Experimental section

General Methods. Reagents and solvents were handled by using standard syringe techniques. Tetrahydrofuran was distilled from sodium and benzophenone; methylene chloride, toluene and benzene from calcium hydride, all under argon. The remaining solvents and chemicals were commercial and used as received. All products were purified by flash chromatography using 230-400 mesh silica gel. Analytical TLC was carried out on silica gel plates. Melting points are uncorrected. ^{1}H NMR and ^{13}C NMR were recorded at 300 and 75 MHz, respectively. When peak multiplicities are reported, the following abbreviations are used: s (singlet); d (doublet); t (triplet); m (multiplet); dd (doublet of doublets); bs (broad singlet). Chemical shifts (δ) are reported in ppm from internal $(CH_3)_4Si$. Elemental analyses were performed at the Universidad Complutense de Madrid.

5-*endo*-chloro-3-*exo*-methyl-6-*exo*-(phenylsulfenyl)-7-oxabicyclo [2.2.1]heptan-2-one, 2. To a solution of HMDS (2.73 ml, 13.20 mmol) in 13 ml of THF cooled to 0ºC, *n*-BuLi (8.25 ml, 13.20 mmol) was added and the mixture was stirred for 20 min. The reaction was cooled to -78ºC and 2.8 g (11 mmol) of **1** dissolved in 60 ml of THF were added. After stirring for 1h at -78ºC, IMe (2.07 ml, 22.8 mmol) was added and the mixture was allowed to warm to 0ºC. The reaction mixture was quenched with saturated aqueous NaCl solution, extracted with ether and dried over $MgSO_4$. Purification *via* flash chromatography eluting with hexanes/ethyl acetate (15:1) afforded 1182 mg of **2** (40%) as a white solid, together with 1260 mg of the starting material **1** (45%). mp: 95-96ºC. ^{1}H NMR ($CDCl_3$): δ 1.28 (d, 3 H, *J*= 7.4 Hz), 2.86 (q, 1 H, *J*= 7.4 Hz), 3.42 (d, 1 H, *J*= 4.0 Hz), 4.23-4.26 (m, 2 H), 4.56 (dd, 1 H, *J*= 5.1, 1.1 Hz), 7.30-7.38 (m, 3 H), 7.43-7.46 (m, 2 H). ^{13}C NMR ($CDCl_3$): δ 13.5, 41.9, 54.9, 60.9, 85.1, 85.4, 128.1, 129.5, 131.9, 137.1, 210.0. Anal. Calcd for $C_{13}H_{13}O_2ClS$: C, 58.10; H, 4.84. Found: C, 58.25; H, 4.76.

5-*endo*-chloro-2,2'-ethylendioxy-3-*exo*-methyl-6-*exo*-(phenyl sulfenyl)-7-oxabicyclo[2.2.1]heptane, 3. To a solution of TfOTMS (0.05 ml, 0.28 mmol) in 3 ml of CH_2Cl_2 cooled at 0ºC, 1.37 ml (5.59 mmol) of 1,2-bis(trimethylsilyloxy)-ethane were added. A solution of **2** (750 mg, 2.79 mmol) in CH_2Cl_2 (25 ml) was added and the reaction mixture was warmed to rt and stirred for

48h. After addition of pyridine (6 ml), the reaction mixture was quenched with saturated aqueous $NaHCO_3$ solution and the aqueous layer was extracted with CH_2Cl_2. The organic layer was dried over $MgSO_4$ and evaporated under reduced pressure. The crude was chromatographed eluting with hexanes/ethyl acetate (10:1) to give **3** (794 mg, 91%) as a colorless oil. ^1H NMR ($CDCl_3$): δ 1.01 (d, 3 H, *J*= 4.9 Hz), 2.65 (q, 1 H, *J*= 4.9 Hz), 3.71 (dd, 1 H, *J*= 7.3, 3.3 Hz), 3.75-3.84 (m, 4 H), 3.90 (d, 1 H, *J*= 7.3 Hz), 3.91 (s, 1 H), 4.06 (d, 1 H, J= 3.3 Hz), 7.16-7.30 (m, 5 H). ^{13}C NMR ($CDCl_3$): δ 134.3, 129.5, 128.6, 128.5, 113.8, 86.3, 81.4, 69.7, 65.3, 64.9, 55.6, 40.1, 12.7. Anal. Calcd for $C_{15}H_{17}O_3ClS$: C, 57.60; H, 5.44. Found: C, 57.79; H, 5.66.

6,6'-(ethylendioxy)-5-*exo*-methyl-2-(phenylsulfonyl)-7-oxabicyclo [2.2.1]hept-2-ene, 4. A solution of **3** (325 mg, 1.04 mmol) in 10 ml of MeOH was cooled to 0°C and 1513 mg (2.60 mmol) of MMPP were added. After stirring for 12h the reaction was quenched with saturated aqueous $NaHCO_3$ solution and concentrated *in vacuo*. The residue was diluted with water and extracted with AcOEt. The organic layer was dried over $MgSO_4$ and removal of the solvent under reduced pressure afforded, after purification by chromatography (hexanes/ethyl acetate, 4:1), 344 mg (96%) of the corresponding chlorosulfone intermediate. This compound was then dissolved in CH_2Cl_2 (7 ml) and cooled to 0°C. DBU (0.30 ml, 2.0 mmol) was added dropwise and stirring was maintained for 2h. The reacion mixture was quenched with a 0.5 N HCl solution, extracted with CH_2Cl_2 and dried over $MgSO_4$. After removal of the solvent *in vacuo*, purification by chromatography eluting with hexanes/ethyl acetate (2:1) gave 261 mg of **4** (85%) as a white solid. mp: 111-112 °C; ^1H NMR ($CDCl_3$): δ 1.12 (d, 3 H, *J*= 7.1 Hz), 1.88 (q, 1 H, *J*= 7.1 Hz), 3.72-4.02 (m, 4 H), 4.60 (s, 1 H), 4.64 (t, 1 H, *J*= 1.5 Hz), 7.15 (d 1 H, *J*= 1.5 Hz), 7.53-7.63 (m, 3 H), 7.93 (dd, 2 H, *J*= 8.2, 1.6 Hz). ^{13}C NMR ($CDCl_3$): δ 82.1, 85.9, 112.8, 128.2, 129.3, 133.8, 140.4, 146.5, 150.4. Anal. Calcd for $C_{15}H_{16}O_5S$: C, 58.44; H, 5.19. Found: C, 58.25; H, 5.21.

