REVISED 12/03/01

SUPPORTING INFORMATION

EXPERIMENTAL DETAILS

Although kynuramine dihydrobromide is available commercially, we favor the following preparation as a lower cost alternative for larger scale preparations:

To a degassed stirring biphase of EtOAc (200 mL) and 1 N NaOH (125 mL 125 mmol) was added tryptamine (20.0 g 125 mmol), followed by dropwise addition of methyl chloroformate (1.05 eq. 131 mmol 10.1 mL) at 25 °C. After stirring 30 minutes at 25 °C under N_2, the organics were separated, dried with sodium sulfate, and evaporated under reduced pressure. The resulting thick yellow oil was flashed through a short plug of silica (1:2 hexanes/EtOAc) onto a flask of hexanes where the methyl carbamate[1] precipitated as an off white microcrystalline solid (26.0 g 119 mmol 95%).

An AcOH solution (400 mL) of tryptamine methyl carbamate (10.0 g 46.0 mmol) was cooled in an ice bath while O_3 was bubbled through until the exotherm of the reaction was no longer sufficient to prevent the acetic acid from freezing (~30 minutes @ 90V 2.1 L/min). The solution was degassed with N_2 (5 min.), concentrated HCl (10 mL) was added, and the solvent was removed under reduced pressure. To the resulting crude orange semisolid was added CH_2Cl_2 (300 mL), followed by concentrated pH 7 phosphate buffer till neutral. The organics were separated, dried with sodium sulfate, and removed under reduced pressure to yield a yellow/orange solid. Silica gel chromatography (2:1 hexanes:EtOAc) followed by crystallization from the column solvent provided kynuramine methyl carbamate[2] as pretty yellow needles (7.50 g 32.0 mmol 70%) suitable for long term storage.

A solution of the methyl carbamate (750 mg 3.20 mmol) in HBr sat. AcOH (8 mL) was heated to 80 °C 12 h under N_2. The resulting brown solution was cooled to 25 °C, THF (25 mL) was added, and the resulting suspension was filtered under N_2 to provide kynuramine dihydrobromide as a white powder (2.70 mmol 887 mg 85%).

1. Somei, M.; Yamada, F.; Morikawa, H. *Heterocycles* **1997**, *46*, 91-94.
2. Nakagawa, M.; Maruyama, T.; Hirakoso, K.; Kato, S.; Hino, T. *Heterocycles* **1981**, *16*, 172.

SUPPORTING INFORMATION

EXPERIMENTAL DETAILS

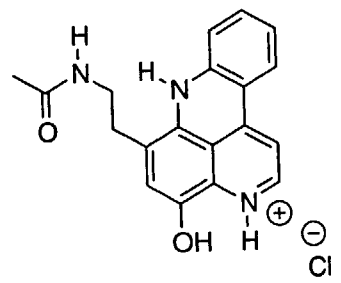
Styelsamine B

To a solution of N-acetyl dopamine (100 mg 0.51 mmol) in degassed 2:1 MeoH:AcOH (6 mL) was added kynuramine dihydrobromide (1.05 eq. 0.54 mmol 175 mg) followed by $CeCl_3$ (15 mol% 0.08 mmol 28.5 mg). To the rapidly stirring yellow solution under N_2 was added Ag_2O (2.0 eq. 1.02 mmol 236 mg) and the suspension was warmed to 40 °C for 1.5 h. The red/violet solution was filtered through Celite to remove the insoluble silver metal formed and added dropwise to stirring 6N HCl (15 mL) at 90 °C. After 30 min the purple suspension was cooled to rt and filtered under N_2 to provide styelsamine B as a purple solid (64 mg 0.18 mmol 35%).

