Enantioselective total synthesis of the indole alkaloid 16-episilicine

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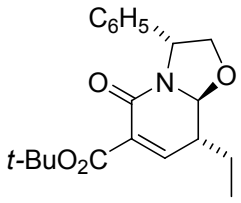
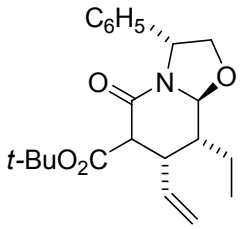
Supporting Information Available

Experimental procedures and spectroscopic data for compounds

General Procedures. All reactions were performed under an argon atmosphere with dry, freshly distilled solvents using standard procedures. Drying of organic extracts during the work-up of reactions was performed over anhydrous Na_2SO_4. Evaporation of solvent was accomphished with a rotatory evaporator. Thin-layer chromatography was done on SiO_2 (silica gel 60 F_{254}), and the spots were located by UV and either a 1% $KMnO_4$ solution or hexachloroplatinate reagent. Chromatography refers to flash column chromatography and was carried out on SiO_2 (silica gel 60, 230-400 mesh). Melting points were determined in a capillary tube and are uncorrected. Unless otherwise indicated NMR spectra were recorded in $CDCl_3$. The chemical shifts are reported as δ values, in parts per million (ppm) relative to Me_4Si (0 ppm) or relative to residual chloroform (7.26 ppm, 77.0 ppm) as an internal standard. Data are reported in the following manner: chemical shift, integrated intensity, multiplicity, coupling constant (*J*) in hertz (Hz) and assignment (when possible). Multiplicities are reported using the following abbreviations: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad; ap, apparent. Assignments and stereochemical determinations are given only when they are derived from definitive two-dimensional NMR experiments (HSQC-COSY). Only noteworthy IR absorptions (cm^{-1}) are listed. Mass spectra (MS) data are reported as *m/z* (%).

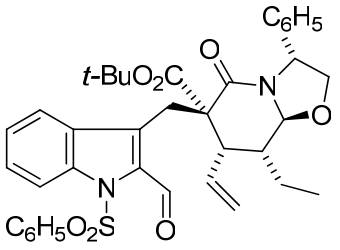


(3*R*,8*R*,8a*S*)-6-(*tert*-Butoxycarbonyl)-8-ethyl-5-oxo-3-phenyl-2,3,8,8a-tetrahydro-5*H*-oxazolo[3,2-*a*]pyridine (2). Lithium bis(trimethylsilyl)amide (13.5 mmol of a 1.0 M solution in THF) was slowly added at –78 ºC to a solution of lactam **1** (1.56 g, 6.13 mmol) in anhydrous THF (100 mL), and the resulting mixture was stirred for 1 h. Then, $(Boc)_2O$ (1.47 g, 6.74 mmol) and, after 30 min of continuous stirring at –78 ºC, a solution of PhSeCl (1.64 g, 8.58 mmol) in anhydrous THF (10 mL) were sequentally added. The resulting mixture was stirred for 2 h and poured into saturated aqueous NH_4Cl. The aqueous layer was extracted with EtOAc, and the combined organic extracts were dried and concentrated. Flash chromatography (9:1 to 4:1 hexane-EtOAc) of the mixture afforded the corresponding selenides as a mixture of C-6 epimers. A stream of ozone gas was bubbled through a cooled (–78 ºC) solution of selenides (2.60 g, 5.20 mmol) in anhydrous CH_2Cl_2 (100 mL) until it turned pale blue. Then, the solution was purged with O_2, and the temperature was slowly raised to 25 ºC. After 30 min of stirring, the mixture was poured intro brine, and the aqueous layer was extracted with CH_2Cl_2. The combined organic extracts were dried and concentrated under reduced pressure to give unsaturated lactam **2** (1.78 g) as an oil, which was used in the next reaction without further purification: δ_H (400 MHz; $CDCl_3$; Me_4Si) 1.11 (3H, t, *J* 7.3 Hz, CH_3 ethyl), 1.50 [9H, s, $C(CH_3)_3$], 1.56-1.65 (1H, m, CH_2 ethyl), 1.82-1.89 (1H, m, CH_2 ethyl), 2.53 (1H, dddd, *J* 9.6, 8.0, 5.2 and 2.0 Hz, H-8), 3.93 (1H, dd, *J* 9.2 and 6.0 Hz, H-2), 4.43 (1H, dd, *J* 9.2 and 7.2 Hz, H-2), 5.10 (1H, d, *J* 9.6 Hz, H-8a), 5.27 (1H, t, *J* 6.3 Hz, H-3), 6.98 (1H, d, *J* 2.0 Hz, H-7), 7.24-7.91 (5H, m, ArH); δ_C (100.6 MHz; $CDCl_3$; Me_4Si) 11.0 (CH_3 ethyl), 23.5 (CH_2 ethyl), 28.0 [$C(CH_3)_3$], 42.4 (C-8), 58.3 (C-3), 73.1 (C-2), 82.0 [$C(CH_3)_3$], 90.7 (C-8a), 126.3 (C-*o*), 127.7 (C-*p*), 128.7 (C-*m*), 131.5 (C-6), 138.9 (C-*ipso*), 144.7 (C-7), 157.8 (NCO), 162.5 (CO).



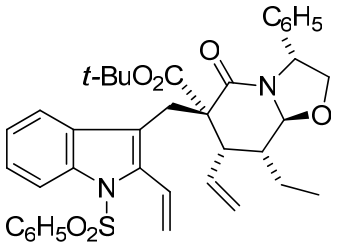
(3*R*,7*S*,8*R*,8a*S*)-6-(*tert*-Butoxycarbonyl)-8-ethyl-5-oxo-3-phenyl-7-vinyl-2,3,6,7,8,8a-hexahydro-5*H*-oxazolo[3,2-*a*]pyridine (3). LiCl (0.88 g, 20.8 mmol) was heated at 80 ºC for 1 h under vacuum (10-15 mmHg) in a three-necked round-bottomed flask. Then, CuI (2.30 g, 20.8 mmol) and THF (50 mL) were added at room temperature, and the mixture was stirred for 5 min. The suspension was cooled at –78 ºC, and vinylmagnesium bromide (1M in THF, 20.8 mL),

TMSCl (2.70 mL, 20.8 mmol) and the crude unsaturated lactam **2** (1.78 g, 5.2 mmol) in THF (100 mL) were successively added. The resulting mixture was stirred at −78 ºC for 20 h. The reaction was quenched with saturated aqueous NH_4Cl, and the organic layer was extracted with EtOAc. The combined organic extracts were dried and concentrated. Flash chromatography (hexane to 1:9 hexane-EtOAc) gave a mixture of lactams **3** and 6-*epi*-**3** (1.62 g, 84% overall yield from **1**). Pure isomers were isolated after a subsequent chromatography. **3**: $[\alpha]^{22}_D$ − 87.4 (*c* 1.0 in $CHCl_3$); δ_H (400 MHz; $CDCl_3$; Me_4Si) 1.01 (3H, t, *J* 7.3 Hz, CH_3 ethyl), 1.36-1.64 (1H, m, CH_2 ethyl), 1.47 [9H, s, $C(CH_3)_3$], 1.70-1.80 (1H, m, CH_2 ethyl), 2.02-2.09 (1H, m, H-8), 2.97 (1H, ddd, *J* 8.0, 3.6 and 1.2 Hz, H-7), 3.45 (1H, d, *J* 1.2 Hz, H-6), 3.70 (1H, dd, *J* 13.6 and 9.0 Hz, H-2), 4.51 (1H, dd, *J* 13.6 and 8.4 Hz, H-2), 4.63 (1H, d, *J* 8.8 Hz, H-8a), 5.20-5.29 (3H, m, H-3 and HC=C*H*$_2$), 5.79-5.90 (1H, m, *H*C=CH_2), 7.20-7.35 (5H, m, ArH); δ_C (100.6 MHz; $CDCl_3$; Me_4Si) 11.1 (CH_3 ethyl), 21.2 (CH_2 ethyl), 27.8 [C(*C*H_3)$_3$], 40.8 (C-8), 41.0 (C-7), 53.4 (C-6), 58.7 (C-3), 72.5 (C-2), 82.0 [*C*$(CH_3)_3$], 90.5 (C-8a), 118.1 (HC=*C*H_2), 125.8 (C-*o*), 127.4 (C-*m*), 128.7 (C-*p*), 134.3 (H*C*=CH_2), 139.4 (C-*ipso*), 164.2 (NCO), 169.2 (CO); HMRS calcd for [$C_{22}H_{29}NO_4$ +H] 372.2169, found: 372.2166. 6-*epi*-**3**: δ_H (400 MHz; $CDCl_3$; Me_4Si) 1.03 (3H, t, *J* 7.4 Hz, CH_3 ethyl), 1.36-1.64 (1H, m, CH_2 ethyl), 1.42 [9H, s, $C(CH_3)_3$], 1.70-1.80 (1H, m, CH_2 ethyl), 2.02-2.09 (1H, m, H-8), 3.06 (1H, ddd, *J* 10.8, 6.0 and 3.2 Hz, H-7), 3.48 (1H, d, *J* 6.0 Hz, H-6), 3.69 (1H, t, *J* 8.5 Hz, H-2), 4.53 (1H, dd, *J* 8.5 and 4.8 Hz, H-2), 4.66 (1H, d, *J* 9.2 Hz, H-8a), 5.20-5.37 (3H, m, H-3 and HC=C*H*$_2$), 5.79-5.90 (1H, m, *H*C=CH_2), 7.20-7.35 (5H, m, ArH); δ_C (100.6 MHz; $CDCl_3$; Me_4Si) 11.0 (CH_3 ethyl), 21.6 (CH_2 ethyl), 27.9 [C(*C*H_3)$_3$], 42.2 (C-8), 44.4 (C-7), 54.6 (C-6), 58.1 (C-3), 72.2 (C-2), 81.7 [*C*$(CH_3)_3$], 90.4 (C-8a), 120.2 (HC=*C*H_2), 125.4 (C-*o*), 127.3 (C-*m*), 128.7 (C-*p*), 132.4 (H*C*=CH_2), 139.0 (C-*ipso*), 164.9 (NCO), 167.7 (CO); HMRS calcd for [$C_{44}H_{58}N_2O$ + Na]: 765.4085, found: 765.4080.



(3*R*,6S,7*S*,8*R*,8a*S*)-6-[(1-Benzenesulfonyl-2-formyl-3-indolyl)methyl]-6-(*tert*-butoxycarbonyl)-8-ethyl-5-oxo-3-phenyl-7-vinyl-2,3,6,7,8,8a-hexahydro-5*H*-oxazolo[3,2-*a*]pyridine (5). NaH (60% dispersion in mineral oil) (65 mg, 1.62 mmol) was slowly added at 0 ºC to a solution of lactams **3** and 6-*epi*-**3** (500 mg, 1.35 mmol) in dry DMF (20 mL), and the mixture was stirred at room temperature for 1 h. Then, a solution of indole

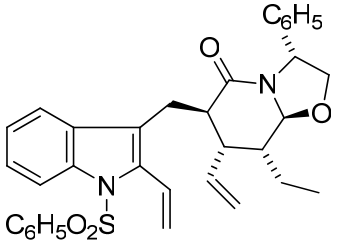
4[1] (1.02 g, 2.69 mmol) in dry DMF (25 mL) was slowly added, and the mixture was stirred at room temperature for 8 h. The reaction was quenched with saturated aqueous NH_4Cl, and the aqueous layer was extracted with EtOAc. The combined organic extracts were concentrated, and the residue was redissolved in Et_2O. The organic extract was washed with water, dried, filtered, and concentrated. Flash chromatography (9:1 to 1:1 hexane-EtOAc) gave lactam **5** (1.81 g, 75%): $[\alpha]^{22}_D$ – 137.7 (*c* 0.5 in $CHCl_3$); ν_{max} (KBr) / cm^{-1} 1671 (NCO), 1727 (CO); δ_H (400 MHz; $CDCl_3$; Me_4Si) 0.87 (3H, t, *J* 7.3 Hz, CH_3 ethyl), 1.22 [9H, s, $C(CH_3)_3$], 1.27-1.37 (1H, m, CH_2 ethyl), 1.68-1.74 (1H, m, CH_2 ethyl), 2.00 (1H, ddd, *J* 13.2, 9.0 and 3.6 Hz, H-8), 2.86 (1H, dd, *J* 10.0 and 3.6 Hz, H-7), 3.66 (1H, t, *J* 8.4 Hz, H-2), 3.70 (1H, d, *J* 13.2 Hz, CH_2-ind), 3.85 (1H, d, *J* 13.2 Hz, CH_2-ind), 4.49 (1H, t, *J* 8.4 Hz, H-2), 4.68 (1H, d, *J* 9.0 Hz, H-8a), 5.04 (1H, t, *J* 8.4 Hz, H-3), 5.22 (1H, dd, *J* 10.0 and 1.6 Hz, $HC=CH_2$), 5.25 (1H, dd, *J* 17.6 and 1.6 Hz, $HC=CH_2$), 5.81 (1H, dt, *J* 17.6 and 10.0 Hz, $HC=CH_2$), 7.20-7.30 (7H, m, ArH, H-7 ind), 7.39 (2H, dd, *J* 8.0 and 1.2 Hz, ArH), 7.43 (1H, dd, *J* 8.0 and 1.2 Hz, H-5 ind), 7.74-7.76 (2H, m, ArH), 8.00 (1H, d, *J* 8.0 Hz, H-6 ind), 8.09 (1H, d, *J* 8.8 Hz, H-4 ind), 10.52 (1H, s, CHO); δ_C (100.6 MHz; $CDCl_3$; Me_4Si) 10.8 (CH_3 ethyl), 21.4 (CH_2 ethyl), 27.8 [$C(CH_3)_3$], 31.5 (CH_2-ind), 40.5 (C-8), 48.9 (C-7), 59.1 (C-3), 59.7 (C-6), 72.1 (C-2), 82.5 [$C(CH_3)_3$], 90.4 (C-8a), 115.0 (C-7 ind), 120.6 ($HC=CH_2$), 123.9 (C-6 ind), 124.1 (C-5 ind), 125.7 (C-4 ind), 126.8 (C-*o*), 127.2 (C-*m*), 128.4 (C-*p*), 128.7 (C-*o*), 129.0 (C-*m*), 129.9 (C-3 ind), 132.0 (C-2 ind), 132.7 ($HC=CH_2$), 133.8 (C-*p*), 134.8 (C-3a ind), 137.3 (C-*ipso*), 137.6 (C-7a ind), 139.4 (C-*ipso*), 166.0 (NCO), 170.3 (CO), 184.8 (CHO); HMRS calcd for [$C_{38}H_{40}N_2O_7S$ + Na]: 691.2447, found: 691.2448.



(3*R*,6*S*,7*S*,8*R*,8a*S*)-6-[(1-Benzenesulfonyl-2-vinyl-3-indolyl)methyl]-6-(*tert*-butoxycarbonyl)-8-ethyl-5-oxo-3-phenyl-7-vinyl-2,3,6,7,8,8a-hexahydro-5*H*-oxazolo[3,2-*a*]pyridine. KHMDS (0.5 M in toluene, 8.48 mL) was added to a solution of $MePh_3PBr$ (1.52 g, 4.24 mmol) in anhydrous THF (20 mL) at 25 ºC, and the resulting mixture was stirred for 30 min. Then, this solution was transfered to a solution of indole **5** (1.45 g, 2.12 mmol) in anhydrous THF (20 mL), and the resulting mixture was heated at reflux for 6 h. The crude mixture

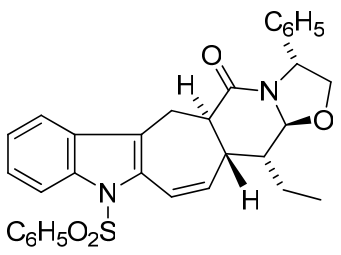
[1] Indole **4** was obtained by NBS bromination of 1-benzenesulfonyl-3-methylindole-2-carbaldehyde, which was prepared according to : D. W. M. Benzies, P. Martinez-Fresneda and R. A. Jones, *Synth. Commun*., 1986, **16**, 1799.

was poured into water (20 mL), the aqueous layer was extracted with Et_2O, and the combined organic extracts were dried and concentrated. Flash chromatrography of the resulting yelow foam (9:1 to 4:1 hexane-EtOAc) afforded pure vinylindole (1.05 g, 74%): $[\alpha]^{22}_D$ + 18.6 (*c* 0.5 in $CHCl_3$); ν_{max} (KBr) / cm^{-1} 1655 (NCO), 1729 (CO); δ_H (400 MHz; $CDCl_3$; Me_4Si) 0.56 (3H, t, *J* 7.4 Hz, CH_3 ethyl), 0.97-1.09 (1H, m, CH_2 ethyl), 1.26-1.38 (2H, m, CH_2 ethyl and H-8), 1.36 [9H, s, $C(CH_3)_3$], 2.73 (1H, dd, *J* 11.2 and 4.0 Hz, H-7), 3.58 (1H, dd, *J* 8.4 and 7.6 Hz, H-2), 3.64 (1H, d, *J* 14.8 Hz, CH_2-ind), 3.97 (1H, d, *J* 14.8 Hz, CH_2-ind), 4.08 (1H, t, *J* 8.4 Hz, H-2), 4.54 (1H, d, *J* 9.2 Hz, H-8a), 5.09-5.14 (2H, m, $HC=CH_2$), 5.19 (1H, t, *J* 7.6 Hz, H-3), 5.58 (1H, dd, *J* 18.0 and 1.2 Hz, ind-$HC=CH_2$), 5.69-5.78 (1H, m, $HC=CH_2$), 5.77 (1H, dd, *J* 11.6 and 1.2 Hz, ind-$HC=CH_2$), 7.12 (1H, dd, *J* 18.0 and 11.6 Hz, ind-$HC=CH_2$), 7.22-7.38 (10H, m, ArH), 7.48 (1H, t, *J* 7.6 Hz, H-7 ind), 7.70 (1H, d, *J* 8.0 Hz, H-5 ind), 7.75 (1H, d, *J* 7.6 Hz, H-6 ind), 8.21 (1H, d, *J* 8.4 Hz, H-4 ind); δ_C (100.6 MHz; $CDCl_3$; Me_4Si) 10.3 (CH_3 ethyl), 20.9 (CH_2 ethyl), 28.0 [$C(CH_3)_3$], 30.4 (CH_2-ind), 41.6 (C-8), 46.1 (C-7), 59.0 (C-3), 59.3 (C-6), 71.7 (C-2), 82.6 [$C(CH_3)_3$], 89.4 (C-8a), 114.8 (C-7 ind), 118.4 (C-3 ind), 119.7 ($HC=CH_2$), 121.2 (C-4 ind), 122.6 (ind-$HC=CH_2$), 123.5 (C-5 ind), 125.4 (C-6 ind), 125.9 (C-*o*), 126.8 (C-*m*), 127.4 (C-*p*), 127.6 (C-*o*), 128.6 (C-*m*), 131.1 (C-2 ind), 133.2 (C-*p*), 133.7 (ind-$HC=CH_2$), 135.7 (C-*ipso*), 136.9 (C-3a ind), 138.3 (C-7a ind), 139.0 ($HC=CH_2$), 168.2 (NCO), 170.3 (CO); HMRS calcd for [$C_{39}H_{42}N_2O_6S$ + Na]: 689.2662, found: 689.2655.



