CHAPTER - V

ATTEMPTS TOWARDS THE SYNTHESIS OF SPIROHOMOPENTAPRISMANE

V.1 Abstract

In this chapter an approach towards synthesis of spiro-homopentaprismane (8) from readily available spirocyclic diones (1 & 2) is described. The strategy is schematically presented in Scheme-V.1. The spiro cage diones (1 & 2) on zinc reduction gave polycyclic diones (9 & 10) respectively. The reduction of the dione 10 with Lithium Aluminium hydride furnished the key intermediate endo-endo diol (11) which was transformed into its dimesylate (12) by its treatment with methanesulphonyl chloride in pyiridine. However, the dimesylate (12) failed to undergo elimination to give 7 upon treatment with KO^{t}Bu in dimethyl sulphoxide.

V.2 Introduction

In the previous chapters of this thesis it has been demonstrated that spirocyclic diones 1 and 2 which are readily available from spirodine-benzoquinone Diels-Alder adducts,[1] can serve as useful precursors to a variety of interesting novel carbocyclic systems. The Ce(IV) ion oxidation and Schmidt fragmentation of the diones 1 & 2 described earlier (Chapter-III and IV) were mediated through carbenium intermediates and involved cyclobutyl ----> cyclopropylcarbinyl ----> homoallylic carbenium ion type rearrangements.

In this chapter, we wish to describe our brief attempts towards synthesis of spiroprismanes of type (8) from the spirocagediones (1 & 2).

Prismanes are a fascinating class of $(CH)_n$ polyhedranes, whose synthetic appeal has been sustained through the prediction and expectancy of novel structural characteristics and unusual chemical reactivity.[2-6] After the synthesis of triprismane[7] tetraprismane[8] and pentaprismane,[9] the attention has now shifted towards synthesis of higher prismanes.[10] The higher homologue, of pentaprismane, the homopentaprismane (5) was although first reported by Underwood and Ramamoorthy[11] from Cookson's dione (3), which was later found to be incorrect.[12] However, Eaton and his associates[13] reported the synthesis and also provided the unambiguous proof of the structure of homopentaprismane 5 and its precursor homohypostrophene (6) (Fig.V.1). The synthetic strategies and the efforts in the synthesis of some of the prismanes have been described earlier (Chapter-I). We became interested in the synthesis of novel spiroannulated pentaprismane (8) and its precursor 7 from readily available cage diones 1 & 2. Our efforts in this direction is described in the following sections.

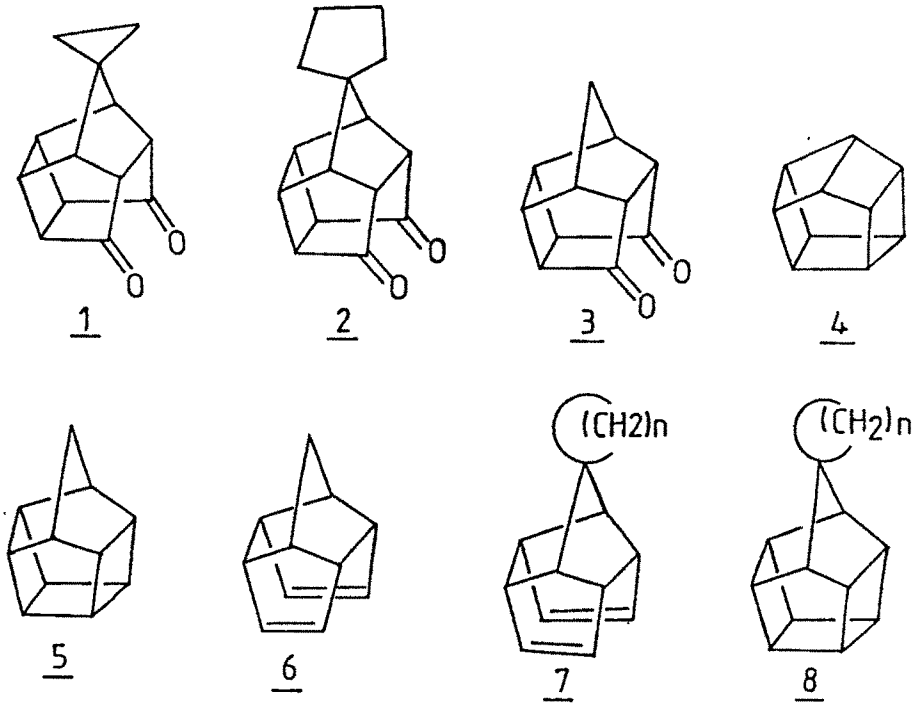
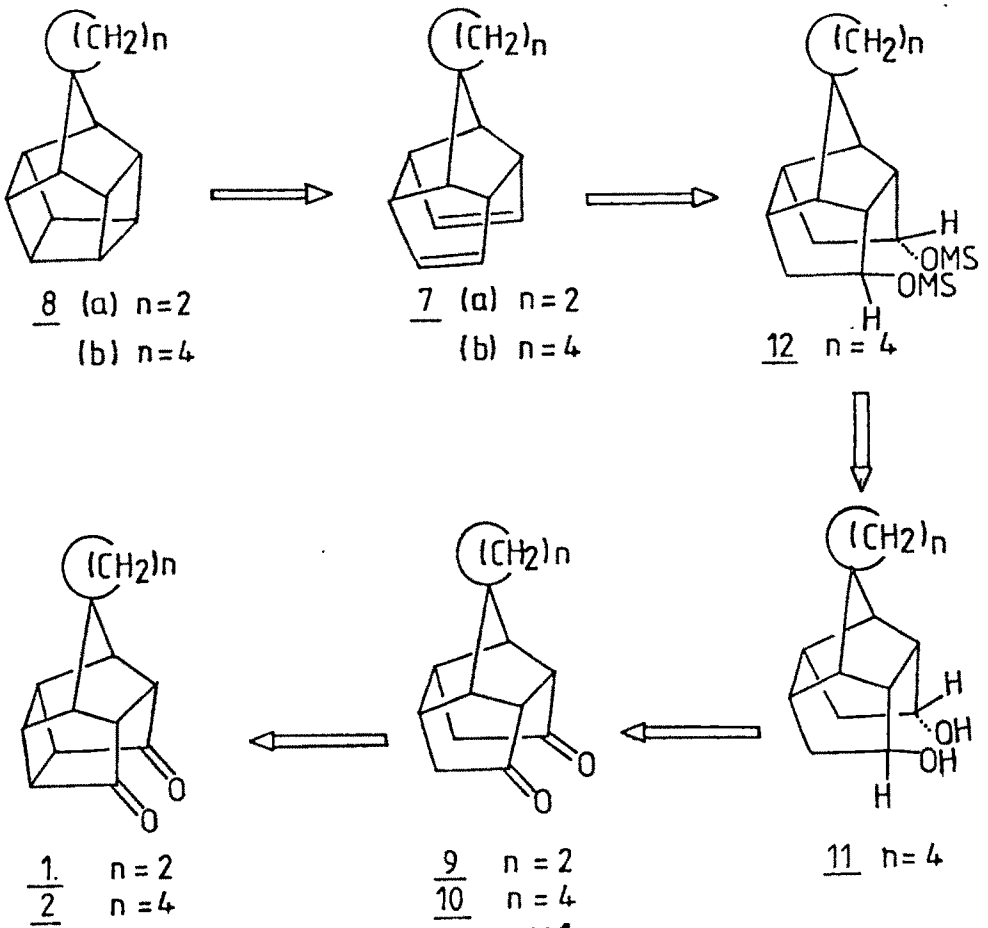


Fig. V.1

V.3 Strategy

Our approach for the synthesis of spirohomopentaprismanes in outlined, in retrosynthetic sense in the Scheme-V.1. It was thought that intramolecular $\pi^{2s} + \pi^{2s}$ cycloaddition of homohypostrophene analogue 7 would readily provide access to 8. It was further envisaged that bis elimination of the dimesylate (12) would be a reasonable process leading to the key intermediate spirohomohyostrophene 7. The dimesylate (12) was thought to be easily derived from the corres-



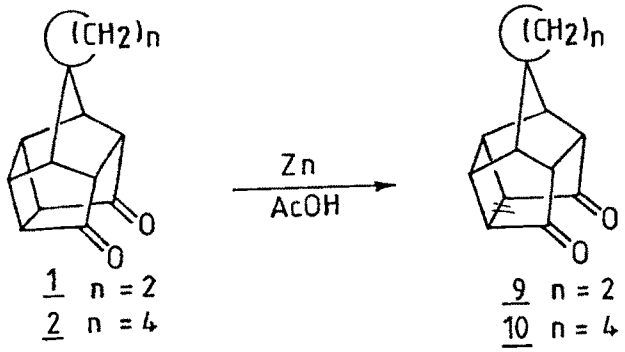
Scheme-V,1

ponding endo, endo diol (11) which inturn, could be obtained from the reduction of dione (10). The dione 10, having one less sigma bond than the parent spirodiones (1 & 2) was hoped to be easily prepared from the parent diones. Since it is known[14] that the strained cyclobutane σ bond of the parent system 3 undergoes a rapid reductive cleavage upon treatment with zinc in acidic medium, although this reductive cleavage of cyclobutane σ bond is quite susceptible

to structural changes from one polycyclic dione to another. In many cases this reduction has failed.[15] None the less, we set out to explore the above strategy, the results of which is described in the following section.