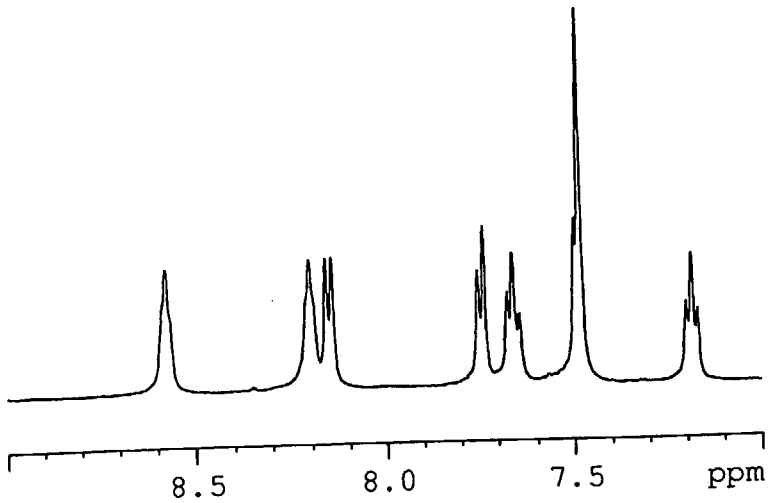
Cystodytin J

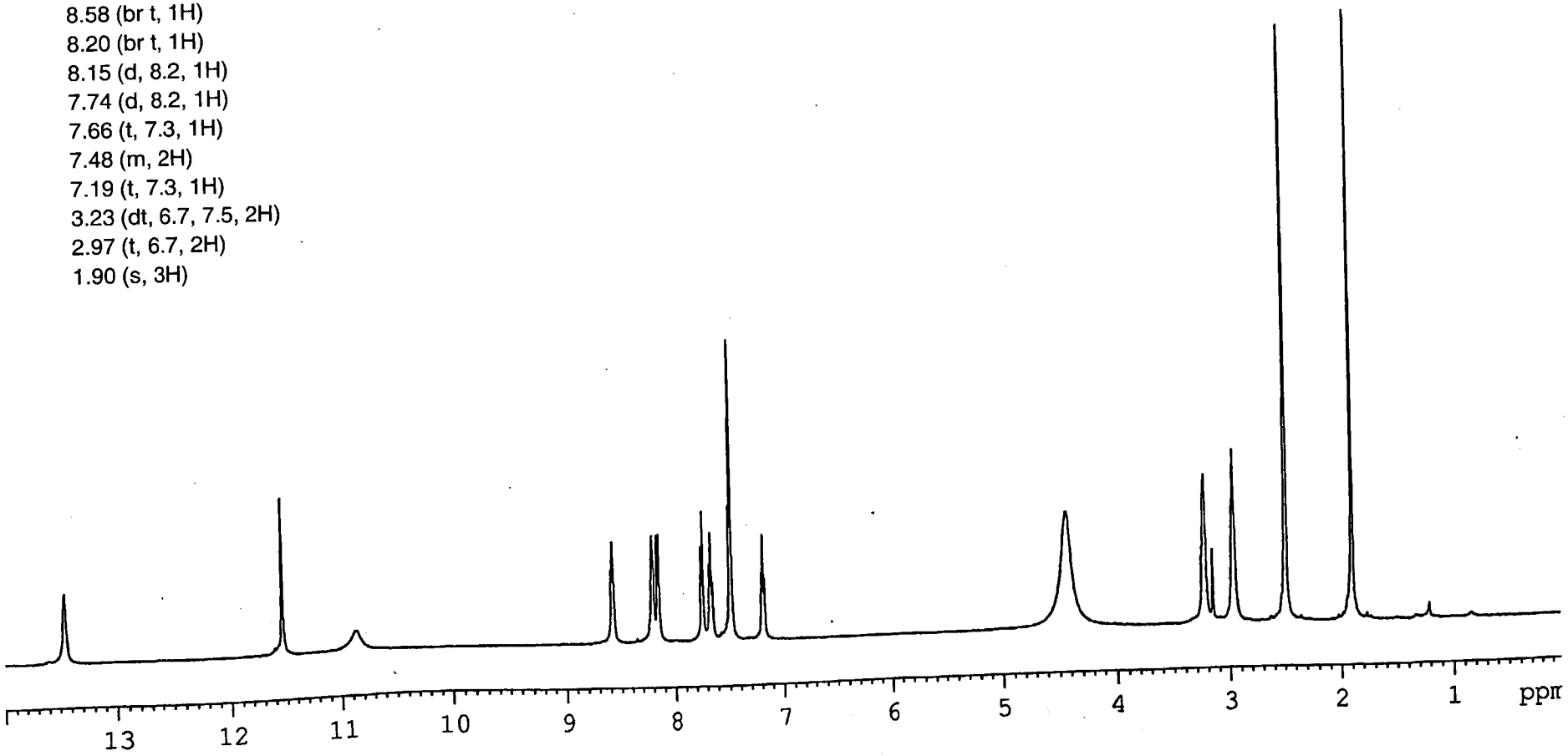
To a rapidly stirring solution of styelsamine B (30.0 mg 0.08 mmol) in MeOH (2 mL) at 25 °C was added Ag_2O (1.0 eq 0.08 mmol 19.5 mg) followed by sat. $NaHCO_3$ dropwise until the purple color of the starting material was no longer evident. The orange solution was filtered through Celite, H_2O (1 mL) and EtOAc (5 mL) were added, the organics were separated and solvent was evaporated to provide crude cystodytin J as a dirty yellow solid (18 mg 0.06 mmol 68%).