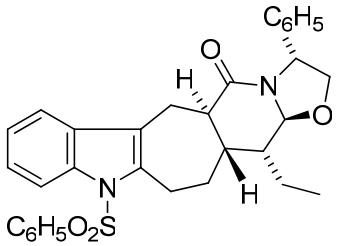
(3*R*,6*R*,7*S*,8*R*,8a*S*)-6-[(1-Benzenesulfonyl-2-vinyl-3-indolyl)methyl]-8-ethyl-5-oxo-3-phenyl-7-vinyl-2,3,6,7,8,8a-hexahydro-5*H*-oxazolo[3,2-*a*]pyridine (6). TFA (5.0 mL, 10.2 mmol) was added to a solution of above vinylindole (1.15 g, 1.73 mmol) in anhydrous CH_2Cl_2 (150 mL). The mixture was stirred at room temperature until disappearence of the starting compound was observed by TLC (3 h). The reaction was quenched with saturated aqueous $NaHCO_3$ (pH = 7) and extracted with CH_2Cl_2. The combined organic extracts were dried, filtered, and concentrated to give a foam, which was dissolved in anhydrous toluene (250 mL). The resulting solution was heated at reflux for 7 h and concentrated to dryness. Flash chromatography (hexane to 9:1 hexane-EtOAc) afforded **6** (717 mg, 77%) and its 6-epimer (136.5 mg, 14%). **6** (6*R*, major): $[\alpha]^{22}_D$ – 96.0 (*c* 0.5 in $CHCl_3$); ν_{max} (KBr) / cm^{-1} 1653 (NCO); δ_H (400 MHz; $CDCl_3$; Me_4Si) 1.12 (3H, t, *J* 7.2 Hz, CH_3 ethyl), 1.46-1.56 (1H, m, CH_2 ethyl), 1.87-1.95 (2H, m, CH_2 ethyl and H-8), 2.45 (1H, dd, *J* 8.0 and 2.4 Hz, H-7), 3.06 (1H, dd, *J* 12.0 and 3.2 Hz,

H-6), 3.23 (1H, dd, *J* 14.0 and 12.0 Hz, C*H*$_2$-ind), 3.55 (1H, dd, *J* 14.0 and 3.2 Hz, C*H*$_2$-ind), 3.86 (1H, t, *J* 8.5 Hz, H-2), 4.69 (1H, t, *J* 8.5 Hz, H-2), 4.81 (1H, d, *J* 8.8 Hz, H-8a), 4.87 (1H, d, *J* 16.8 Hz, HC=C*H*$_2$), 5.15 (1H, d, *J* 10.4 Hz, HC=C*H*$_2$), 5.41 (1H, d, *J* 8.5 Hz, H-3), 5.67 (1H, dd, *J* 17.6 and 1.5 Hz, ind-HC=C*H*$_2$), 5.84 (1H, dd, *J* 11.2 and 1.5 Hz, ind-HC=C*H*$_2$), 5.82-5.92 (1H, m, *H*C=CH$_2$), 7.31 (1H, dd, *J* 17.6 and 11.2 Hz, ind-*H*C=CH$_2$), 7.38-7.54 (9H, m, ArH and H-7 ind), 7.63-7.67 (2H, m, ArH), 7.79 (1H, d, *J* 8.0 Hz, H-5 ind), 7.90 (1H, dd, *J* 8.0 and 1.2 Hz, H-6 ind), 8.40 (1H, d, *J* 8.4 Hz, H-4 ind); δ_C (100.6 MHz; $CDCl_3$; Me_4Si) 11.4 (CH_3 ethyl), 21.7 (CH_2 ethyl), 26.1 (*C*H$_2$-ind), 39.3 (C-7), 40.0 (C-8), 45.7 (C-6), 58.9 (C-3), 72.8 (C-2), 90.9 (C-8a), 115.1 (C-7 ind), 117.5 (HC=*C*H$_2$), 119.8 (C-6 ind), 120.6 (C-2 ind), 121.2 (ind-HC=*C*H$_2$), 123.9 (C-4 ind), 125.4 (C-5 ind), 126.0 (C-*o*), 126.6 (C-*m*), 127.6 (ind-H*C*=CH$_2$), 127.8 (C-*p*), 128.9 (C-*o*), 128.9 (C-*m*), 130.3 (C-3 ind), 133.6 (C-*p*), 135.5 (H*C*=CH$_2$), 135.8 (C-3a ind), 136.2 (C-7a ind), 138.1 (C-*ipso*), 139.6 (C-*ipso*), 170.2 (NCO); HMRS calcd for [$C_{34}H_{34}N_2O_4S$ + H]: 567.2316, found: 567.2312. 6-*epi*-**6** (6*S*, minor): $[\alpha]^{22}_D$ – 16.0 (*c* 0.2 in $CHCl_3$); ν_{max} (KBr) / cm^{-1} 1656 (NCO); δ_H (400 MHz; $CDCl_3$; Me_4Si) 0.85 (3H, t, *J* 7.3 Hz, CH_3 ethyl), 1.24-1.36 (1H, m, CH_2 ethyl), 1.48-1.64 (2H, m, CH_2 ethyl and H-8), 2.30 (1H, dt, *J* 6.4 and 3.6 Hz, H-7), 2.83 (1H, m, C*H*$_2$-ind), 2.90 (1H, dd, *J* 12.4 and 4.4 Hz, H-6), 3.59 (1H, d, *J* 13.2 Hz, C*H*$_2$-ind), 3.71 (1H, t, *J* 8.5 Hz, H-2), 4.52 (1H, t, *J* 8.5 Hz, H-2), 4.62 (1H, d, *J* 8.8 Hz, H-8a), 4.98 (1H, dd, *J* 17.0 and 1.4 Hz, CH=C*H*$_2$), 5.26 (1H, t, *J* 8.5 Hz, H-3), 5.32 (1H, dd, *J* 10.0 and 1.4 Hz, CH=C*H*$_2$), 5.39 (1H, dd, *J* 17.8 and 1.6 Hz, ind-CH=C*H*$_2$), 5.55 (1H, dd, *J* 11.4 and 1.6 Hz, ind-CH=C*H*$_2$), 5.62 (1H, dt, *J* 17.0 and 10.0 Hz, C*H*=CH$_2$), 7.04 (1H, dd, *J* 17.8 and 11.4 Hz, ind-C*H*=CH$_2$), 7.22 (1H, dt, *J* 8.0 and 1.2 Hz, H-7 ind), 7.25-7.39 (9H, m, ArH), 7.47 (1H, dt, *J* 7.2 and 1.2 Hz, H-5 ind), 7.57 (1H, d, *J* 8.0 Hz, ArH), 7.72 (2H, dd, *J* 8.0 and 1.2 Hz, H-6 ind), 8.21 (1H, d, *J* 8.4 Hz, H-4 ind); δ_C (100.6 MHz; $CDCl_3$; Me_4Si) 11.4 (CH_3 ethyl), 22.7 (CH_2 ethyl), 23.0 (*C*H$_2$-ind), 42.1 (C-7), 44.9 (C-8), 47.1 (C-6), 58.9 (C-3), 73.0 (C-2), 91.6 (C-8a), 115.0 (C-7 ind), 119.9 (C-4 ind), 120.8 (C-3 ind), 121.4 (*C*H$_2$=CH), 122.0 (ind-CH=*C*H$_2$), 123.6 (C-5 ind), 125.1 (C-6 ind), 126.0 (C-*o*), 126.7 (C-*m*), 127.6 (C-*p*), 127.7 (C-*p*), 128.8 (C-*o*), 128.9 (C-*m*), 130.6 (C-2 ind), 132.9 (*C*H=CH$_2$), 133.5 (ind-*C*H=CH$_2$), 135.6 (C-*ipso*), 136.2 (C-*ipso*), 138.2 (C-3a ind), 140.0 (C-7a ind), 167.0 (NCO); HMRS calcd for [$C_{34}H_{34}N_2O_4S$ + Na]: 589.2131, found: 589.2132.



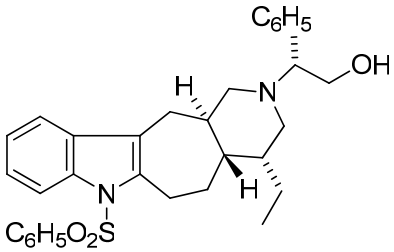
(1*R*,3a*S*,4*R*,4a*S*,12a*R*)-7-(Benzenesulfonyl)-4-ethyl-13-oxo-1-phenyl-1,2,3a,4,4a,12,12a,13-octahydrooxazolo[2",3":6',1']pyrido[3',4':4,5]cyclohepta[1,2-

***b*]indole (7).** Second-generation Grubbs catalyst (263 mg) was added to a solution of vinylindole **6** (1.31 g, 2.32 mmol) in anhydrous toluene (300 mL) under argon atmosphere. The mixture was stirred at reflux for 5 days and concentrated. The resulting residue was purified by flash column chormatography (4:1 to 1:1 hexane-EtOAc) to yield pentacyclic lactam **7** (1.09 g, 87%): mp 161-163 ºC (from MeOH); $[\alpha]^{22}_D$ – 244.0 (*c* 0.3 in $CHCl_3$); (Found: C, 70.53; H, 5.74; N, 5.09; S, 5.89. Calc. for $C_{32}H_{30}N_2O_4S{\cdot}1/2H_2O$**:** C, 70.57; H, 5.67; N, 5.14; S, 5,89%); ν_{max} (KBr) / cm^{-1} 1656 (NCO); δ_H (400 MHz; $CDCl_3$; Me_4Si) 0.99 (3H, t, *J* 7.4 Hz, CH_3), 1.53-1.64 (2H, m, CH_2 ethyl), 1.89-1.95 (1H, m, H-4), 2.62 (1H, dt, *J* 10.0 and 3.6 Hz, H-12a), 2.77 (1H, ddd, *J* 10.0, 5.4 and 2.1 Hz, H-4a), 2.87 (1H, dd, *J* 16.8 and 10.0 Hz, H-12), 3.46 (1H, dd, *J* 16.8 and 3.6 Hz, H-12), 3.84 (1H, dd, *J* 9.0 and 6.6 Hz, H-2), 4.40 (1H, dd, *J* 9.0 and 7.8 Hz, H-2), 4.92 (1H, d, *J* 4.8 Hz, H-3a), 5.31 (1H, t, *J* 6.9 Hz, H-1), 6.10 (1H, dd, *J* 11.7 and 5.1 Hz, H-5), 7.23-7.50 (13H, m, ArH, H-6, H-9, H-10), 7.66 (1H, dd, *J* 8.4 and 1.2 Hz, H-8), 8.24 (1H, d, *J* 8.1 Hz, H-11); δ_C (100.6 MHz; $CDCl_3$; Me_4Si) 12.1 (CH_3 ethyl), 19.9 (CH_2 ethyl), 24.3 (C-12), 39.8 (C-4), 43.8 (C-4a), 44.3 (C-5a), 58.6 (C-1), 71.8 (C-2), 90.2 (C-3a), 115.5 (C-8), 118.9 (C-9), 121.1 (C-6a), 123.8 (C-11), 124.1 (C-10), 125.5 (C-10), 126.1 (C-11b), 126.4 (C-*o*), 127.6 (C-*m*), 128.7 (C-*p*), 128.8 (C-*o*), 130.8 (C-6), 132.6 (C-5), 132.8 (C-*m*), 133.5 (C-*p*), 136.7 (C-*ipso*), 137.9 (C-11a), 139.4 (C-*ipso*), 170.8 (NCO).

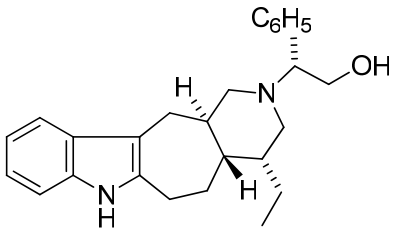


(1*R*,3a*S*,4*R*,4a*S*,12a*R*)-7-(Benzenesulfonyl)-4-ethyl-13-oxo-1-phenyl-1,2,3a,4,4a,5,6,12,12a,13-decahydrooxazolo[2",3":6',1']pyrido[3',4':4,5]cyclohepta[1,2-*b*]indole. A suspension of compound **7** (500 mg, 0.93 mmol) in EtOAc (50 mL) and 20% PtO_2 (100 mg) was hydrogenated at room temperature and atmospheric pressure for 24 h. The catalyst was removed by filtration, the solvent was evaporated, and the resulting residue was chromatographed (9:1 hexane-EtOAc) to afford the saturated pentacycle (360 mg, 72%): $[\alpha]^{22}_D$ – 22.5 (*c* 1.0 in $CHCl_3$); (Found: C, 66.57; H, 5.81; N, 4.58; S, 5.13. Calc. for $C_{32}H_{32}N_2O_4S{\cdot}1/3CHCl_3$: C, 66.94; H, 5.62; N, 4.83; S, 5.53%); ν_{max} (KBr) / cm^{-1} 1662 (NCO); δ_H (400 MHz; $CDCl_3$; Me_4Si) 1.00 (3H, t, *J* 7.6 Hz, CH_3 ethyl), 1.43-1.62 (2H, m, CH_2 ethyl), 1.75 (1H, ddd, *J* 18.0, 9.2 and 3.6 Hz, H-5), 1.87-1.95 (2H, m, H-4, H-5), 2.08-2.16 (1H, m, H-4a), 2.57 (1H, ddd, *J* 11.2, 8.4 and 4.0 Hz, H-12a), 2.87 (1H, dd, *J* 16.0 and 8.4 Hz, H-12), 3.21 (1H, ddd, *J* 17.2, 9.2 and 4.4 Hz, H-6), 3.41-3.50 (1H, m, H-6), 3.43 (1H, dd, *J* 16.0 and 4.0 Hz, H-12), 3.78 (1H, dd, *J* 9.2 and 7.4 Hz, H-2), 4.38 (1H, t, *J* 8.4 Hz, H-2), 4.74 (1H, d, *J* 2.8 Hz, H-3a), 5.36 (1H, t, *J* 7.4 Hz, H-3), 7.23-7.55 (11H, m, H-8, H-9, H-10 and ArH), 7.70 (2H, dd, *J* 8.8 and 1.2 Hz, ArH), 8.19 (1H, dd, *J* 6.4 and 1.6 Hz, H-11); δ_C

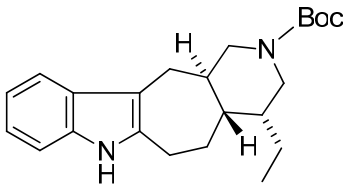
(100.6 MHz; $CDCl_3$; Me_4Si) 12.6 (CH_3 ethyl), 19.6 (CH_2 ethyl), 22.2 (C-12), 25.3 (C-6), 28.1 (C-5), 37.6 (C-4a), 41.2 (C-12a), 44.6 (C-4), 58.5 (C-1), 71.4 (C-2), 89.8 (C-3a), 114.8 (C-8), 118.5 (C-9), 119.5 (C-6a), 123.6 (C-10), 124.2 (C-11), 126.0 (C-*o*), 126.2 (C-*m*), 127.6 (C-*p*), 128.8 (C-*o*), 129.2 (C-*m*), 130.7 (C-11b), 133.5 (C-*p*), 136.4 (C-11a), 136.6 (C-7a), 139.2 (C-*ipso*), 139.9 (C-*ipso*), 172.1 (NCO); HMRS calcd for $[C_{32}H_{32}N_2O_4S + H]$: 541.2155, found: 541.2160.



(4*R*,4a*S*,12a*R*)-7-(Benzenesulfonyl)-4-ethyl-2-[(1*R*)-2-hydroxy-1-phenylethyl]-1,3,4,4a,5,6,12,12a-octahydropyrido[3',4':4,5]cyclohepta[1,2-*b*]indole (8). $LiAlH_4$ (436 mg, 11.5 mmol) was slowly added to a suspension of $AlCl_3$ (498 mg, 3.73 mmol) in THF (50 mL) at 0 ºC. After the mixture was stirred at 25 ºC for 30 min and cooled to –78 ºC, the above hydrogenated pentacycle (940 mg, 1.17 mmol) in anhydrous THF (40 mL) was slowly added. The stirring was continued at –78 ºC for 10 min and at 0 ºC for 1 h 30 min. The mixture was cooled to 0 ºC, and the reaction was quenched with water. The aqueous layer was extracted with EtOAc, and the combined organic extracts were dried and concentrated to give a foam, which was chromatographed (9:1 to 4:1 hexane-EtOAc) to afford compound **8** (710 mg, 88%): $[\alpha]^{22}_D$ + 73.2 (*c* 0.37 in $CHCl_3$); (Found: C, 72.62; H, 7.12; N, 5.01. Calc. for $C_{32}H_{36}N_2O_3S$: C, 72.70; H, 6.86; N, 5.30%); ν_{max} (KBr) / cm^{-1} 3441 (OH); δ_H (400 MHz; $CDCl_3$; Me_4Si) 0.90 (3H, t, *J* 7.2 Hz, CH_3 ethyl), 1.17-1.54 (7H, m, CH_2 ethyl, H-4, H-4a, H-5 and H-12a), 2.10 (1H, dd, *J* 15.2 and 10.8 Hz, H-3), 2.28 (1H, d, *J* 11.6 Hz, H-12), 2.57 (1H, dd, *J* 15.2 and 1.6 Hz, H-3), 2.66 (1H, dd, *J* 15.2 and 10.8 Hz, H-6), 2.85 (1H, d, *J* 8.8 Hz, H-1), 2.95 (1H, d, *J* 11.6 Hz, H-12), 3.62-3.77 (m, 3H, H-6, NC*H* and C*H*$_2$O), 4.01-4.09 (1H, m, CH_2O), 7.19-7.51 (11H, m, H-8, H-9, H-10 and ArH), 7.66 (2H, dd, *J* 8.4 and 0.8 Hz, ArH), 8.20-8.23 (1H, m, H-11); δ_C (100.6 MHz; $CDCl_3$; Me_4Si) 12.7 (CH_3 ethyl), 18.8 (CH_2 ethyl), 25.4 (C-12), 28.8 (C-6), 31.5 (C-5), 35.3 (C-4a), 43.7 (C-12a), 49.7 (C-4), 53.4 (C-3), 55.6 (C-1), 60.2 (CH_2O), 70.0 (NCH), 115.3 (C-8), 117.7 (C-9), 121.1 (C-6a), 123.4 (C-10), 123.9 (C-11), 126.2 (C-*o*), 127.9 (C-*p*), 128.2 (C-*m*), 128.9 (C-*o*), 129.1 (C-*m*), 130.4 (C-11b), 133.5 (C-*p*), 135.2 (C-11a), 136.3 (C-7a), 139.3 (C-*ipso*), 139.6 (C-*ipso*); HMRS calcd for $[C_{32}H_{36}N_2O_3S + H]$: 529.2519, found: 529.2526.

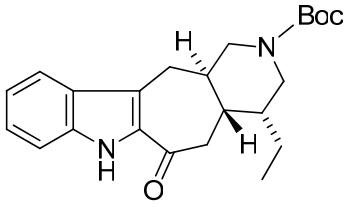


(4*R*,4a*S*,12a*R*)-4-Ethyl-2-[(1*R*)-2-hydroxy-1-phenylethyl]-1,3,4,4a,5,6,12,12a-octahydropyrido[3',4':4,5]cyclohepta[1,2-*b*]indole. Mg turnings (207 mg, 8.50 mmol) were added to a solution of compound **8** (710 mg, 1.53 mmol) in anhydrous MeOH (60 mL) at 0 ºC. The resulting mixture was warmed to room temperature and vigorously stirred for 4 h. The reaction was quenched with brine, and the resulting solution was extracted with CH_2Cl_2. The combined organic extracts were dried and concentrated, and the resulting residue was chromatographed (hexane to 4:1 hexane-EtOAc) to give the *N*-unsubstituted indole (480 mg, 81%): $[\alpha]^{22}_D$ + 8.3 (*c* 0.29 in $CHCl_3$); (Found: C, 79.03; H, 8.41; N, 6.67. Calc. for $C_{26}H_{32}N_2O \cdot 1/4EtOAc$: C, 78.99; H, 8.35; N, 6.82%); ν_{max} (KBr) / cm^{-1} 2925 (OH), 3411 (NH); δ_H (400 MHz; $CDCl_3$; Me_4Si) 0.94 (3H, t, *J* 7.2 Hz, CH_3 ethyl), 1.21-1.74 (7H, m, CH_2 ethyl, H-4, H-4a, H-5 and H-12a), 2.22 (1H, dd, *J* 14.8 and 11.2 Hz, H-12), 2.32 (1H, d, *J* 12.4 Hz, H-3), 2.72-2.84 (3H, m, H-1 and H-12), 2.94-3.01 (2H, m, H-3 and H-6), 2.65-3.75 (2H, m, NCH and CH_2O), 4.07-4.16 (1H, m, CH_2O), 7.08 (2H, m, H-8, H-9, H-10, H-11 and ArH), 7.24-7.46 (7H, m, ArH, H-ind), 7.75 (1H, brs, NH); δ_C (100.6 MHz; $CDCl_3$; Me_4Si) 12.8 (CH_3 ethyl), 18.8 (CH_2 ethyl), 27.9 (C-12), 29.4 (C-6), 32.5 (C-5), 36.5 (C-4a), 44.2 (C-12a), 49.4 (C-4), 53.6 (C-3), 55.6 (C-1), 60.3 (CH_2O), 70.1 (NCH), 110.3 (C-8), 110.9 (C-6a), 117.4 (C-9), 119.2 (C-10), 120.6 (C-11), 127.9 (C-11b), 128.2 (C-*o*), 128.8 (C-*p*), 129.0 (C-*m*), 134.1 (C-11a), 135.3 (C-7a), 138.0 (C-*ipso*); HMRS calcd for [$C_{26}H_{32}N_2O$ + H]: 389.2594, found: 389.2599.