(1*S, 2*R**, 6*S**)-3,3'-(ethylendioxy)-5-(phenylsulfonyl)-2,6-dimethylcyclohex-4-en-1-ol, 5**. To a solution of **4** (285 mg, 0.92 mmol) in THF (7 ml) cooled at -78°C, 1.73 ml (2.77 mmol) of MeLi were added. After stirring for 1h at -78°C, the reaction mixture was quenched with water and extracted with AcOEt. The organic layer was dried over $MgSO_4$ and concentrated under reduced pressure.

Purification *via* flash chromatography eluting with hexanes/ethyl acetate (1:1) afforded **5** (285 mg, 95%) as a white solid. mp: 121-122 °C; ^{1}H NMR ($CDCl_3$): δ 1.09 (d, 3 H, *J*= 6.8 Hz), 1.10 (d, 3 H, *J*= 7.1 Hz), 2.15 (qd, 1 H, *J*= 6.8, 2.2 Hz), 2.50 (d, 1 H, *J*= 8.8 Hz), 2.55 (m, 1 H), 3.69 (ddd, 1 H, *J*= 8.8, 3.7, 2.2 Hz), 3.93-4.19 (m, 4 H), 7.52-7.61 (m, 3 H), 7.83 (dd, 2 H, *J*= 8.2, 1.5 Hz). ^{13}C NMR ($CDCl_3$): δ 9.9, 15.0, 37.0, 40.8, 64.2, 66.3, 74.9, 105.8, 127.4, 129.0, 133.2, 135.8, 140.2, 143.4. Anal. Calcd for $C_{16}H_{20}O_5S$: C, 59.26; H, 6.17. Found: C, 59.29; H, 6.08.

(1*S, 2*R**, 4*S**, 5*R**, 6*S**)-3,3'-(ethylendioxy)-5-(phenylsulfonyl) -2,4,6-trimethylcyclohexan-1-ol, 6**. To a solution of **5** (155 mg, 0.48 mmol) in THF (3.5 ml) cooled at -78°C, 0.90 ml (1.43 mmol) of MeLi were added. The reaction mixture was slowly warmed to 0°C and quenched with a saturated aqueous solution of NH_4Cl. Extraction with CH_2Cl_2, dryness ($MgSO_4$) and concentration under reduced pressure afforded a crude that was purified *via* flash chromatography eluting with hexanes/ethyl acetate (1:1) to give 132 mg of **6** (81%) as a white solid. mp: 105-106°C. ^{1}H NMR ($CDCl_3$): δ 0.97 (d, 3 H, *J*= 7.1 Hz), 1.01 (d, 3 H, *J*= 6.8 Hz), 1.19 (d, 3 H, *J*= 7.1 Hz), 2.16 (qd, 1 H, *J*= 6.8, 3.2 Hz), 2.24 (q, 1 H, *J*= 7.1 Hz), 2.18-2.31 (m, 1 H), 2.82 (d, 1 H, *J*= 9.3 Hz), 3.51-3.59 (m, 1 H), 3.59 (dd, 1 H, *J*= 11.7, 3.2 Hz), 3.86-4.15 (m, 4 H), 7.52-7.60 (m, 3 H), 7.87 (dd, 2 H, *J*= 8.1, 1.5 Hz). ^{13}C NMR ($CDCl_3$): δ 9.7, 10.6, 16.7, 33.5, 37.0, 37.6, 60.3, 64.2, 64.4, 65.8, 112.6, 127.6, 129.0, 133.1, 141.8. Anal. Calcd for $C_{17}H_{24}O_5S$: C, 59.99; H, 7.06. Found: C, 60.10; H, 7.15.

(2*R, 4*S**, 5*R**, 6*S**)-3,3'-(ethylendioxy)-5-(phenylsulfonyl)-2,4,6-trimethylcyclohexan-1-one, 7**. To a solution of $(COCl)_2$ (0.13 ml, 1.52 mmol) in CH_2Cl_2 (7 ml) cooled at -78°C, DMSO (0.13 ml, 1.86 mmol) was added dropwise. After 30 min. a solution of **6** (115 mg, 0.34 mmol) in CH_2Cl_2 (4 ml) was added. The reaction mixture was stirred for 1h at -78°C and 0.38 ml (2.70 mmol) of Et_3N were added. Stirring was maintained for 12h, the reaction mixture was quenched with a saturated aqueous NaCl solution and extracted with CH_2Cl_2. After removal of the solvent *in vacuo*, purification by chromatography eluting with hexanes/ethyl acetate (2:1) gave 94 mg of **7** (82%) as a white solid. mp: 96-97°C. ^{1}H NMR ($CDCl_3$): δ 1.00 (d, 3 H, *J*= 6.3 Hz), 1.01 (d, 3 H, *J*= 6.3 Hz), 1.45 (d, 3 H, *J*= 7.1 Hz), 2.50 (qd, 1 H, *J*=

7.1, 3.9 Hz), 2.96 (qd, 1 H, *J*= 6.3, 1.0 Hz), 3.03 (dq, 1 H, *J*= 12.2, 6.3 Hz), 3.55 (dd, 1 H, *J*= 12.2, 3.9 Hz), 3.91-3.99 (m, 4 H), 7.55-7.64 (m, 3 H), 7.89 (dd, 2 H, *J*= 8.2, 1.5 Hz). ^{13}C NMR ($CDCl_3$): δ 6.5, 11.0, 12.7, 38.2, 40.8, 48.5, 65.6, 65.9, 66.1, 112.1, 127.6, 129.2, 133.5, 141.5, 205.9. Anal. Calcd for $C_{17}H_{22}O_5S$: C, 60.35; H, 6.51. Found: C, 60.48; H, 6.38.