DS6-15 DRX500 d6 dmso



Styelsamine B
^{1}H NMR (500 MHz)
13.46 (br s, 1H)
11.54 (br s, 1H)
10.87 (br s, 1H)
8.58 (br t, 1H)
8.20 (br t, 1H)
8.15 (d, 8.2, 1H)
7.74 (d, 8.2, 1H)
7.66 (t, 7.3, 1H)
7.48 (m, 2H)
7.19 (t, 7.3, 1H)
3.23 (dt, 6.7, 7.5, 2H)
2.97 (t, 6.7, 2H)
1.90 (s, 3H)



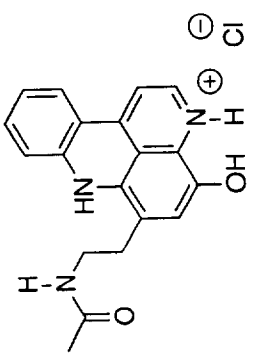


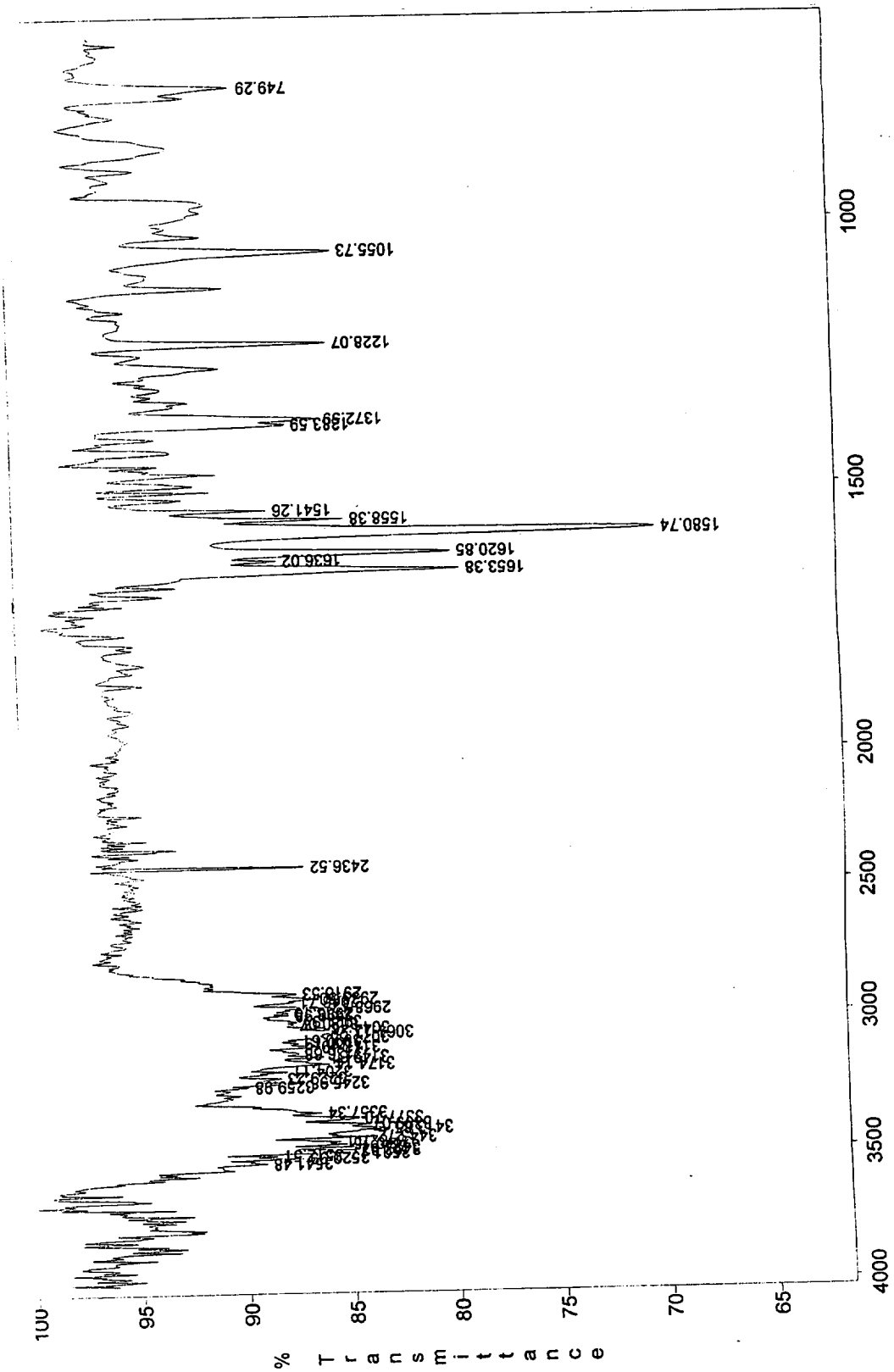
Stylsamine B

M.P. 276.2-277.5

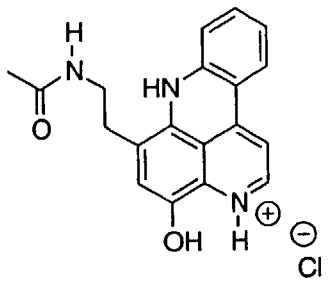
CHN Analysis:
Calcd. for C19H18N3O2Cl:
C, 64.14; H, 5.10; N, 11.81
Found:
C, 63.92; H, 5.17; N, 11.60