V.4 Results and Discussion

Towards realization of our strategy, we first treated the spirodiones 1 and 2 with excess zinc in acetic acid which fortunately, furnished the desired diones 9 and 10 in good yields (Scheme-V.2). That, the reductive cleavage



1 n = 2
2 n = 4

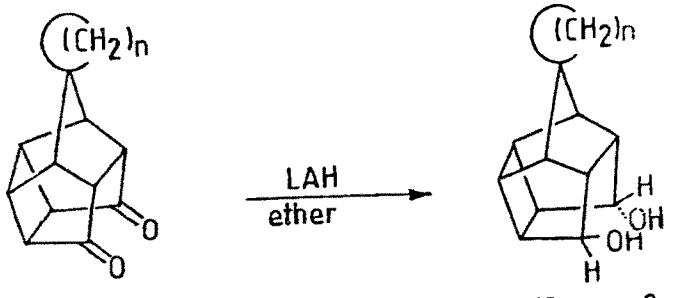
9 n = 2
10 n = 4

Scheme - V.2

of cyclobutane σ bond had occurred was ascertained from the proton nmr and ^{13}CNMR spectra of the resulting ketones (9 & 10). The IR spectrum (Fig. V.3) of 9 showed absorption bands at 2950, 1745, 1720 cm^{-1}. The highfield (300 MHz) proton nmr spectrum (Fig. V.4) displayed signals at δ 2.92 (br s, 4H), 2.28-2.17 (m, 6H) and 0.7 (m, 4H, cyclopropane CH_2). The ^{13}CMR spectrum (Fig. V.5) displayed signals at δ 203.16 (C=O), 59.17, 53.55, 40.12, 39.99, 31.45, 5.45

and 4.45 (cyclopropyl carbons). Similarly the dione 10 also showed IR absorption bands (Fig. V.6) at 2950, 1470 and 1725 cm^{-1} and displayed following signals in its pmr (300 MHz) spectrum (Fig. V.7) δ 2.86 (br s, 4H), 2.41 (br s, 2H), 2.72-2.22 (m, 4H) and 1.92-1.45 (m, 8H, spiroring methylenes). ^{13}CMR spectrum (Fig. V.8) of 10 gave the following signals at δ 203.36 (C=O), 58.76, 57.37, 56.19, 40.21, 38.59, 34.06, 32.44, 30.08, 25.70. These distinct spectral features clearly suggested the assigned structure.

After having the desired diones 9 and 10 in hand, we next turned our attention towards the preparation of endo, endo diol 11. However, before attempting the reduction of diones 9 and 10, we first studied the reduction of the parent cage diones (1 & 2) with lithium aluminium hydride. The treatment of the cage diones 1 & 2 with lithium aluminium hydride proceeded stereospecifically to give crystalline diols 13 and 14 respectively in good yields (Scheme V.3).

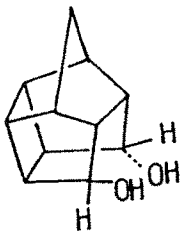


1 n=2
2 n=4

13 n=2
14 n=4

Scheme V.3

The structure and stereochemistry of the diols 13 and 14 were assigned on the basis their spectral and analytical data and also by comparison of their spectral features with that of the endo, endo diol 15 prepared by Dekker et al., [16] by LAH reduction of Cookson's dione (Fig. V.2).



15

Fig. V.2

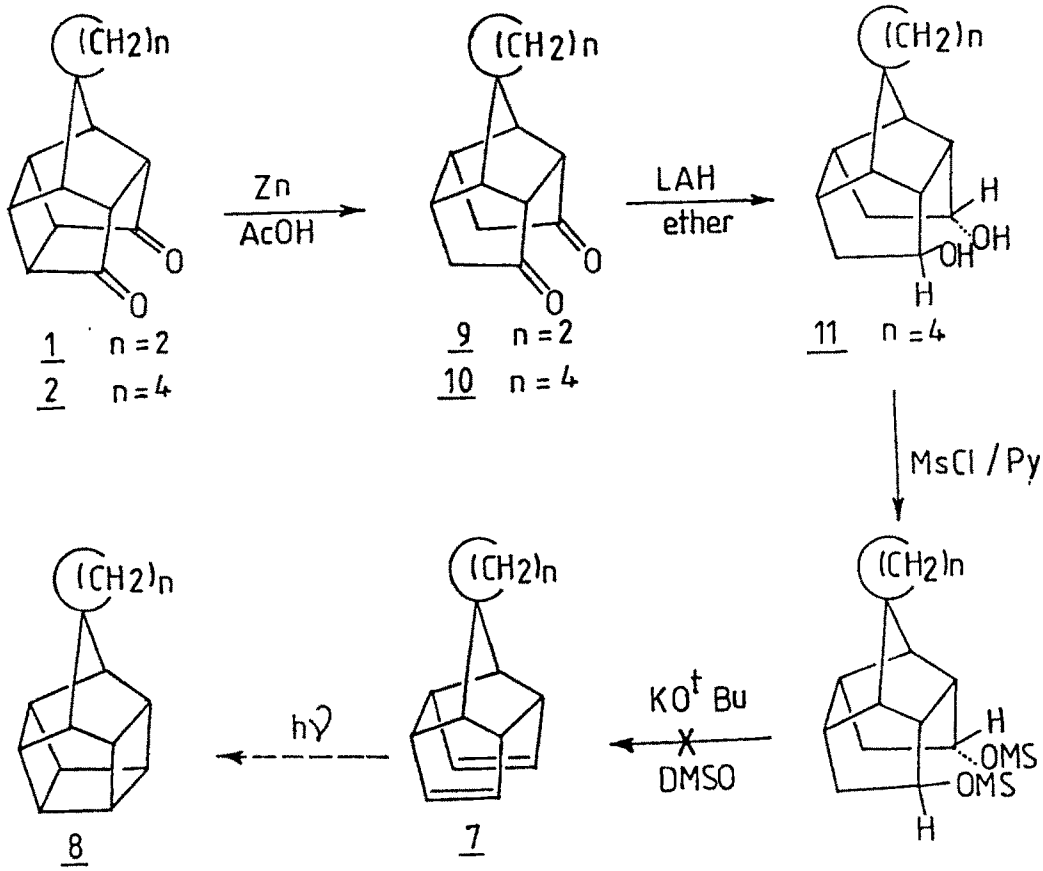
The IR spectrum (Fig. V.9) of 13 (m.p. 164°) showed characteristic absorption bands at 3200-3100 (indicating the presence of a strongly hydrogen bonded O-H group[17]), in addition to bands at 2950 and 1475 cm^{-1}. The proton nmr spectrum ($CDCl_3$, 300 MHz) (Fig. V.10) of 13 displayed signals at δ 6.25 (br, s, 2H, O-H), 3.8 (s, 2H, H-C-OH), 2.75 (d, J=12Hz, 4H, ring H), 2.62 (s, 2H, ring H), 1.65 (s, 2H) and 0.55 & 0.45 (m, 4H, cyclopropane CH_2). Similarly the diol 14 (m.p. 213°) showed followed spectral characteristics. Its IR spectrum (Fig. V.11) showed bands at 3150, 2950, 1510 and 1110 cm^{-1} and proton nmr spectrum (Fig. V.12) gave signals at δ 3.8 (br s, 2H, H-C-OH), 2.65 (br d, J=6Hz, 4H, ring H), 2.5 (m, 2H, ring H), 1.9(m, 2H) and 1.7-1.5 (m, 8H, spiro ring CH_2'S). These spectral features were found similar to that of the endo, endo diol 15.