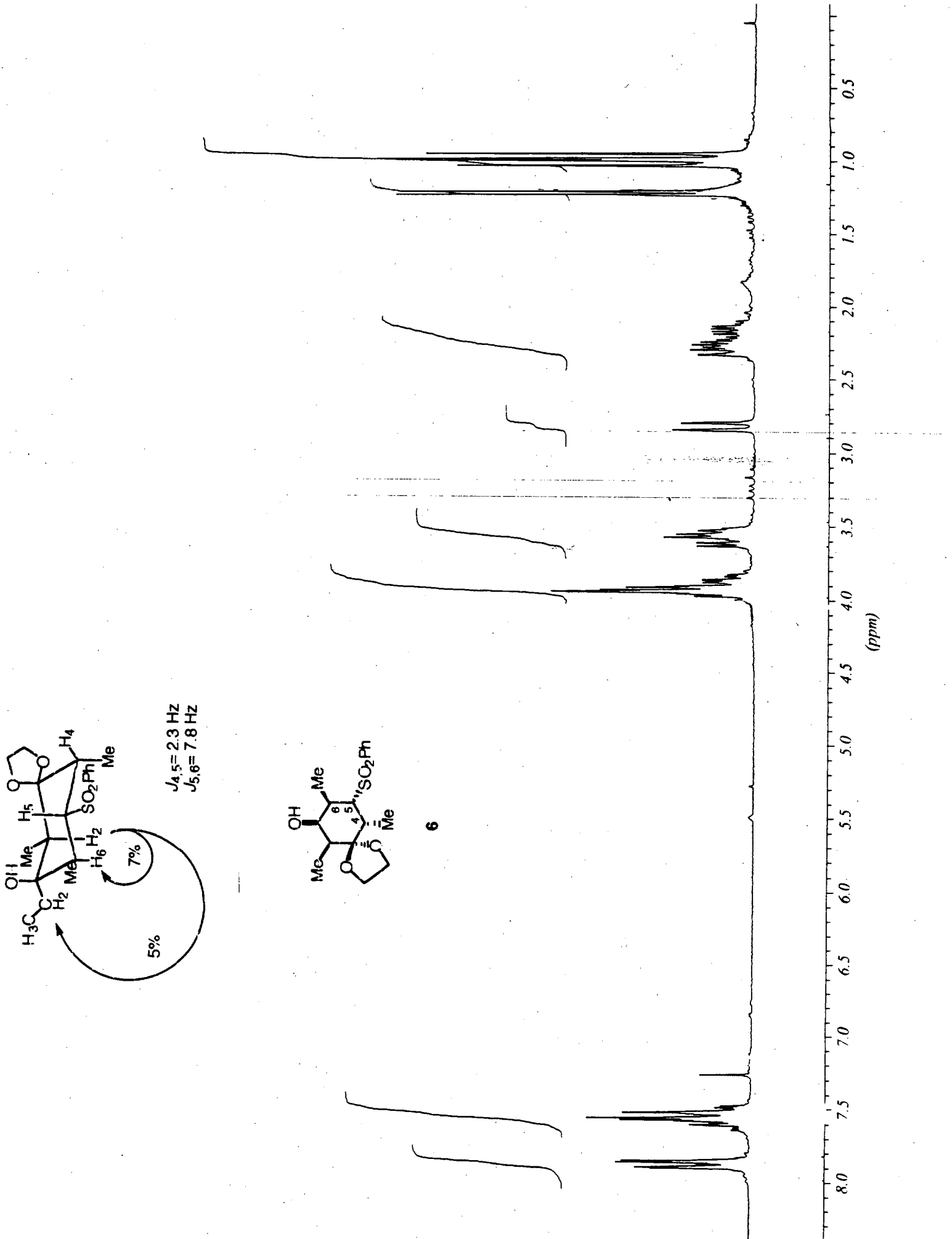
(1*S, 2*R**, 4*S**, 5*R**, 6*S**)-1-(ethyl)-3,3'-(ethylendioxy)-5-(phenylsulfonyl)-2,4,6-trimethylcyclohexan-1-ol, 8**. To a solution of **7** (93 mg, 0.27 mmol) in 3 ml of THF at rt, ethylmagnesium bromide (1.65 ml, 1.65 mmol) was added dropwise. The reaction was stirred for 4h and quenched with a saturated aqueous NH_4Cl solution. The aqueous layer was extracted with AcOEt, dried over $MgSO_4$ and concentrated under reduced pressure. The crude was purified by chromatography eluting with hexanes/ethyl acetate (1:2) to afford **8** (71 mg, 70%) as a white solid. mp: 118-119ºC. ^1H NMR ($CDCl_3$): δ 0.76 (t, 3 H, *J*= 5.2 Hz), 0.88 (d, 3 H, *J*= 4.6 Hz), 0.96 (d, 3 H, *J*= 4.6 Hz), 1.19 (d, 3 H, *J*= 4.6 Hz), 1.58 (q, 2 H, *J*= 5.2 Hz), 2.12 (q, 1 H, *J*= 4.6 Hz), 2.27-2.32 (m, 1 H), 2.30 (dq, 1 H, *J*= 7.8, 4.6 Hz), 3.23 (s, 1 H), 3.65 (dd, 1 H, *J*= 7.8, 2.3 Hz), 3.85-3.99 (m, 4 H), 7.51-7.61 (m, 3 H), 7.88 (dd, 2 H, *J*= 5.1, 1.0 Hz). ^{13}C NMR ($CDCl_3$): δ 6.0, 7.9, 10.7, 12.1, 27.3, 32.6, 36.4, 37.3, 64.3, 65.4, 65.5, 65.7, 112.8, 127.4, 129.0, 133.0, 142.2. Anal. Calcd for $C_{19}H_{28}O_5S$: C, 61.96; H, 7.61. Found: C, 62.01; H, 7.49.