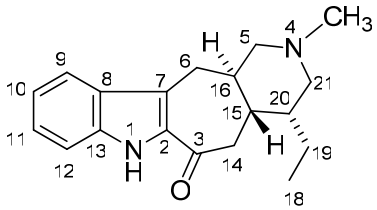


(4*R*,4a*S*,12a*R*)-2-(*tert*-Butoxycarbonyl)-4-ethyl-1,3,4,4a,5,6,12,12a-octahydropyrido[3',4':4,5]cyclohepta[1,2-*b*]indole (9). A solution of deprotected indole (160 mg, 0.41 mmol) and di-*tert*-butyl dicarbonate (94 mg, 0.43 mmol) in EtOAc (25 mL) containing 30% $Pd(OH)_2$-C (48 mg) was hydrogenated at rt for 16 h at atmospheric pressure. The catalyst was removed by filtration, and the solvent was evaporated to give an oil, which was chromatographed (hexane to 4:1 hexane-EtOAc) to afford **9** (91 mg, 60%): $[\alpha]^{22}_D$ – 0.4 (*c* 0.7 in $CHCl_3$); ν_{max} (KBr) / cm^{-1} 1667 (NCO); δ_H (400 MHz; $CDCl_3$; Me_4Si) 0.94 (3H, t, *J* 7.2 Hz, CH_3 ethyl), 1.12-1.45 (3H, m, CH_2 ethyl and H-4), 1.47 [9H, s, $C(CH_3)_3$], 1.60-1.74 (4H, m, H-4a, H-5 and H-12a), 2.29 (1H, dd, *J* 15.2 and 10.0 Hz, H-6), 2.43-2.46 (1H, m, H-1), 2.70-2.92 (4H, m, H-3, H-6 and H-12), 4.16 (1H, d, *J* 12.4 Hz, H-3), 4.30 (1H, d, *J* 12.0 Hz, H-1), 7.07-7.09 (2H, m, H-9 and H-10), 7.24-7.25 (1H, m,

H-8), 7.40-7.47 (1H, m, H-11), 7.82 (1H, brs, NH); δ_C (100.6 MHz; $CDCl_3$; Me_4Si) 12.7 (CH_3 ethyl), 17.2 (CH_2 ethyl), 27.9 (C-3), 28.4 [$C(CH_3)_3$], 29.7 (C-5), 32.8 (C-6), 35.8 (C-4a), 44.2 (C-12a), 46.7 (C-3), 49.7 (C-1), 49.9 (C-3), 79.2 [$C(CH_3)_3$], 110.3 (C-8), 110.6 (C-6a), 117.4 (C-9), 119.2 (C-10), 120.6 (C-11), 128.8 (C-11b), 134.2 (C-11a), 138.0 (C-7a), 155.1 (NCO); HMRS calcd for [$C_{23}H_{33}N_2O_4$ + HCOOH]: 401.2435, found: 401.2429.



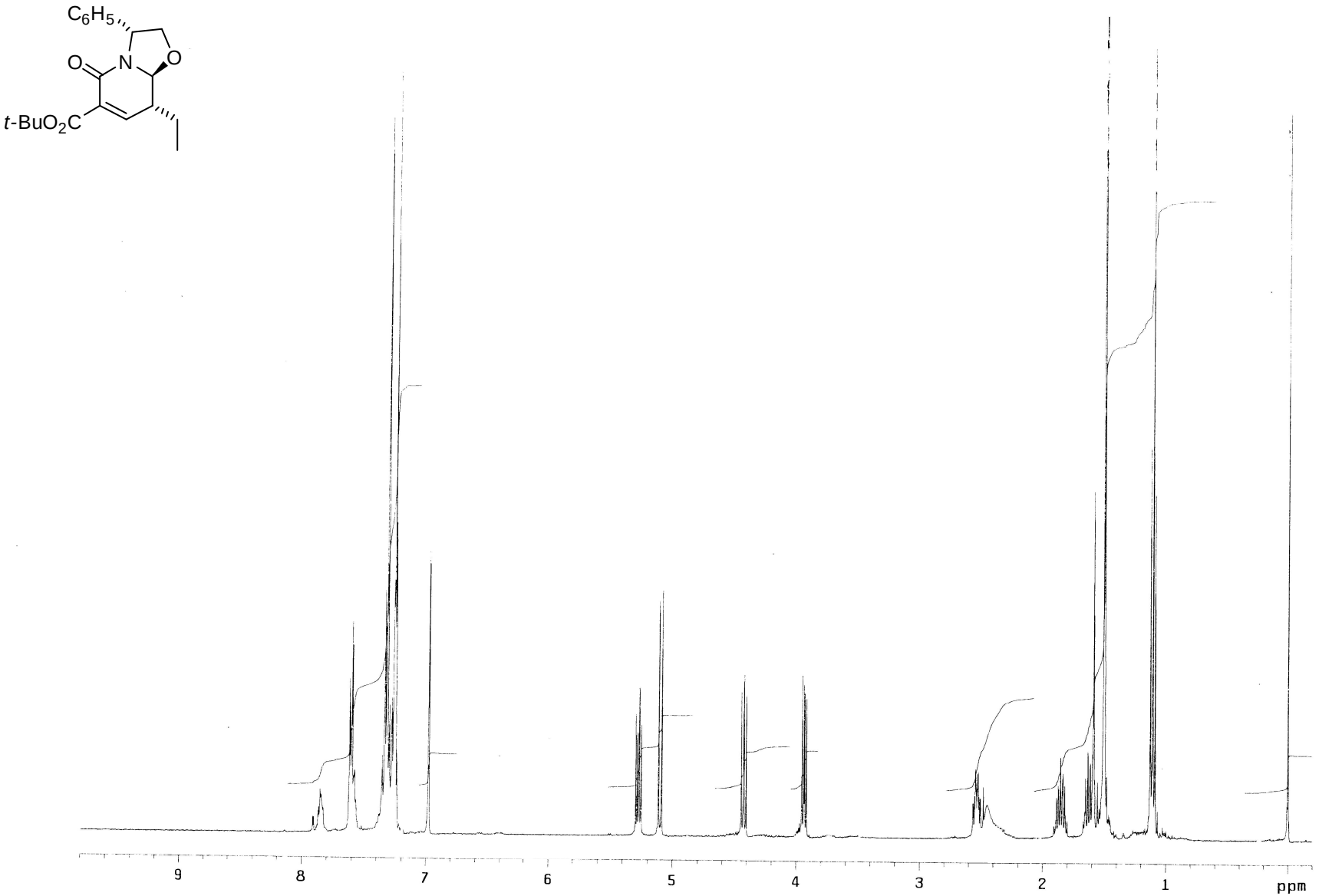
(4*R*,4a*S*,12a*R*)-2-(*tert*-Butoxycarbonyl)-4-ethyl-6-oxo-1,3,4,4a,5,6,12,12a-octahydropyrido[3',4':4,5]cyclohepta[1,2-*b*]indole (10). I_2O_5 (84 mg, 0.25 mmol) was added to a solution of compound **9** (78 mg, 0.21 mmol) in THF-H_2O (9:1, 10 mL) at 0 ºC, and the mixture was stirred at room temperature for 5 h 30 min. The mixture was poured into saturated aqueous $NaHCO_3$, and the aqueous layer was extracted with EtOAc. The combined organic extracts were washed with 20% aqueous $Na_2S_2O_3$ and brine, dried, filtered, and concentrated. The resulting oil was chromatographed (CH_2Cl_2) affording compound **10** (67 mg, 83%): $[\alpha]^{22}_D$ – 22.9 (*c* 0.24 in $CHCl_3$); ν_{max} (KBr) / cm^{-1} 1692 (NCO), 1729 (CO); δ_H (400 MHz; $CDCl_3$; Me_4Si) 1.00 (3H, t, *J* 7.2 Hz, CH_3 ethyl), 1.24-1.34 (2H, m, CH_2 ethyl), 1.46 [9H, s, $C(CH_3)_3$], 1.60 (1H, m, H-4), 1.91-2.00 (1H, m, H-4a), 2.02-2.11 (1H, m, H-12a), 2.47-2.53 (1H, m, H-1), 2.72-2.87 (2H, m, H-5), 2.77 (1H, dd, *J* 15.6 and 7.2 Hz, H-3), 2.84 (1H, dd, *J* 16.4 and 4.8 Hz, H-12), 3.16 (1H, dd, *J* 16.4 and 6.0 Hz, H-12), 4.10 (1H, m, H-3), 4.31 (1H, d, *J* 12.0 Hz, H-1), 7.16 (1H, ddd, *J* 8.0, 6.0 and 1.2 Hz, H-11), 7.33-7.39 (2H, m, H-9, H-10), 7.64 (1H, d, *J* 8.0 Hz, H-8), 8.86 (1H, brs, NH); δ_C (100.6 MHz; $CDCl_3$; Me_4Si) 12.7 (CH_3 ethyl), 17.9 (CH_2 ethyl), 26.7 (C-12), 29.1 (CH_3), 36.2 (C-12a), 42.6 (C-4a), 43.2 (C-4), 46.3 (C-5), 46.8 (C-1), 49.8 (C-3), 79.6 [$C(CH_3)_3$], 112.0 (C-8), 120.4 (C-10), 120.8 (C-11), 123.0 (C-11b), 126.6 (C-9), 127.6 (C-11a), 132.6 (C-6a), 136.4 (C-7a), 155.5 (NCO), 193.9 (CO); HMRS calcd for [$C_{23}H_{31}N_2O_3$ + H]: 383.2329, found: 383.2329.



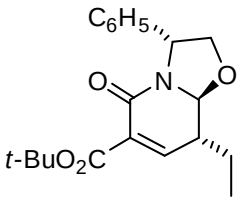
(–)-16-episilicine

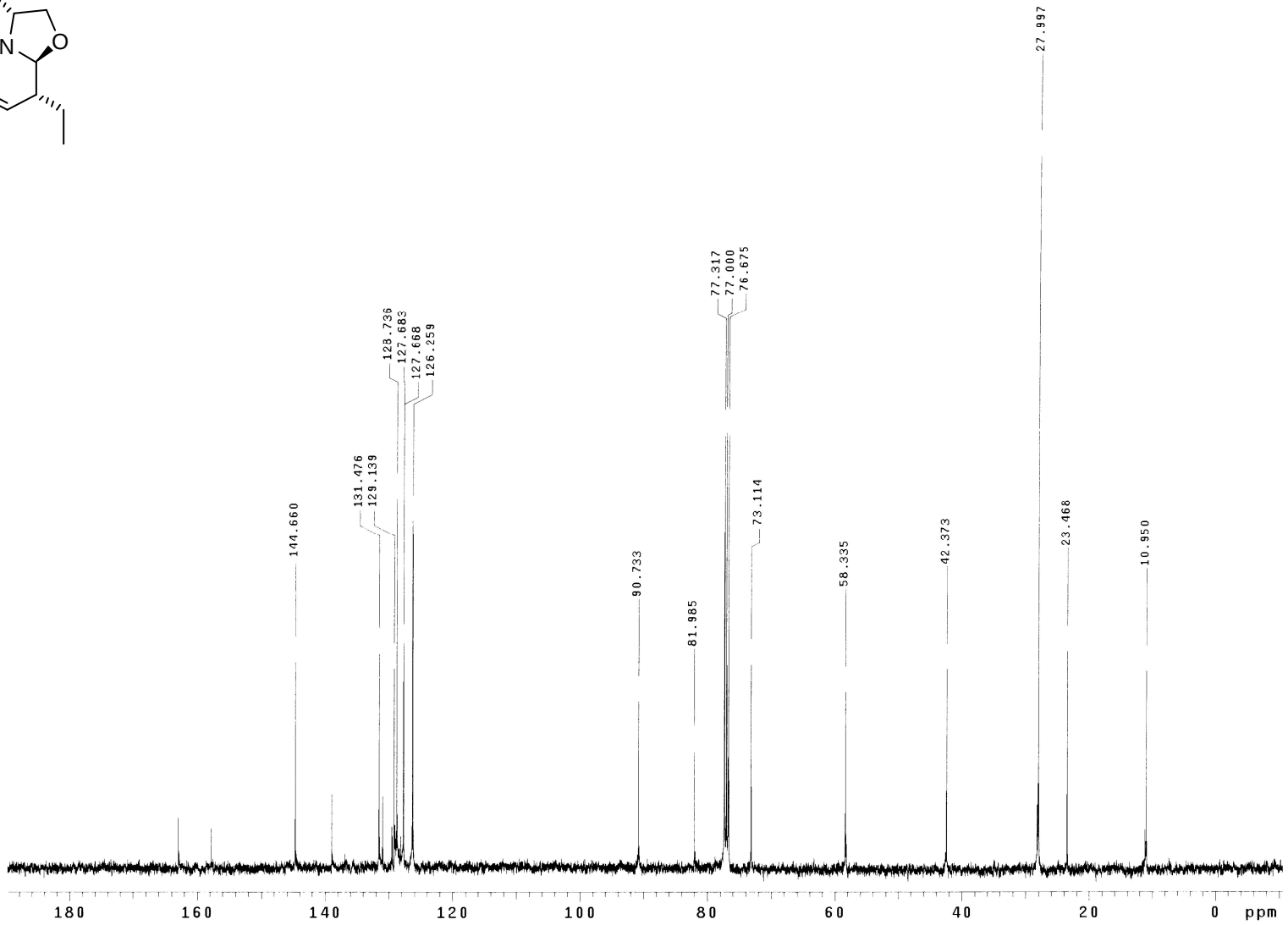
TFA (50 µl, 0.65 mmol) was added to a solution of indole **10** (70 mg, 0.18 mmol) in anhydrous CH_2Cl_2 (10 mL). The mixture was stirred at room temperature for 5 h and brought to pH 7 by

addition of saturated aqueous $NaHCO_3$. The aqueous layer was extracted with CH_2Cl_2, and the combined organic extracts were dried and concentrated. The residue was dissolved in anhydrous CH_3CN (5 mL), MeI (18 µl, 0.29 mmol) was added, and the mixture was stirred at room temperature for 3 h. The solution was washed with saturated aqueous $NaHCO_3$, and the aqueous phase was extracted with EtOAc. The combined organic extracts were dried, filtered, and concentrated. Flash chromatography using a cartridge containing amine functionalized silica (EtOAc) afforded pure (–)-16-episilicine (29 mg, 55%): $[\alpha]^{22}_D$ – 20.0 (*c* 1.0 in $CHCl_3$); δ_H (400 MHz; $CDCl_3$; Me_4Si) 0.97 (3H, t, *J* 7.2 Hz, CH_3 ethyl), 1.34-1.46 (2H, m, CH_2 ethyl), 1.56-2.02 (5H, m, H-15, H-20, H-21 and H-5), 2.20-2.40 (1H, m, H-16), 2.29 (3H, brs, NCH_3), 2.81 (2H, d, *J* 6.4 Hz, H-14), 2.84 (1H, m, H-21), 2.90-3.09 (2H, m, H-5 and H-6), 3.18 (1H, dd, *J* 16.4 and 6.4 Hz, H-6), 7.14 (1H, ddd, *J* 8.0, 6.4 and 1.0 Hz, H-10), 7.33 (1H, ddd, *J* 8.0, 6.4 and 1.0 Hz, H-11), 7.37 (1H, d, *J* 8.0 Hz, H-12), 7.65 (1H, d, *J* 8.0 Hz, H-9), 8.79 (1H, brs, NH); δ_C (100.6 MHz; $CDCl_3$; Me_4Si) 12.9 (C-18), 18.9 (C-19), 27.1 (C-6), 35.7 (C-16), 41.9 (C-15), 43.0 (C-20), 46.2 (NCH_3), 46.8 (C-14), 57.8 (C-21), 63.4 (C-5), 112.1 (C-12), 120.3 (C-10), 120.7 (C-9), 123.1 (C-7), 126.5 (C-11), 127.7 (C-8), 132.6 (C-2), 136.4 (C-13), 194.3 (CO).

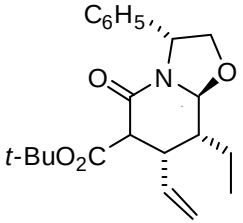


(3*R*,8*R*,8a*S*)-6-(*tert*-Butoxycarbonyl)-8-ethyl-5-oxo-3-phenyl-2,3,8,8a-tetrahydro-5*H*-oxazolo[3,2-*a*]pyridine (2)

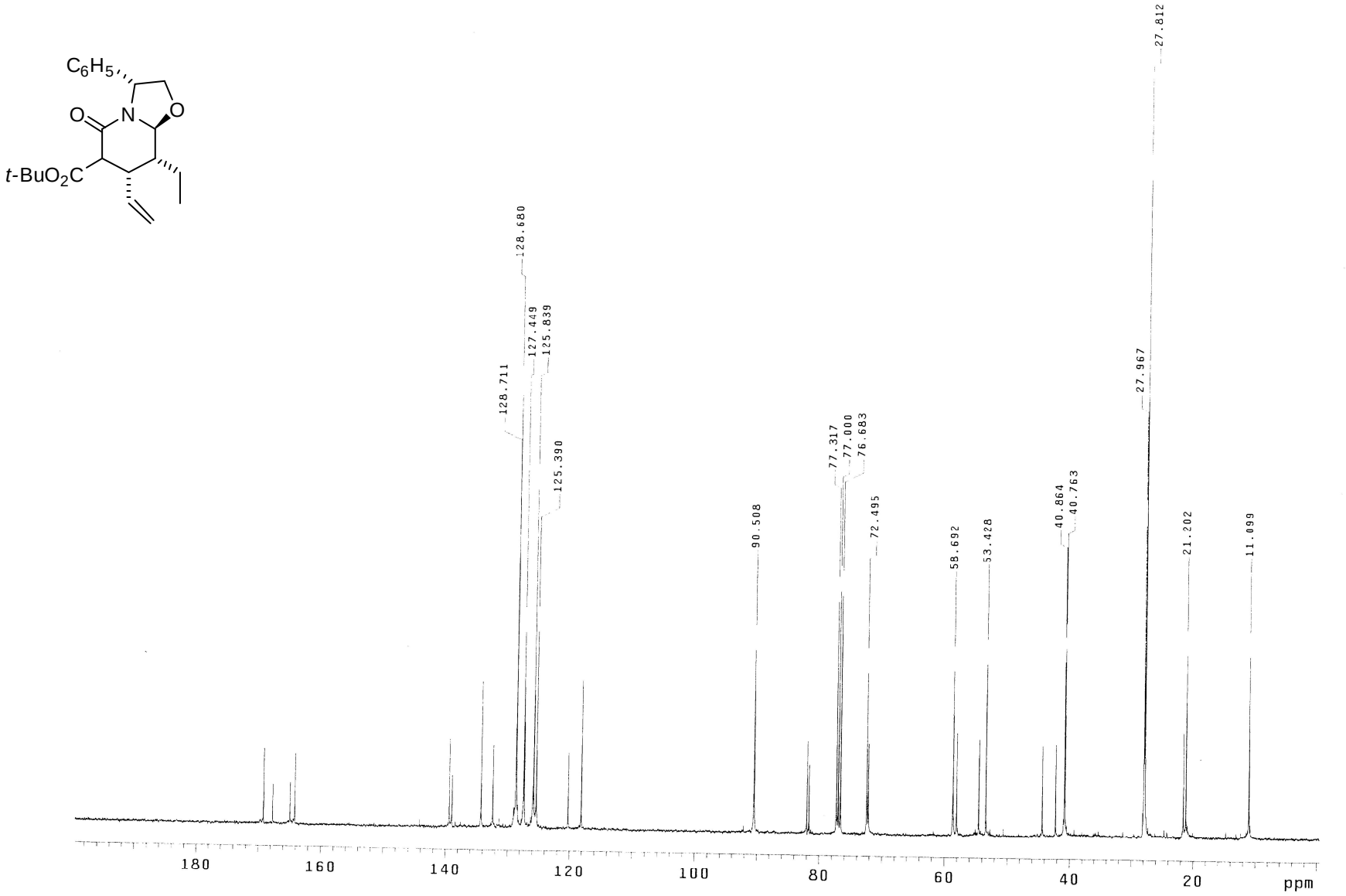




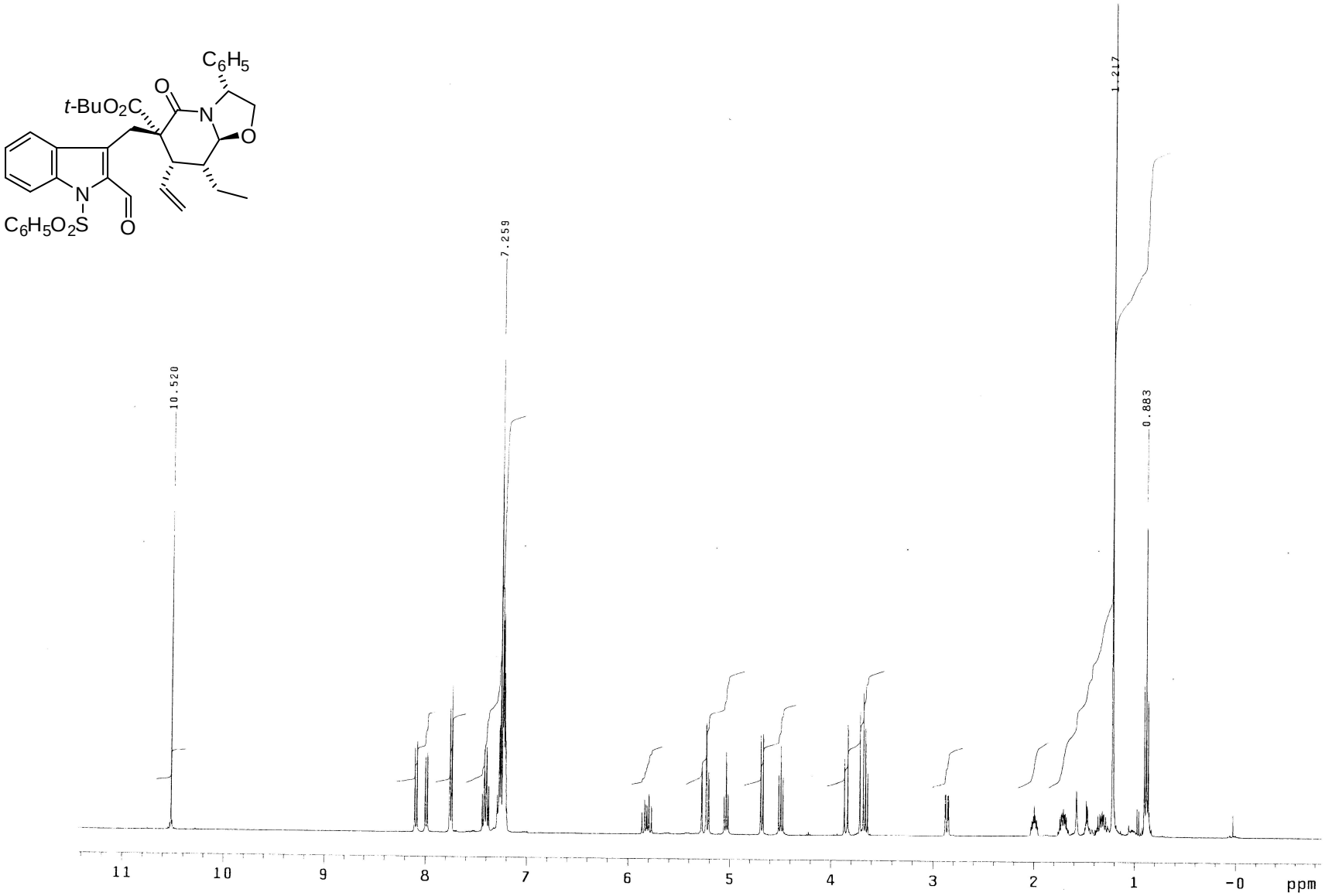
(3*R*,8*R*,8a*S*)-6-(*tert*-Butoxycarbonyl)-8-ethyl-5-oxo-3-phenyl-2,3,8,8a-tetrahydro-5*H*-oxazolo[3,2-*a*]pyridine (2)