After the studies on reduction of parent cage ketones 1 & 2, we treated the dione 10 with lithium aluminium hydride in dry ether which produced the crystallin diol 11 in excellent yield (86%). The structure and stereochemistry of the diol 11 was assigned on the basis of the spectral characteristics which was found similar to the endo, endo diol 14 and 15. The IR spectrum (Fig.V.13) of 11 showed characteristic absorption bands at 3150 (OH group) 2950 (C-H stretching), 1120 and 1075 cm^{-1}. The proton nmr spectrum (90 MHz, $CDCl_3$) (Fig. V.14) displayed following resonances at δ 6..40 (br s, 2H, O-H exchangeable with D_2O), 4.3 (br m, 2H, H-C-OH), 2.5 (br s, 2H), 2.25 (m, 4H), 1.85 (br s, 4H), 1.65 (br s, 8H, cyclopentane CH_2).

The spiro diol 11 was mesylated with methanesulphonyl chloride in pyridine which gave a dimesylate 12 in good yield (65%). The dimesylate showed absorption bands at 2950, 1335, 1325, 1180 and 1160 cm^{-1} (methane sulphonoxy group) in its IR spectrum (Fig. V.15). The proton nmr spectrum (90 MHz, $CDCl_3$) (Fig. V.16) gave signals at δ 5.0 (br s, 2H, H-C-OMs), 3.05 (s, 6H, -OMs), 2.65 (br m, 2H), 2.3 (br s, 4H), 1.9 (br s, 4H) and 1.55 (br s, 8H, spiroring methylenes). It was also analyzed correctly for $C_{17}H_{26}O_6S_2$.

However much to our disappointment, when we treated the dimesylate 12 with KO^tBu in dimethyl sulphoxide, it failed to

give the desired spirohomohypostrophene derivative (7). The overall sequence in outlined in the following Scheme-V.4.



1 n = 2
2 n = 4
9 n = 2
10 n = 4
11 n = 4
12 n = 4
7
8

Scheme-V. 4

While the inertness of 12 towards Ko^t Bu was beyond expectation, several reasons can be conceived. The mesyloxy groups lacks assistance from solvent probably because they are tightly hidden in the small space.

V.5 Experimental

General Remarks : Please refer Chapter-II, Section-5.

Reduction of pentacyclo [5.4.0.$0^{2,6}0^{3,10}0^{5,9}$] undecane-8,11-dione-4-spiro-1'-cyclopropane (1) with Zinc-AcOH.

The diketone (1) (1 g,0.005 mol) and zinc dust (2 g) were refluxed in glacial acetic acid (20-30 ml) at 120° for about 4 h (tlc). The reaction mixture was filtered over celite bed and the filtrate was poured into a saturated solution of $NaHCO_3$. It was extracted with ether (3 x 50 ml) and the combined extract was washed with water (2 x 20 ml), brine (2 x 15 ml) and dried over anhydrous sodium sulphate. Stripping off the solvent under reduced pressure gave a residue, which was chromatographed over silica gel. Elution with pet. ether - ethylacetate mixture (70:30) gave the reduced polycyclic dione (9) (0.76 g, 75%), m.p. 138-9°, UV λ_{max}^{MeOH} :204 nm, IR (KBr) ν_{max} : (Fig.V.3) : 2950, 1745, 1725 cm^{-1}. NMR ($CDCl_3$, 300 MHz) (Fig.V.4): δ 2.92 (s, 4H, methylenic H), 2.38-2.23 (m, 6H, ring H) and 0.84-0.56 (m, 4H, cyclopropane CH_2). ^{13}CNMR ($CDCl_3$) (Fig. V.5): δ 203.16 (C=O) 59.77, 53.55, 40.12, 39.95, 30.45, 5.45 and 4.43. Analysis : Found C, 77.30 ; H, 7.35% requires C, 77.22 ; H, 6.93% for $C_{13}H_{14}O_2$.

Reduction of pentacyclo [5.4.0.$0^{2,6}0^{3,10}0^{5,9}$] undecane-8,11-dione-4-spiro-1'-cyclopentane (2) with Zinc-AcOH

The diketone (2) (1 g, 0.0044 mol) and zinc dust (3 g)

were refluxed in glacial acetic acid (20-25 ml) at 120° for about 4-5 h (tlc). The reaction mixture was filtered over celite bed and the filtrated was poured into a saturated solution of $NaHCO_3$. It was extracted with ether (3 x 50 ml) and the combined extract was washed with water (2 x 20 ml), brine (2 x 15 ml) and dried over anhydrous sodium sulphate. Removal of solvent under reduced pressure gave the residue, which was chromatographed over silica gel. Elution with pet. ether - ethylacetate mixture (70:30) furnished the reduced polycyclic dione (10) (0.8 g, 79%). m.p. 165°, UV λ_{max}^{MeOH} : 206 nm, IR (KBr) ν_{max} (Fig.V.6) : 2950, 1740, 1725 cm^{-1}. NMR ($CDCl_3$, 300 MHz) (Fig.V.7) : δ 2.86 (s, 4H, methylenic H), 2.41 (s, 2H, ring H), 2.27-2.22 (m, 4H, ring H) and 1.92-1.45 (m, 8H, cyclopentane CH_2). ^{13}CNMR ($CDCl_3$) (Fig. V.8) : δ 203.36 (C=O), 58.76, 57.37, 56.19, 40.21, 38.59, 34.06, 32.44, 30.08, 25.70. Analysis : Found C, 78.57 ; H, 7.44% requires C, 78.26 ; 7.83% for $C_{15}H_{18}O_2$.

LAH reduction of pentacyclo [5.4.0.$0^{2,6}$.$0^{3,10}$.$0^{5,9}$] undecane-8,11-dione-4-spiro-1'-cyclopropane (1)

To a slurry of LAH (1 g) in dry ether (75 ml) was added a solution of 1 (0.5 g, 0.002 mol) in dry ether dropwise at 0° and further stirred at 0° for 1 h, followed by reflux for 5 h. It was worked up carefully by adding 30% H_2SO_4 to destroy the excess LAH and extracted with ether (3 x 50 ml). The combined etheral layer was washed with water (2 x 15 ml), brine (2 x 10 ml) and dried over anhydrous sodium

sulphate. Stripping off the solvent gave the residue, which was chromatographed over silica gel to furnish the endo-endo diol (13) (0.4 g, 80%), m.p. 164°, UV λ_{max}^{MeOH} : 204 nm, IR (KBr) ν_{max} (Fig. V.9) 3100 (OH group), 2950 (C-H stretching) and 1475 cm^{-1}. NMR ($CDCl_3$, 300 MHz) (Fig. V.10) : δ 6.25 (br s, 2H, OH), 3.8 (s, 2H, H-C-OH), 2.75 (d, J=12Hz, 4H, ring H), 2.62 (s, 2H, ring H), 1.65 (s, 2H, ring H) and 0.55& 0.45 (m, 4H, cyclopropane CH_2). Analysis : Found C, 76.00 ; H, 7.87% requires C, 76.47 ; H, 7.84% for $C_{13}H_{16}O_2$.

LAH reduction of pentacyclo [5.4.0.$O^{2,6}O^{3,10}O^{5,9}$] undecane-8,11-dione-4-spiro-1'-cyclopentane (2)

To a slurry of LAH (1 g) in dry ether (75 ml) was added a solution of 2 (0.5 g, 0.0022 mol) in dry ether dropwise at 0° and after stirring or 1 h at 0°, it was refluxed for 5 h. It was worked up carefully by adding 30% H_2SO_4 to destroy the excess LAH and extracted with ether (3 x 50 ml). The combined organic layer was washed with water (2 x 15 ml), brine (2 x 10 ml) and dried over anhydrous sodium sulphate. Removal of solvent under reduced pressure gave the residue, which was chromatographed over silica gel. Elution with pet. ether - ethylacetate mixture (50:50) gave the endo-endo diol (14) (0.38 g, 75%), m.p. 213°, UV λ_{max}^{MeOH} : 203 nm, IR (KBR) ν_{max} (Fig. V.11) : 3150 (hydroxyl group), 2950, 1510, 1110 cm^{-1}. NMR ($CDCl_3$, 90 MHz) (Fig. V.12) : δ 3.8 (br s, 2H, H-C-OH), 2.65 (br d, 4H, ring H), 2.5 (br m, 2H, ring

H), 1.9 (br m, 2H) and 1.7-1.5 (br m, 8H, cyclopentane CH_2). Analysis : Found C, 76.35 ; H, 8.76% requires C, 77.58 ; H, 8.62% for $C_{15}H_{20}O_2$.