(2*S, 3*, 4*R**, 6*)-5,5'-(ethylendioxy)-3-(ethyl)-3'-(hydroxy)-2,4,6-trimethylcyclohexan-1-one, 9**. A solution of diisopropylamine (0.08 ml, 0.54 mmol) in 5 ml of THF and 1 ml of DMPU was cooled to -20ºC. *n*-BuLi (0.35 ml, 0.56 mmol) was added and, after 15 min., 99 mg (0.27 mmol) of **8** dissolved in 3 ml of THF were added. The reaction was stirred for other 15 min. before O_2 was bubbled into the solution for 1h. The mixture was quenched with saturated aqueous NH_4Cl solution, extracted with ether and dried over $MgSO_4$. After removal of the solvent *in vacuo*, purification by chromatography eluting with hexanes/ethyl acetate (4:1) gave 35 mg of **9** (54%) as a colorless oil. ^1H NMR ($CDCl_3$): δ 0.70 (t, 3 H, *J*= 5.8 Hz), 0.79 (d, 3 H, *J*= 6.1 Hz), 0.81 (d, 3 H, *J*= 6.8 Hz), 0.96 (d, 3 H, *J*= 7.1 Hz), 1.50 (q, 2 H, *J*= 5.8 Hz), 1.66-1.78 (m, 2 H), 1.96 (q, 1 H, *J*= 6.8 Hz), 3.32 (s , 1 H), 3.83-3.91 (m, 4 H). ^{13}C

NMR ($CDCl_3$): δ 5.8, 8.0, 14.5, 15.0, 27.5, 29.2, 33.7, 35.9, 64.2, 65.3,76.7, 113.8, 204.9. Anal. Calcd for $C_{13}H_{22}O_4$: C, 64.46; H, 9.09. Found: C, 64.68; H, 9.03.

(1*R, 2*R**, 3*R**, 4*R**, 6*R**)-5,5'-(ethylendioxy)-1-(ethyl)-2,4,6-trimethylcyclohexan-1',3-diol, 10**. To a solution of **9** (16 mg, 0.07 mmol) in THF (1 ml) cooled at 0°C, $BH_3{\cdot}SMe_2$ (0.016 ml, 0.16 mmol) was added dropwise and the reaction was stirred for 90 min. The mixture was quenched with a 5% aqueous solution of $NaHCO_3$, extracted with AcOEt and dried over $MgSO_4$. After removal of the solvent *in vacuo*, purification by chromatography eluting with hexanes/ethyl acetate (2:1) gave 12 mg of **10** (74%) as a colorless oil. ^1H NMR ($CDCl_3$): δ 0.74 (t, 3 H, *J*= 5.2 Hz), 0.86 (d, 3 H, *J*= 4.6 Hz), 0.93 (d, 3 H, *J*= 4.2 Hz), 1.17 (d, 3 H, *J*= 4.6 Hz), 1.59-1.71 (m, 2 H), 2.07 (d, 1 H, *J*= 10.0 Hz), 2.16 (q, 1 H, *J*= 4.6 Hz), 2.30-2.42 (m, 2 H), 3.28 (s , 1 H), 3.72 (ddd, 1 H, *J*= 10.0, 7.3, 2.5 Hz), 3.96-4.09 (m, 4 H). ^{13}C NMR ($CDCl_3$): δ 7.8, 8.6, 11.4, 13.1, 33.2, 35.2, 37.1, 39.3, 64.5, 65.3, 68.1, 72.8, 112.0. Anal. Calcd for $C_{13}H_{24}O_4$: C, 63.93; H, 9.84. Found: C, 64.10; H, 9.96.

