

Supporting Information

Enantioselective Syntheses of (+)-Xylarenal A and *ent*-Xylarenal A

*Sandra Díaz, Asensio González, Ben Bradshaw, Javier Cuesta and Josep Bonjoch**

Laboratori de Química Orgànica, Facultat de Farmàcia, Universitat de Barcelona, Av. Joan XXIII

s/n, 08028-Barcelona, Spain

josep.bonjoch@ub.edu

Contents

- Table 1. ^{13}C NMR Chemical shifts of compounds 1-12	2-3
- Experimental and/or NMR data of compounds 1 and 4-12	4-12
- Copies of ^1H NMR and ^{13}C NMR spectra of all new compounds and terpenoids 1 and 5 , including COSY and HSQC spectra.	13-50

Table 1. ¹³C NMR Chemical shifts of compounds 1-12^{a,b}

	1	2	3	4	5	6	7
C1	74.07	31.7	33.2	73.1	68.7	73.8	73.5
C2	31.33	22.9	26.3	32.8	33.5	34.5	34.6
C3	25.69	37.6	30.3	24.8	28.6	25.0	24.9
C4	43.24	210.8	43.0	43.0	42.7	43.4	43.7
C5	39.51	50.6	38.9	38.3	39.2	38.7	39.3
C6	42.98	29.7	35.4	36.8	35.9	37.2	43.1
C7	43.67	33.6	33.9	34.2	35.6	34.1	42.0
C8	197.82	198.1	199.4	200.8	200.2	200.7	201.5
C9	128.68	125.7	123.8	126.3	119.7	125.6	125.4
C10	162.50	165.7	171.2	168.9	172.8	168.5	167.4
C11	148.93	---	---	---	---	---	33.4
C12	193.52	---	---	---	---	---	136.3
C13	136.07	---	---	---	---	---	116.5
C14	17.57	23.3	15.9	17.9	16.8	18.1	18.3
C15	15.21	---	15.1	15.1	14.7	15.3	15.2
C1'	172.57	---	---	---	---	---	---
C2'	34.99	---	---	---	---	---	---
C3'	25.26	---	---	---	---	---	---
C4'	29.81	---	---	---	---	---	---
C5'	29.65	---	---	---	---	---	---
C6'	29.62	---	---	---	---	---	---
C7'	29.49	---	---	---	---	---	---
C8'	23.05	---	---	---	---	---	---
C9'	32.25	---	---	---	---	---	---
C10'	14.25	---	---	---	---	---	---
CH₃Si	---	---	---	---	---	-5.0	-5.0
CH₃Si	---	---	---	---	---	-4.6	-4.6
CSi	---	---	---	---	---	18.0	18.3
CH₃CSi	---	---	---	---	---	25.7	25.7

^a Diterpene numbering is used in this table. ^b Values for compounds **1**, **3-5**, **7-8**, and **10-12** were assigned on the basis of HSQC spectra.

Table 1 (continued). ¹³C NMR Chemical shifts of compounds 1-12^{a,b}

	8	9^c	10	11	12
C1	73.0	209.4	32.9	73.9	73.7
C2	32.9	45.4	26.4	31.0	31.0
C3	24.8	31.2	30.4	24.9	25.3
C4	43.3	45.2	43.6	43.0	43.0
C5	39.0	41.7	39.5	39.0	39.2
C6	42.7	37.4	41.4	42.8	43.7
C7	42.0	41.9	41.5	42.0	38.1
C8	201.4	211.3	200.4	200.8	200.6
C9	126.3	41.1	123.7	128.6	127.9
C10	167.6	57.7	170.0	161.6	162.3
C11	33.4	33.3	33.4	33.3	43.6
C12	136.0	136.1	136.4	136.0	199.7
C13	116.7	116.6	116.3	116.6	---
C14	18.3	11.7	16.0	17.5	17.4
C15	15.2	14.8	15.1	15.1	15.0
C1'	---	---	---	179.5	172.3
C2'	---	---	---	34.7	34.7
C3'	---	---	---	25.4	24.9
C4'	---	---	---	29.4	29.7
C5'	---	---	---	29.3	29.4
C6'	---	---	---	29.1	29.2
C7'	---	---	---	29.1	29.1
C8'	---	---	---	24.7	22.6
C9'	---	---	---	31.8	31.8
C10'	---	---	---	14.1	14.1

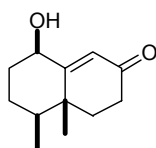
^c Tentative assignments

Experimental Section

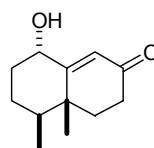
General: All reactions were carried out under an argon atmosphere with dry, freshly distilled solvents under anhydrous conditions. Analytical thin-layer chromatography was performed on SiO₂ (silica gel 60 F₂₅₄), and the spots were located with iodoplatinate reagent or 1% aqueous KMnO₄. Chromatography was carried out on SiO₂ (silica gel 60, 230-240 mesh ASTM). Drying of organic extracts during workup of reactions was performed over anhydrous Na₂SO₄. Evaporation of solvent was accomplished with a rotatory evaporator. Chemical shifts of ¹H and ¹³C NMR spectra are reported in ppm downfield (δ) from Me₄Si

Terpene numbering was used in the NMR assignment of all compounds,

and the IUPAC nomenclature is followed in the headings



4



5

(4aR,5S,8R)-8-Hydroxy-4a,5-dimethyl-4,4a,5,6,7,8-hexahydronaphthalen-2(3H)-one

(4). To a solution of decalone (+)-**3** (1.41 g, 7.91 mmol), trimethylorthoformate (15 mL), methanol (2.74 mL) in DMF (15 mL) was added TsOH (30 mg, 0.16 mmol) and the resulting mixture was stirred for 24 h in the dark. Et₃N (0.87 mL) was added, and the mixture diluted with ether (100 mL), washed three times with saturated NaHCO₃ solution, dried, filtered and concentrated *in vacuo* to give an oil that was used immediately in the following reaction. ¹H NMR of the methyl dienol ether of **3**: (200 MHz, CDCl₃) 0.89 (s, 3H), 0.90 (d, *J* = 6.5 Hz, 3H), 3.58 (s, 3H), 5.16 (d, *J* = 1 Hz, 1H), 5.28 (t, *J* = 2.5 Hz, 1H).

To a mixture of the crude dienol ether (~7.91 mmol), NaHCO₃ (1.99 g, 23.73 mmol) in THF (77 mL) cooled to 0 °C was added a solution of Oxone[®] (7.29 g, 11.87 mmol) in water (46 mL) (c.a. 30 min). The reaction mixture was stirred at 0 °C for 5 h. The reaction was quenched

with saturated NaHCO₃ solution and extracted three times with dichloromethane. The combined organic layers were dried, filtered and concentrated *in vacuo*. Flash column chromatography (from hexane to 20% ethyl acetate in hexane) afforded alcohol **4** (893 mg, 58%) followed by (+)-**1-hydroxyisoondetianone (5)** (216 mg, 14%) as clear oils.

Alcohol 4: [α]_D +138 (*c* 1.15, CHCl₃); ¹H NMR (500 MHz, COSY) 0.93 (d, *J* = 7 Hz, 3H, Me-15), 1.28 (s, 3H, Me-14), 1.40 (m, 2H, H-3_{eq}, H-4_{ax}), 1.66 (tt, *J* = 14, 4 Hz, 1H, H-2_{ax}), 1.70 (td, *J* = 14.5 Hz, 1H, H-6_{ax}), 1.86 (qd, *J* = 13, 3 Hz, H-3_{ax}), 1.97 (dq, *J* = 13, 3 Hz, H-2_{eq}), 2.01 (ddd, *J* = 13.5, 5.3 Hz, 1H, H-6_{eq}), 2.37 (dddd, *J* = 17, 4.5, 3, 1 Hz, H-7_{eq}), 2.51 (ddd, *J* = 17, 15, 5 Hz, H-7_{ax}), 4.31 (t, *J* = 3 Hz, 1H, H-1_{eq}), 5.81 (d, *J* = 1 Hz, 1H, H-9); ¹³C NMR (75 MHz, DEPT, HSQC) 15.1 (C-15), 17.9 (C-14), 24.8 (C-3), 32.8 (C-2), 34.2 (C-7), 36.8 (C-6), 38.3 (C-5), 43.0 (C-4), 73.1 (C-1), 126.3 (C-9), 168.9 (C-10), 200.8 (C-8); HRMS calcd for C₁₂H₁₈O₂: 194.1307, found 194.1312.

(+)-1 α -hydroxyisoondetianone (5): [α]_D +139 (*c* 0.033, CHCl₃) [Lit¹⁰ [α]_D +140 (*c* 0.27, CHCl₃)]; ¹H NMR (400 MHz, COSY) 0.92 (d, *J* = 6.3 Hz, 3H, Me-15), 1.10 (s, 3H, Me-14), 1.45 (m, 1H, H-4), 1.45–1.60 (m, 2H H-3), 1.62 (m, 1H, H-2), 1.77 (td, *J* = 13.5, 4.8 Hz, 1H, H-6_{ax}), 2.01 (ddd, *J* = 13.5, 4.8, 4 Hz, 1H, H-6_{eq}), 2.19 (m, 1H, H-2), 2.33 (dt, *J* = 16.6, 4 Hz, 1H, H-7_{eq}), 2.42 (td, *J* = 16.6, 4 Hz, 1H, H-7_{ax}), 3.58 (br s, 1H, OH), 4.29 (ddd, *J* = 11.5, 5.6, 1.9 Hz, 1H, H-1), 6.19 (s, 1H, H-9); ¹³C NMR (100 MHz, DEPT, HSQC) 14.7 (C-15), 16.8 (C-14), 28.6 (C-3), 33.5 (C-2), 35.6 (C-7), 35.9 (C-6), 39.2 (C-5), 42.7 (C-4), 68.7 (C-1), 119.7 (C-9), 172.8 (C-10), 200.2 (C-8). Anal. Calcd for C₂₂H₃₆O₃·1/2H₂O: C 73.91, H 10.43. Found: C 74.17, H 10.64.

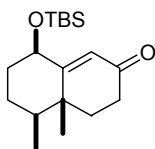
Synthesis of (+)-1 α -hydroxyisoondetianone (5) from 4 via Mitsunobu Process. To a solution of alcohol **4** (32 mg, 0.165 mmol) in benzene (3.2 mL) was added *p*-nitrobenzoic acid (138 mg, 0.825 mmol) and triphenylphosphine (216 mg, 0.825 mmol). The resulting mixture was stirred for 5 min before a solution of DEAD (144 mg, 0.825 mmol) in benzene (1 mL) was added

dropwise via syringe. After stirring for 18 h the reaction mixture was evaporated to dryness and the residue quickly purified through a pad of silica (10% to 25% ethyl acetate in hexane) to afford the crude nitrobenzoate ester which was used immediately in the subsequent step.

