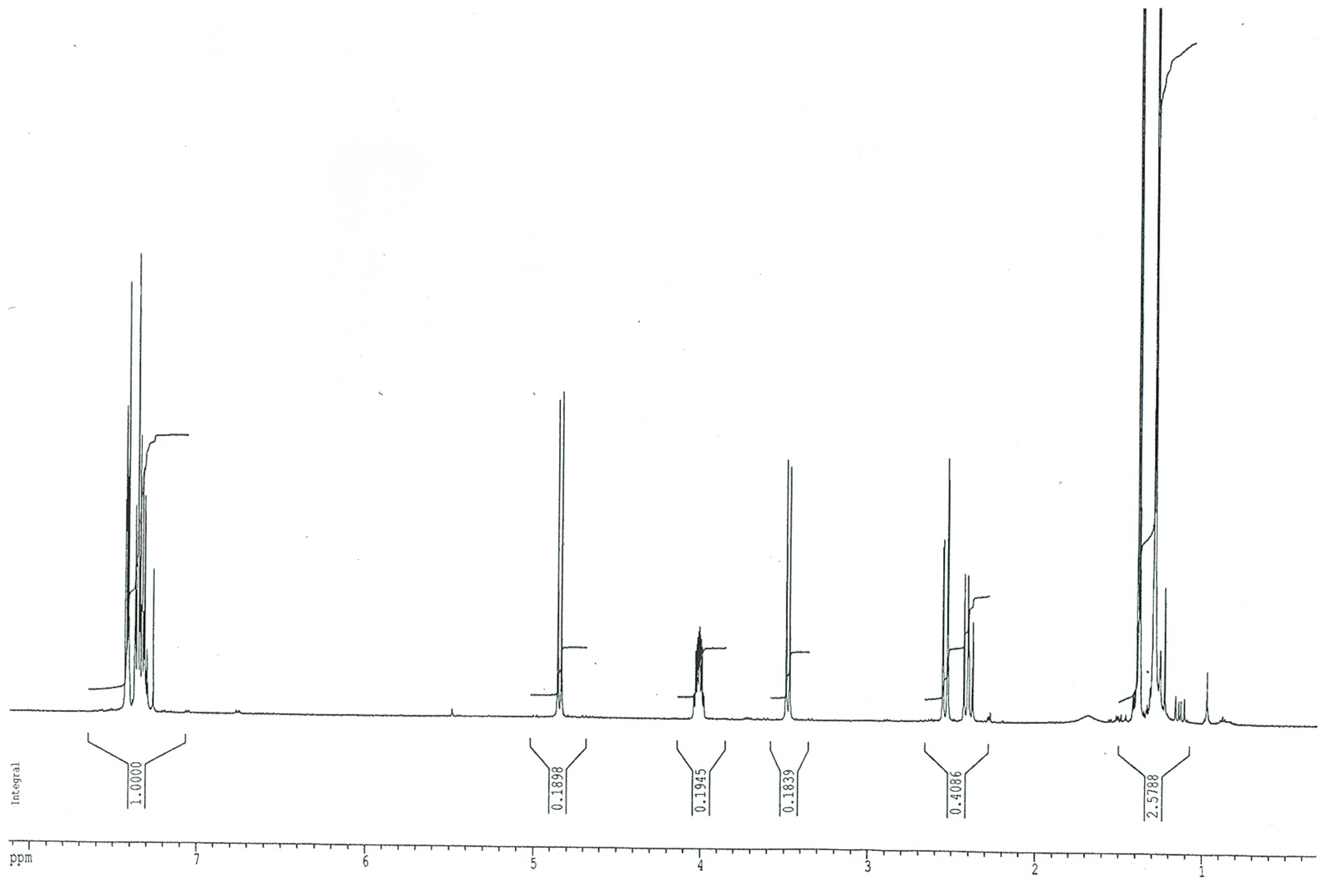
Diffraction data were acquired on a Bruker SMART1000 (**5b**) or a Bruker SMART APEX (**6b**) CCD area detector diffractometer equipped with an Oxford Cryosystems open-flow cryostat operating at 150 K. The structures were solved by direct methods and refined by full-matrix least-squares on F^2.