IR (KBr) cm^{-1}:
3443
3061
1653
1621
1581
1373
1228
1056





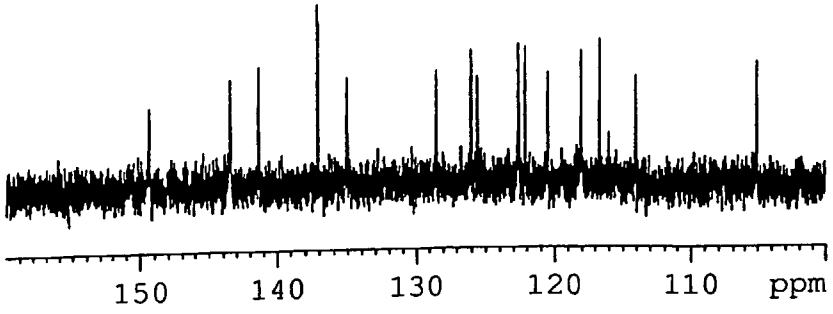
DS6-15 DRX500 d6 dmso

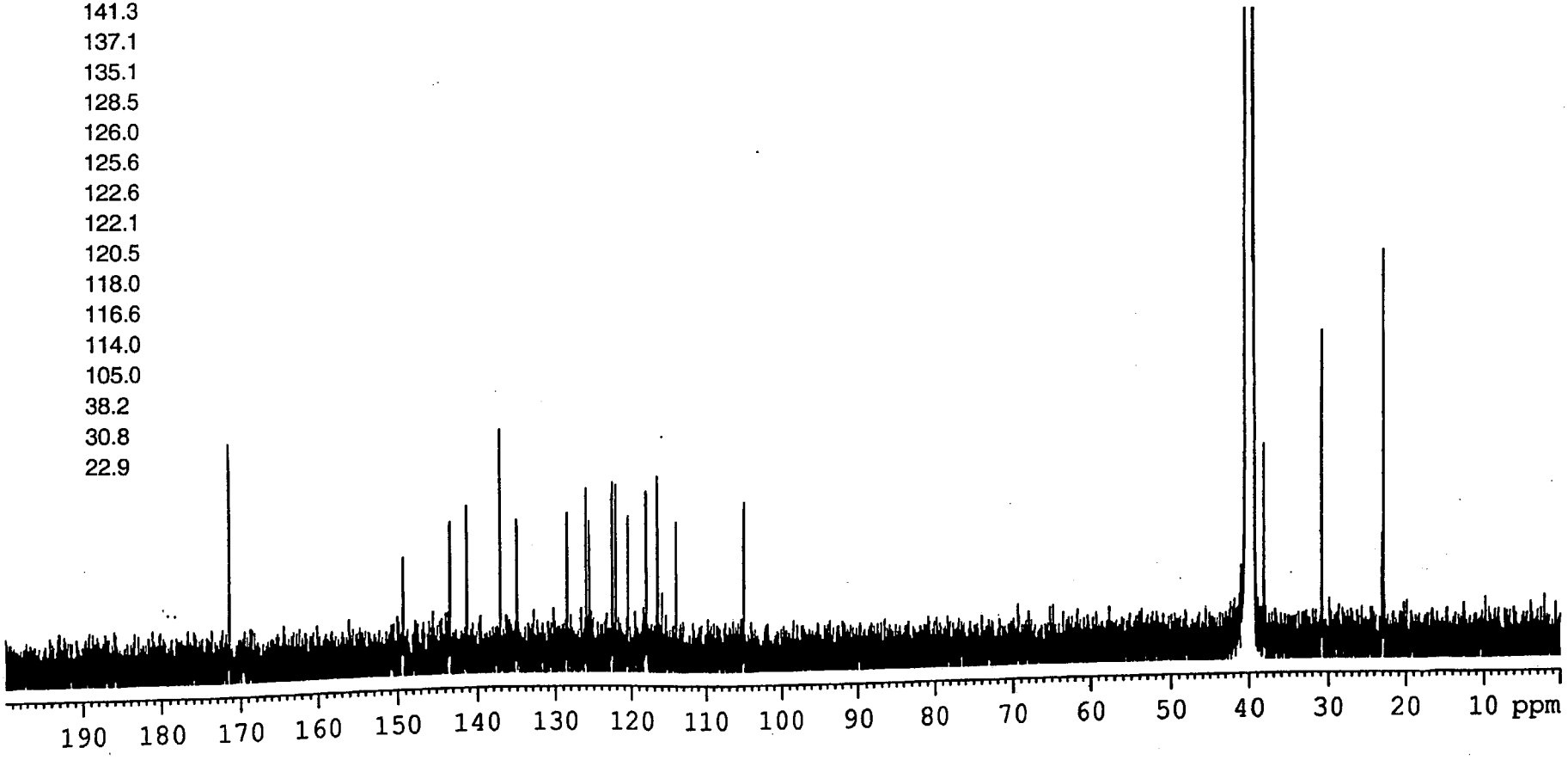


Styelsamine B

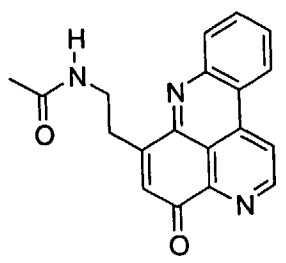
^{13}C NMR (125 MHz)

171.4
149.3
143.4
141.3
137.1
135.1
128.5
126.0
125.6
122.6
122.1
120.5
118.0
116.6
114.0
105.0
38.2
30.8
22.9