To a 0 °C solution of the above crude nitrobenzoate ester (~ 0.165 mmol) in MeOH (5 mL) was LiOH.H₂O (11 mg, 0.27 mmol) in one portion. After stirring for 3 h the reaction mixture was evaporated to dryness and the residue purified by flash chromatography (10% to 50% ethyl acetate in hexane) to afford the alcohol **5** (22 mg, 69%) as a clear oil.

Synthesis of 4 from 5 via Mitsunobu Process. To a solution of alcohol **5** (100 mg, 0.515 mmol) in benzene (10 mL) was added *p*-nitrobenzoic acid (430 mg, 2.58 mmol) and triphenylphosphine (675 mg, 2.58 mmol). The resulting mixture was stirred for 5 min before a solution of DEAD (448 mg, 2.58 mmol) in benzene (2.9 mL) was added dropwise via syringe. After stirring for 18 h the reaction mixture was evaporated to dryness and the residue quickly purified through a pad of silica (10% to 50% ethyl acetate in hexane) to afford the crude nitrobenzoate ester which was used immediately in the subsequent step.

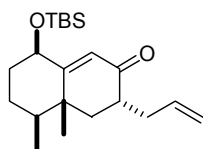
To a 0 °C solution of the above crude nitrobenzoate ester (~ 0.515 mmol) in MeOH (15 mL) was LiOH.H₂O (32 mg, 0.773 mmol) in one portion. After stirring for 3 h the reaction mixture was evaporated to dryness and the residue purified by flash chromatography (10% to 50% ethyl acetate in hexane) to afford the alcohol **4** (67 mg, 67%) as a clear oil.



6

(4aR,5S,8R)-8-(*t*-Butyldimethylsilyloxy)-4a,5-dimethyl-4,4a,5,6,7,8-hexahydro-naphthalen-2(3H)-one (6). To a solution of alcohol **4** (0.69 g, 3.55 mmol), imidazole (1.21g,

17.75 mmol) in DMF (4.4 mL) was added *tert*-butyldimethylsilylchloride in one portion. The mixture was stirred for 24 h at 40 °C. The reaction was quenched with water and extracted three times with ether. The combined organic layers were washed with saturated NH₄Cl solution, brine, dried, filtered and concentrated *in vacuo*. Flash column chromatography (from hexane to 3% ethyl acetate in hexane) afforded TBS ether **6** (924 mg, 84%) as a clear oil: [α]_D +50 (*c* 0.7, CHCl₃); ¹H NMR (300 MHz) 0.00 (s, 3H, Me-Si), 0.05 (s, 3H, Me-Si), 0.87 (s, 9H, Me₃C-Si), 0.92 (d, *J* = 6.5 Hz, 3H, Me-15), 1.25 (s, 3H, Me-14), 1.30–1.45 (m, 2H, H-3_{eq}, H-4_{ax}), 1.59 (tt, *J* = 14, 4 Hz, 1H, H-2_{ax}), 1.70 (td, *J* = 13.5, 4 Hz, 1H, H-6_{ax}), 1.84 (dm, *J* = 13.5 Hz, 1H, H-2_{eq}), 1.86 (qd, *J* = 13.3 Hz, 1H, H-3_{ax}), 2.01 (ddd, *J* = 13.5, 5, 3 Hz, 1H, H-6_{eq}), 2.35 (dm, *J* = 16.5 Hz, 1H, H-7_{eq}), 2.48 (ddd, *J* = 17, 15, 5 Hz, 1H, H-7_{ax}), 4.23 (s, 1H, H-1_{eq}), 5.74 (s, 1H, H-9); ¹³C NMR (75 MHz, DEPT) -5.0 (CH₃-Si), -4.6 (CH₃-Si), 15.3 (C-15), 18.0 (C-Si), 18.1 (C-14), 25.0 (C-3), 25.7 (CH₃C-Si), 34.1 (C-7), 34.5 (C-2), 37.2 (C-6), 38.7 (C-5), 43.4 (C-4), 73.8 (C-1), 125.6 (C-9), 168.5 (C-10), 200.7 (C-8). Anal. Calcd for C₁₈H₃₂O₂Si·1/3H₂O: C 68.75, H 10.47. Found: C 68.71, H 10.37.

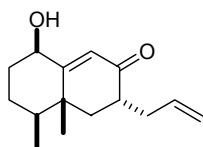


7

(3*S*,4*aR*,5*S*,8*R*)-3-Allyl-8-(*t*-butyldimethylsilyloxy)-4*a*,5-dimethyl-4,4*a*,5,6,7,8-

hexahydronaphthalen-2(3*H*)-one (7). To solution of LiN(SiMe₃)₂ (1 M in THF, 1.87 mL, 1.87 mmol) in THF (3 mL) at -78 °C was added ketone **6** (115 mg, 0.37 mmol) dissolved in THF (4 mL). After stirring for 30 min HMPA (325 μL, 1.87 mmol) was added. After stirring for a further 20 min allyl bromide (315 μL, 3.73 mmol) was added slowly. After stirring for 5 h at -78 °C the mixture was warmed to room temperature and then stirred for a further 16 h. The reaction was quenched with 1N HCl (7 mL) and extracted three times with ether. The combined organic layers

were washed with brine, dried, filtered and concentrated *in vacuo*. Flash column chromatography (hexane to 2% ethyl acetate in hexanes) afforded the allylated ketone **7** (71 mg, 55%) as a clear oil and 33 mg of **6** (75% yield based on recovered starting material): $[\alpha]_D +46$ (*c* 1.81, CHCl₃); ¹H NMR (500 MHz, COSY) 0.06 (s, 6H, Me-Si), 0.87 (s, 9H, Me₃C-Si), 0.92 (d, *J* = 6.5 Hz, 3H, Me-15), 1.27 (s, 3H, Me-14), 1.32-1.37 (m, 2H, H-3_{eq}, H-4_{ax}), 1.40 (t, *J* = 13.5 Hz, 1H, H-6_{ax}), 1.58 (tt, *J* = 13.5, 3.5 Hz, 1H, H-2_{ax}), 1.82 (dq, *J* = 13, 3.5 Hz, 1H, H-3_{ax}), 1.87 (qd, *J* = 13, 3.5 Hz, 1H, H-3_{ax}), 2.03 (dd, *J* = 13.5, 4.5 Hz, 1H, H-6_{eq}), 2.05 (dt, *J* = 12.5, 8 Hz, H-11), 2.52 (dddd, *J* = 13.5, 8, 4.5, 3.5 Hz, 1H, H-7_{ax}), 2.70 (m, 1H, H-11), 4.23 (t, *J* = 2.5 Hz, H-1), 5.03 (dm, *J* = 10 Hz, H-13), 5.05 (dq, *J* = 16, 1.5 Hz, H-13), 5.73 (s, 1H, H-9), 5.79 (dddd, *J* = 17, 11, 7, 6 Hz, 1H, H-12); ¹³C NMR (75 MHz, DEPT, HSQC) -5.0 (CH₃-Si), -4.6 (CH₃-Si), 15.2 (C-15), 18.3 (C-14), 24.9 (C-3), 25.7 (CH₃C-Si), 33.4 (C-11), 34.6 (C-2), 39.3 (C-5), 42.0 (C-7), 43.1 (C-6), 43.7 (C-4), 73.5 (C-1), 116.5 (C-13), 125.4 (C-9), 136.3 (C-12), 167.4 (C-10), 201.5 (C-8).

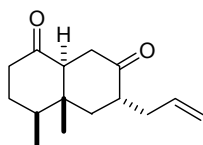


8

(3R,4aR,5S,8R)-3-Allyl-8-hydroxy-4a,5-dimethyl-4,4a,5,6,7,8-hexahydronaphthalen-

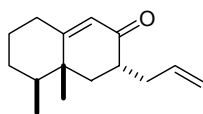
2(3H)-one (8). To a solution of TBS ether **7** (253 mg, 0.725 mmol) in THF (15 mL) was added a solution of TBAF (1 M in THF, 1.45 mL, 1.45 mmol). After stirring for 18 h the reaction was quenched with water and extracted three times with dichloromethane. The combined organic layers were washed with brine, dried, filtered and concentrated *in vacuo*. Flash chromatography (5% to 25% ethyl acetate in hexane) afforded alcohol **8** (150 mg, 88%) as a clear oil: $[\alpha]_D +63$ (*c* 1.46, CH₂Cl₂); ¹H NMR (300 MHz, COSY, NOESY) 0.94 (d, *J* = 6.5 Hz, 3H, Me-15), 1.30 (s, 3H, Me-14), 1.35–1.50 (m, 3H, H-3, H-4_{ax}, H-6), 1.66 (tt, *J* = 13.5, 3.5 Hz, 1H, H-2_{ax}), 1.88 (qd, *J* = 13.5, 3.5 Hz, 1H, H-3_{ax}), 2.00 (dq, *J* = 13, 2.5 Hz, 1H, H-2_{eq}), 2.03 (masked, 1H, H-6), 2.06 (t, *J* = 13

Hz, 1H, H-11_R), 2.51 (dddd, $J = 13, 9, 6.5, 2$ Hz, 1H, H-7_{ax}), 2.68 (dddd, $J = 13, 6.5, 2, 1$ Hz, 1H, H-11_S), 4.33 (t, $J = 2.7$ Hz, 1H, H-1_{eq}), 5.04 (dd, $J = 10$ Hz, 1H, H-13), 5.05 (dd, $J = 17, 1$ Hz, 1H, H-13), 5.76 (dddd, $J = 17, 11, 7, 6$ Hz, 1H, H-12), 5.81 (s, 1H, H-9); ¹³C NMR (75 MHz, DEPT, HSQC) 15.2 (C-15), 18.3 (C-14), 24.8 (C-3), 32.9 (C-2), 33.4 (C-11), 39.0 (C-5), 42.0 (C-7), 42.7 (C-6), 43.3 (C-4), 73.0 (C-1), 116.7 (C-13), 126.3 (C-9), 136.0 (C-12), 167.6 (C-10), 201.4 (C-8).
 Anal. Calcd for C₁₅H₂₂O₂·1/3H₂O: C 74.88, H 9.51. Found: C 74.82, H 9.68.