LAH reduction of reduced polycyclic dione (10)

To a slurry of LAH (2 g) in dry ether (100 ml) was added a solution of 10 (1 g, 4.3 m mol) in dry ether dropwise at 0° and the reaction mixture was stirred at 0° for 1 h followed by reflux for 4 h (tlc). It was worked-up as described earlier, which furnished the cage diol (11) (0.88 g, 86%), m.p. 136°, UV λ_{max}^{MeOH} : 203 nm ; IR (KBr) ν_{max} (Fig.V.13) 3150 (OH group), 2950, 1120 and 1075 cm^{-1}. NMR ($CDCl_3$, 90 MHz) (Fig. V.14) : δ 6.40 (br s, 2H, OH), 4.3 (br m, 2H, H-C-OH), 2.5 (br s, 2H), 2.25 (br m, 4H, ring H), 1.85 (br s, 4H) and 1.65 (br s, 8H, cyclopentane CH_2). Analysis : Found C, 77.27; H, 9.55% requires C, 76.92 ; H, 9.40% for $C_{15}H_{22}O_2$.

Conversion of diol (11) in to its dimesylate (12)

Methanesulphonyl chloride (2 ml) was added to a solution of diol (11) (0.5 g, 2.14 m mol) in dry benzene (20 ml) and dry pyridine (2 ml) at 0° with stirring. The reaction mixture was continued stirring for further 1 h (tlc) and then diluted with ice cold water, neutralize it with saturated $NaHCO_3$ solution, extract it with ether (3 x 50 ml). The combined etheral layer was washed with water (2 x 15 ml), brine (2 x 10 ml) and dried over anhydrous sodium sul-

phate. Solvent was stripped off and the residue was chromatographed over silica gel to furnish the dimesylate (12) (0.54 g, 65%), m.p. 122°, UV λ_{max}^{MeOH} : 206 nm ; IR (KBr) ν_{max} (Fig. V.15) : 2950, 1355, 1325, 1180 and 1160 cm^{-1}. NMR ($CDCl_3$, 90 MHz) (Fig. V.16) δ 5.0 (br, with fine structure 2H, H-C-OMs), 3.05 (s, 6H, OMs), 2.65 (br m, 2H), 2.3 (br s, 4H, ring H), 1.9 (br s, 4H) and 1.55 (br s, 8H, cyclopentane CH_2). Analysis : Found C, 52.71 ; H, 7.05% requires C, 52.30 ; H, 6.67% for $C_{17}H_{26}O_6S_2$.

Attempted reaction of dimesylate (12) with KO^tBu in DMSO

Potassium tertiary butoxide (1.0 g) was added to a solution of dimesylate (12) (0.5 g, 2.16 m mol) in dry dimethyl sulphoxide (20 ml). The reaction mixture was stirred at 0° and further stirring at room temperature for 6 h (tlc). No reaction was observed (tlc) either in cold or at room temperature.