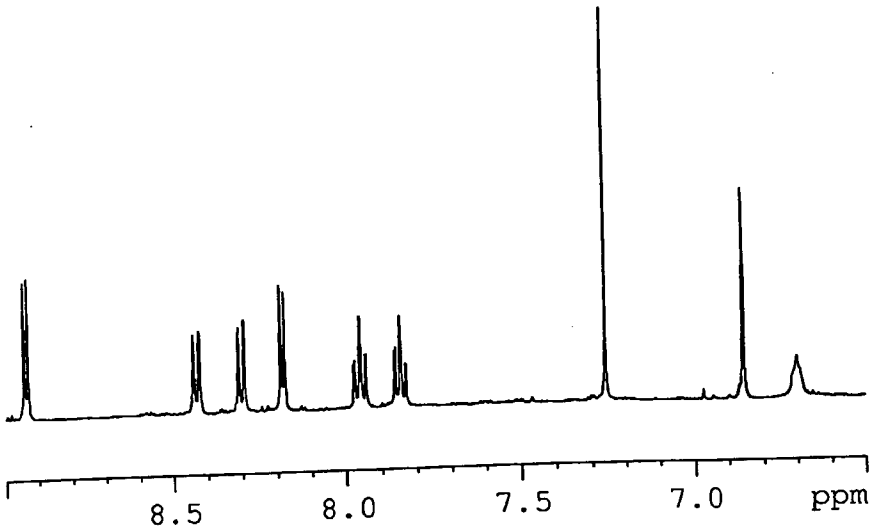


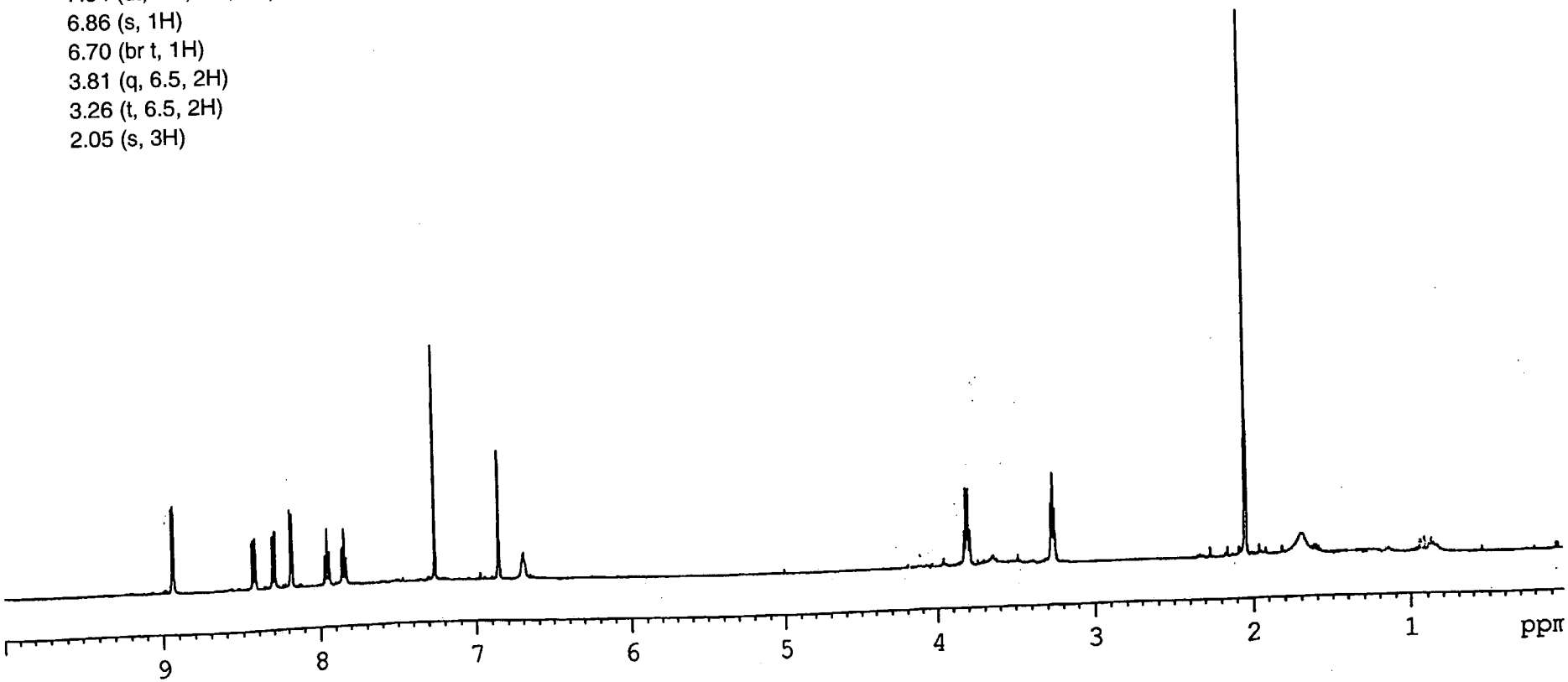


DS6-21 CYSTODYTIN J DRX500 cdcl3



Cystodytin J
^{1}H NMR (500 MHz)
8.94 (d, 5.5,1H)
8.43 (d, 7.5,1H)
8.30 (d, 8.1, 1H)
8.18 (d, 5.5, 1H)
7.96 (dt, 7.0, 1.3,1H)
7.84 (dt, 7.0, 1.3, 1H)
6.86 (s, 1H)
6.70 (br t, 1H)
3.81 (q, 6.5, 2H)
3.26 (t, 6.5, 2H)
2.05 (s, 3H)