9

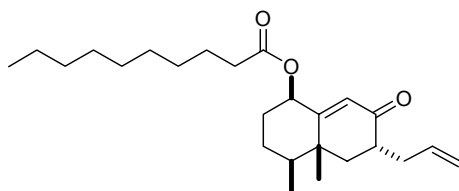
(4S,4aR,6R,8aS)-6-Allyl-4,4a-dimethyloctahydronaphthalene-1,7-dione (9). ¹H NMR (300 MHz) 0.92 (s, 3H), 0.97 (d, $J = 6$ Hz), 1.31 (t, $J = 13$ Hz, 1H), 1.65-1.85 (m, 2H), 1.90-2.02 (m, 2H), 2.12 (dd, $J = 13.5, 5$ Hz, 1H), 2.32-2.50 (m, 2H), 2.54-2.63 (m, 2H), 5.04 (dd, $J = 10$ Hz, 1H), 5.05 (dd, $J = 17, 1$ Hz, 1H), 5.76 (dddd, $J = 17, 11, 7, 6$ Hz, 1H); ¹³C NMR (75 MHz, DEPT) 11.7 (CH₃), 14.8 (CH₃), 31.2 (CH₂), 33.3 (CH₂), 37.4 (CH₂), 41.1 (CH₂), 41.7 (C), 41.9 (CH), 45.2 (CH), 45.4 (CH₂), 57.7 (CH), 116.6 (CH₂), 136.1 (CH), 209.4 (CO), 211.3 (CO).



10

(3R,4aR,5S)-3-Allyl-4a,5-dimethyl-4,4a,5,6,7,8-hexahydronaphthalen-2(3H)-one (10): $[\alpha]_D^{25} +137$ (c 1.6, CH₂Cl₂); ¹H NMR (300 MHz, COSY, NOESY) 0.90 (d, $J = 6.3$ Hz, 3H, Me-15), 1.12 (s, 3H, Me-14), 1.40-1.47 (m, 2H, H-2, H-6), 1.44 (m, 1H, H-4), 1.87 (m, 1H, H-2), 2.08-2.10 (m, 2H, H-6 and H-11), 2.3 (m, 2H, H-1), 2.41 (dddd, $J = 13, 9.5, 4.5, 4.5$ Hz, 1H, H-7_{ax}), 2.72 (m, 1H, H-11), 5.06 (dm, $J = 17$ Hz, 1H, H-13), 5.07 (dm, $J = 11$ Hz, 1H, H-13), 5.72 (d, $J = 1.5$ Hz, 1H,

H-9), 5.80 (dddd, $J = 17, 11, 7, 6$ Hz, 1H, H-12); ^{13}C NMR (75 MHz, DEPT, HSQC) 15.1 (C-15), 16.0 (C-14), 26.4 (C-2), 30.4 (C-3), 32.9 (C-1), 33.4 (C-11), 39.5 (C-5), 41.4 (C-6), 41.5 (C-7), 43.6 (C-4), 116.3 (C-13), 123.7 (C-9), 136.4 (C-12), 170.0 (C-10), 200.2 (C-8). Anal. Calcd for $\text{C}_{15}\text{H}_{22}\text{O} \cdot 1/6 \text{H}_2\text{O}$: C 81.51, H 10.17. Found: C 81.63, H 10.15.

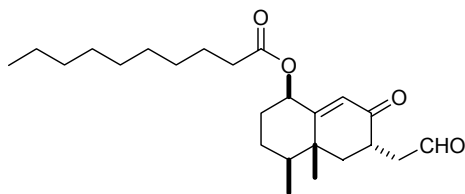


11

(1R,4S,4aR,6R)-6-Allyl-4,4a-dimethyl-7-oxo-1,2,3,4,4a,5,6,7-octahydronaphthalen-1-yl

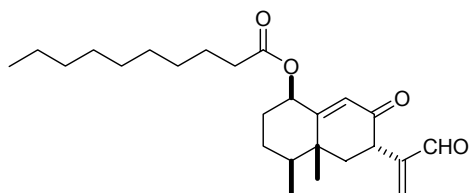
Decanoate (11). To a solution of **8** (140 mg, 0.587 mmol) in THF (21 mL) was added DMAP (132 mg, 1.08 mmol), decanoic anhydride (293 mg, 0.897 mmol) and triethylamine (2.45 mL). The reaction mixture was heated to reflux for 24 h, allowed to cool to room temperature, poured into 1N HCl/ice, stirred for 10 min and then extracted three times with ether. The combined organic layers were washed with saturated NaHCO_3 , brine, dried (Na_2SO_4), filtered and concentrated *in vacuo*. Flash chromatography (from hexane to 3% ethyl acetate in hexane) afforded the ester **11** (214 mg, 92%) as a clear oil: $[\alpha]_{\text{D}} +34.5$ (c 1.45, CH_2Cl_2); ^1H NMR (400 MHz, COSY, NOESY) 0.88 (t, $J = 7, 3$ Hz, 3H, H-10'), 0.95 (d, $J = 6.8$ Hz, 3H, Me-15), 1.23 (s, 3H, Me-14), 1.25–1.30 (m, 12H), 1.45 (m, 3H, H-3_{eq}, H-4, H-6), 1.62 (m, 2H, H-3'), 1.70 (m, H-2), 1.75 (qd, $J = 13, 2.5$ Hz, H-3_{ax}), 1.99 (dq, $J = 13, 2.5$ Hz, H-2_{eq}), 2.07 (m, 2H, H-6, H-11), 2.28 (td, $J = 7.5, 4$ Hz, 2H, H-2'), 2.50 (dddd, $J = 14, 8.5, 4, 4$ Hz, H-7_{ax}), 2.69 (m, 1H, H-11), 5.04 (dm, $J = 10$ Hz, 1H, H-13), 5.06 (dm, $J = 17$ Hz, 1H, H-13), 5.4 (t, $J = 3$ Hz, 1H, H-1_{eq}), 5.76 (dddd, $J = 17, 11, 7, 6$ Hz, 1H, H-12), 5.94 (s, 1H, H-9); ^{13}C NMR (100 MHz, DEPT, HSQC) 14.1 (C-10'), 15.1 (C-15), 17.5 (C-14), 24.7 (C-8'), 24.9 (C-3), 25.4 (C-3'), 29.1, 29.1, 29.3, 29.4, (C-4', C-5', C-6', C-7'), 31.0 (C-2), 31.8 (C-9'), 33.3 (C-11), 34.7 (C-2'), 39.0 (C-5), 42.0 (C-7), 42.8 (C-6), 43.0 (C-4), 73.9

(C-1), 116.6 (C-13), 128.6 (C-9), 136.0 (C-12), 161.6 (C-10), 179.5 (C-1'), 200.8 (C-8). Anal. Calcd for C₂₅H₄₀O₃ 3/4H₂O: C 74.68, H 10.40. Found: C 74.59, H 11.22.



12

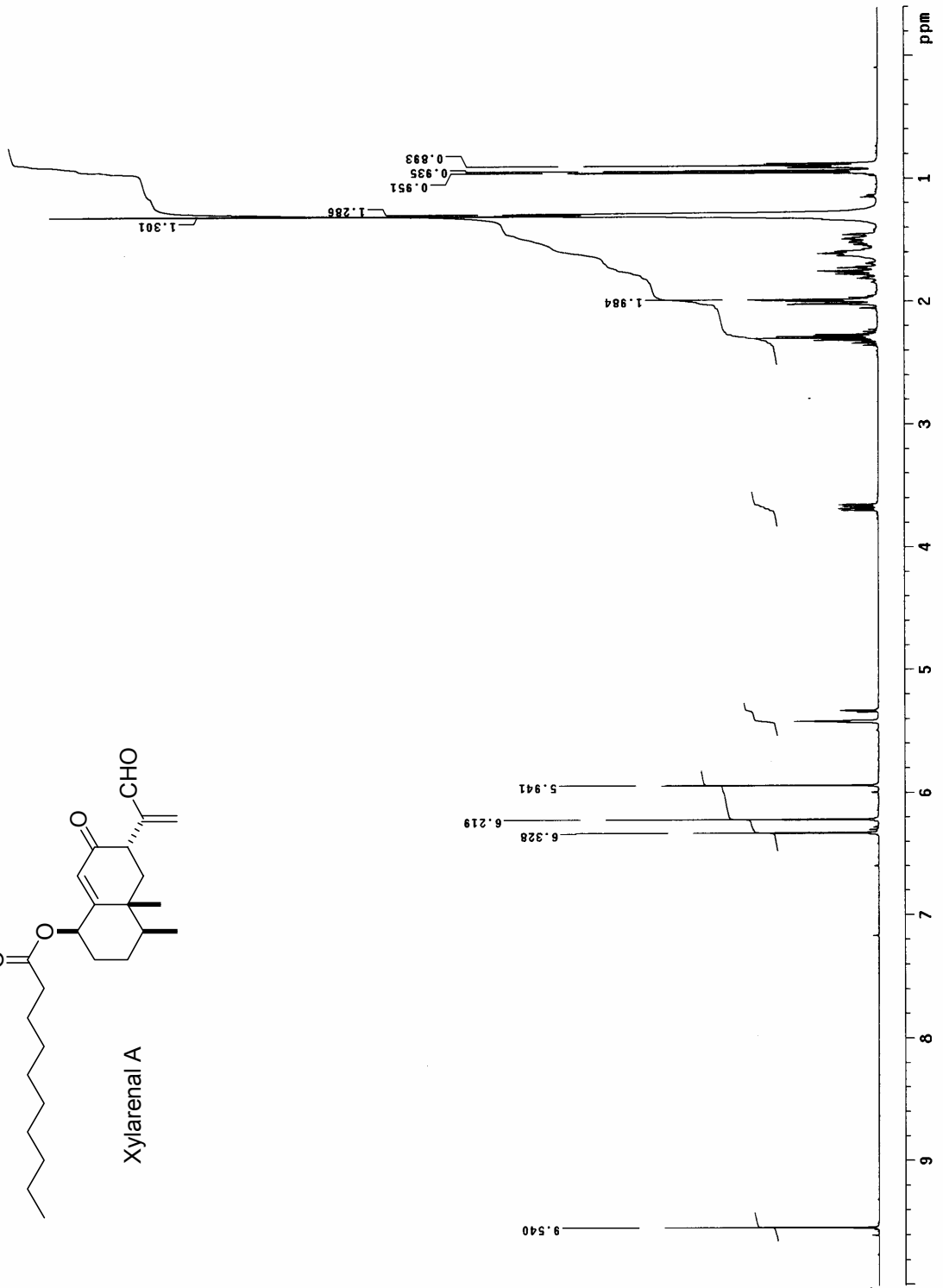
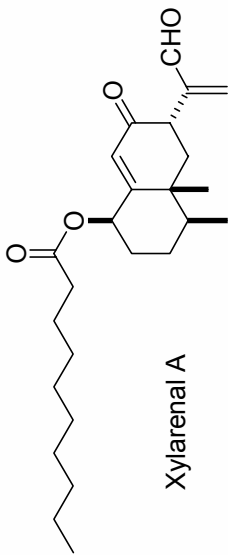
(1R,4S,4aR,6S)-4,4a-Dimethyl-7-oxo-6-(2-oxoethyl)-1,2,3,4,4a,5,6,7-octahydro-naphthalen-1-yl Decanoate (12). To a solution of **11** (150 mg, 0.386 mmol) in dioxane (3 mL) and H₂O (1 mL) was added 2,6 lutidine (90 μL, 0.772 mmol), NaIO₄ (330 mg, 1.546 mmol) and 4% aqueous solution of OsO₄ (0.031 mL, 0.0077 mmol). After stirring for 4 h, the reaction was quenched with water and extracted 4 times with dichloromethane. The combined organic layers were washed with brine, dried, filtered and concentrated *in vacuo*. Flash chromatography (hexane to 10% ethyl acetate in hexane) afforded the aldehyde **12** (113 mg, 75%) as a clear oil: ¹H NMR (400 MHz, COSY, NOESY) 0.88 (t, *J* = 6.5 Hz, 3H, Me-10'), 0.94 (d, *J* = 6.5 Hz, 3H, Me-15), 1.26 (s, 3H, Me-14), 1.43 (m, 1H, H-4), 1.45 (m, 1H, H-3), 1.57 (m, 1H, H-6_{ax}), 1.61 (m, 1H, H-3'), 1.64 (m, 1H, H-2_{ax}), 1.73 (qd, *J* = 14, 2.5 Hz, H-3_{ax}), 1.98 (dq, *J* = 14, 5 Hz, 1H, H-2_{eq}), 2.05 (dd, *J* = 12.5, 4.5 Hz, 1H, H-6), 2.28 (m, H-2'), 2.36 (ddd, *J* = 17.5, 6, 1 Hz, H-11), 3.01 (ddd, *J* = 17.5, 6, 1 Hz, H-11), 3.14 (dq, *J* = 14.5, 5 Hz, 1H, H-7_{ax}), 5.41 (s, 1H, H-1), 5.98 (s, 1H, H-9), 9.85 (s, 1H, H-12); ¹³C-NMR (100 MHz, DEPT, HSQC) 14.1 (C-10'), 15.0 (C-15), 17.4 (C-14), 22.6 (C-8'), 24.9 (C-3'), 25.3 (C-3), 29.1 (C-7'), 29.2 (C-6'), 29.4 (C-5'), 29.7 (C-4'), 31.0 (C-2), 31.8 (C-9'), 34.7 (C-2'), 38.1 (C-7), 39.2 (C-5), 43.0 (C-4), 43.6 (C-11), 43.7 (C-6), 73.7 (C-1), 127.9 (C-9), 162.3 (C-10), 172.3 (C-1'), 199.7 (C-12), 200.6 (C-8).