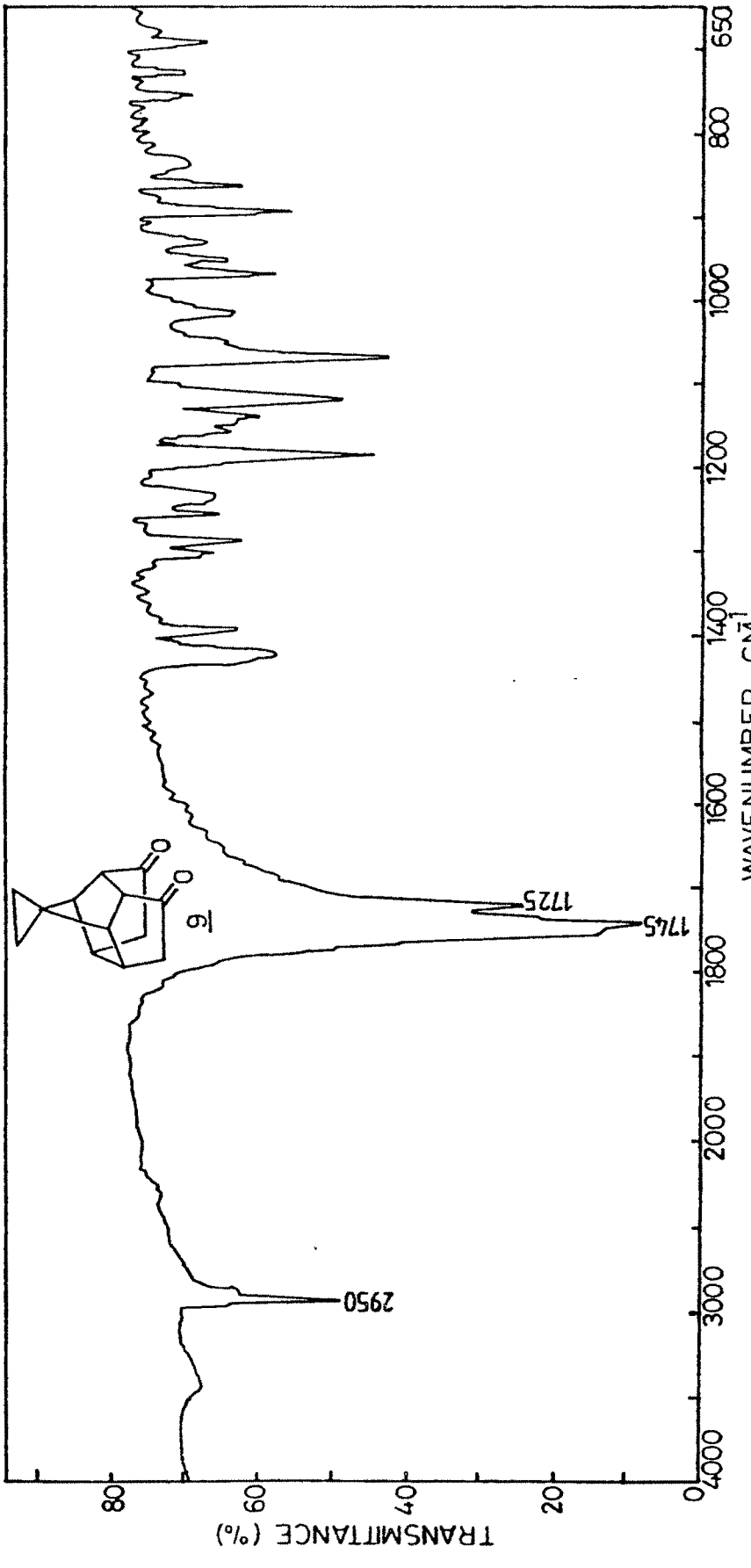


Fig. V.3 : IR (KBr) spectrum of compound 9

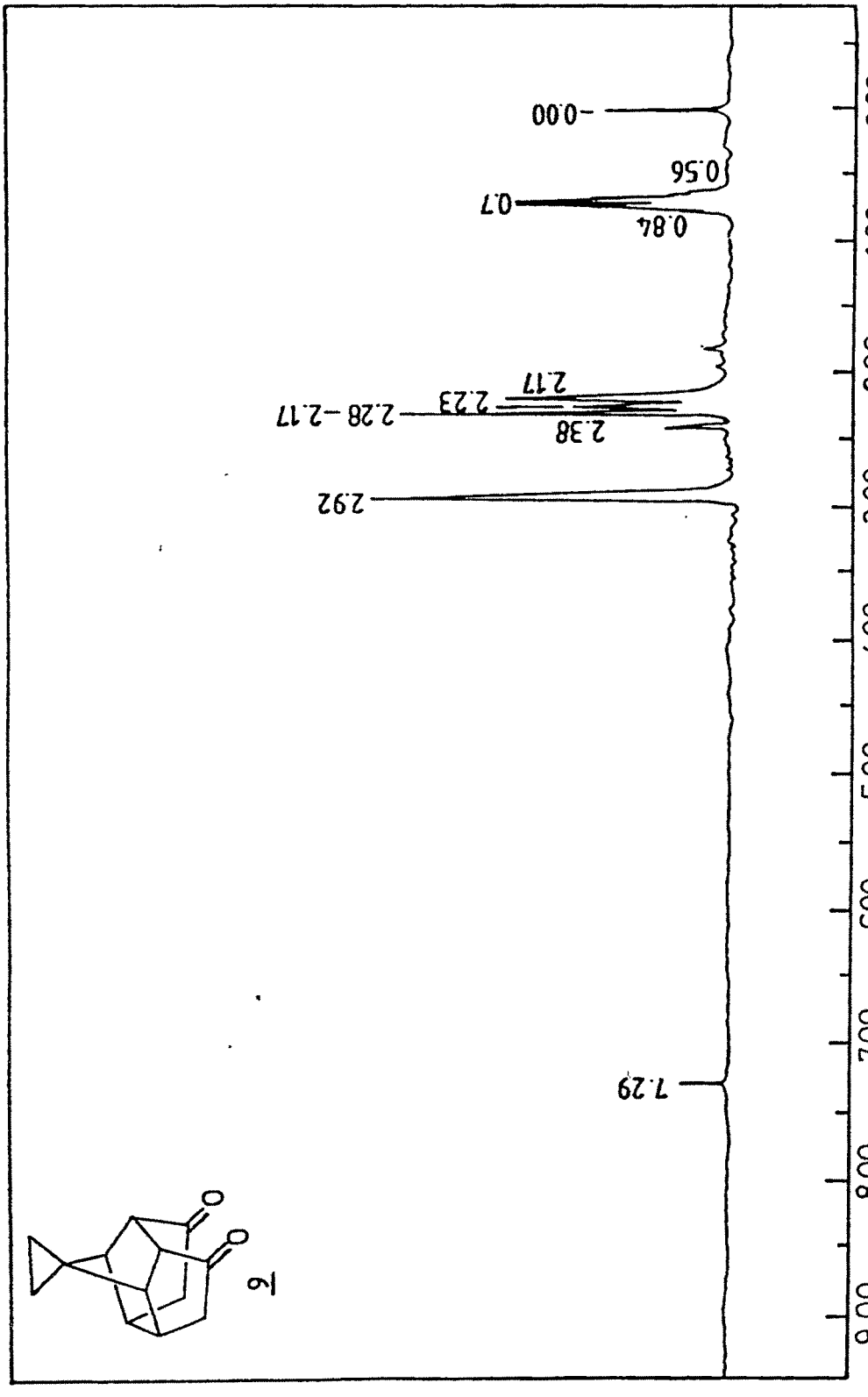


Fig. V.4 : NMR ($CDCl_3$, 300 MHz) spectrum of compound 9

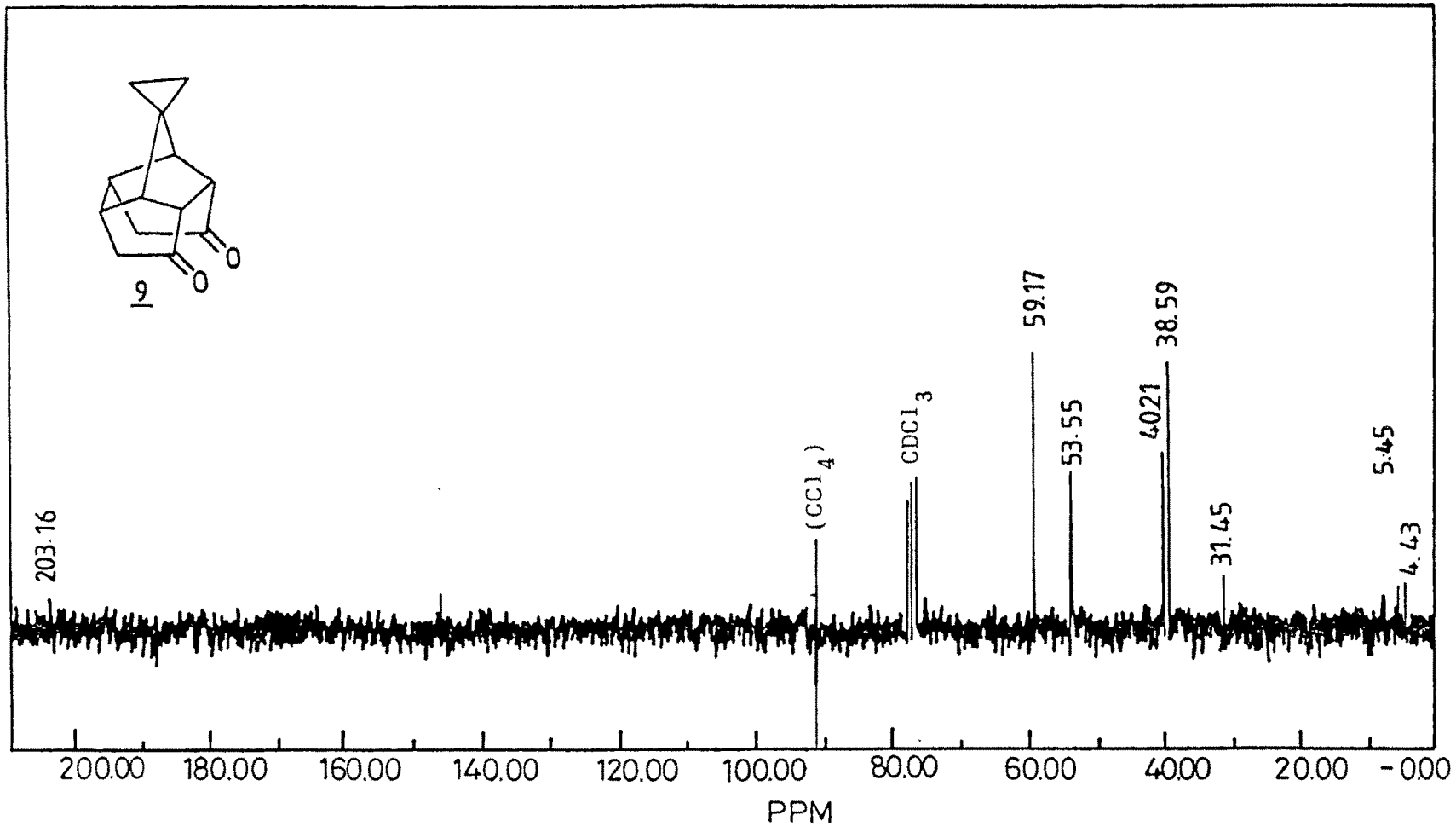