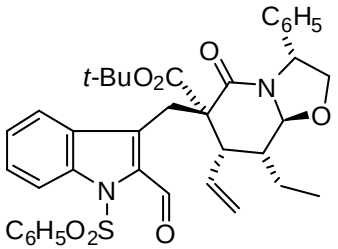
(3*R*,7*S*,8*R*,8a*S*)-6-(*tert*-Butoxycarbonyl)-8-ethyl-5-oxo-3-phenyl-7-vinyl-2,3,6,7,8,8a-hexahydro-5*H*-oxazolo[3,2-*a*]pyridine (3)

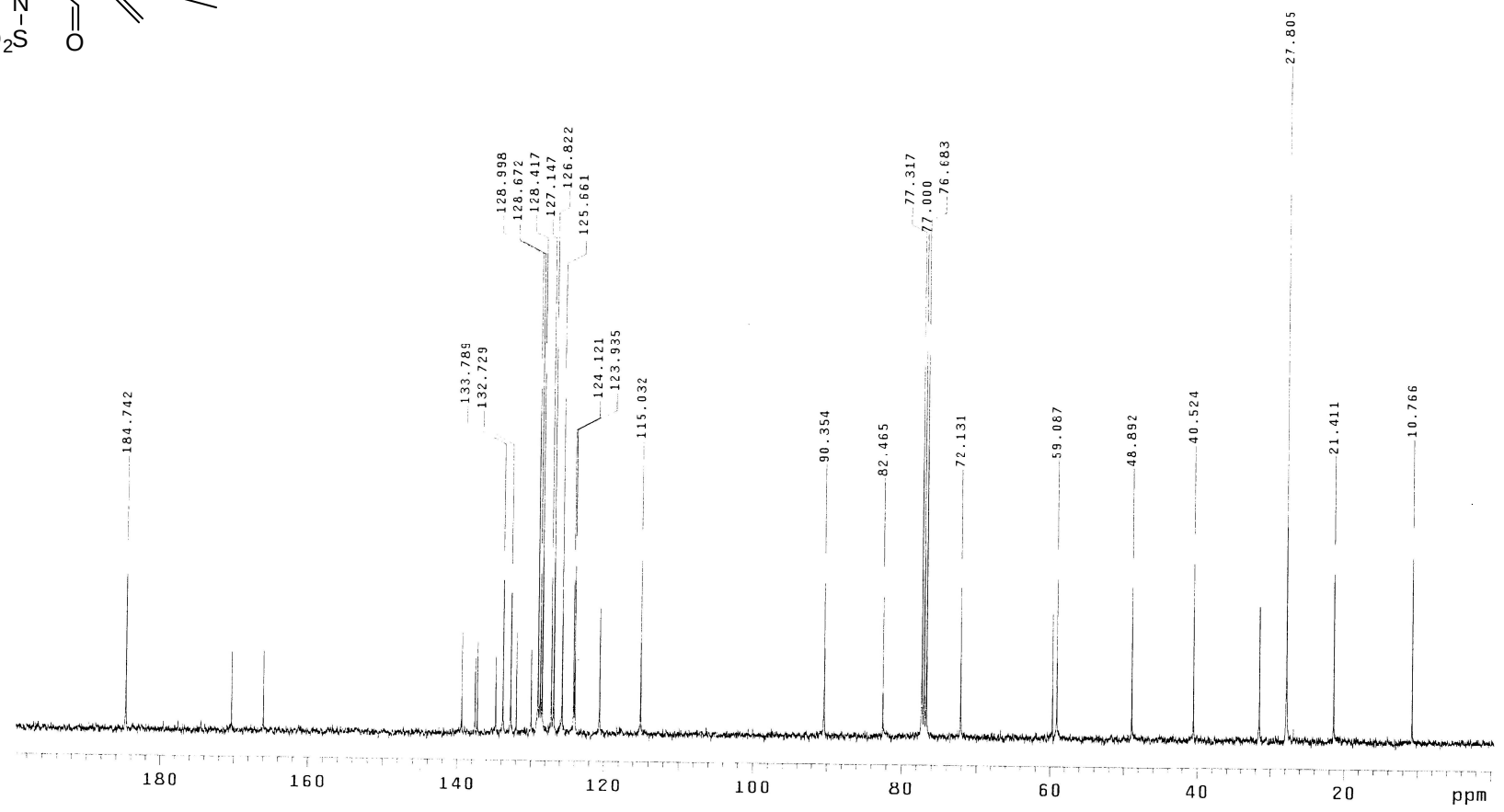


(3*R*,7*S*,8*R*,8a*S*)-6-(*tert*-Butoxycarbonyl)-8-ethyl-5-oxo-3-phenyl-7-vinyl-2,3,6,7,8,8a-hexahydro-5*H*-oxazolo[3,2-*a*]pyridine (3)

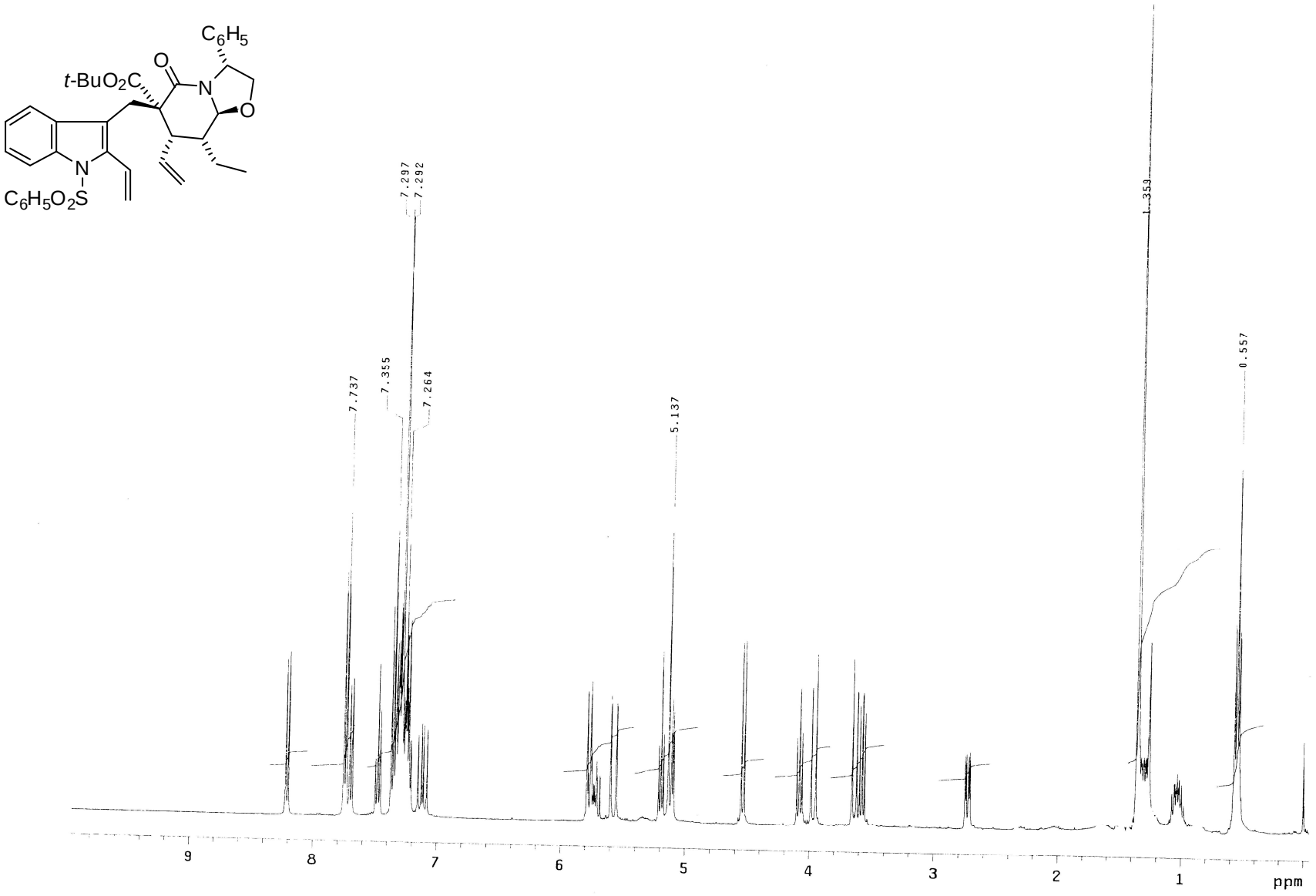


(3*R*,6S,7*S*,8*R*,8a*S*)-6-[(1-Benzenesulfonyl-2-formyl-3-indolyl)methyl]-6-(*tert*-butoxycarbonyl)-8-ethyl-5-oxo-3-phenyl-7-vinyl-2,3,6,7,8,8a-hexahydro-5*H*-oxazolo[3,2-*a*]pyridine (5)

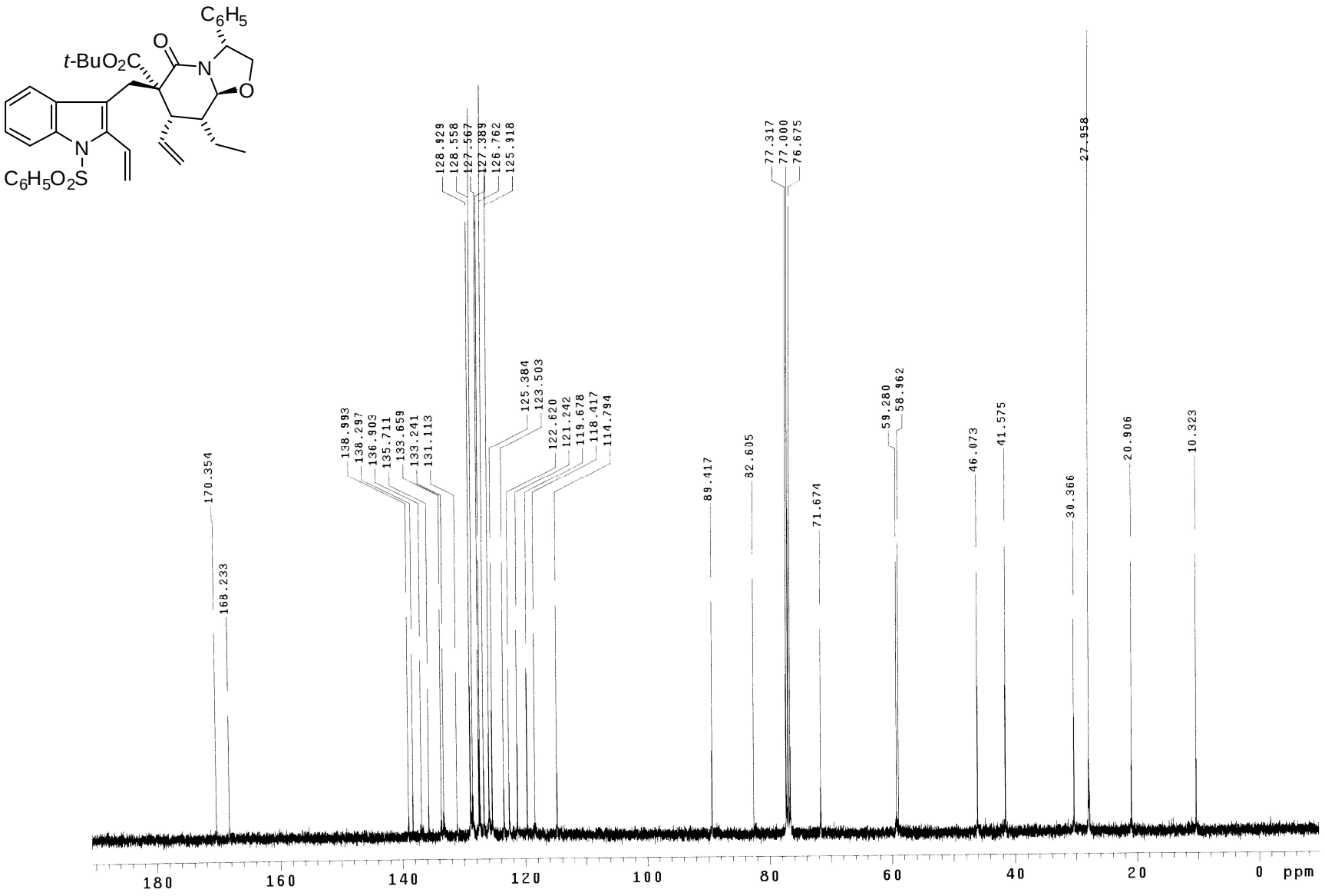




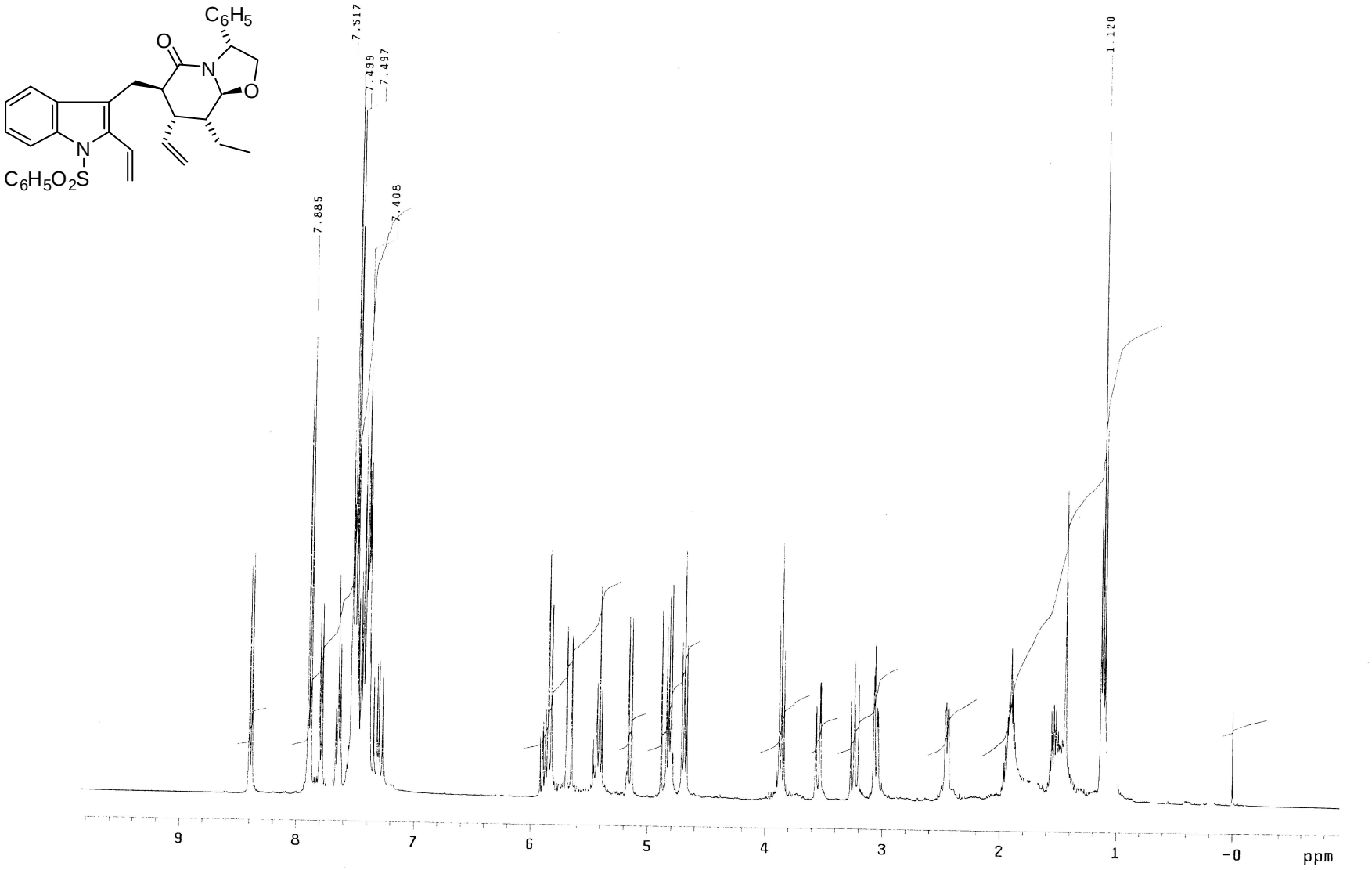
(3*R*,6S,7*S*,8*R*,8a*S*)-6-[(1-Benzenesulfonyl-2-formyl-3-indolyl)methyl]-6-(*tert*-butoxycarbonyl)-8-ethyl-5-oxo-3-phenyl-7-vinyl-2,3,6,7,8,8a-hexahydro-5*H*-oxazolo[3,2-*a*]pyridine (5)