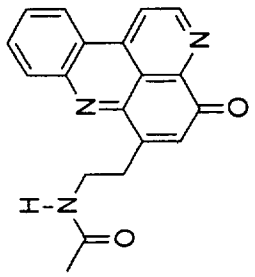


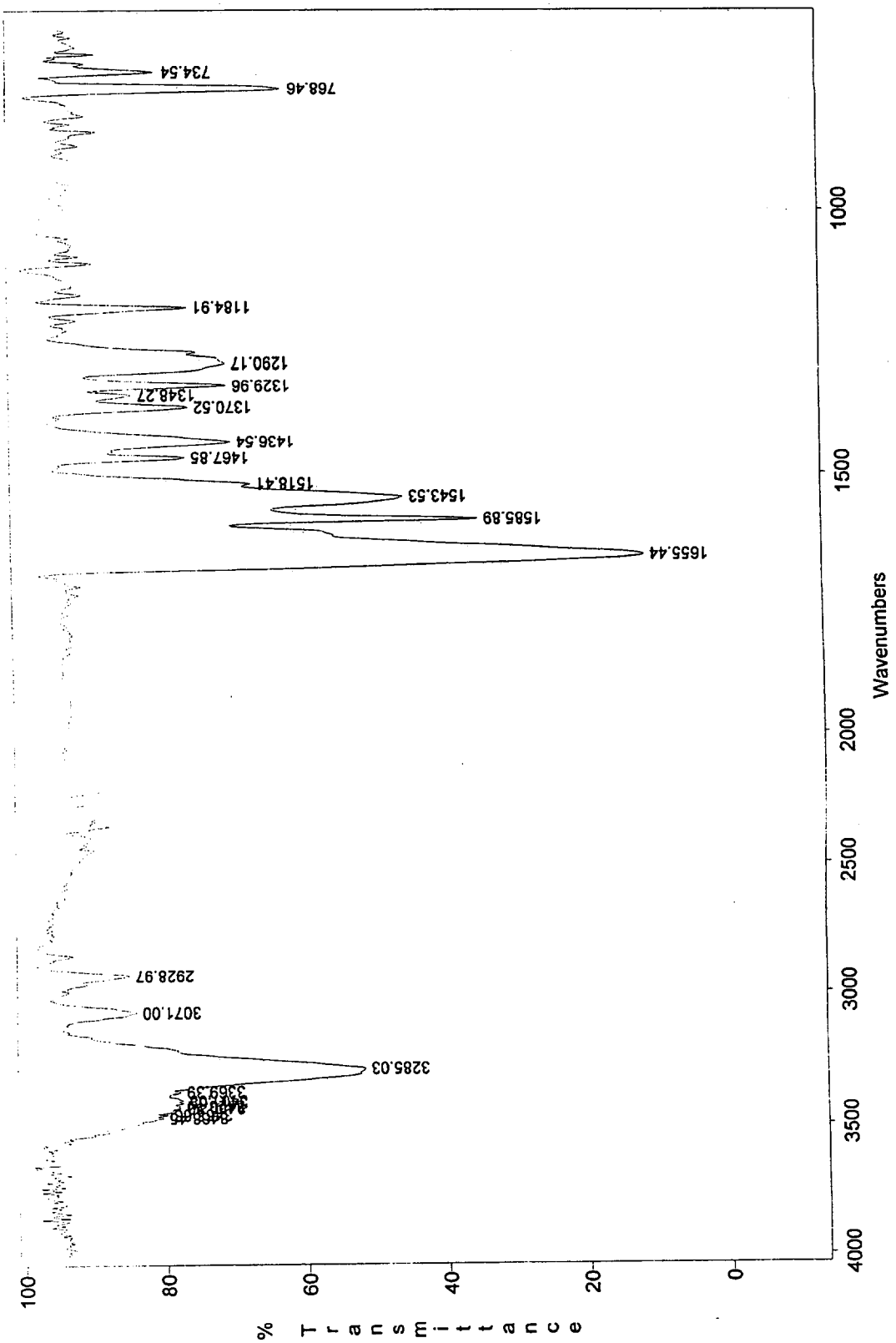
Cystodytin J

M.P. 195.8-196.9

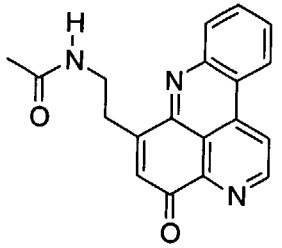
IR (KBr) cm^{-1}:

3285
3071
1655
1586
1544
1437
1330
1290





DS6-31 CYSTODYTIN J DRX500 CDC13



Cystodytin J
^{13}C NMR (125 MHz)

183.3
170.5
152.1
150.3
149.7
146.4
145.3
136.9
132.8
131.8
129.8
122.8
121.7
119.0
117.8
39.2
31.7
23.2