Fig. V.5 : ^{13}CNMR ($CDCl_3$) spectrum of compound 9

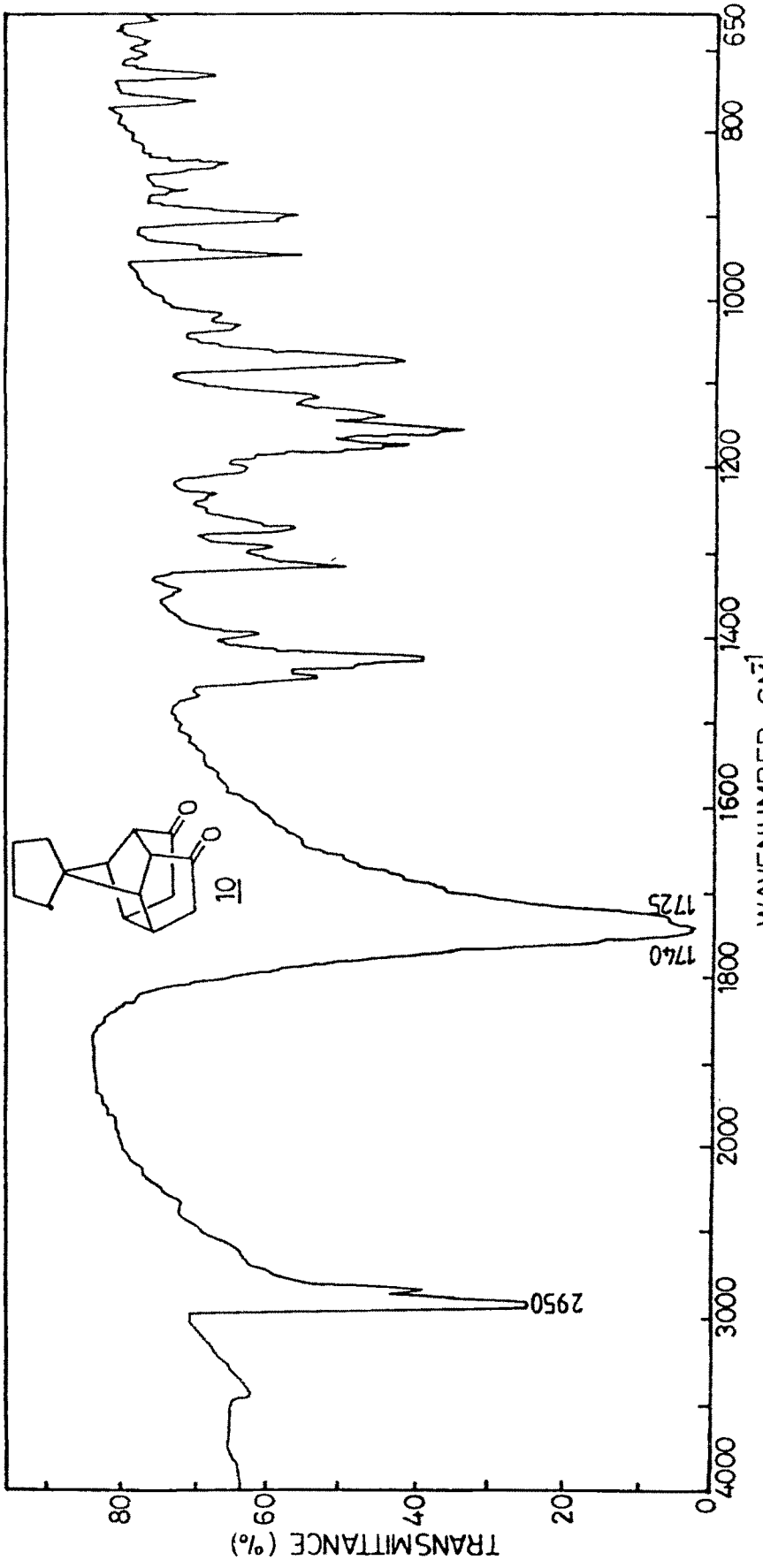


Fig. V.6 : IR (KBr) spectrum of compound 10

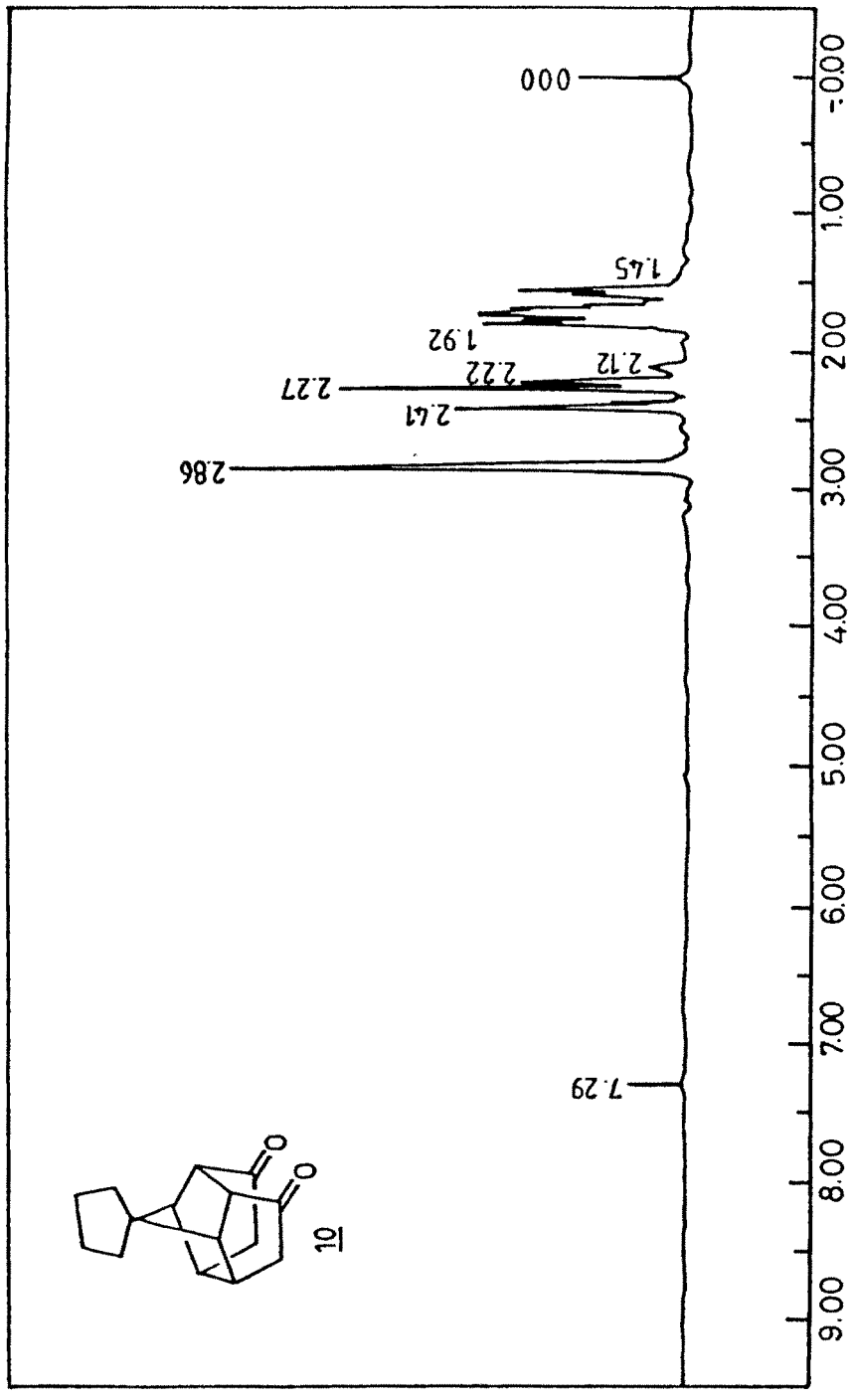


Fig. V.7 : NMR ($CDCl_3$, 300 MHz) spectrum of compound 10