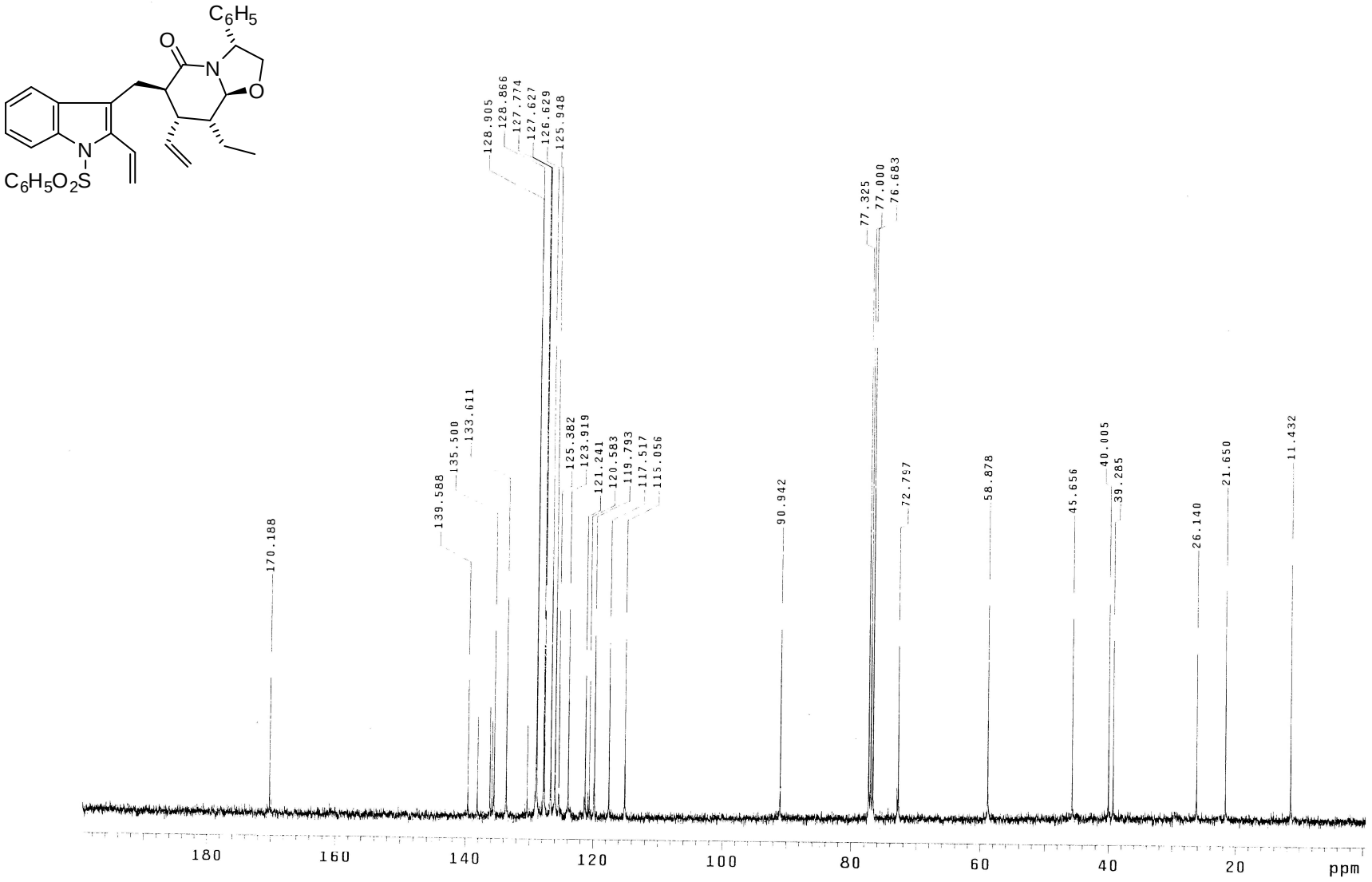
(3*R*,6*S*,7*S*,8*R*,8a*S*)-6-[(1-Benzenesulfonyl-2-vinyl-3-indolyl)methyl]-6-(*tert*-butoxycarbonyl)-8-ethyl-5-oxo-3-phenyl-7-vinyl-2,3,6,7,8,8a-hexahydro-5*H*-oxazolo[3,2-*a*]pyridine



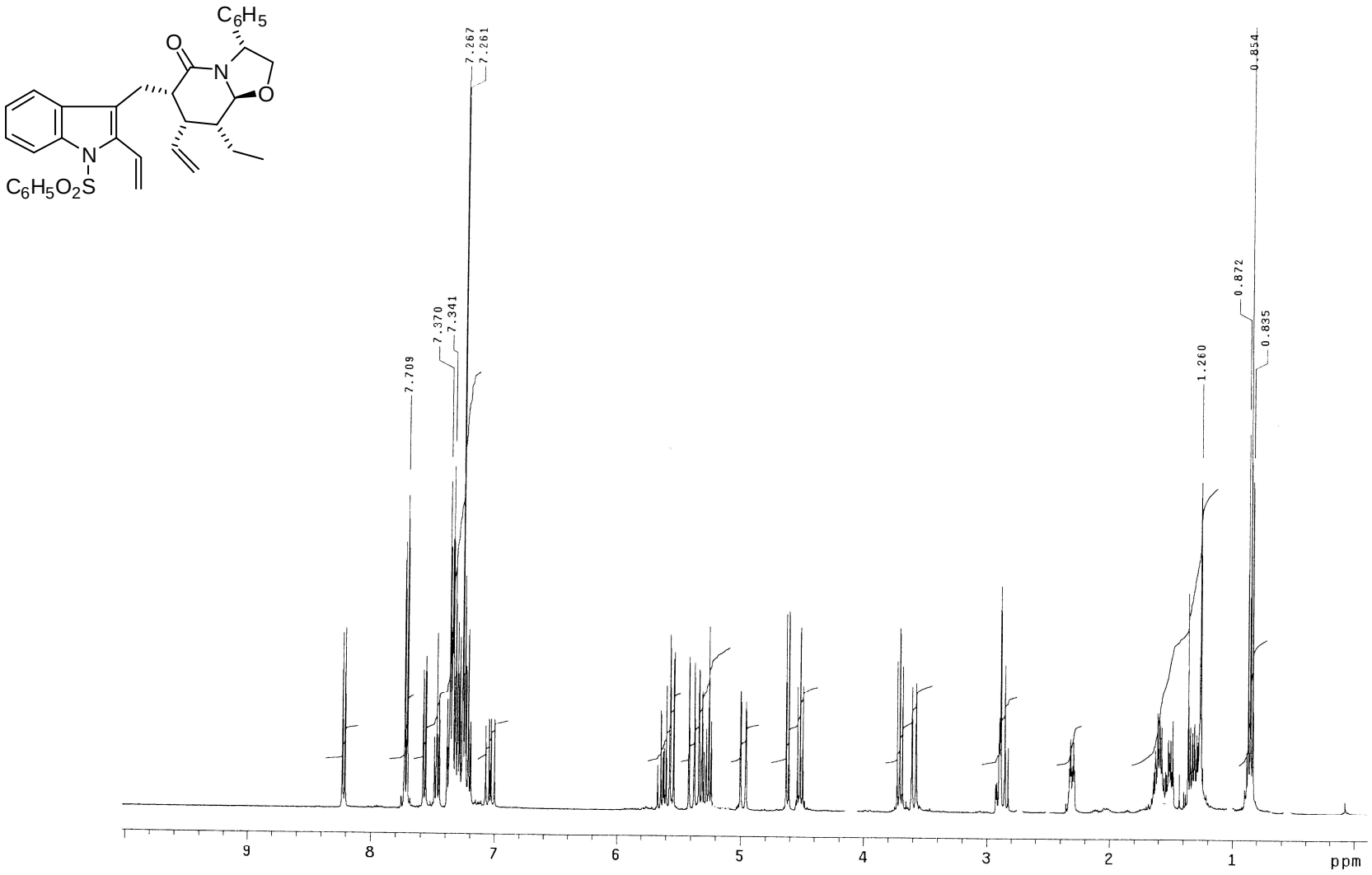
(3*R*,6*S*,7*S*,8*R*,8a*S*)-6-[(1-Benzenesulfonyl-2-vinyl-3-indolyl)methyl]-6-(*tert*-butoxycarbonyl)-8-ethyl-5-oxo-3-phenyl-7-vinyl-2,3,6,7,8,8a-hexahydro-5*H*-oxazolo[3,2-*a*]pyridine



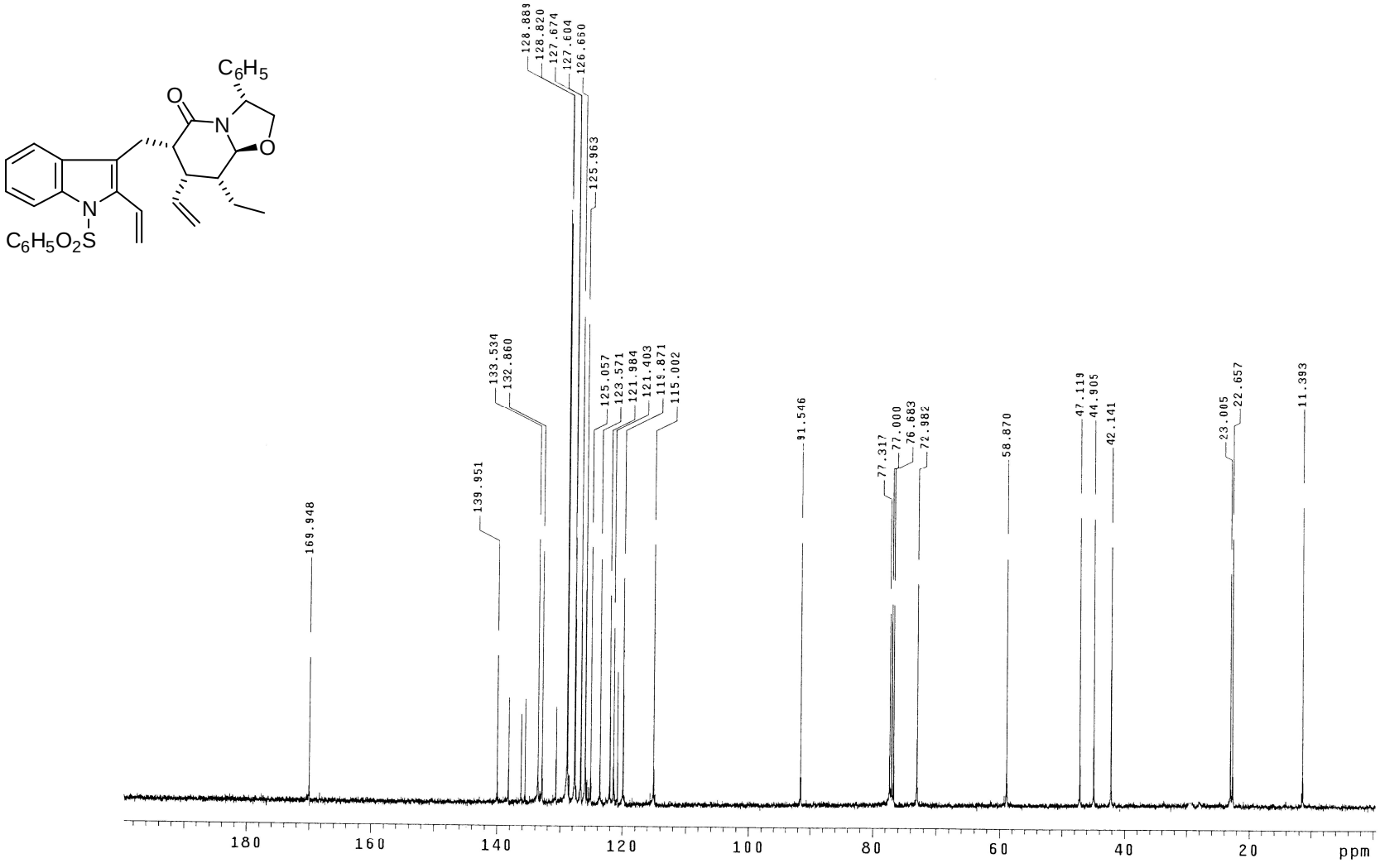
(3*R*,6*R*,7*S*,8*R*,8a*S*)-6-[(1-Benzenesulfonyl-2-vinyl-3-indolyl)methyl]-8-ethyl-5-oxo-3-phenyl-7-vinyl-2,3,6,7,8,8a-hexahydro-5*H*-oxazolo[3,2-*a*]pyridine (6)



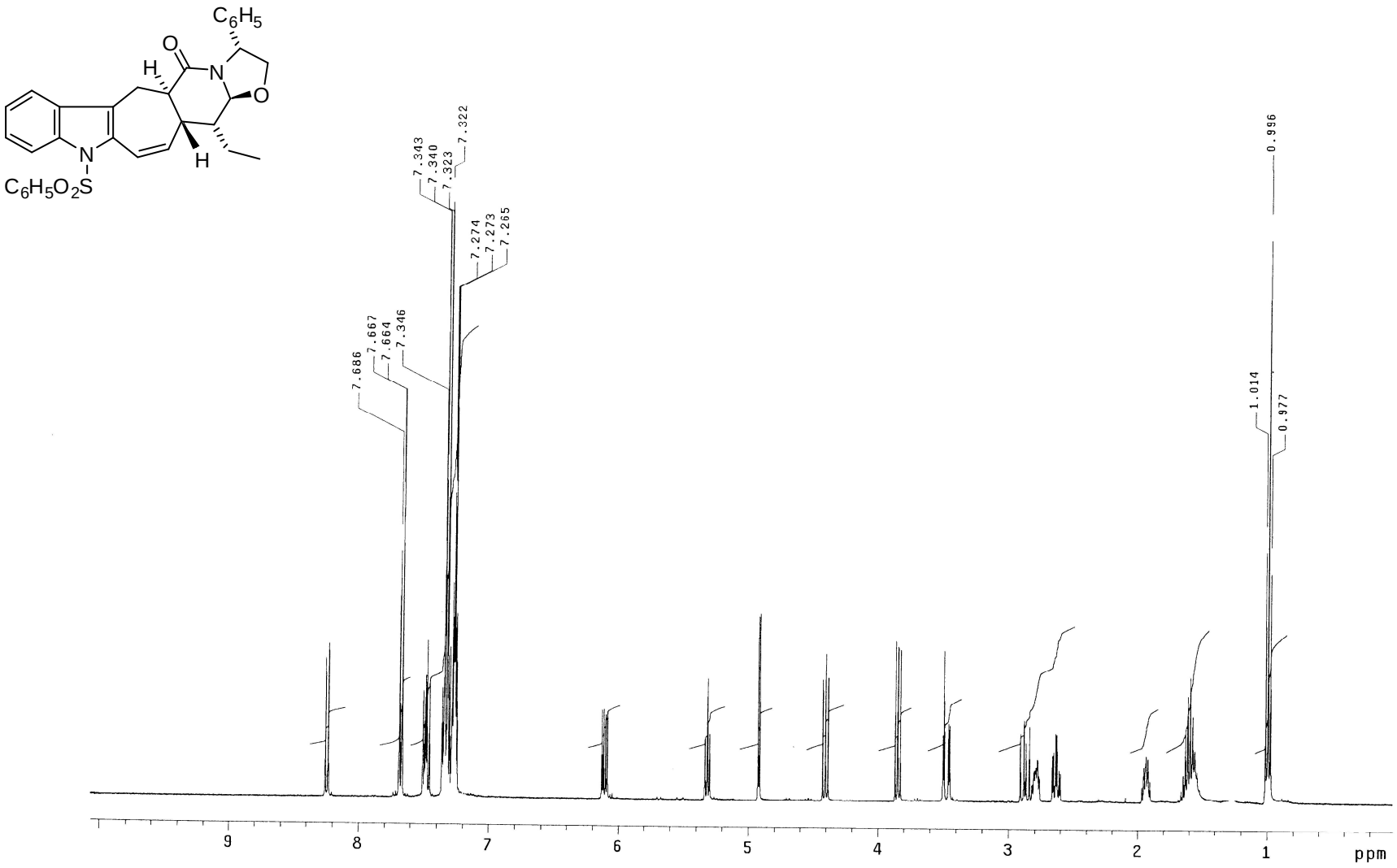
(3*R*,6*R*,7*S*,8*R*,8a*S*)-6-[(1-Benzenesulfonyl-2-vinyl-3-indolyl)methyl]-8-ethyl-5-oxo-3-phenyl-7-vinyl-2,3,6,7,8,8a-hexahydro-5*H*-oxazolo[3,2-*a*]pyridine (6)



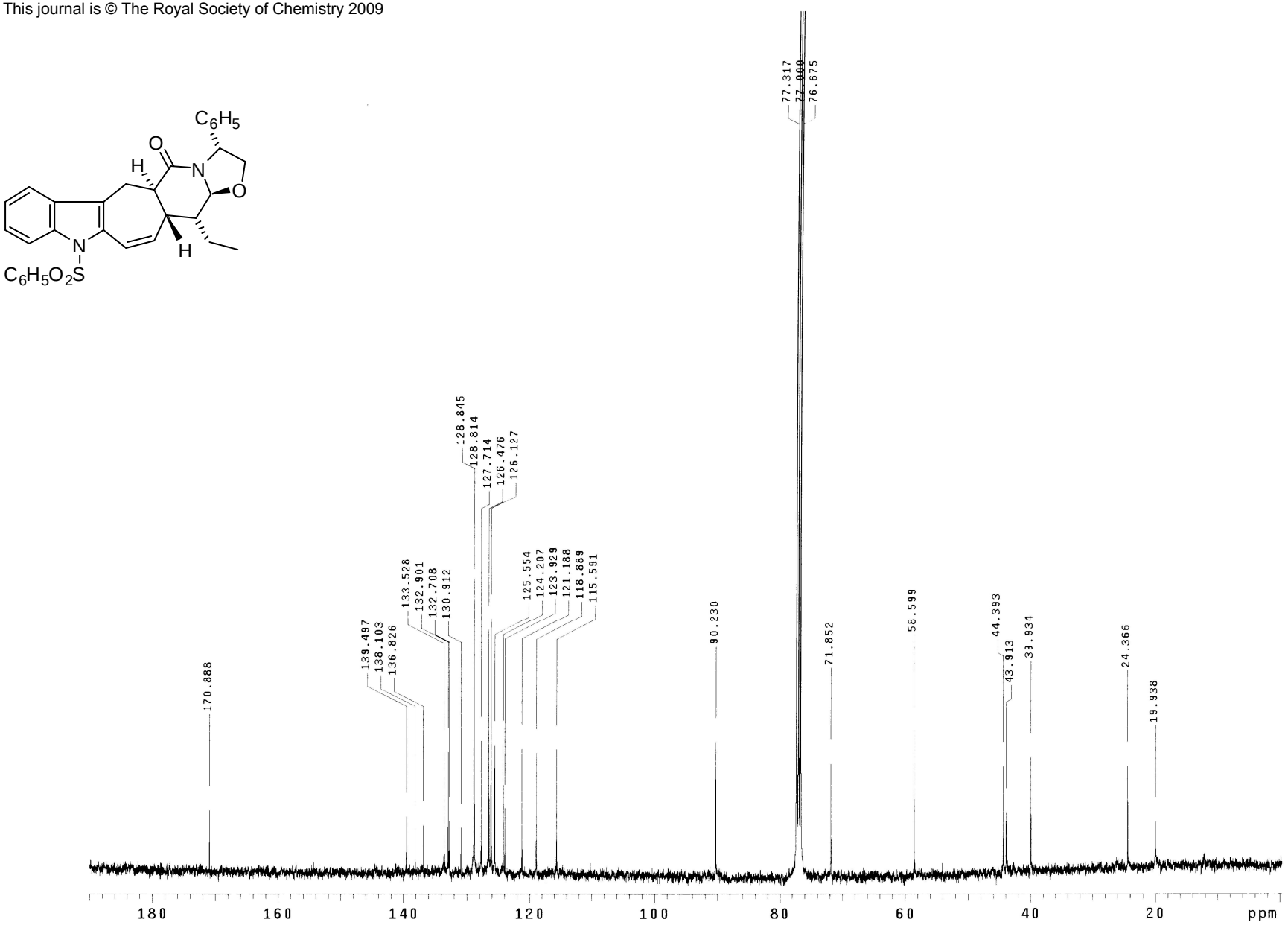
(3*R*,6*S*,7*S*,8*R*,8a*S*)-6-[(1-Benzenesulfonyl-2-vinyl-3-indolyl)methyl]-8-ethyl-5-oxo-3-phenyl-7-vinyl-2,3,6,7,8,8a-hexahydro-5*H*-oxazolo[3,2-*a*]pyridine (6-*epi*-**6)**