Crystal data for **5b**. $C_{19}H_{18}O_4$, M = 310.33, monoclinic, a = 13.0132(10), b = 8.6004(7), c = 14.1620(11) Å, β = 91.558(2)°, V = 1584.4(2) Å^3, T = 150(2) K, Z = 4, D_x = 1.301 g cm^{-3}. Final R_1 [2746 $F > 4\sigma(F)$] = 0.0375, wR_2 [all 3656 F^2] = 0.105.



Crystal data for **6b**. $C_{19}H_{18}O_4$, M = 310.33, triclinic, a = 5.5429(5), b = 9.5351(8), c = 15.1955(13) Å, α = 82.937(2), β = 85.273(2), γ= 77.190(2)°, V = 775.9(2) Å^3, T = 150(2) K, Z = 2, D_x = 1.328 g cm^{-3}. Final R_1 [2913 $F > 4\sigma(F)$] = 0.0401, wR_2 [all 3507 F^2] = 0.111.

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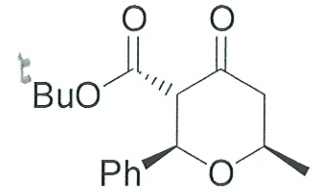
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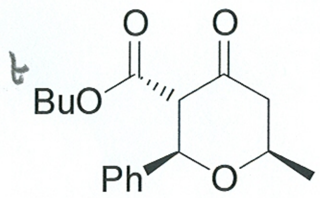