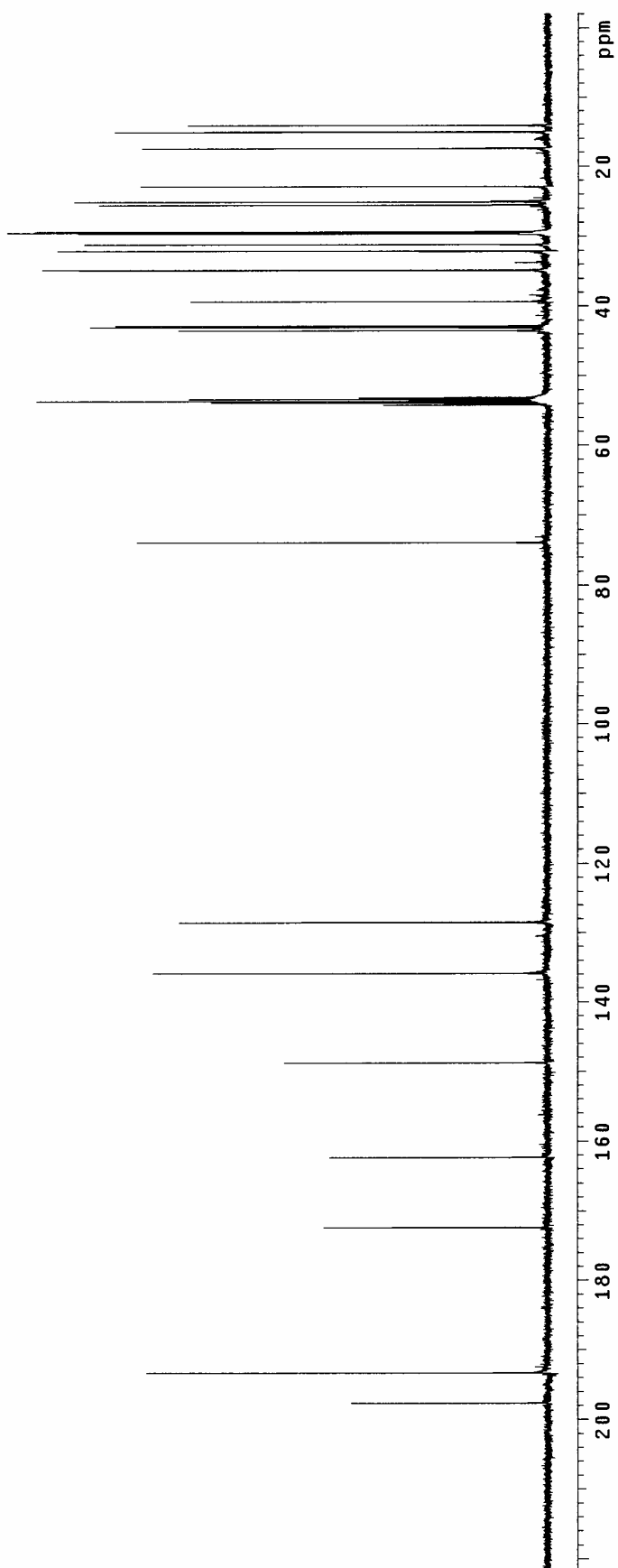
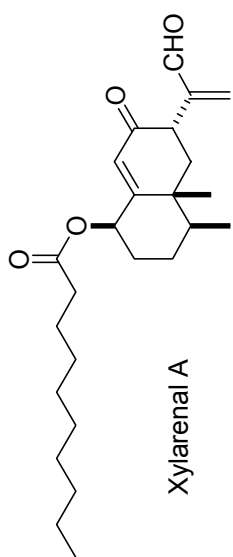


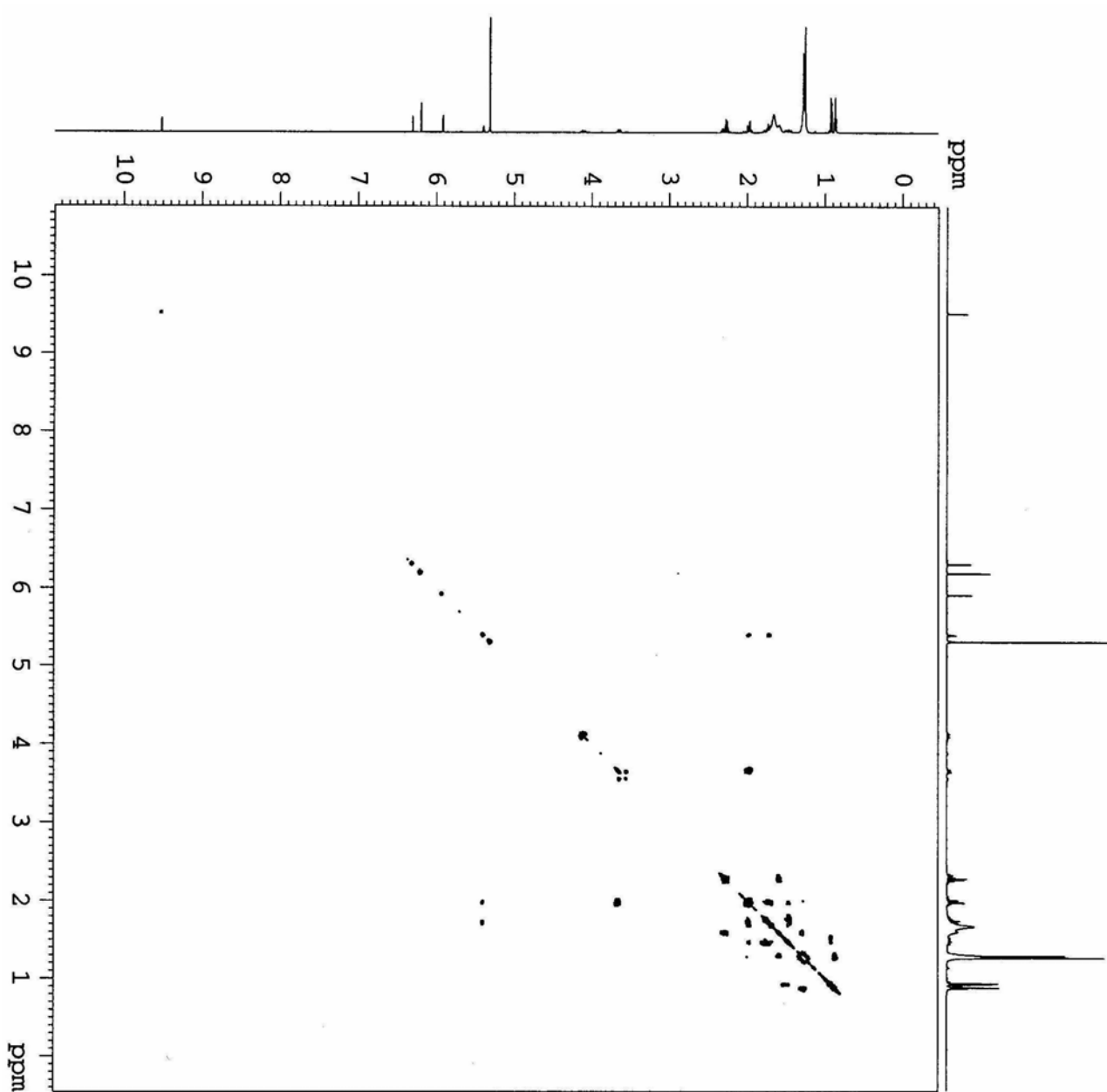
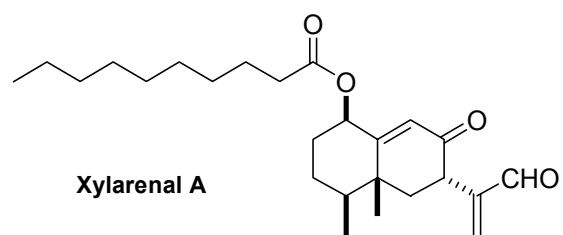
1