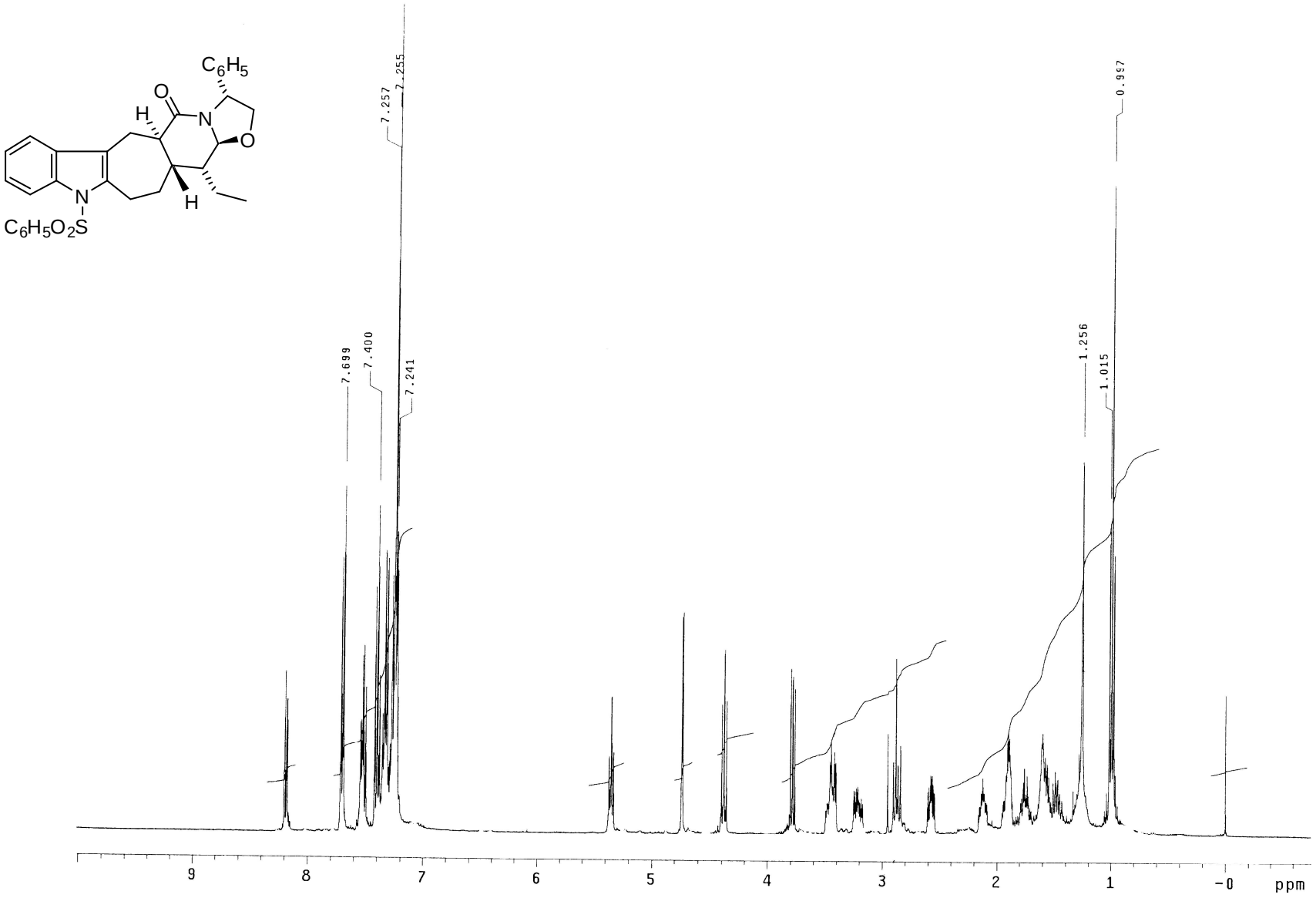
(3*R*,6*S*,7*S*,8*R*,8a*S*)-6-[(1-Benzenesulfonyl)-2-vinyl-3-indolyl)methyl]-8-ethyl-5-oxo-3-phenyl-7-vinyl-2,3,6,7,8,8a-hexahydro-5*H*-oxazolo[3,2-*a*]pyridine (6-*epi*-**6)**



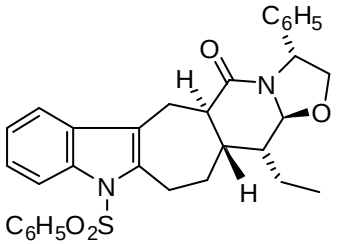
(1*R*,3a*S*,4*R*,4a*S*,12a*R*)-7-(Benzenesulfonyl)-4-ethyl-13-oxo-1-phenyl-1,2,3a,4,4a,12,12a,13-octahydrooxazolo[2",3":6',1']pyrido[3',4':4,5]cyclohepta[1,2-*b*]indole (7)

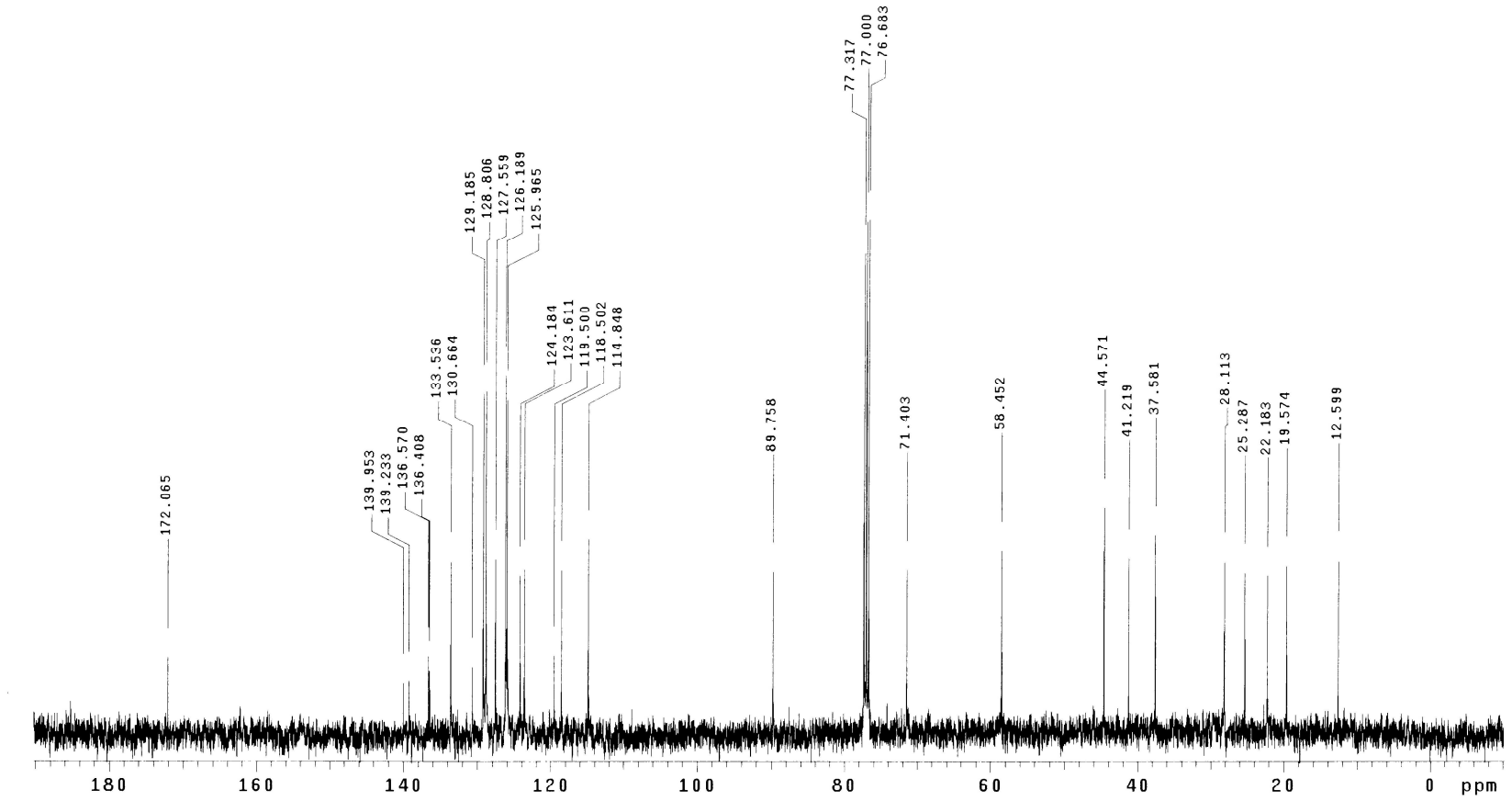


(1*R*,3a*S*,4*R*,4a*S*,12a*R*)-7-(Benzenesulfonyl)-4-ethyl-13-oxo-1-phenyl-1,2,3a,4,4a,12,12a,13-octahydrooxazolo[2",3":6',1']pyrido[3',4':4,5]cyclohepta[1,2-*b*]indole (7)

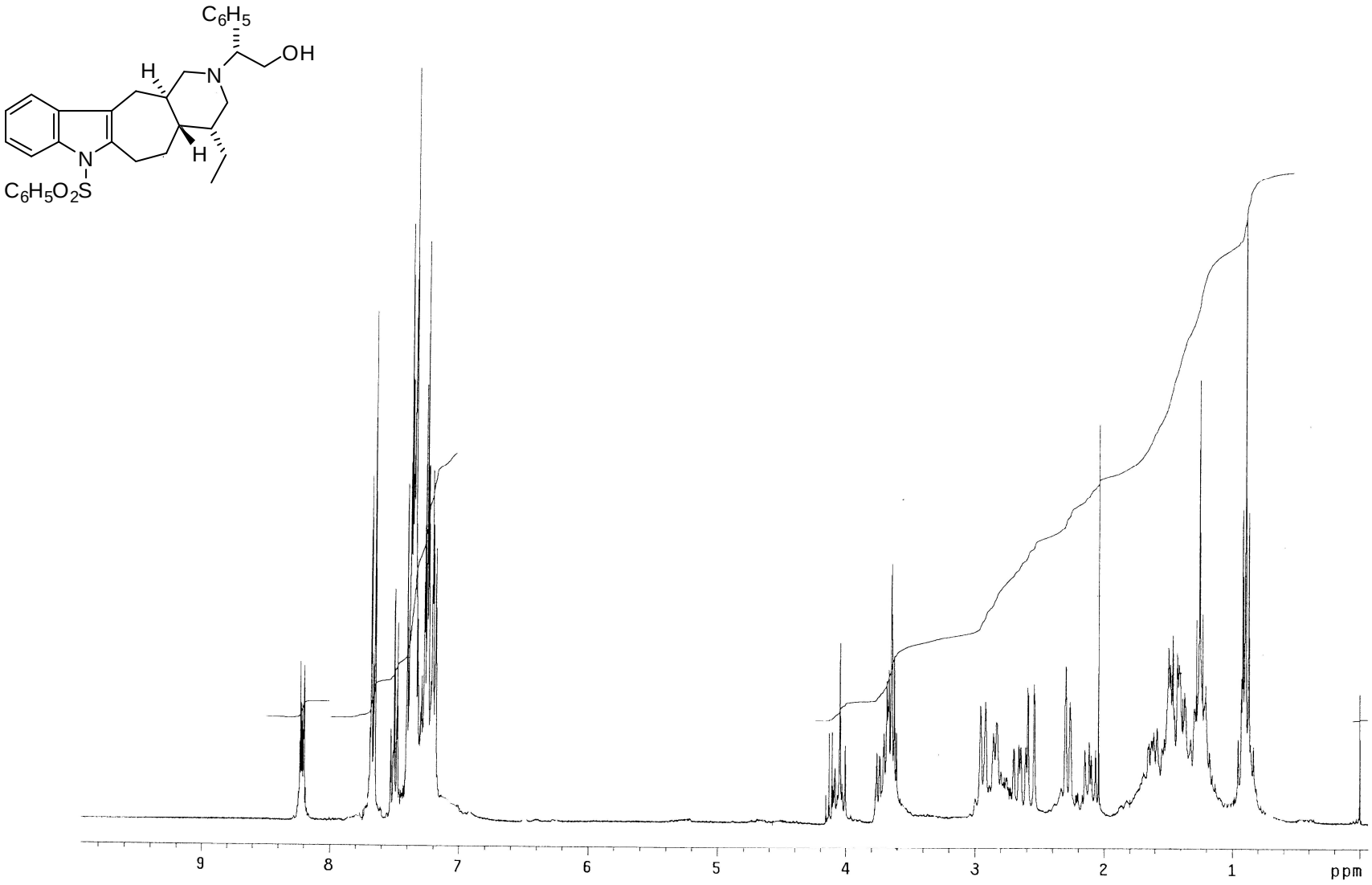


(1*R*,3a*S*,4*R*,4a*S*,12a*R*)-7-(Benzenesulfonyl)-4-ethyl-13-oxo-1-phenyl-1,2,3a,4,4a,5,6,12,12a,13-decahydrooxazolo[2",3":6',1']pyrido[3',4':4,5]cyclohepta[1,2-*b*]indole

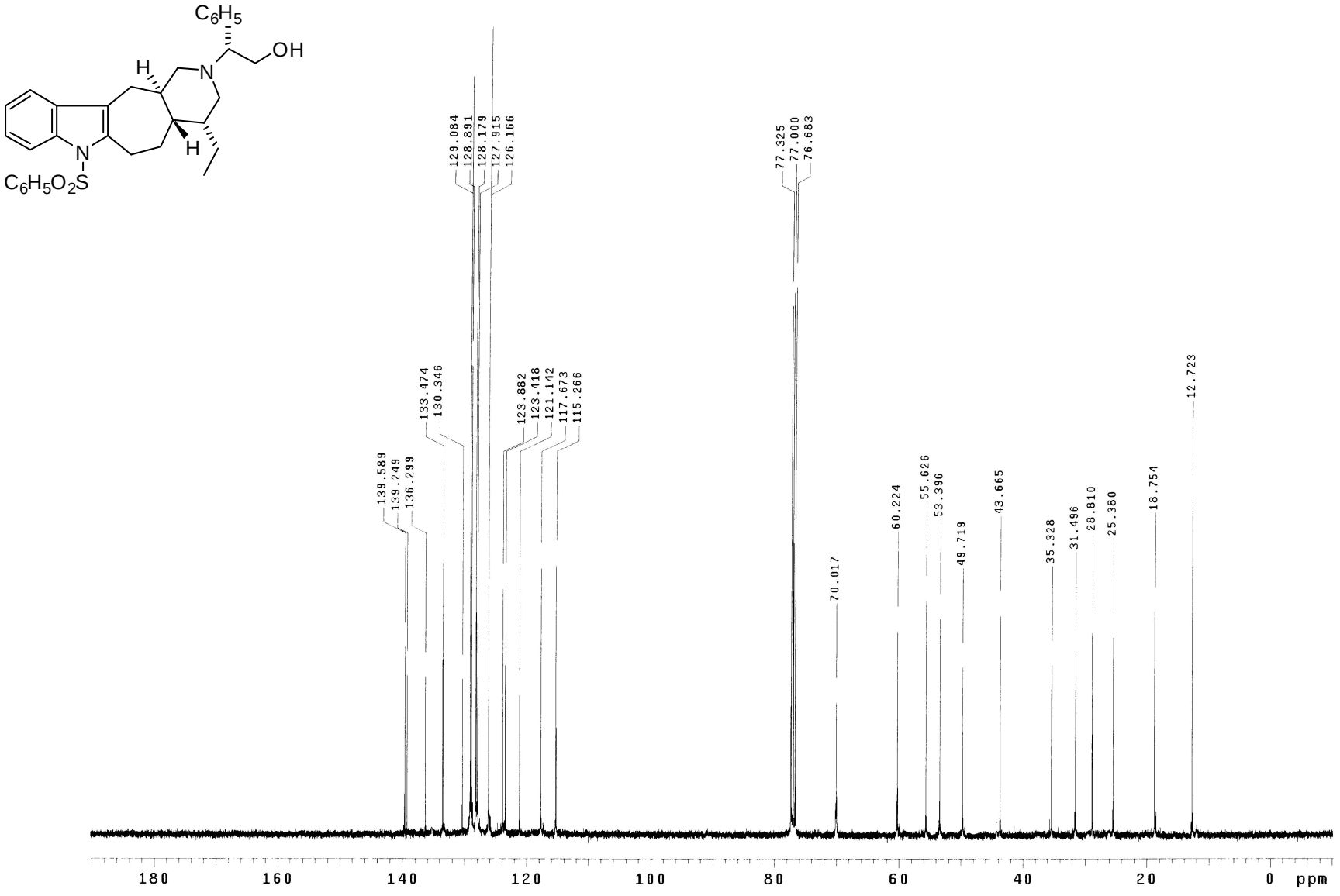




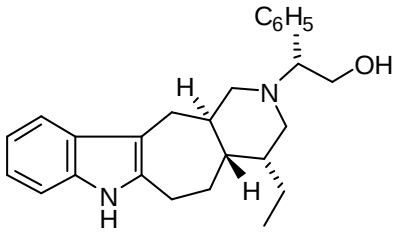
(1*R*,3a*S*,4*R*,4a*S*,12a*R*)-7-(Benzenesulfonyl)-4-ethyl-13-oxo-1-phenyl-1,2,3a,4,4a,5,6,12,12a,13-decahydrooxazolo[2”,3”:6’,1’]pyrido[3’,4’:4,5]cyclohepta[1,2-*b*]indole

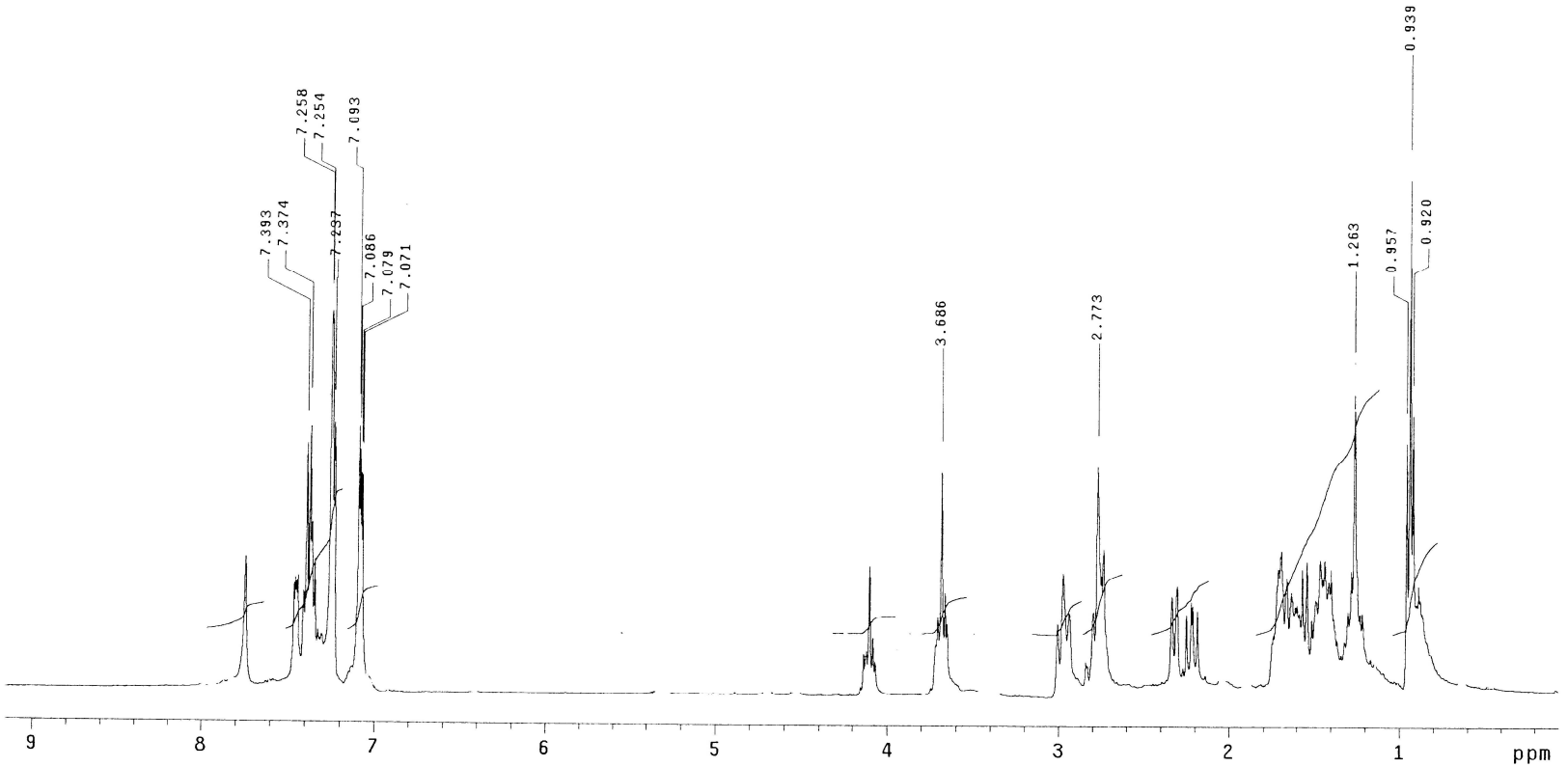


(4*R*,4a*S*,12a*R*)-7-(Benzenesulfonyl)-4-ethyl-2-[(1*R*)-2-hydroxy-1-phenylethyl]-1,3,4,4a,5,6,12,12a-octahydropyrido[3',4':4,5]cyclohepta[1,2-*b*]indole (8)