(2*R, 3*R**, 4*R**, 5*R**, 6*R**)-3-(ethyl)-3',5-(dihydroxy)-2,4,6-trimethylcyclohexan-1-one, 11**. To a solution of **10** (9 mg, 0.04 mmol) in CH_3CN (1 ml) at rt were added NaI (1 mg, 0.007 mmol) and $CeCl_3{\cdot}7H_2O$ (27.9 mg, 0.07 mmol). The reaction was warmed to 65°C and stirred for 3h. After cooling to rt, the mixture was quenched with a 0.5N HCl solution. The aqueous layer was extracted with ether and dried over $MgSO_4$. After removal of the solvent *in vacuo*, purification by chromatography eluting with hexanes/ethyl acetate (2:1) gave 6.4 mg of **11** (87%) as a colorless oil. ^1H NMR ($CDCl_3$): δ 0.90 (t, 3 H, *J*= 5.0 Hz), 0.98 (d, 3 H, *J*= 4.2 Hz), 1.20 (d, 3 H, *J*= 4.9 Hz), 1.22 (d, 3 H, *J*= 4.2 Hz), 1.46-1.58 (m, 2 H), 2.54 (m, 1 H), 2.66 (q, 1 H, *J*= 4.2 Hz), 2.98 (s, 1 H), 3.06 (q , 1 H, *J*= 4.9 Hz), 3.37 (d, 1 H, *J*= 8.1 Hz), 3.64 (dd, 1 H, *J*= 8.1, 7.0 Hz). ^{13}C NMR ($CDCl_3$): δ 8.3, 11.9, 13.8, 15.2, 30.1, 32.6, 33.4, 35.4, 71.3, 74.3, 204.2. Anal. Calcd for $C_{11}H_{20}O_3$: C, 66.00; H, 10.00. Found: C, 65.89; H, 9.91.