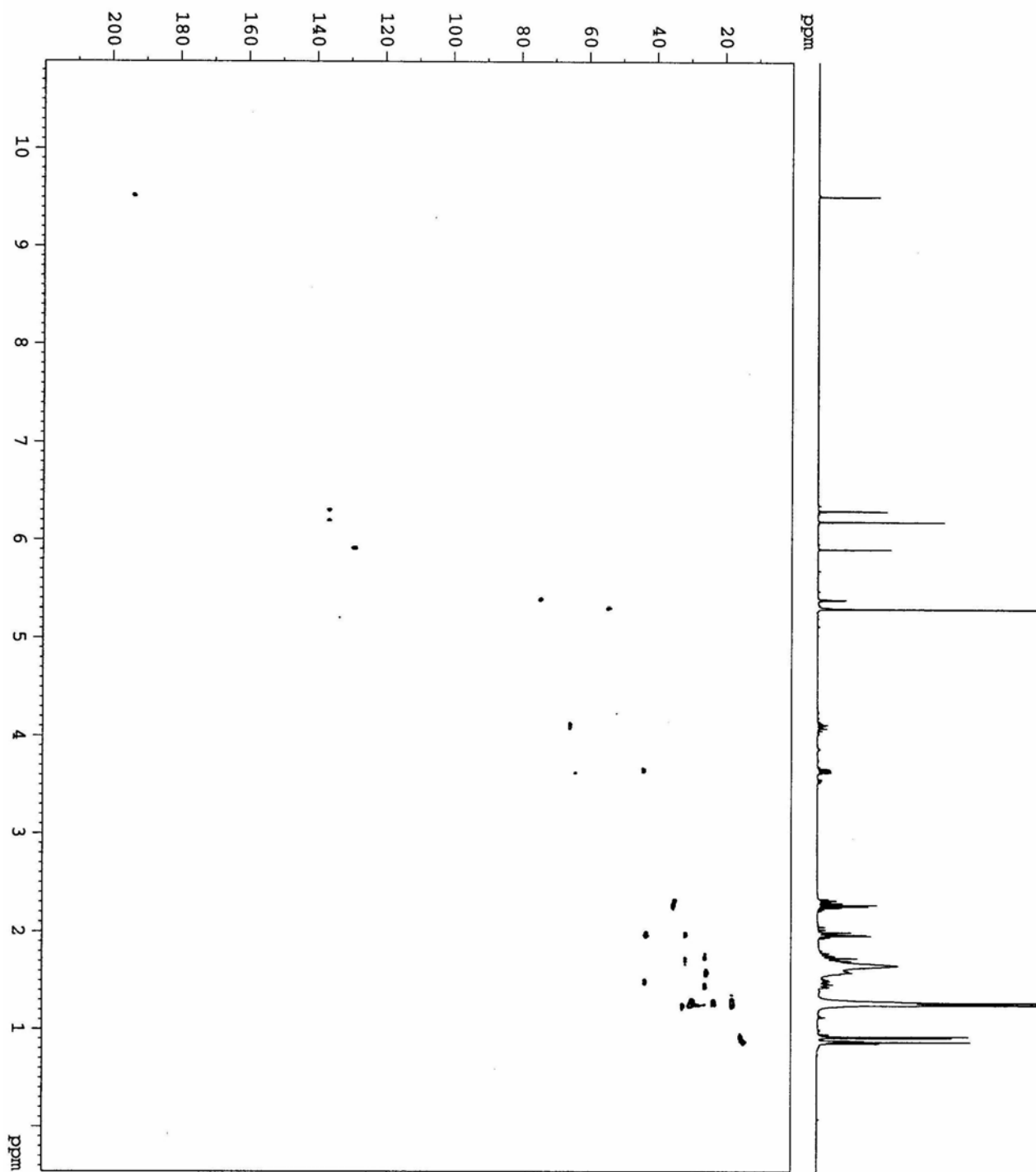
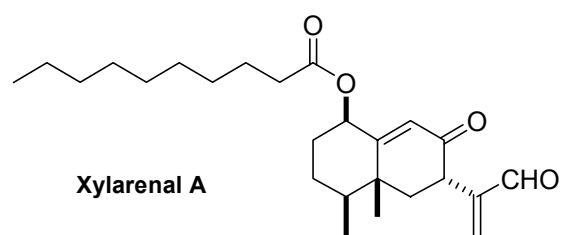
Xylarenal A (1). To a solution of **12** (105 mg, 0.269 mmol) in dichloromethane (20.15 mL) and triethylamine (1.36 g, 1.87 mL, 13.44 mmol) was added Eschenmoser's salt (249 mg, 1.345 mmol). After stirring for 18 h the reaction was quenched with saturated NaHCO₃ and extracted three times with dichloromethane. The combined organic layers were washed with brine, dried (Na₂SO₄), filtered and concentrated *in vacuo*. Flash chromatography (from hexane to 10% ethyl acetate in hexane) afforded synthetic Xylarenal A (**1**, 84 mg, 78%) as a clear oil: [α]_D +28.2 (*c* 0.45, CH₂Cl₂); [Lit.⁴ Xylarenal A [α]_D +30 (*c* 0.4, CH₂Cl₂)]; ¹H NMR (400 MHz, COSY, NOESY) 0.88 (t, *J* = 6.7 Hz, 3H, Me-10'), 0.93 (d, *J* = 6.7 Hz, 3H, Me-15), 1.27 (s, 3H, Me-14), 1.27-1.29 (m, 12H), 1.45 (m, 1H, H-3), 1.50 (m, 1H, H-4), 1.59 (m, 2H, H-3'), 1.72 (m, 1H, H-2), 1.75 (m, 1H, H-3), 1.98 (m, 2H, H-6), 1.99 (m, 1H, H-2), 2.28 (pseudo q, *J* = 7.5 Hz, H-2'), 3.66 (dd, *J* = 13.2, 5.5 Hz, H-7), 5.41 (pseudo t, *J* = 3 Hz, 1H, H-1), 5.93 (s, 1H, H-9), 6.21 (s, 1H, H-13), 6.32 (s, 1H, H-13), 9.53 (s, 1H, H-12); ¹³C NMR (100 MHz, DEPT, HSQC) 14.25 (C-10'), 15.21 (C-15), 17.57 (C-14), 23.05 (C-8'), 25.26 (C-3'), 25.69 (C-3), 31.33 (C-2), 29.49, 29.62, 29.65, 29.81 (C-4', C-5', C-6' y C-7'), 32.25 (C-9'), 34.99 (C-2'), 39.51 (C-5), 42.98 (C-6), 43.24 (C-4), 43.67 (C-7), 74.07 (C-1), 128.68 (C-9), 136.07 (C-13), 148.93 (C-11), 162.50 (C-10), 172.57 (C-1'), 193.52 (C-12), 197.82 (C-8).

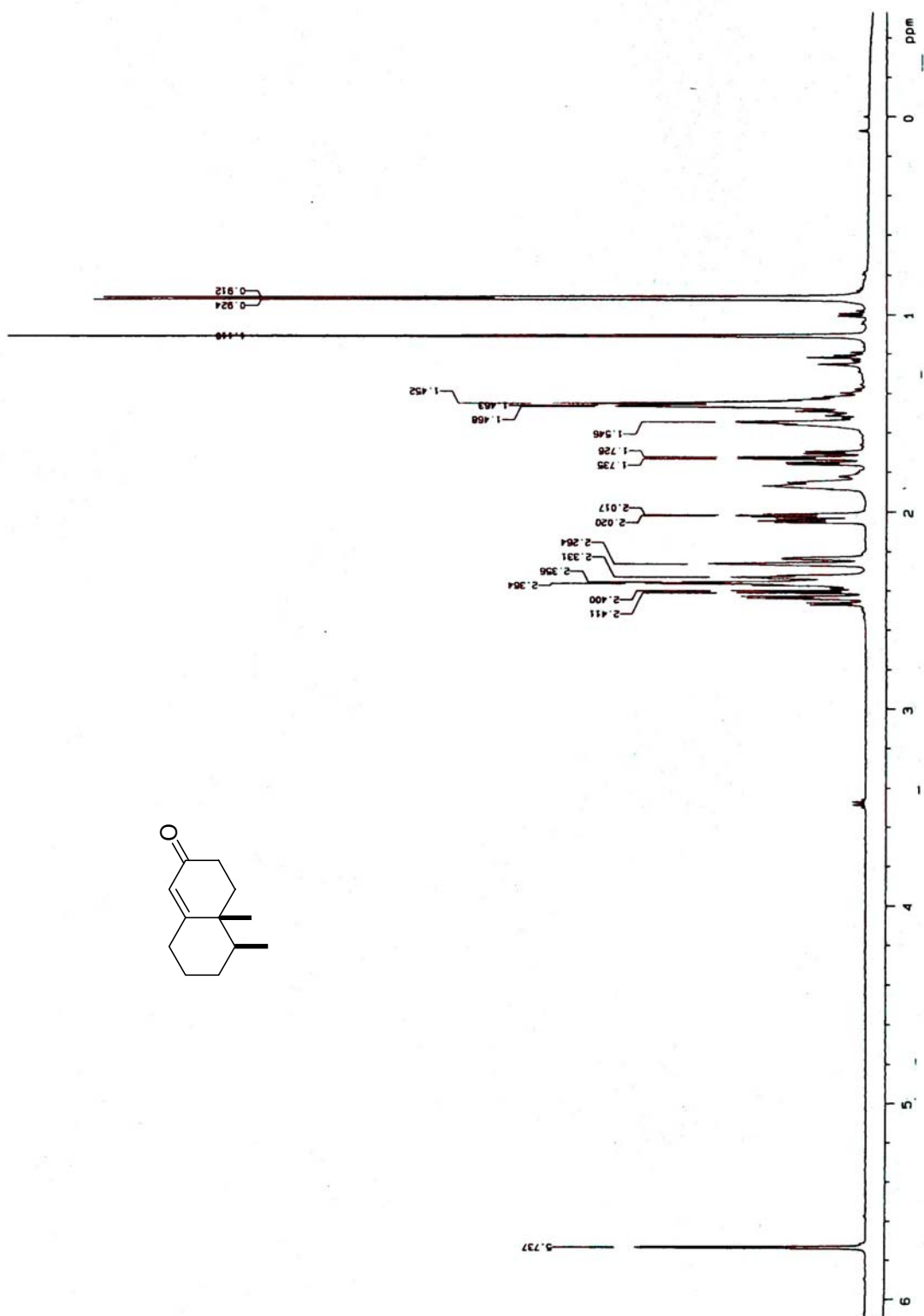
[α] _D For compounds in the enantiomeric series:	
(-)- 4 [α] _D - 142 (<i>c</i> 1.7, CHCl ₃)	(-)- 8 [α] _D - 41 (<i>c</i> 2.34, CH ₂ Cl ₂)
(-)- 6 [α] _D - 50 (<i>c</i> 0.7, CHCl ₃)	(-)- 11 [α] _D - 39 (<i>c</i> 0.13, CH ₂ Cl ₂)
(-)- 7 [α] _D - 45 (<i>c</i> 1.34, CH ₂ Cl ₂)	(-)- 1 [α] _D - 32.7 (<i>c</i> 0.85, CH ₂ Cl ₂);