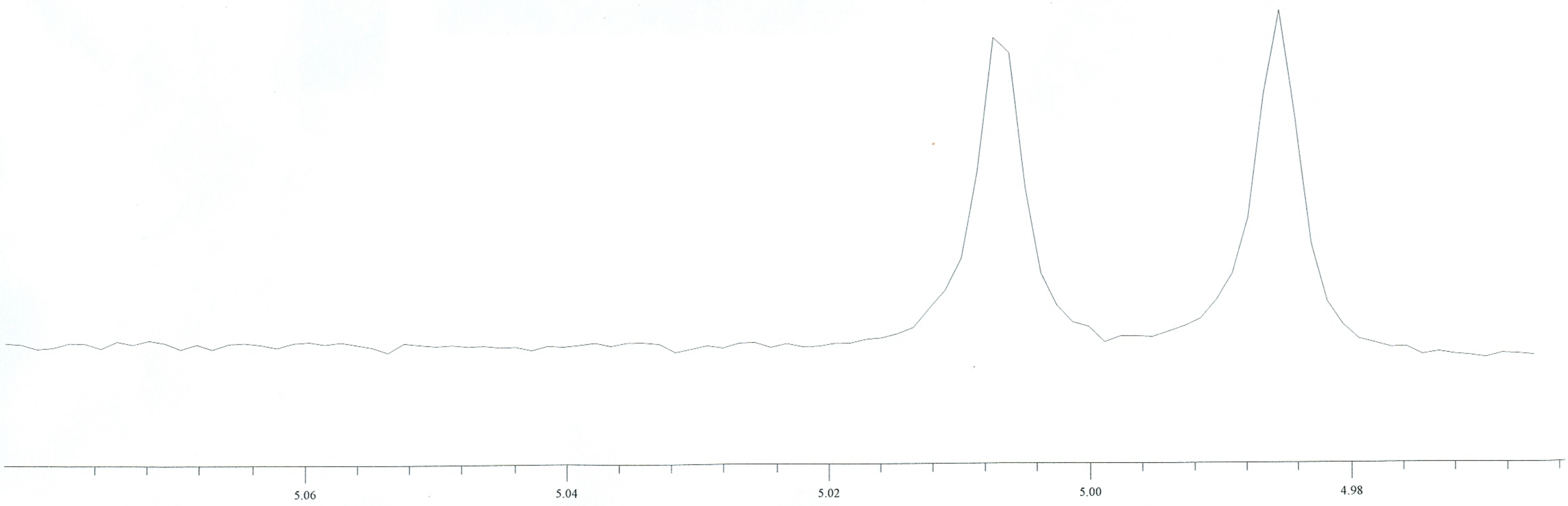
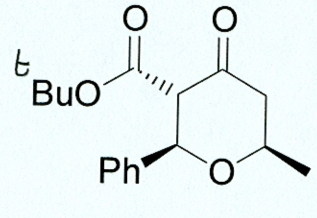
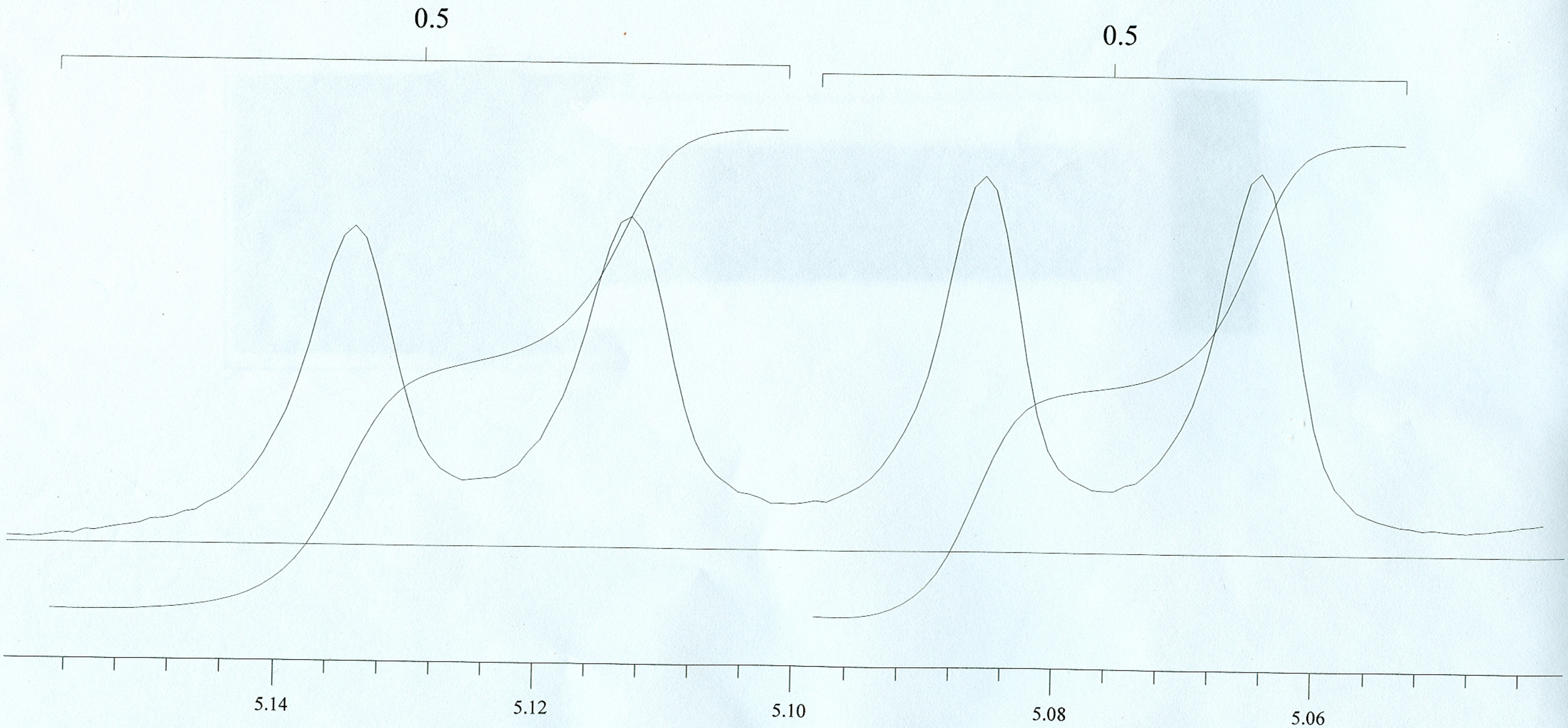


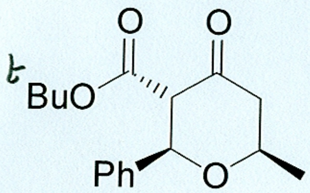
single enantiomer



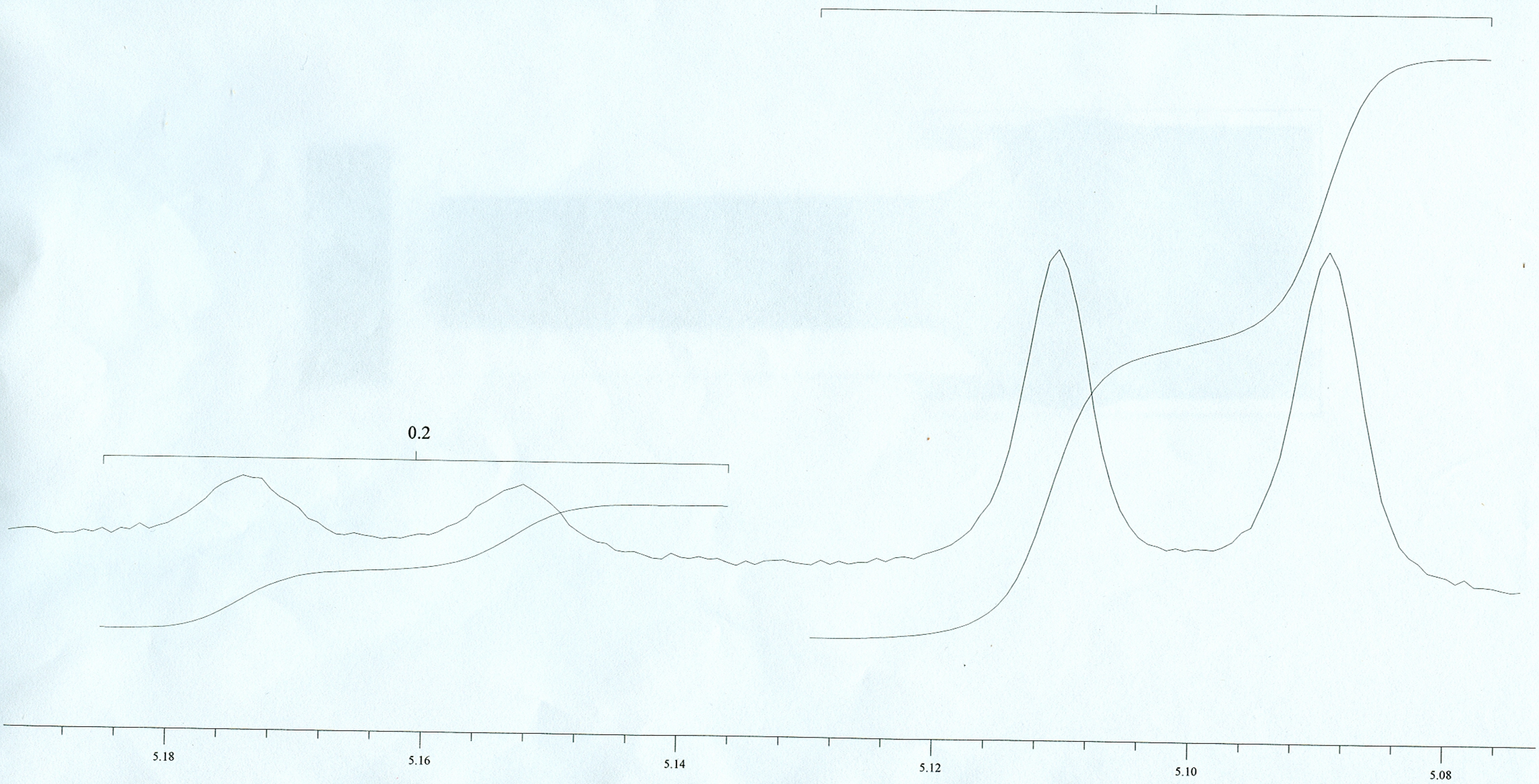