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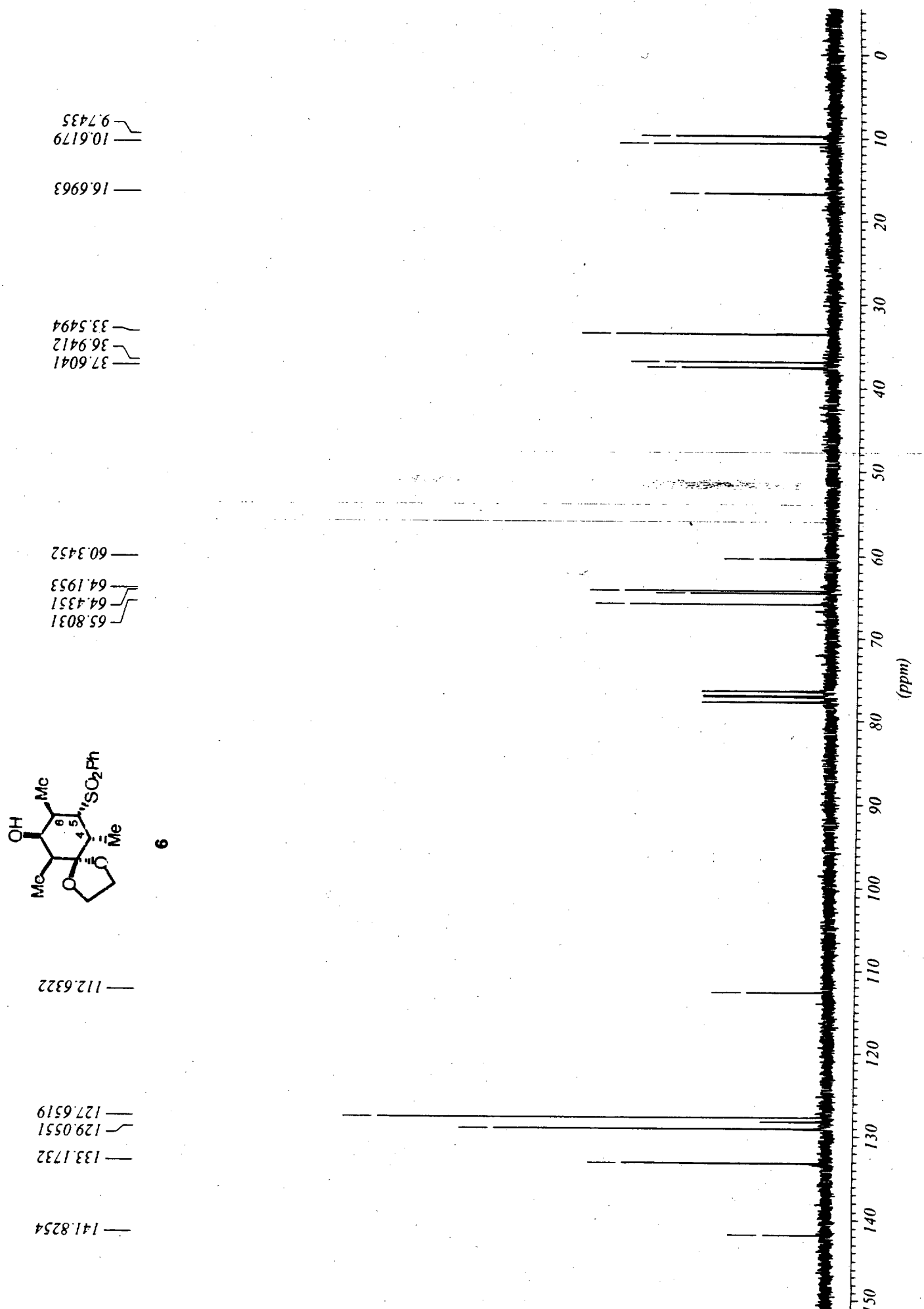
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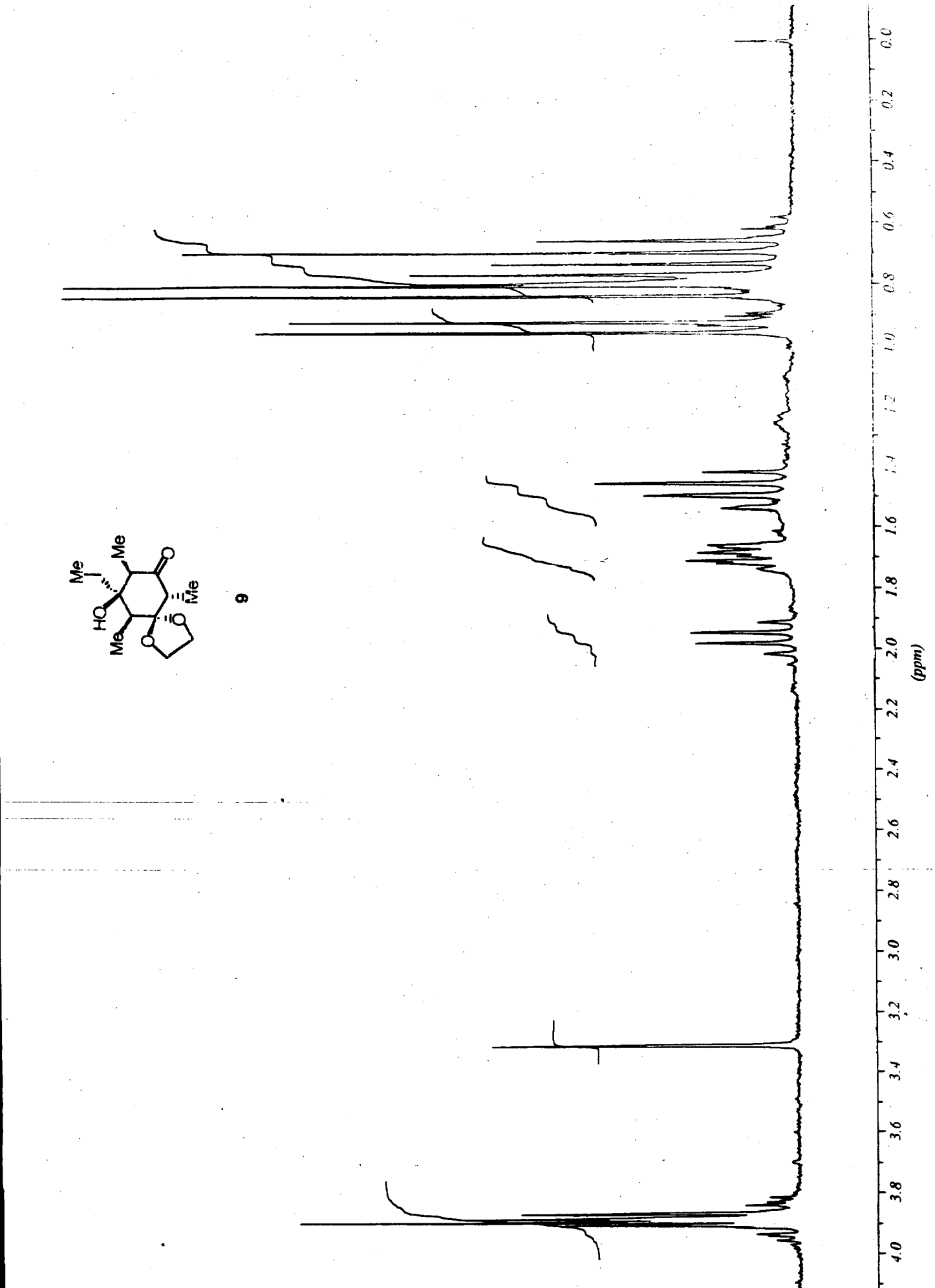
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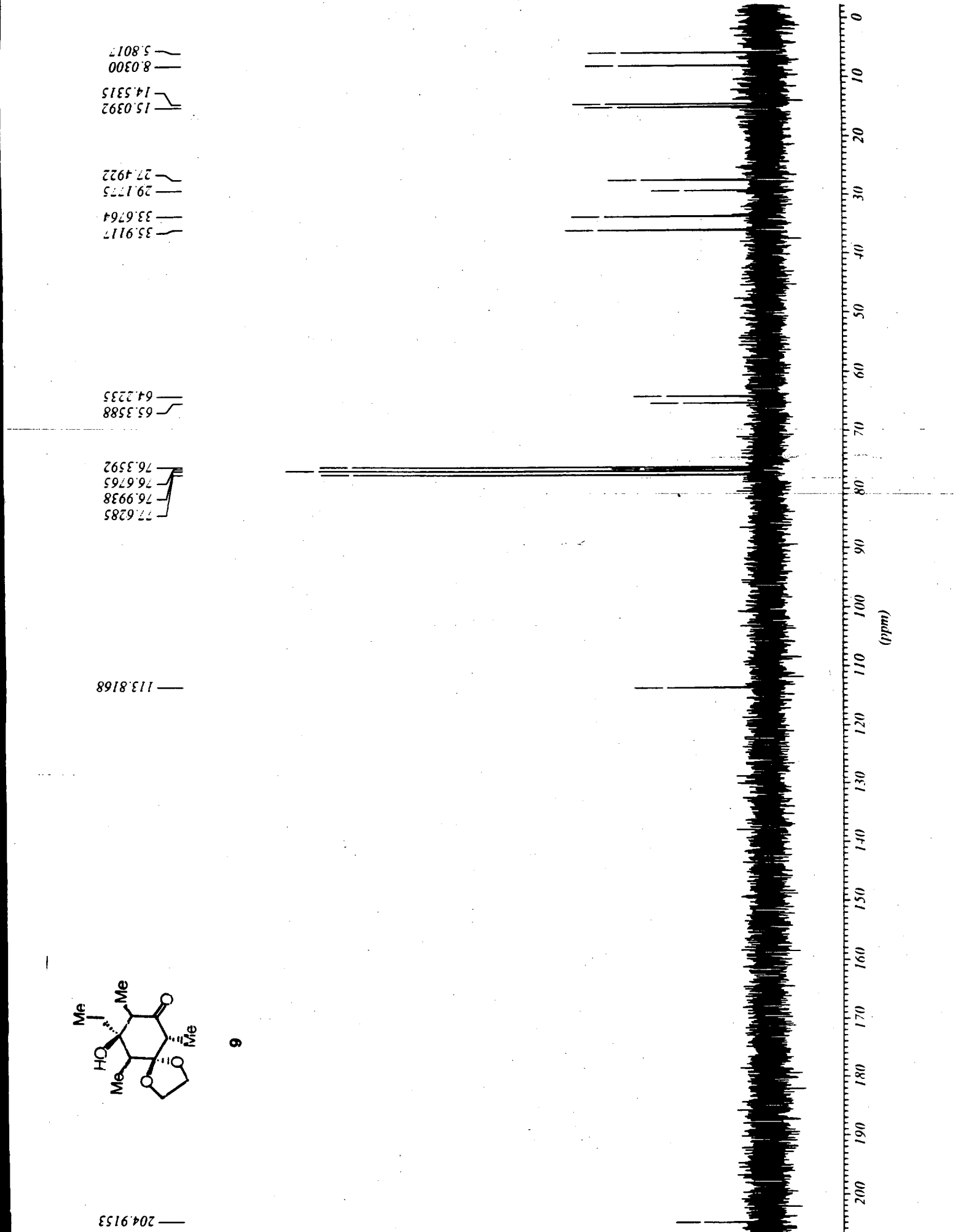
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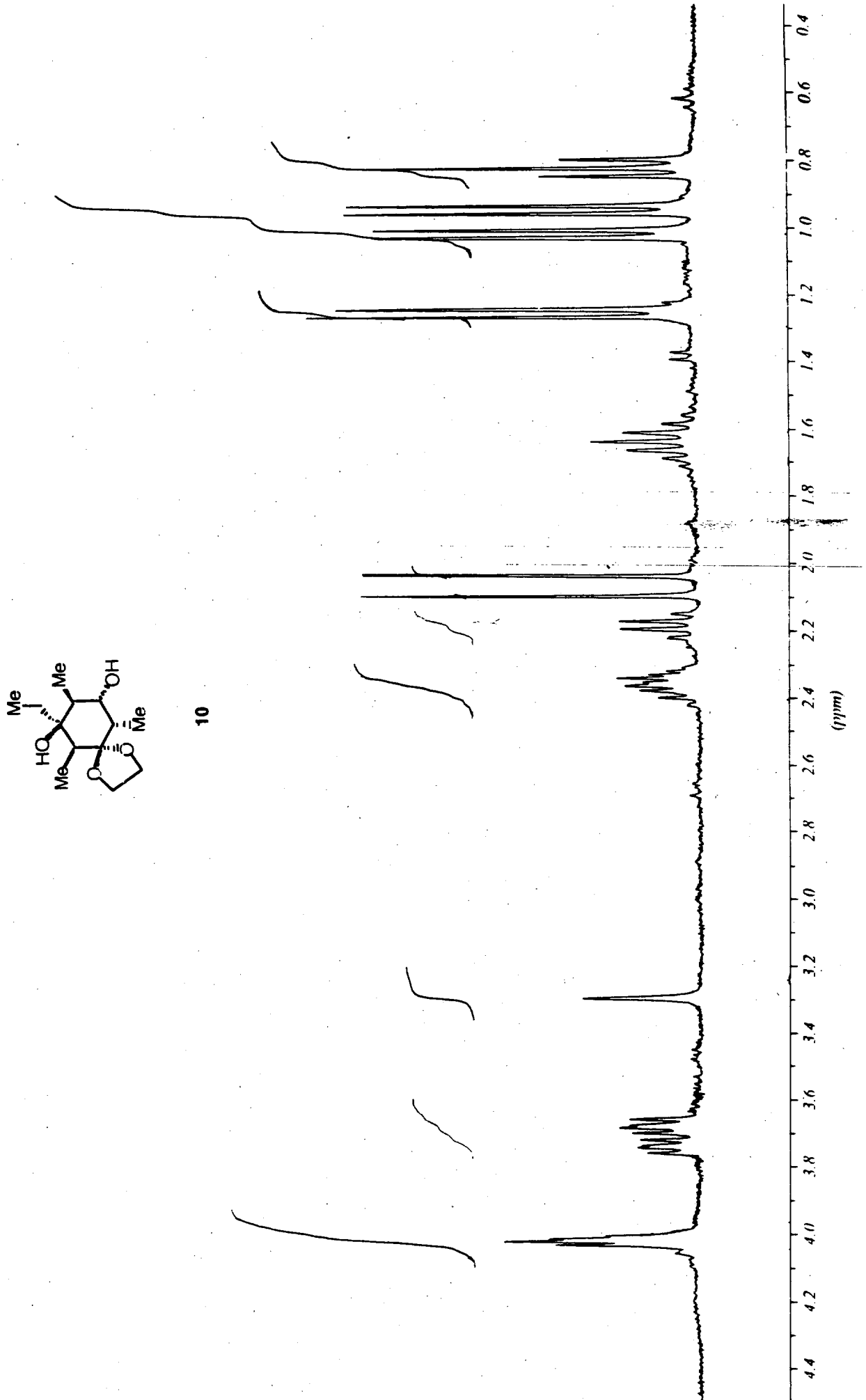
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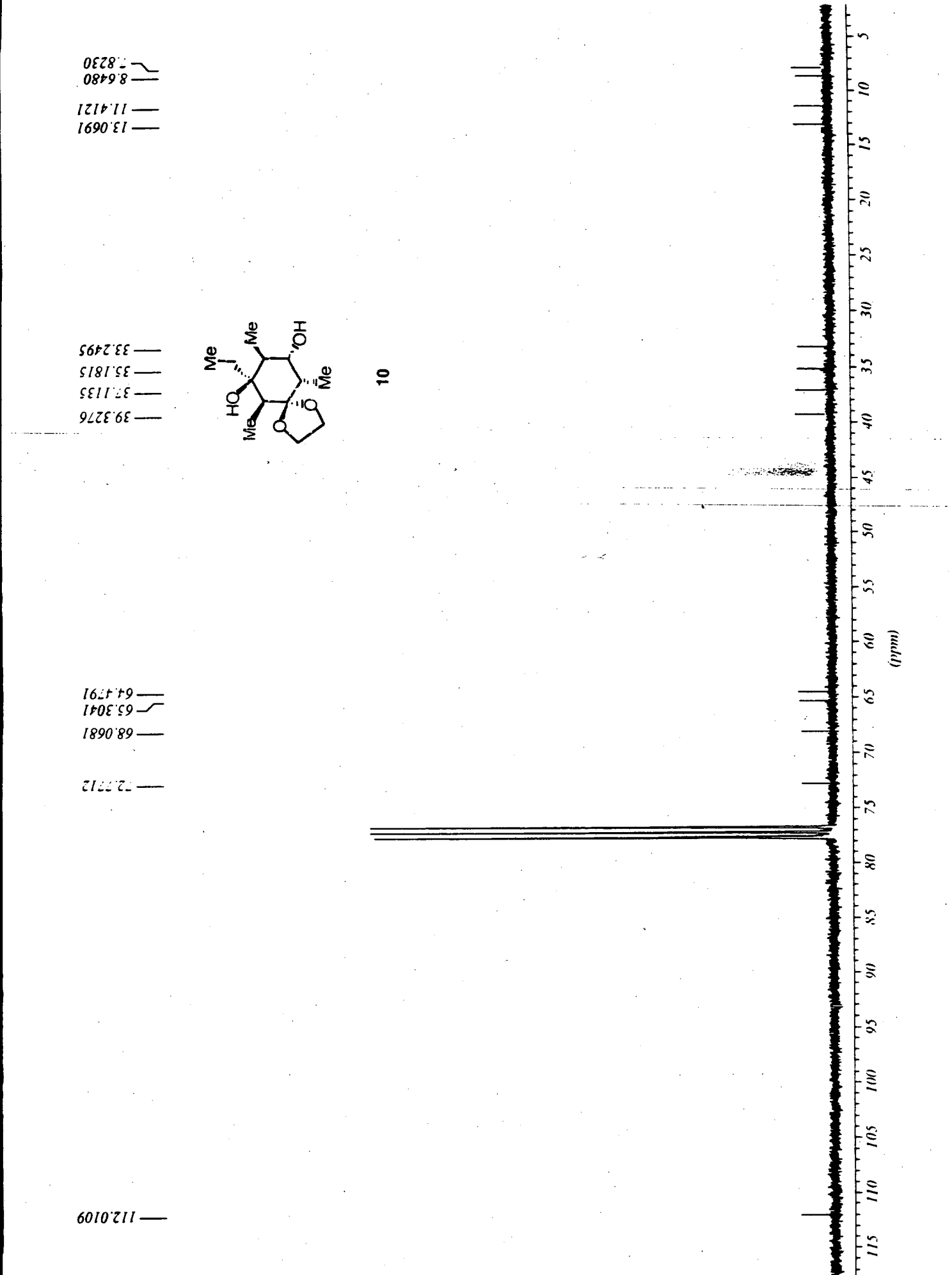