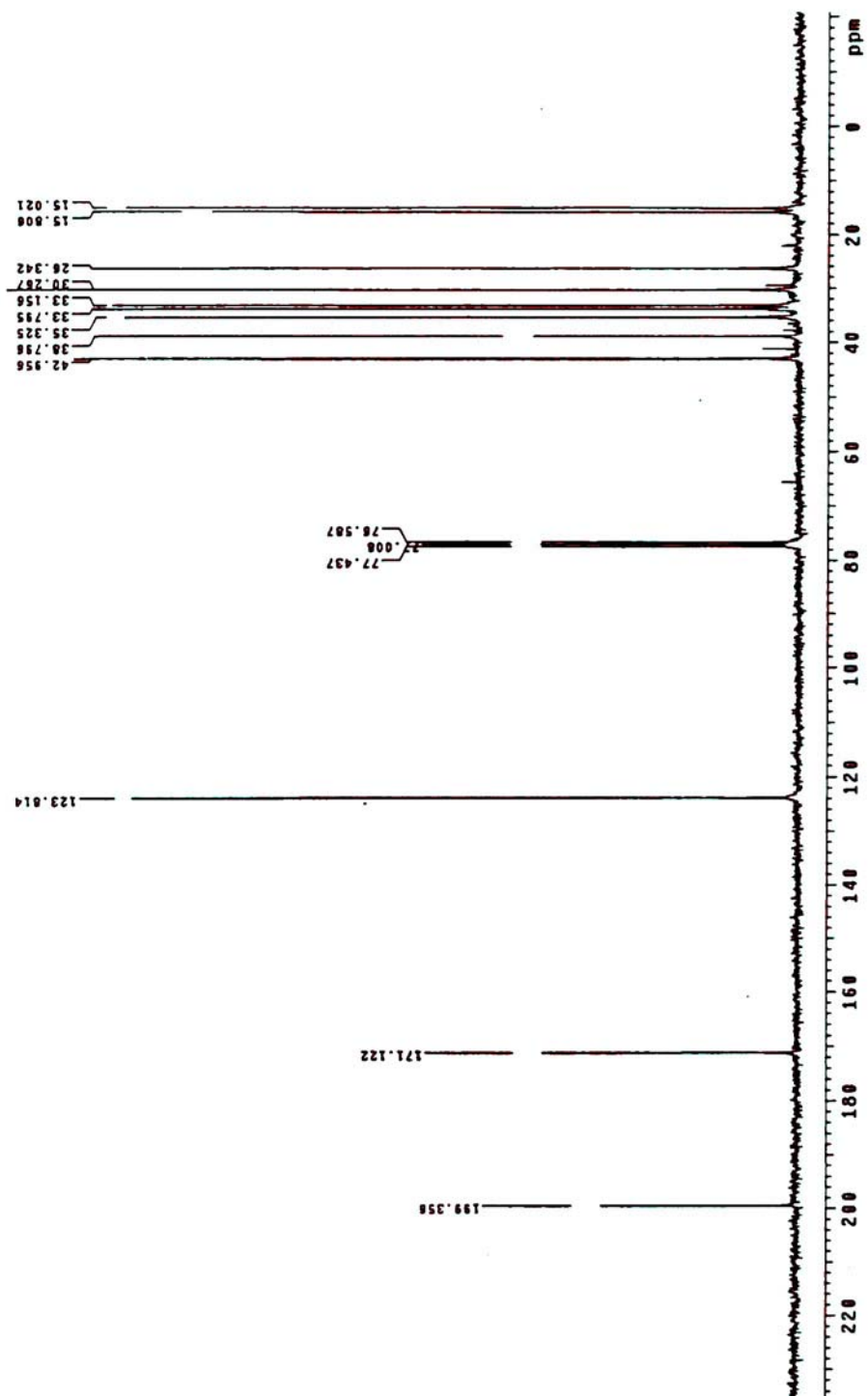
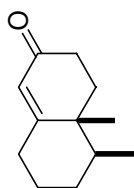