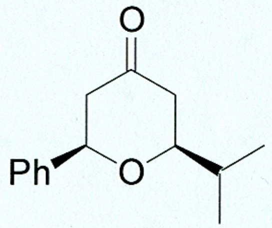
racemate

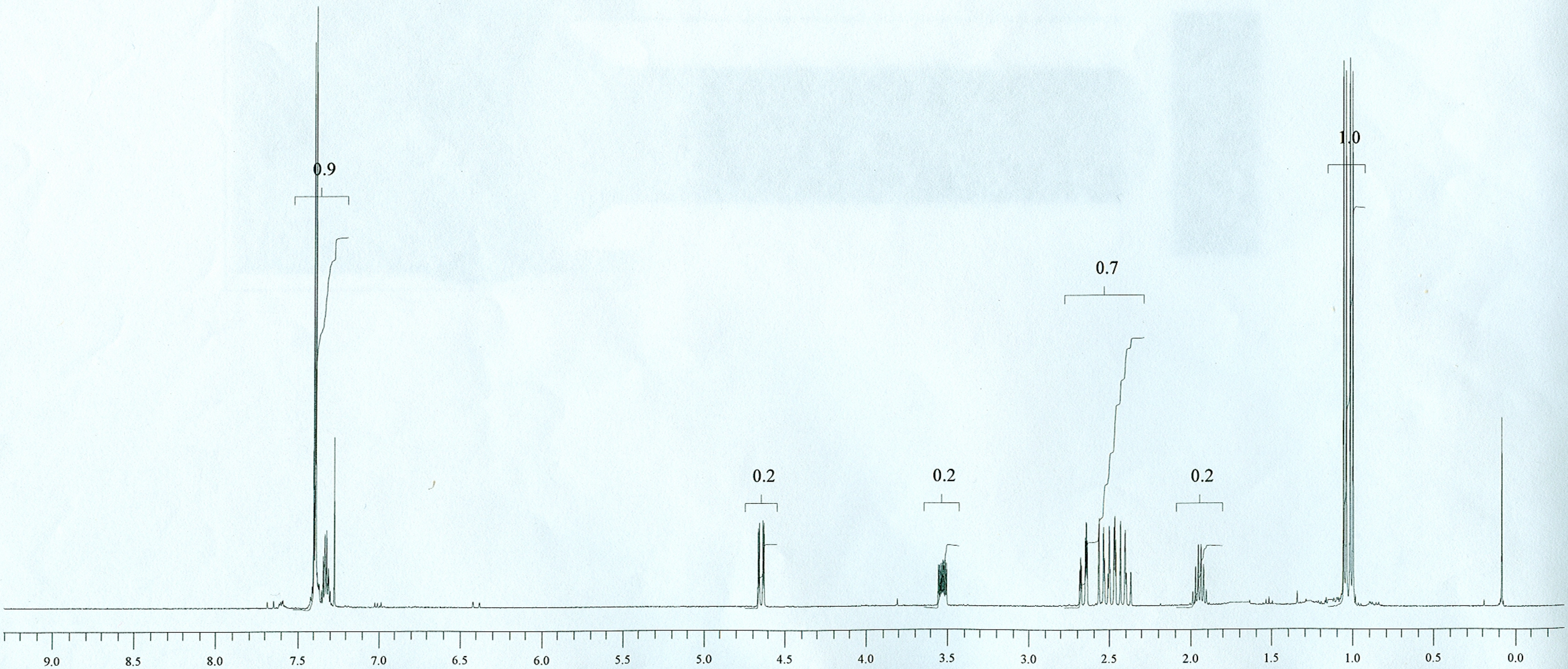




single enantiomer doped with racemate







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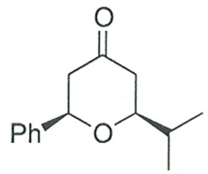