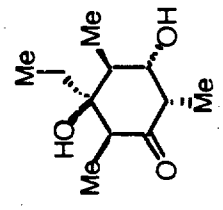
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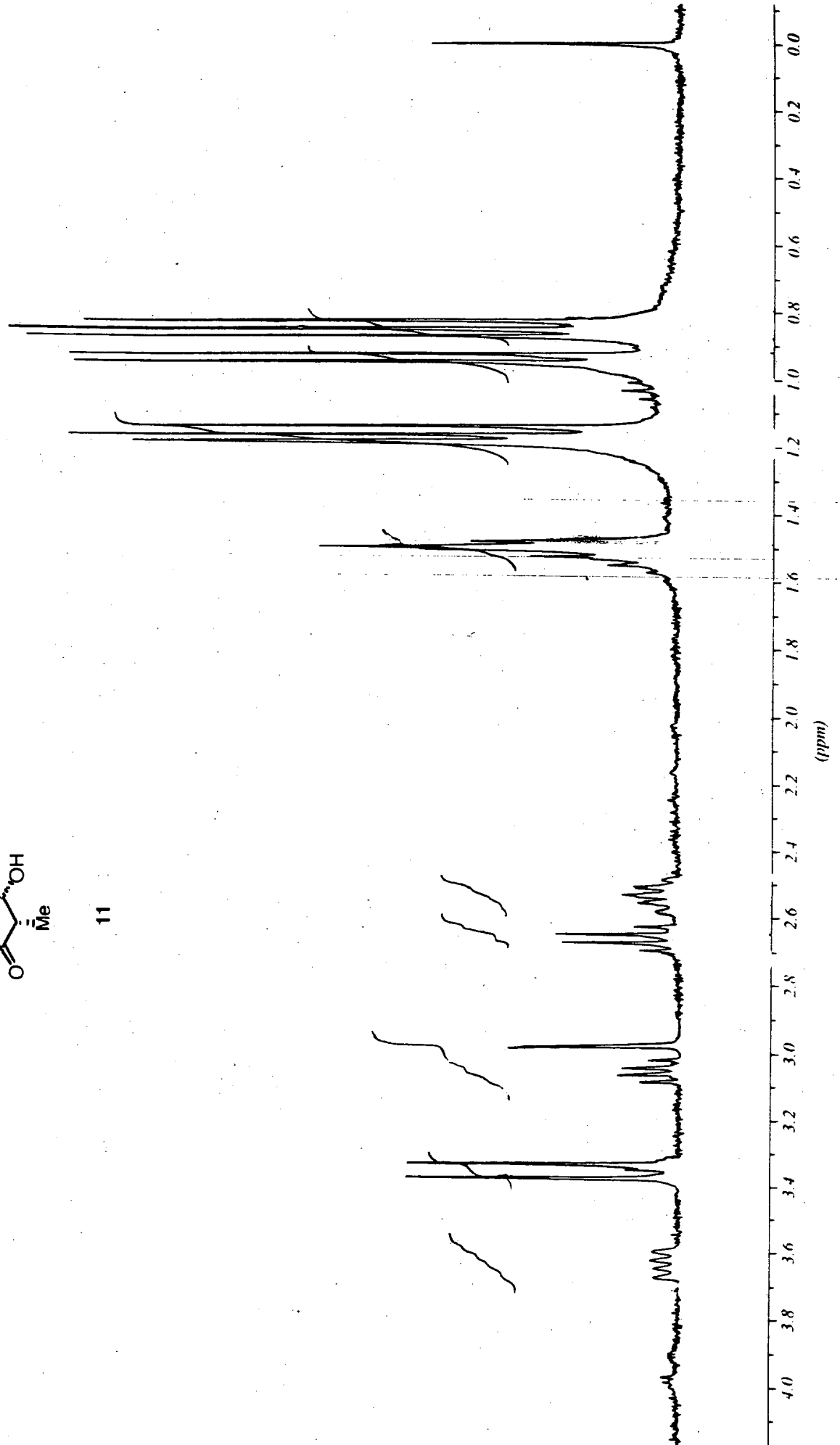
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