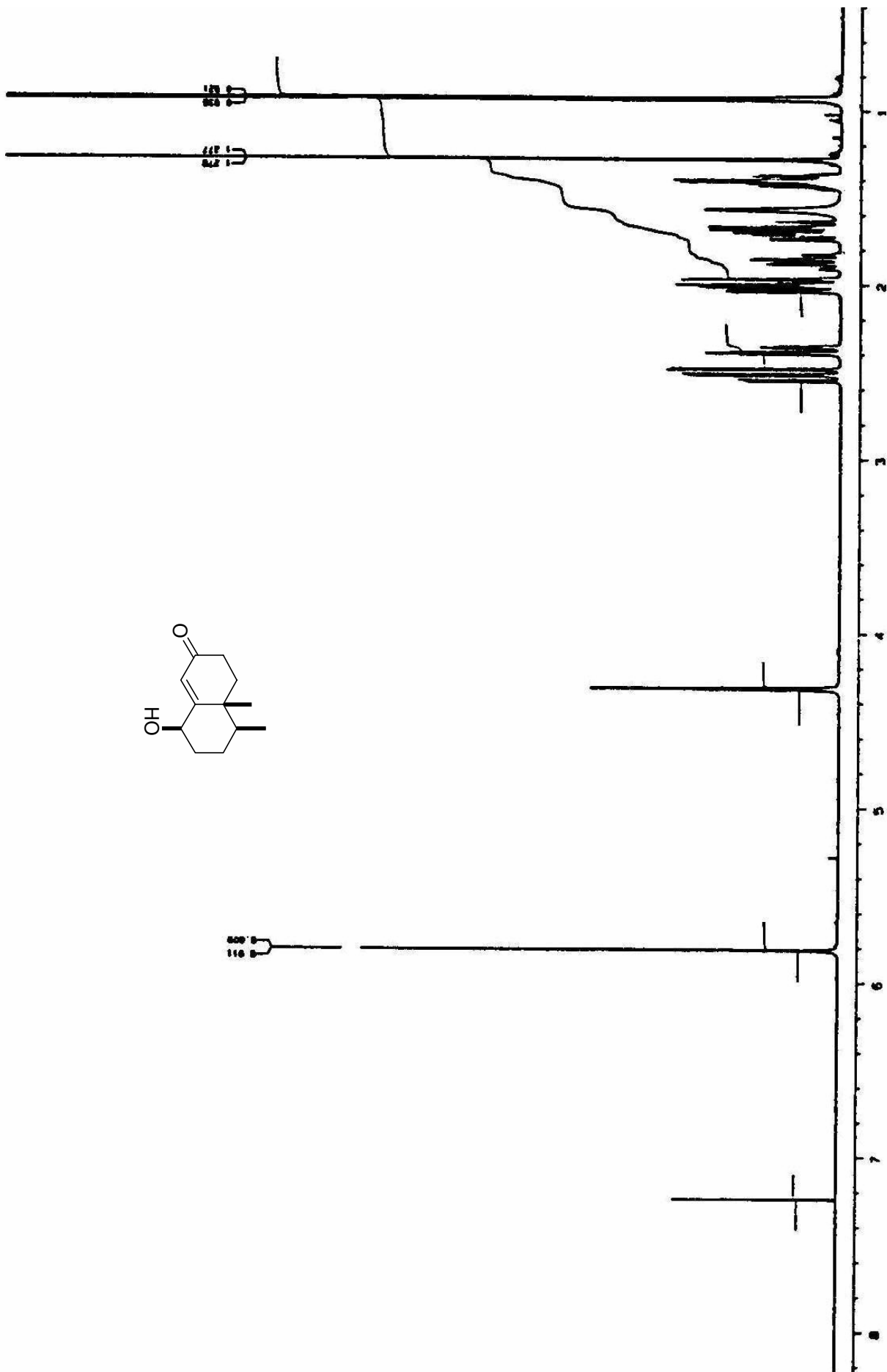


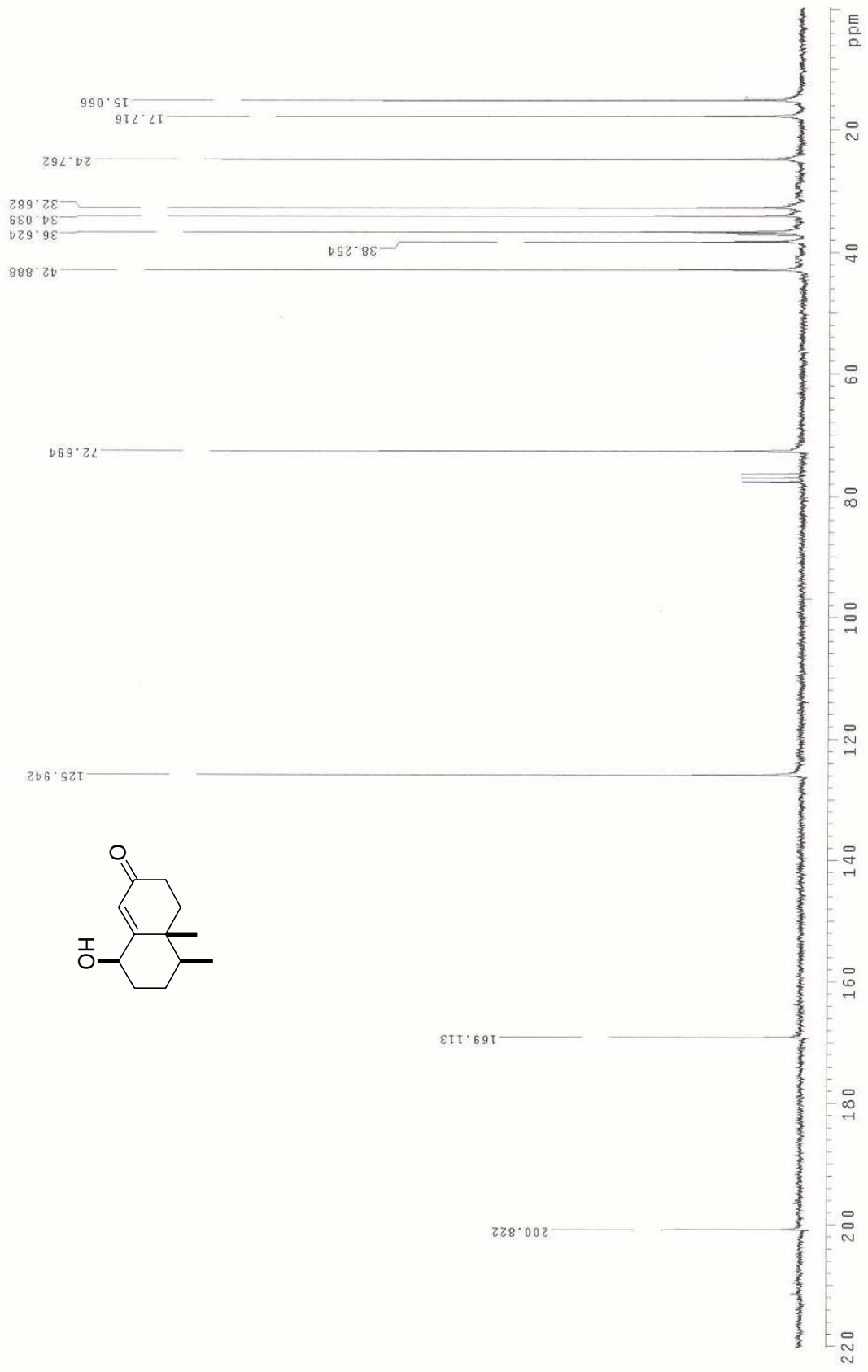


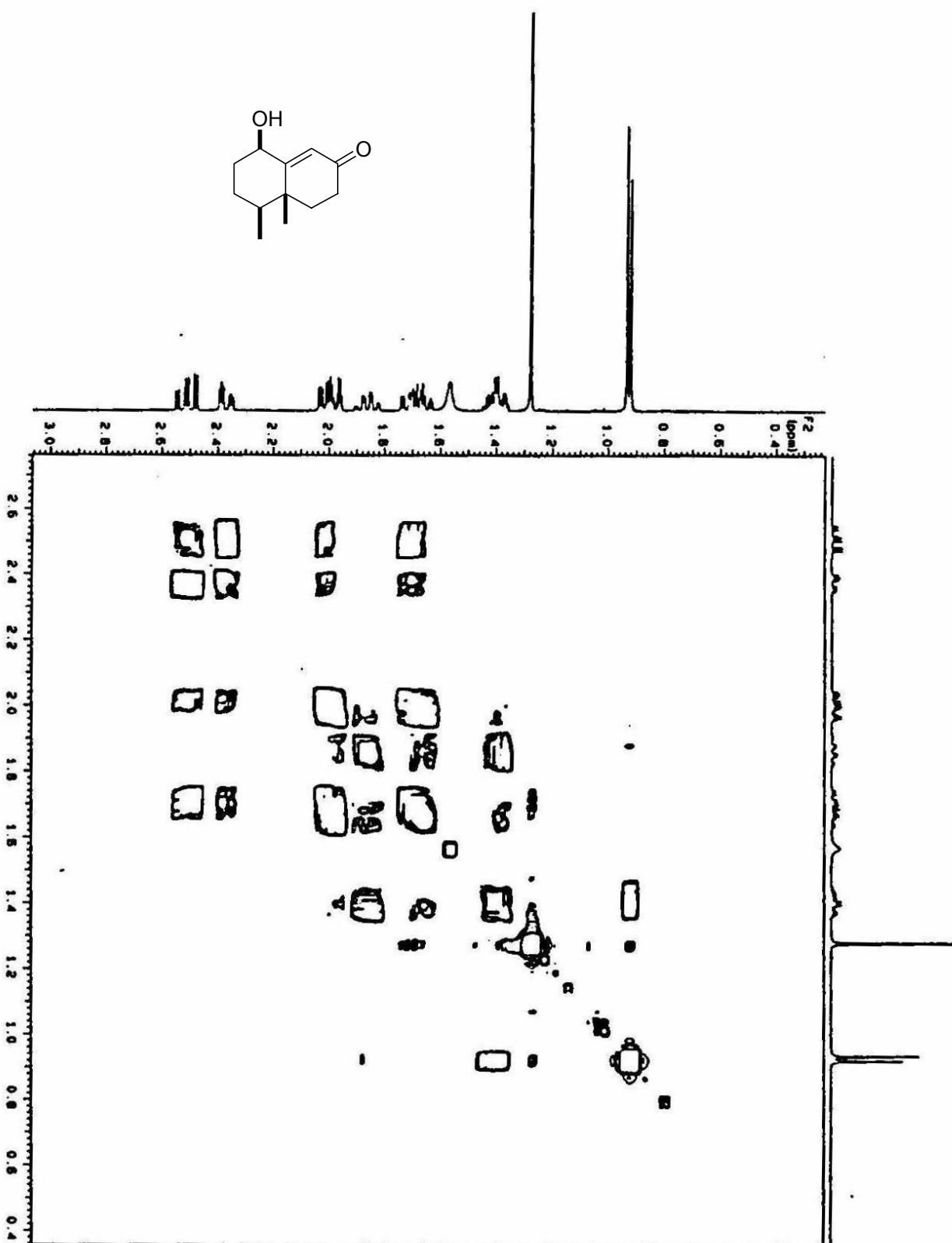


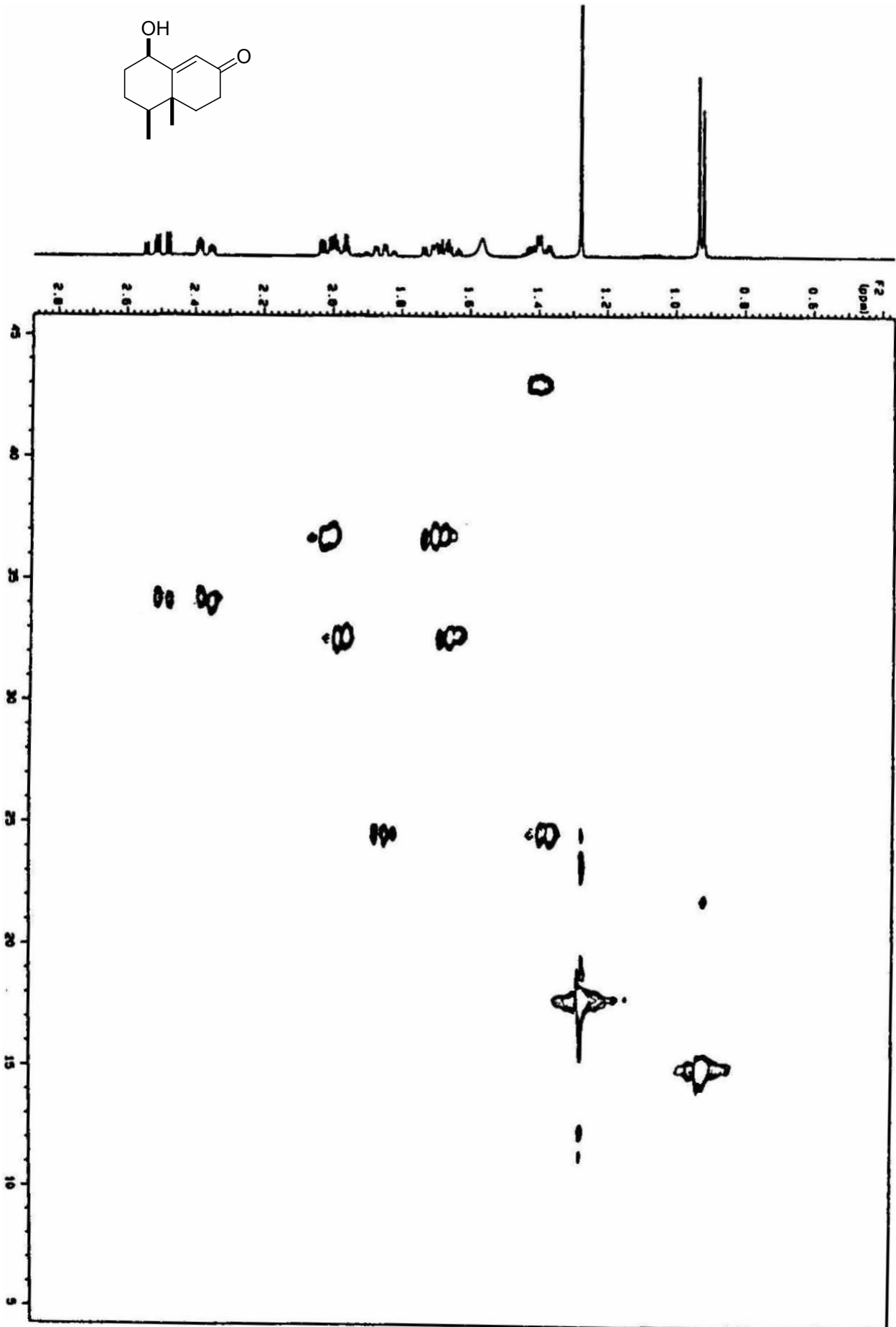
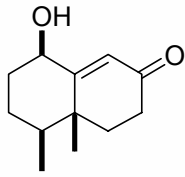