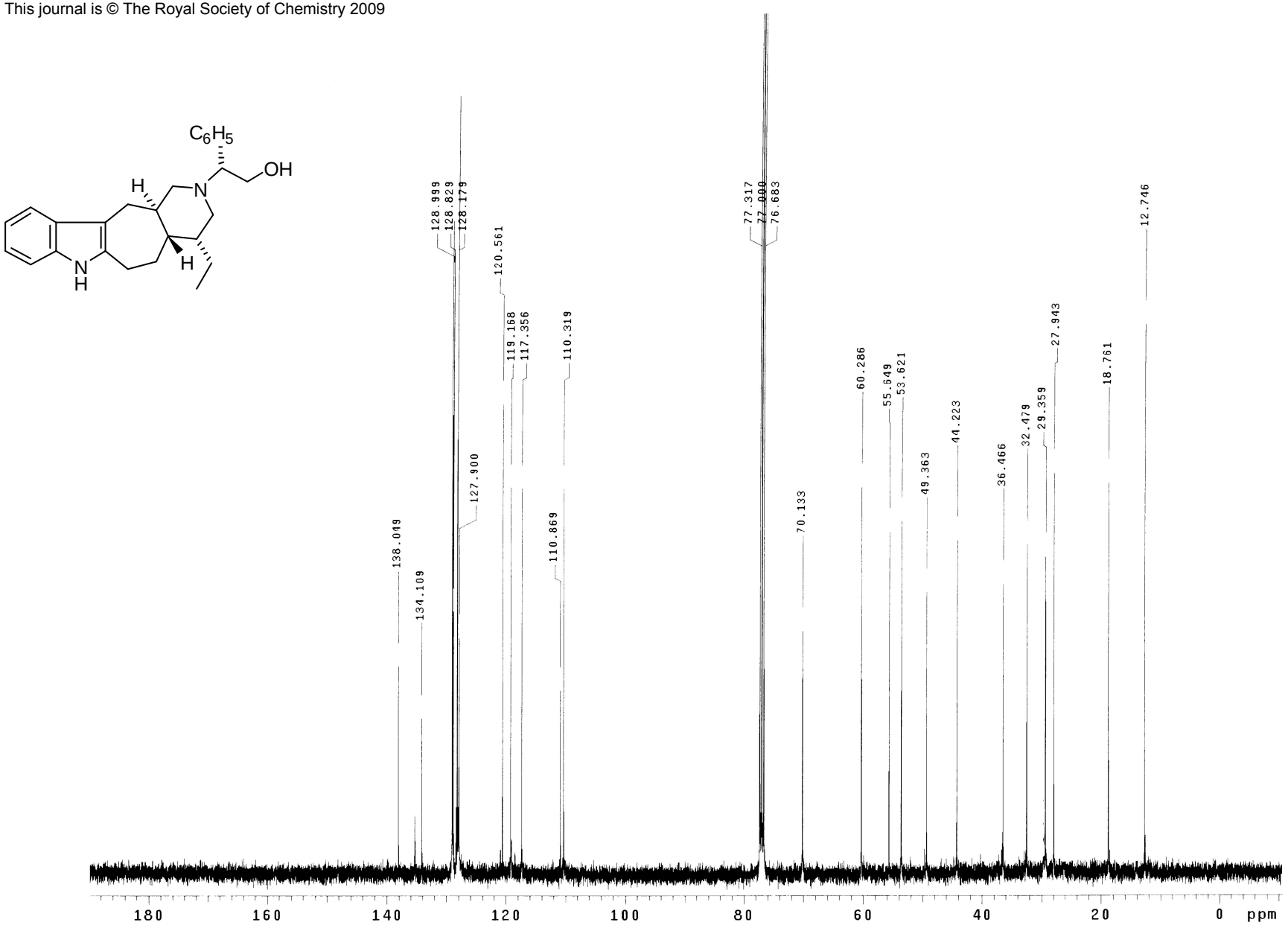


(4*R*,4a*S*,12a*R*)-7-(Benzenesulfonyl)-4-ethyl-2-[(1*R*)-2-hydroxy-1-phenylethyl]-1,3,4,4a,5,6,12,12a-octahydropyrido[3',4':4,5]cyclohepta[1,2-*b*]indole (8)

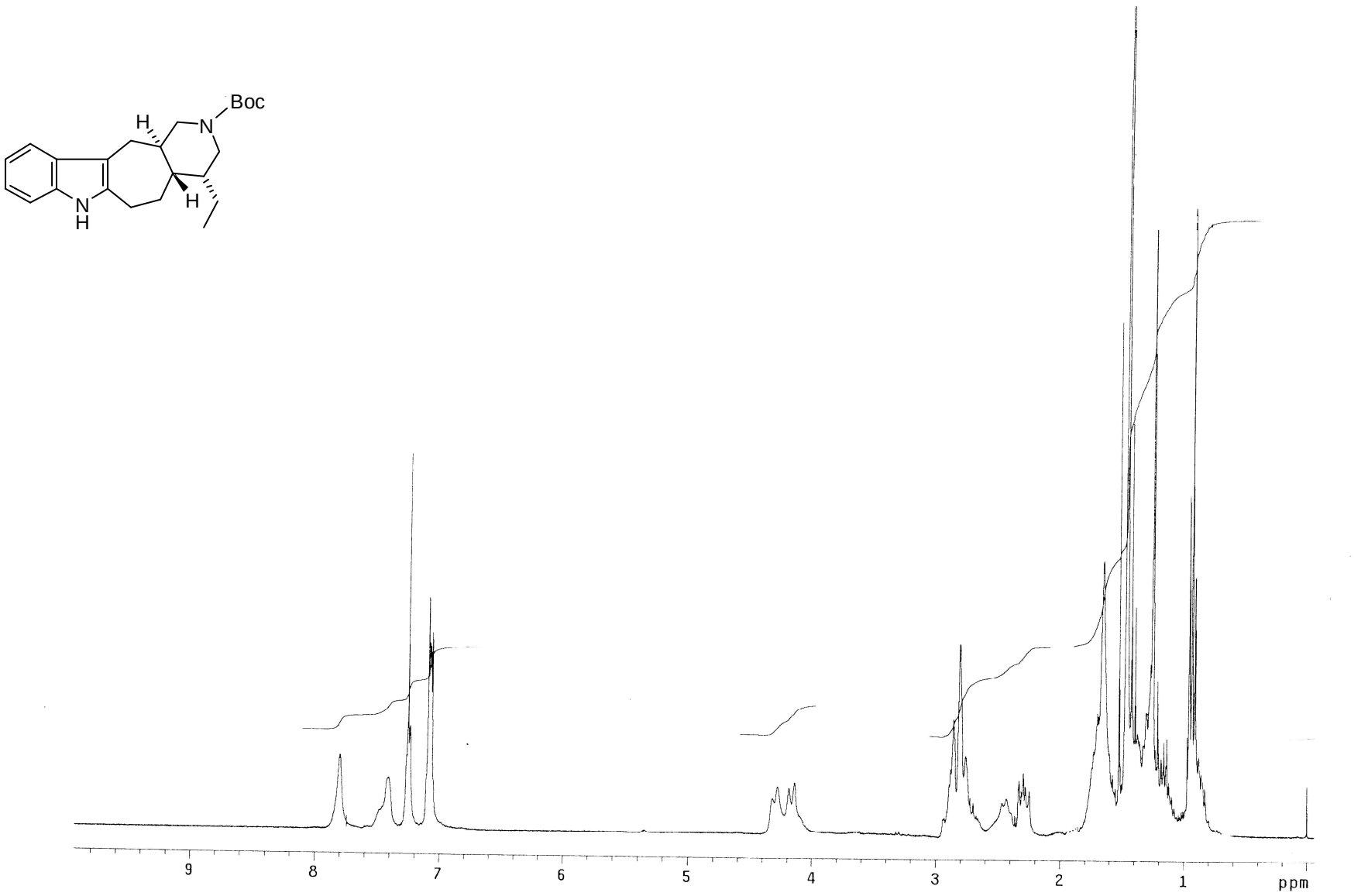




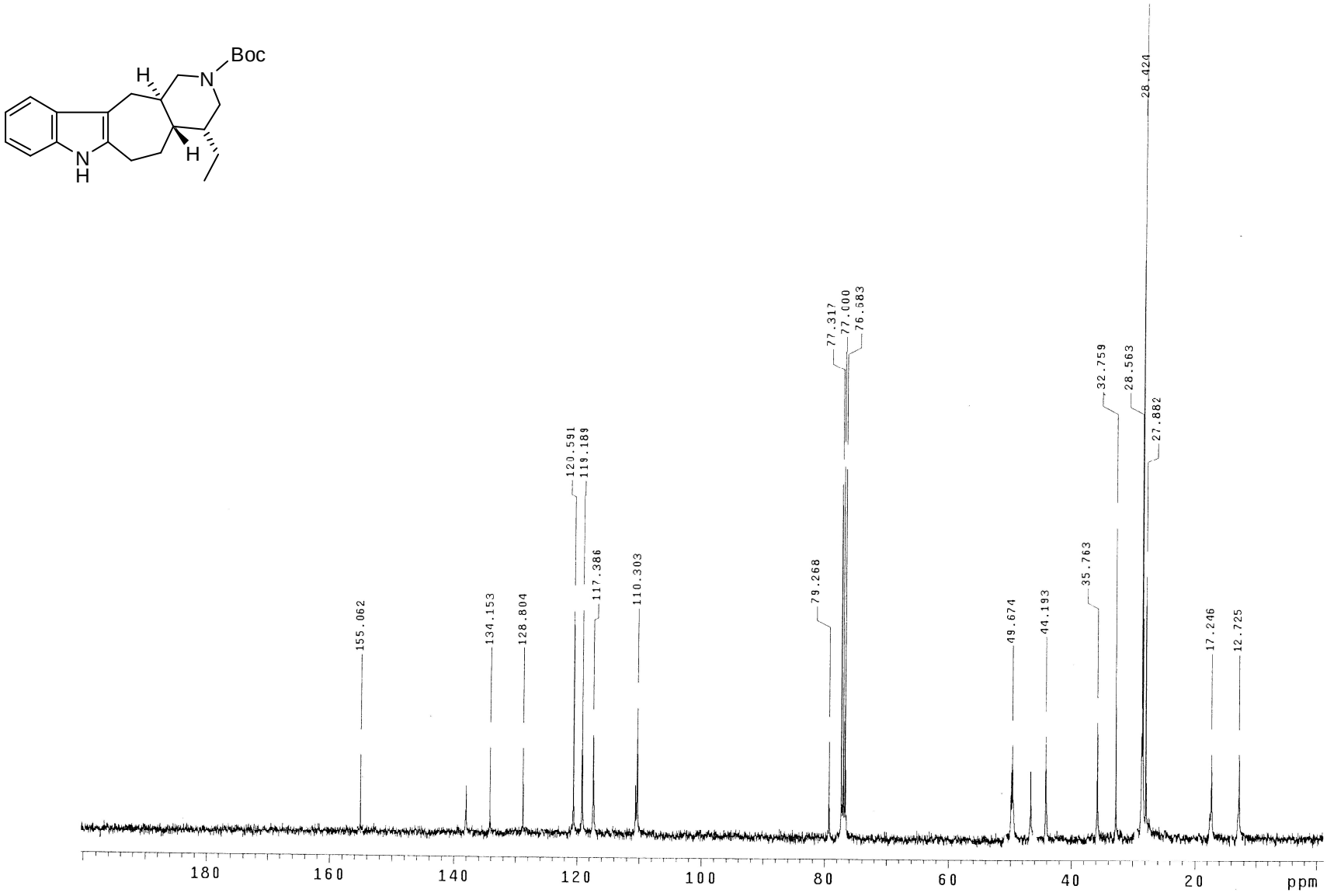
(4*R*,4a*S*,12a*R*)-4-Ethyl-2-[(1*R*)-2-hydroxy-1-phenylethyl]-1,3,4,4a,5,6,12,12a-octahydropyrido[3',4':4,5]cyclohepta[1,2-*b*]indole



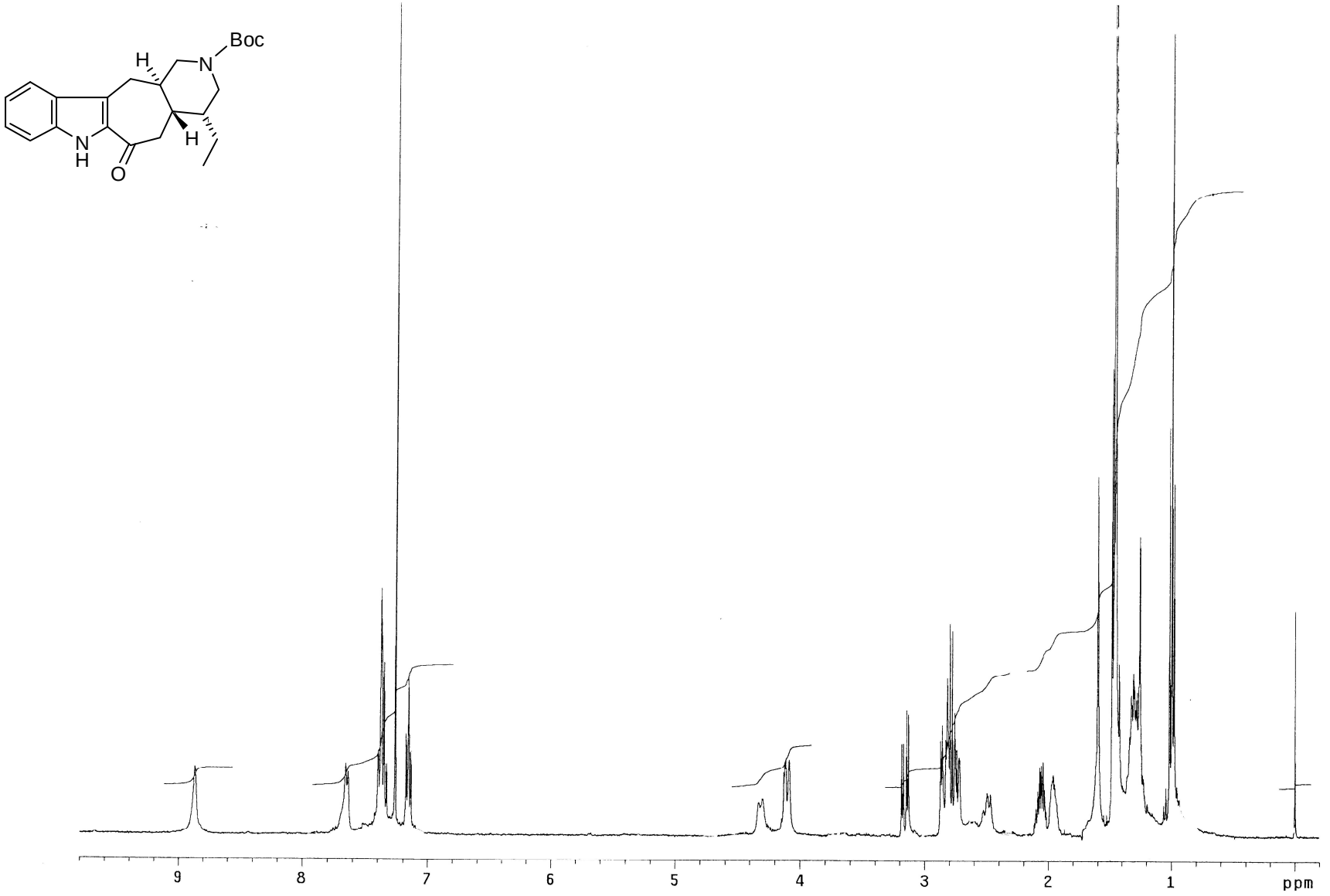
(4*R*,4a*S*,12a*R*)-4-Ethyl-2-[(1*R*)-2-hydroxy-1-phenylethyl]-1,3,4,4a,5,6,12,12a-octahydropyrido[3',4':4,5]cyclohepta[1,2-*b*]indole



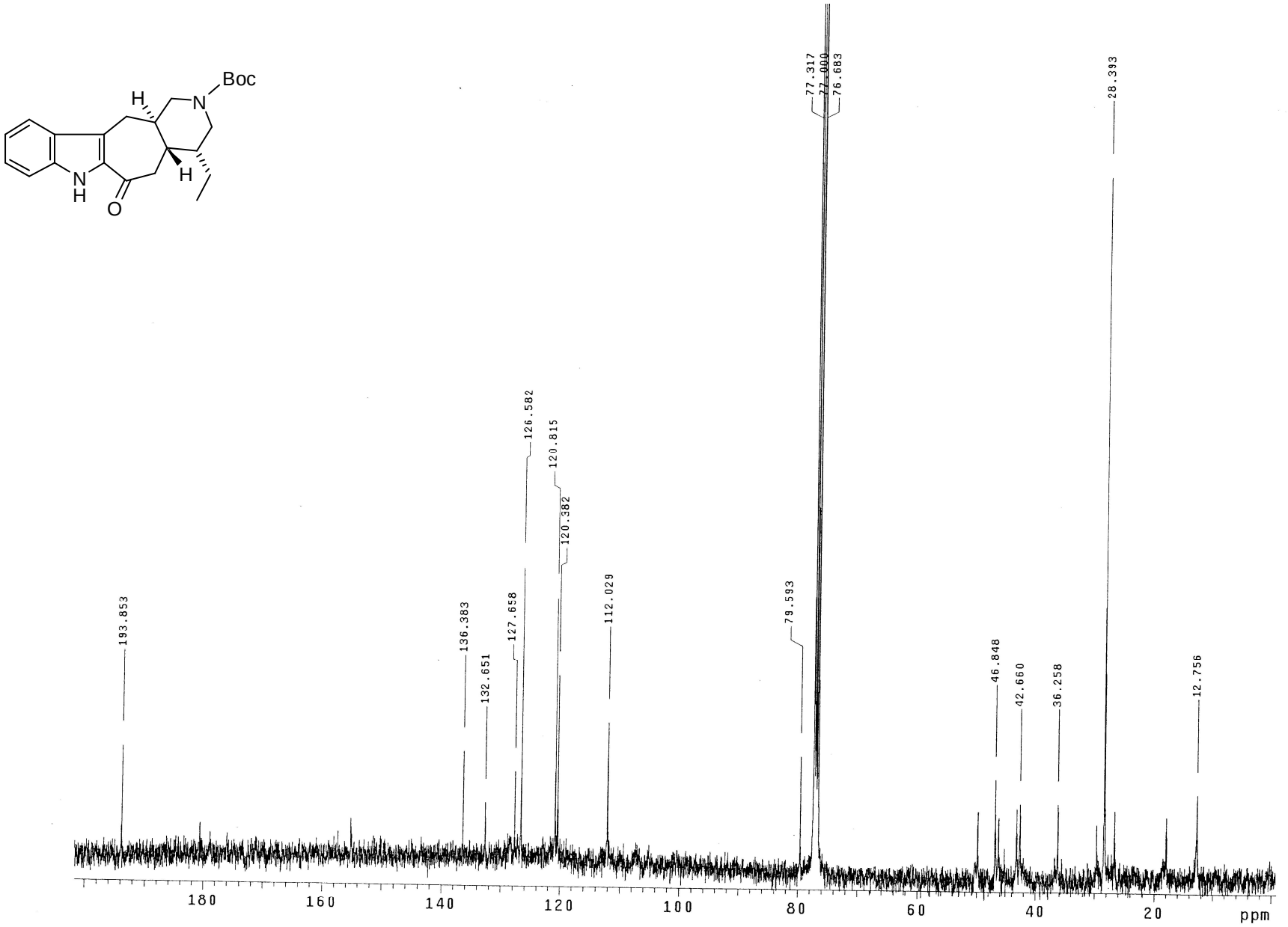
(4*R*,4a*S*,12a*R*)-2-(*tert*-Butoxycarbonyl)-4-ethyl-1,3,4,4a,5,6,12,12a-octahydropyrido[3',4':4,5]cyclohepta[1,2-*b*]indole (9)