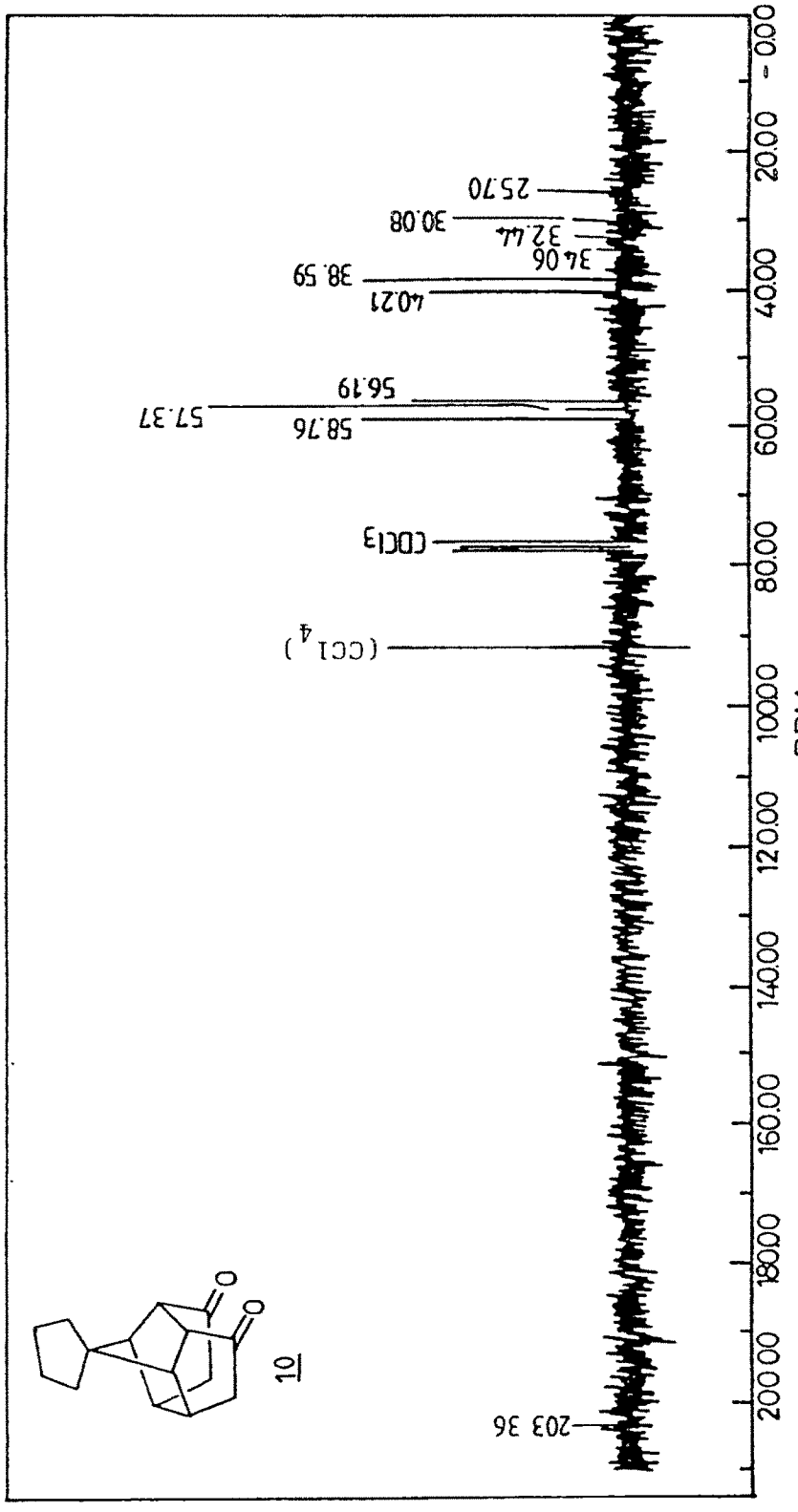


Fig. V.8 : ^{13}CNMR ($CDCl_3$) spectrum of compound 10

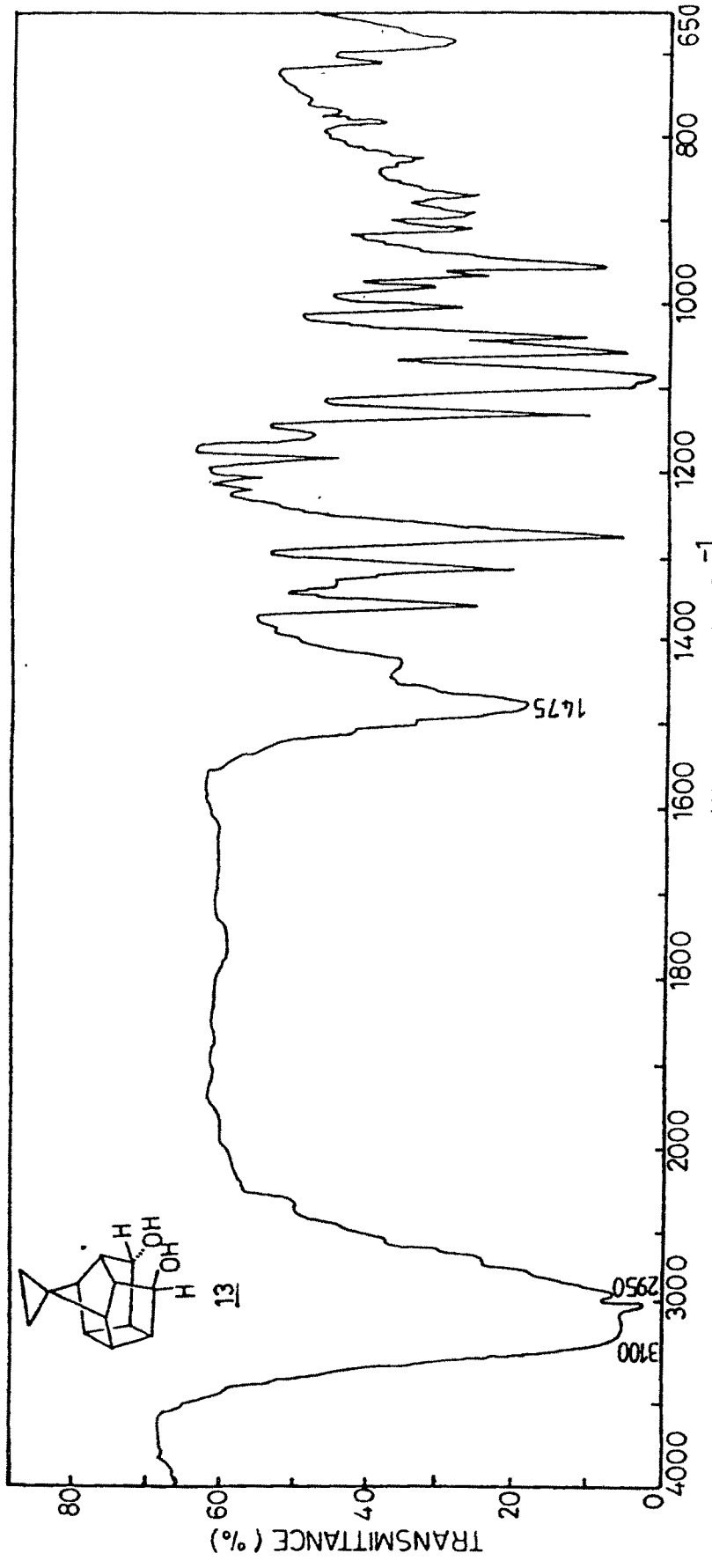


Fig. V.9 : IR (KBr) spectrum of compound 13

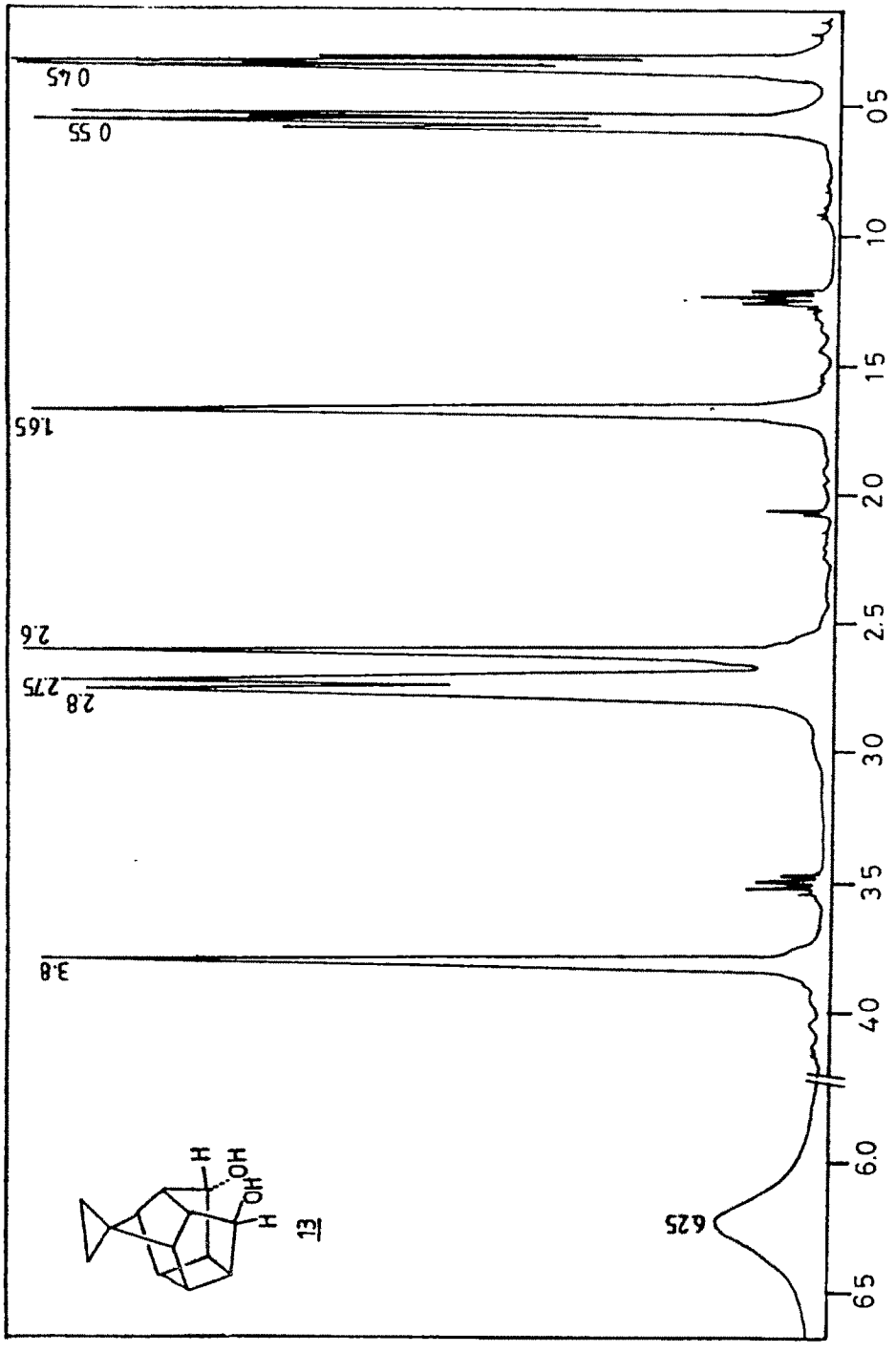