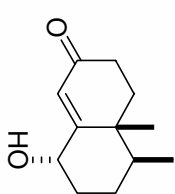




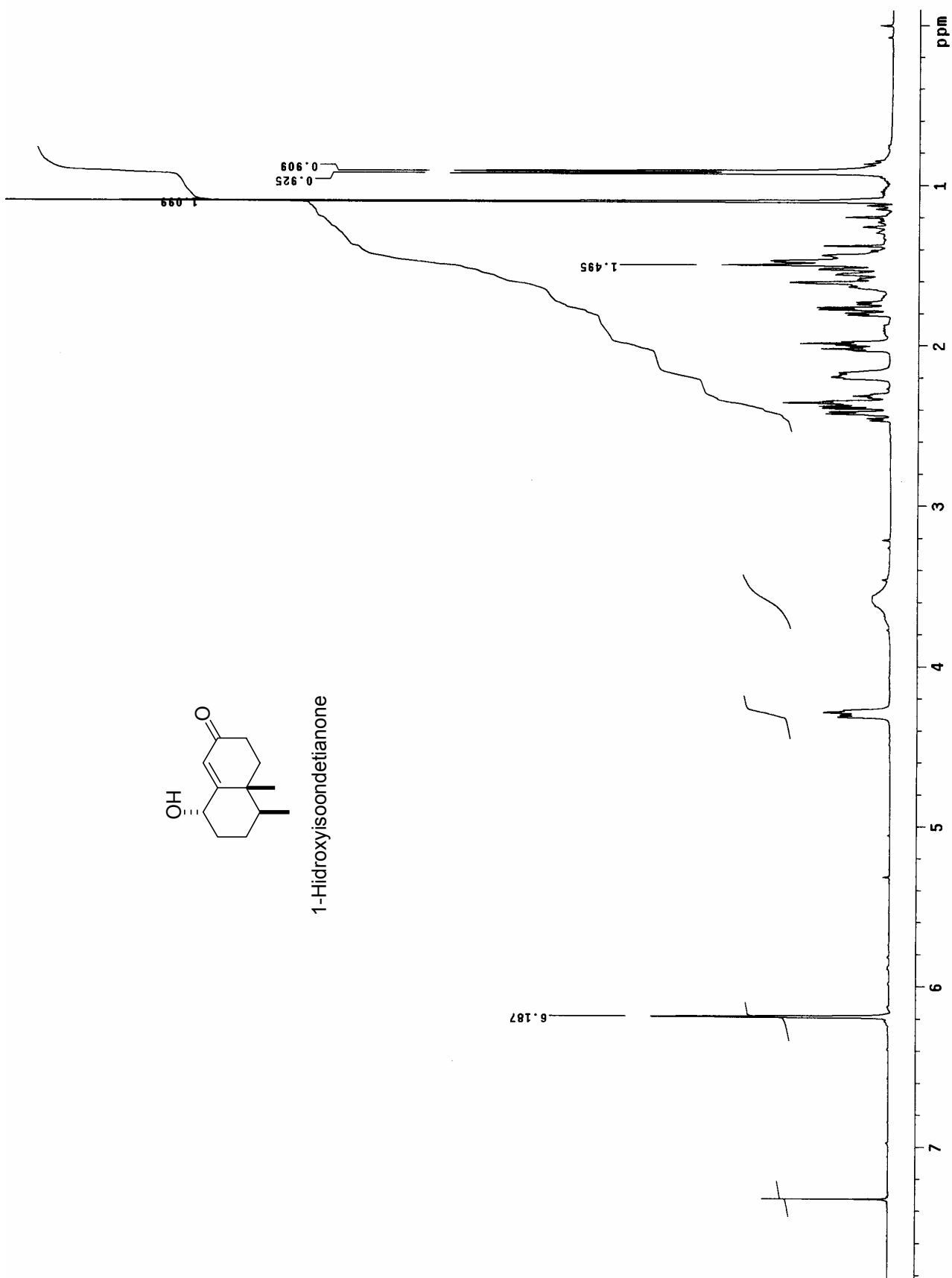


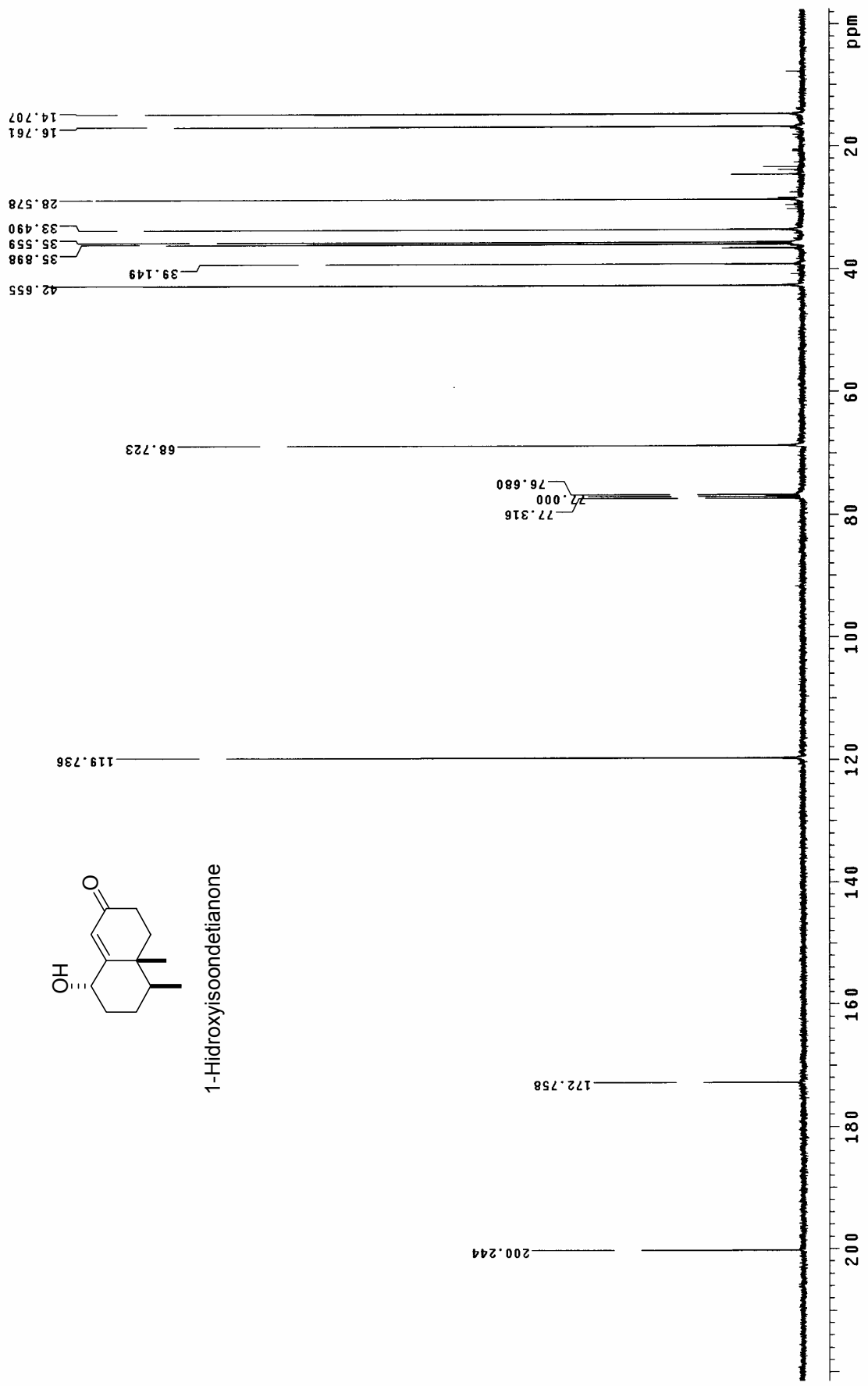


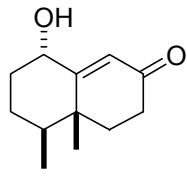




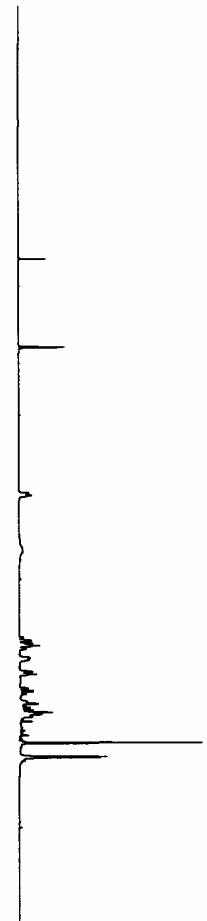
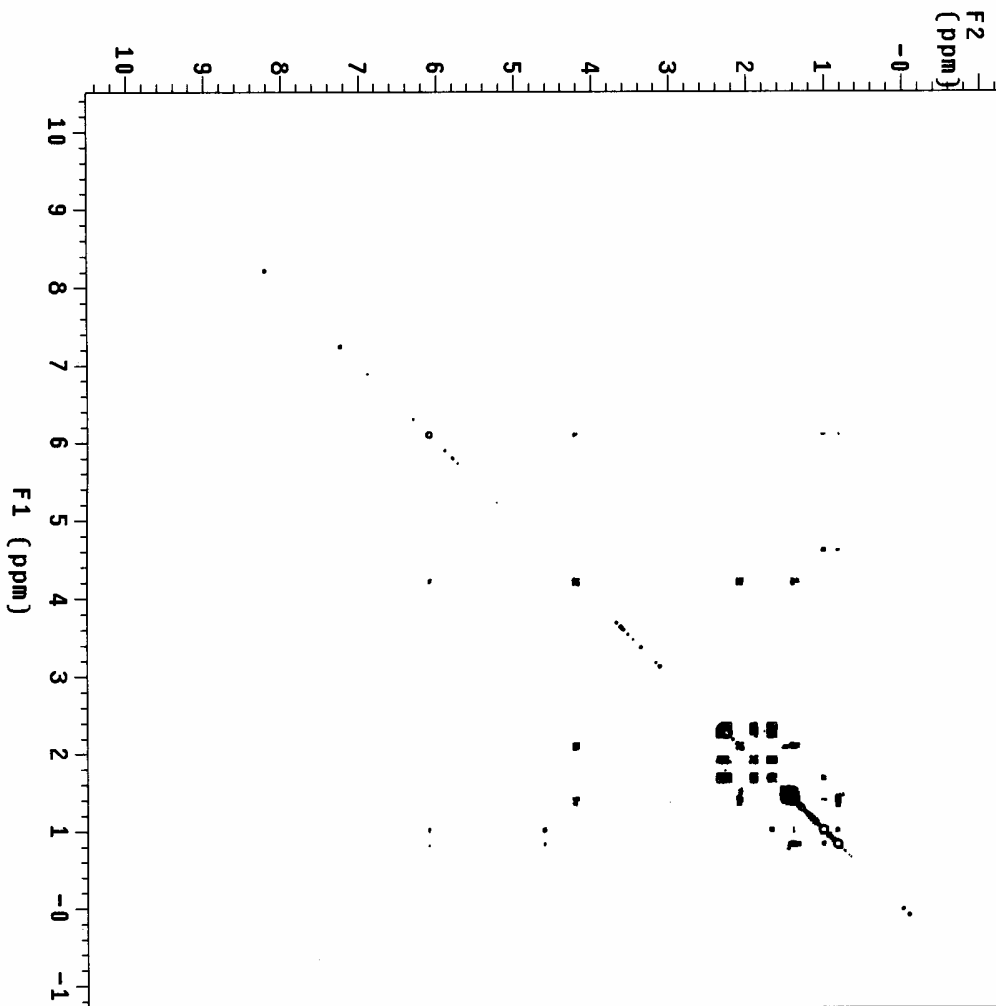
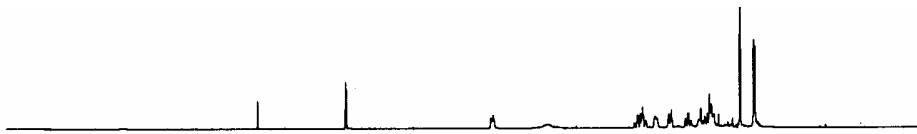
1-Hidroxyisondetianone

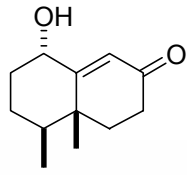






1-Hydroxyisoondetianone





1-Hydroxyisoondetianone