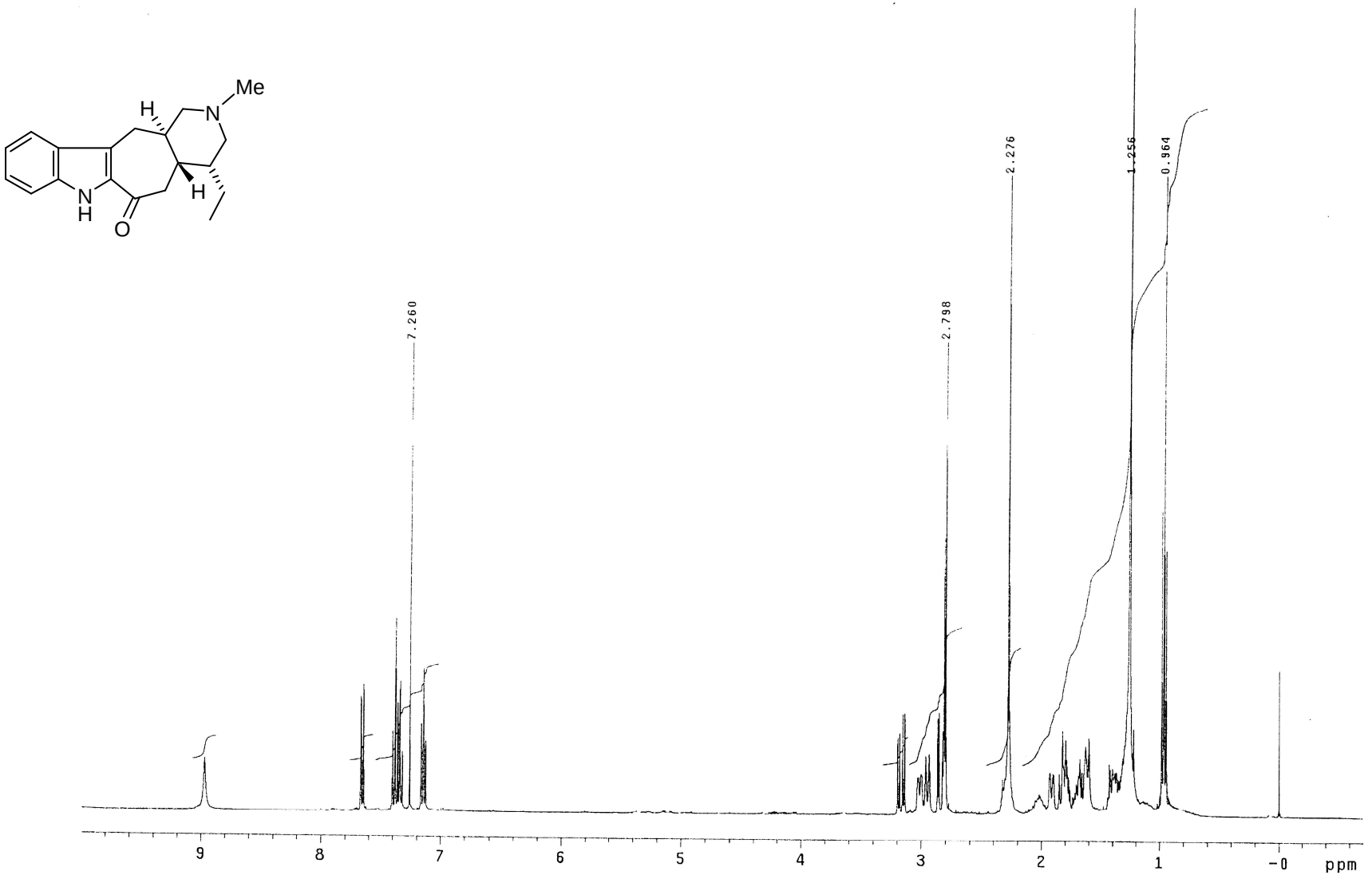
(4*R*,4a*S*,12a*R*)-2-(*tert*-Butoxycarbonyl)-4-ethyl-1,3,4,4a,5,6,12,12a-octahydropyrido[3',4':4,5]cyclohepta[1,2-*b*]indole (9)



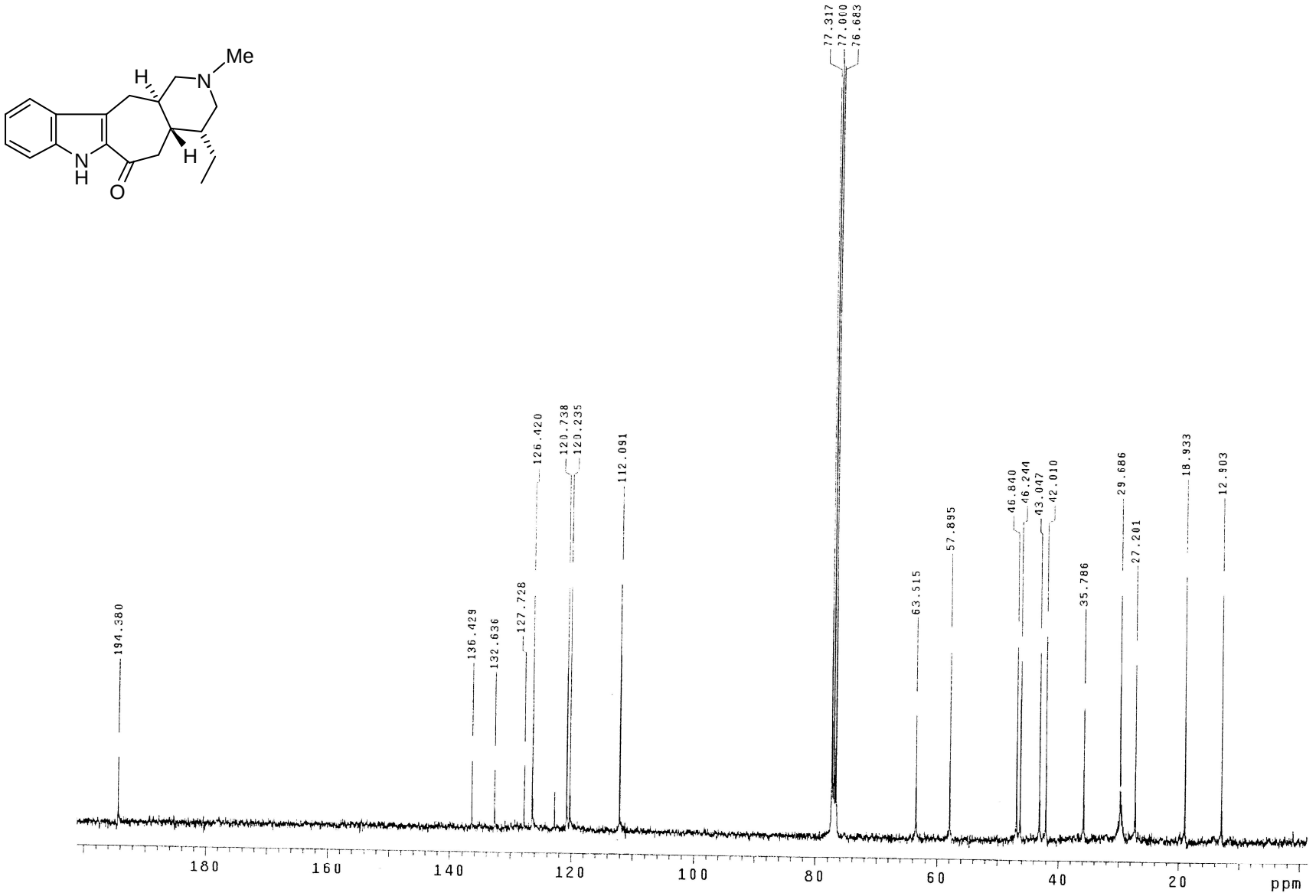
(4*R*,4a*S*,12a*R*)-2-(*tert*-Butoxycarbonyl)-4-ethyl-6-oxo-1,3,4,4a,5,6,12,12a-octahydropyrido[3',4':4,5]cyclohepta[1,2-*b*]indole (10)



(4*R*,4a*S*,12a*R*)-2-(*tert*-Butoxycarbonyl)-4-ethyl-6-oxo-1,3,4,4a,5,6,12,12a-octahydropyrido[3',4':4,5]cyclohepta[1,2-*b*]indole (10)



(-)-16-Episilicine



(-)-16-Episilicine

Table 1. Crystal data and structure refinement for **7**

Identification code	jb68d	
Empirical formula	C32 H30 N2 O4 S	
Formula weight	538.64	
Temperature	565(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P 21 21 21	
Unit cell dimensions	a = 9.004(5) Å	α= 90°.
	b = 14.264(3) Å	β= 90°.
	c = 20.840(6) Å	γ = 90°.
Volume	2676.5(18) $Å^3$	
Z	4	
Density (calculated)	1.337 Mg/m^3	
Absorption coefficient	0.163 mm^{-1}	
F(000)	1136	
Crystal size	0.47 x 0.23 x 0.21 mm^3	
Theta range for data collection	1.73 to 24.94°.	
Index ranges	0<=h<=10, 0<=k<=16, 0<=l<=24	
Reflections collected	2660	
Independent reflections	2660	
Completeness to theta = 24.94°	99.8 %	
Max. and min. transmission	0.9667 and 0.9275	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	2660 / 0 / 353	
Goodness-of-fit on F^2	1.016	
Final R indices [I>2sigma(I)]	R1 = 0.0477, wR2 = 0.0833	
R indices (all data)	R1 = 0.0948, wR2 = 0.0970	
Absolute structure parameter	-0.18(15)	
Largest diff. peak and hole	0.170 and -0.223 $e.Å^{-3}$	

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (Å^{2}x 10^3) for **7**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
S(1)	2863(1)	947(1)	8883(1)	52(1)
O(1)	5025(4)	6802(2)	8552(2)	61(1)
O(2)	3005(4)	-44(2)	8858(2)	70(1)
O(3)	1497(3)	1381(2)	8708(2)	65(1)
O(5)	8295(4)	4911(2)	7879(2)	69(1)
N(4)	6938(4)	5781(2)	8567(2)	43(1)
N(69)	4163(4)	1384(2)	8396(2)	43(1)
C(2)	6317(5)	7367(3)	8470(3)	57(2)
C(3)	7612(5)	6664(3)	8346(2)	49(1)
C(5)	7210(6)	4972(3)	8230(2)	44(1)
C(6)	6110(4)	4179(3)	8310(2)	39(1)
C(7)	4539(4)	4609(3)	8324(2)	41(1)
C(8)	4418(5)	5235(3)	8925(2)	45(1)
C(8A)	5562(5)	6007(3)	8899(2)	47(1)
C(31)	8997(5)	6952(4)	8686(3)	56(2)
C(32)	9363(7)	6607(4)	9284(3)	84(2)
C(33)	10616(8)	6922(6)	9609(4)	115(3)
C(34)	11502(9)	7574(7)	9315(6)	138(5)
C(35)	11164(9)	7930(6)	8739(5)	124(4)
C(36)	9907(6)	7617(4)	8415(3)	82(2)
C(61)	6324(5)	3429(3)	7804(2)	45(1)
C(62)	5720(5)	2503(3)	8021(2)	41(1)
C(63)	6514(5)	1626(3)	8047(2)	40(1)
C(64)	7977(6)	1371(3)	7878(2)	53(1)
C(65)	8433(6)	477(4)	7983(2)	59(2)
C(66)	7491(6)	-180(3)	8257(2)	57(1)
C(67)	6047(6)	47(3)	8416(2)	51(1)
C(68)	5569(5)	948(3)	8302(2)	44(1)
C(71)	3237(5)	3965(3)	8282(2)	47(1)
C(72)	3131(5)	3027(3)	8266(2)	47(1)
C(73)	4324(5)	2353(3)	8238(2)	43(1)

C(74)	3383(5)	1329(3)	9643(2)	51(1)
C(75)	4326(6)	788(4)	10010(3)	72(2)
C(76)	4687(7)	1081(6)	10617(3)	87(2)
C(77)	4149(7)	1904(6)	10851(3)	82(2)
C(78)	3217(8)	2441(4)	10489(3)	79(2)
C(79)	2808(6)	2154(4)	9878(3)	65(2)
C(81)	4543(6)	4685(3)	9558(2)	63(2)
C(82)	3881(7)	5184(4)	10130(3)	91(2)

Table 3. Bond lengths [Å] and angles [°] for **7**

S(1)-O(2)	1.420(3)
S(1)-O(3)	1.425(3)
S(1)-N(69)	1.669(4)
S(1)-C(74)	1.741(5)
O(1)-C(2)	1.425(5)
O(1)-C(8A)	1.430(5)
O(5)-C(5)	1.223(5)
N(4)-C(5)	1.372(6)
N(4)-C(8A)	1.456(5)
N(4)-C(3)	1.472(5)
N(69)-C(68)	1.424(5)
N(69)-C(73)	1.428(5)
C(2)-C(3)	1.559(6)
C(3)-C(31)	1.492(6)
C(5)-C(6)	1.513(6)
C(6)-C(61)	1.514(6)
C(6)-C(7)	1.543(6)
C(7)-C(71)	1.492(6)
C(7)-C(8)	1.543(6)
C(8)-C(8A)	1.509(6)
C(8)-C(81)	1.538(6)
C(31)-C(36)	1.375(7)
C(31)-C(32)	1.380(7)
C(32)-C(33)	1.391(8)
C(33)-C(34)	1.370(11)
C(34)-C(35)	1.339(12)
C(35)-C(36)	1.392(9)
C(61)-C(62)	1.499(5)
C(62)-C(73)	1.353(6)
C(62)-C(63)	1.441(6)
C(63)-C(68)	1.393(6)
C(63)-C(64)	1.412(6)
C(64)-C(65)	1.359(6)
C(65)-C(66)	1.386(6)

C(66)-C(67)	1.380(6)
C(67)-C(68)	1.376(6)
C(71)-C(72)	1.342(6)
C(72)-C(73)	1.442(6)
C(74)-C(79)	1.376(6)
C(74)-C(75)	1.378(7)
C(75)-C(76)	1.372(8)
C(76)-C(77)	1.360(8)
C(77)-C(78)	1.363(8)
C(78)-C(79)	1.387(7)
C(81)-C(82)	1.511(6)

O(2)-S(1)-O(3)	120.1(2)
O(2)-S(1)-N(69)	106.6(2)
O(3)-S(1)-N(69)	106.8(2)
O(2)-S(1)-C(74)	108.7(2)
O(3)-S(1)-C(74)	109.2(3)
N(69)-S(1)-C(74)	104.3(2)
C(2)-O(1)-C(8A)	103.5(3)
C(5)-N(4)-C(8A)	125.5(4)
C(5)-N(4)-C(3)	119.1(4)
C(8A)-N(4)-C(3)	108.1(3)
C(68)-N(69)-C(73)	107.5(4)
C(68)-N(69)-S(1)	123.0(3)
C(73)-N(69)-S(1)	124.9(3)
O(1)-C(2)-C(3)	105.5(4)
N(4)-C(3)-C(31)	115.6(4)
N(4)-C(3)-C(2)	100.9(3)
C(31)-C(3)-C(2)	111.7(4)
O(5)-C(5)-N(4)	120.5(4)
O(5)-C(5)-C(6)	122.3(4)
N(4)-C(5)-C(6)	117.1(4)
C(5)-C(6)-C(61)	111.6(4)
C(5)-C(6)-C(7)	107.7(4)
C(61)-C(6)-C(7)	114.2(4)
C(71)-C(7)-C(8)	110.3(4)

C(71)-C(7)-C(6)	118.3(3)
C(8)-C(7)-C(6)	108.0(4)
C(8A)-C(8)-C(81)	110.6(4)
C(8A)-C(8)-C(7)	110.2(4)
C(81)-C(8)-C(7)	113.4(4)
O(1)-C(8A)-N(4)	102.8(4)
O(1)-C(8A)-C(8)	111.5(4)
N(4)-C(8A)-C(8)	115.9(4)
C(36)-C(31)-C(32)	118.4(6)
C(36)-C(31)-C(3)	119.5(6)
C(32)-C(31)-C(3)	122.1(5)
C(31)-C(32)-C(33)	121.3(7)
C(34)-C(33)-C(32)	118.3(9)
C(35)-C(34)-C(33)	121.8(9)
C(34)-C(35)-C(36)	119.9(9)
C(31)-C(36)-C(35)	120.4(7)
C(62)-C(61)-C(6)	111.5(4)
C(73)-C(62)-C(63)	108.1(4)
C(73)-C(62)-C(61)	125.2(4)
C(63)-C(62)-C(61)	126.6(4)
C(68)-C(63)-C(64)	119.1(4)
C(68)-C(63)-C(62)	108.3(4)
C(64)-C(63)-C(62)	132.6(4)
C(65)-C(64)-C(63)	118.9(5)
C(64)-C(65)-C(66)	121.1(5)
C(67)-C(66)-C(65)	121.1(5)
C(68)-C(67)-C(66)	118.1(5)
C(67)-C(68)-C(63)	121.6(4)
C(67)-C(68)-N(69)	131.5(4)
C(63)-C(68)-N(69)	107.0(4)
C(72)-C(71)-C(7)	132.2(4)
C(71)-C(72)-C(73)	127.7(4)
C(62)-C(73)-N(69)	108.9(4)
C(62)-C(73)-C(72)	126.9(4)
N(69)-C(73)-C(72)	124.1(4)
C(79)-C(74)-C(75)	120.9(5)

C(79)-C(74)-S(1)	119.4(5)
C(75)-C(74)-S(1)	119.7(5)
C(76)-C(75)-C(74)	119.1(6)
C(77)-C(76)-C(75)	120.6(7)
C(76)-C(77)-C(78)	120.4(6)
C(77)-C(78)-C(79)	120.3(6)
C(74)-C(79)-C(78)	118.6(6)
C(82)-C(81)-C(8)	114.1(4)

Table 4. Anisotropic displacement parameters ($Å^2 x\ 10^3$)for **7**. The anisotropic displacement factor exponent takes the form: $-2\pi^2[\ h^2a^{*2}U^{11} + ... + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
S(1)	43(1)	48(1)	65(1)	2(1)	-1(1)	-18(1)
O(1)	51(2)	40(2)	91(3)	10(2)	-7(2)	-1(2)
O(2)	69(2)	40(2)	100(3)	0(2)	1(2)	-26(2)
O(3)	35(2)	74(2)	86(3)	14(2)	-6(2)	-11(2)
O(5)	56(2)	56(2)	94(3)	-10(2)	29(2)	-15(2)
N(4)	39(2)	35(2)	56(2)	-3(2)	4(2)	-3(2)
N(69)	36(2)	43(2)	49(2)	2(2)	-1(2)	-8(2)
C(2)	54(3)	43(3)	75(4)	11(3)	-6(3)	-5(3)
C(3)	52(3)	34(3)	59(3)	6(2)	-1(3)	-7(2)
C(5)	40(3)	46(3)	47(3)	3(2)	-1(3)	-6(3)
C(6)	36(3)	39(3)	41(3)	6(2)	2(2)	-2(2)
C(7)	35(3)	39(3)	50(3)	6(2)	1(2)	1(2)
C(8)	33(2)	47(3)	53(3)	-1(3)	4(3)	3(2)
C(8A)	46(3)	43(3)	52(3)	0(3)	-2(3)	0(3)
C(31)	45(3)	41(3)	81(4)	-9(3)	4(3)	-3(3)
C(32)	63(4)	69(4)	121(6)	-9(4)	-32(4)	-12(4)
C(33)	69(5)	128(7)	149(8)	-35(6)	-48(5)	-3(5)
C(34)	44(5)	162(10)	206(12)	-112(10)	-15(7)	-4(6)
C(35)	64(6)	119(7)	190(10)	-87(8)	50(6)	-41(5)
C(36)	63(4)	75(4)	108(5)	-30(4)	31(4)	-15(4)
C(61)	41(3)	41(3)	53(3)	0(2)	2(3)	-9(2)
C(62)	38(3)	43(3)	43(3)	-2(2)	2(2)	-6(2)
C(63)	39(3)	41(3)	41(3)	-12(2)	1(2)	-3(2)
C(64)	54(3)	49(3)	55(3)	-12(3)	10(3)	-6(3)
C(65)	46(3)	53(3)	78(4)	-16(3)	5(3)	6(3)
C(66)	65(4)	44(3)	62(4)	-7(3)	-11(3)	1(3)
C(67)	61(4)	39(3)	53(3)	-4(3)	-4(3)	-6(3)
C(68)	45(3)	39(3)	47(3)	-1(3)	-5(3)	-3(3)
C(71)	36(3)	52(3)	52(3)	0(3)	-2(2)	-1(3)
C(72)	29(3)	53(3)	60(3)	5(3)	6(3)	-4(2)
C(73)	44(3)	36(3)	48(3)	-1(2)	0(3)	-3(2)

C(74)	42(3)	52(3)	60(3)	5(3)	3(3)	-18(3)
C(75)	57(4)	83(4)	76(4)	11(4)	2(3)	5(4)
C(76)	60(4)	137(7)	64(5)	8(5)	-7(3)	-2(5)
C(77)	70(5)	117(6)	61(4)	-15(4)	13(4)	-42(4)
C(78)	97(5)	76(4)	65(4)	-3(4)	13(4)	-11(4)
C(79)	67(4)	68(4)	60(4)	8(3)	6(3)	-2(3)
C(81)	67(4)	55(3)	66(4)	1(3)	12(3)	-13(3)
C(82)	93(5)	111(5)	69(4)	-9(4)	21(4)	-4(4)