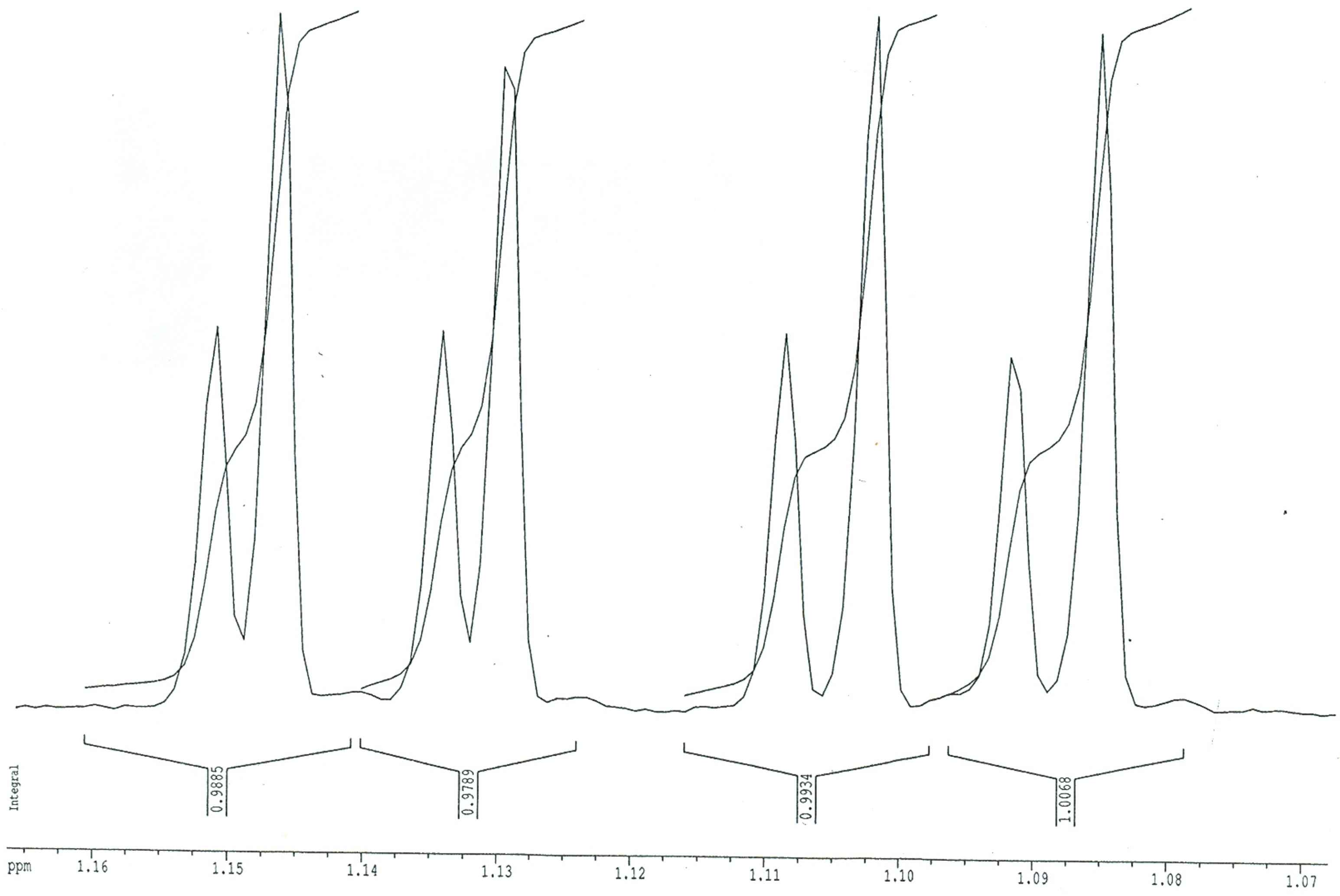
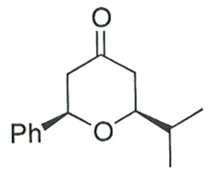
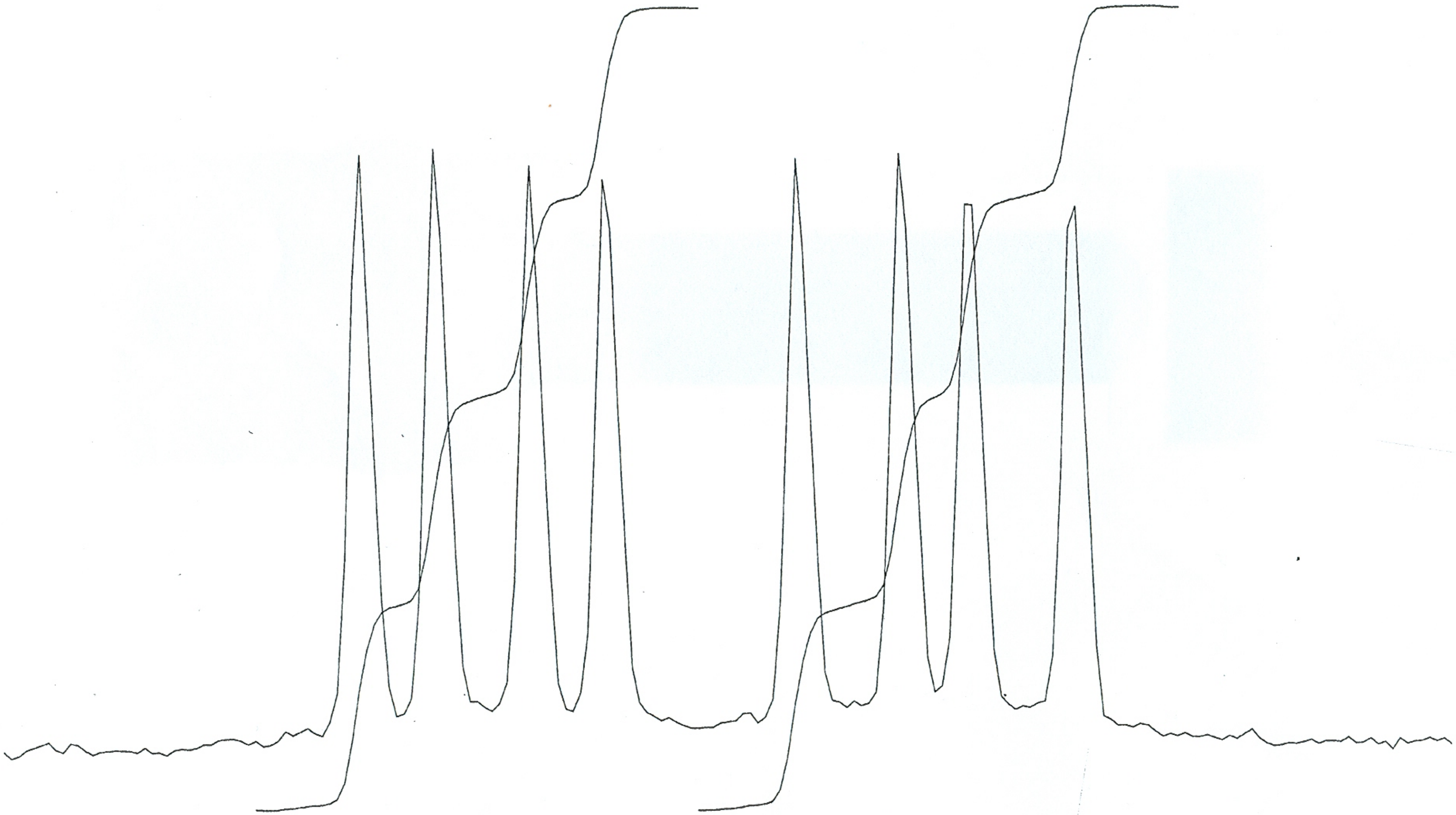


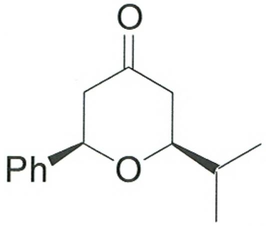
single enantiomer doped with racemate





racemate





single enantiomer