Fig. V.10 : NMR ($CDCl_3$, 300 MHz) spectrum of compound 13

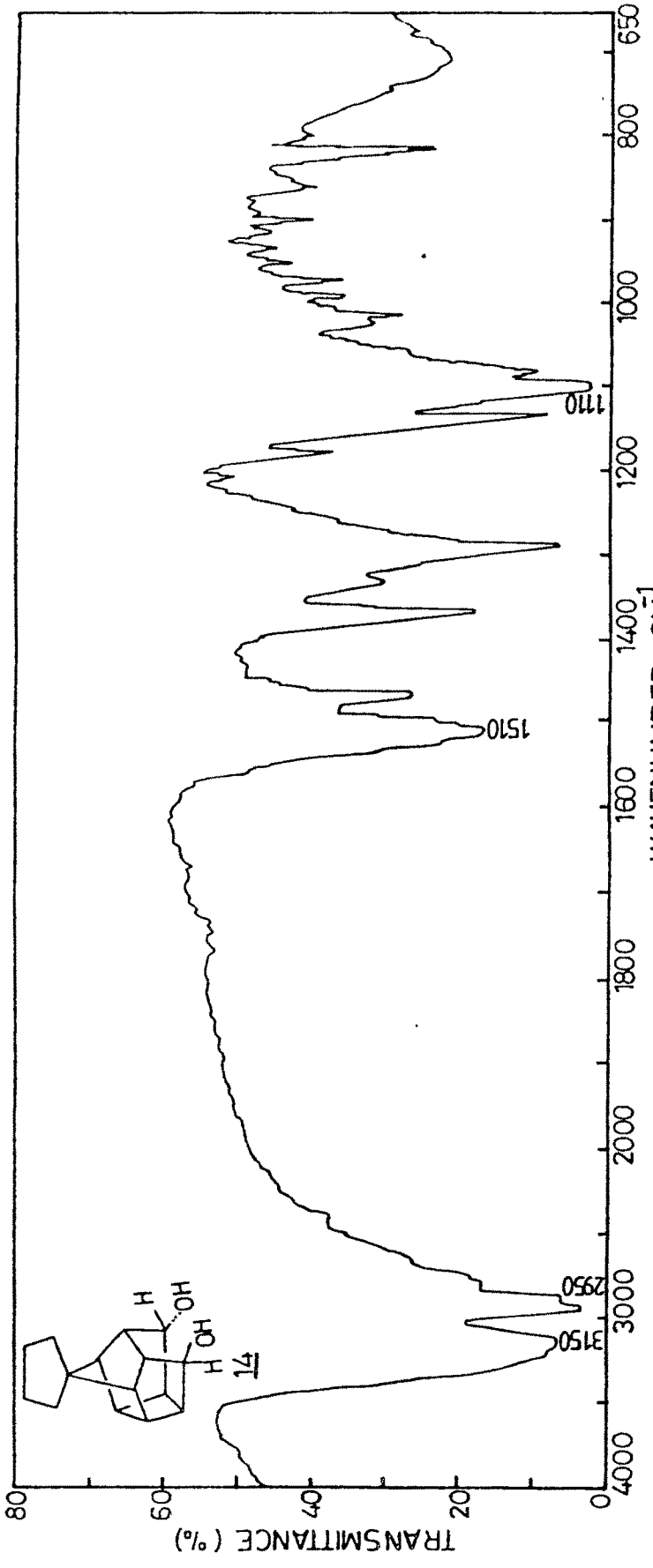


Fig. V.11 : IR (KBr) spectrum of compound 14

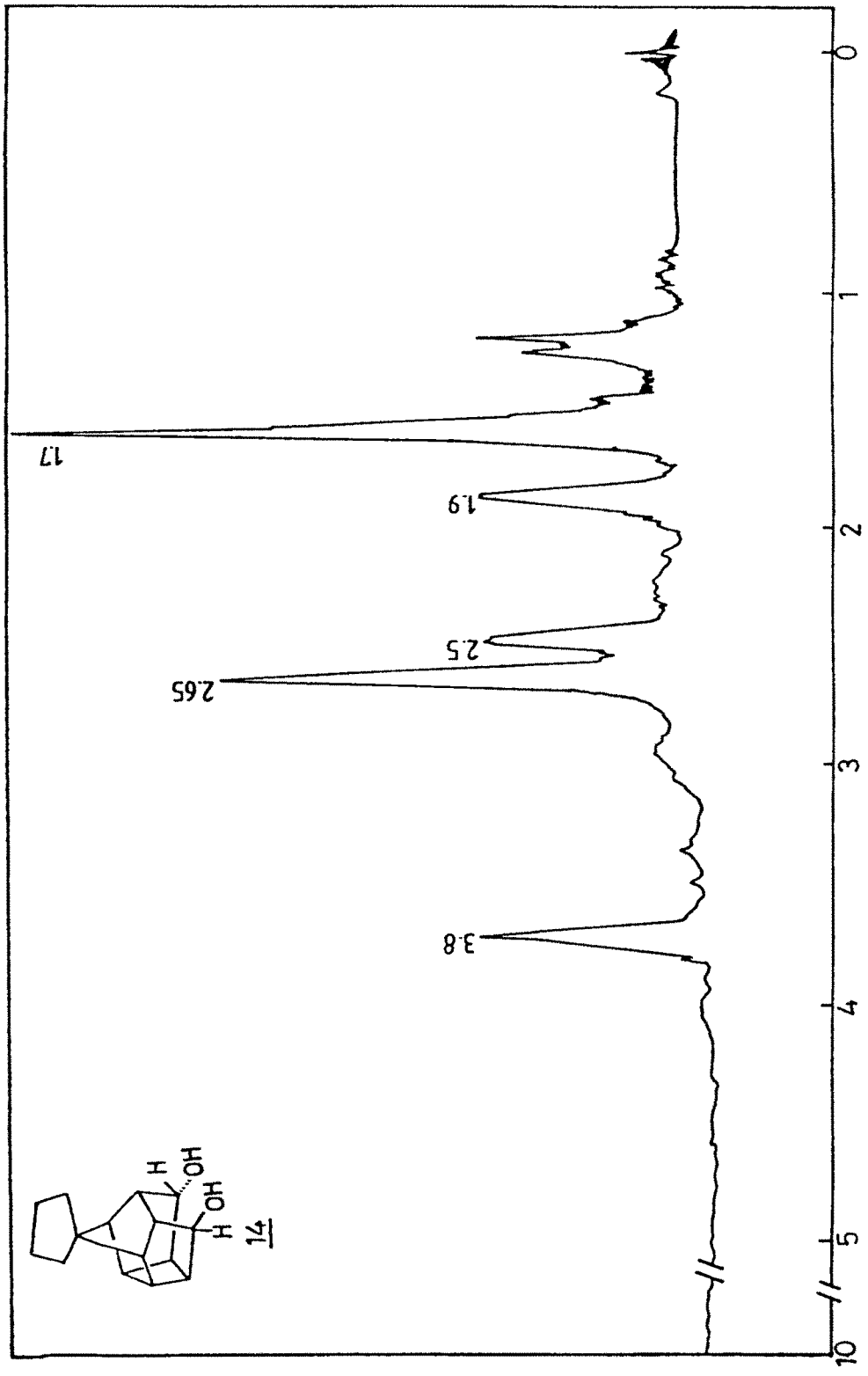


Fig. V.12 : NMR ($CDCl_3$, 90 MHz) spectrum of compound 14

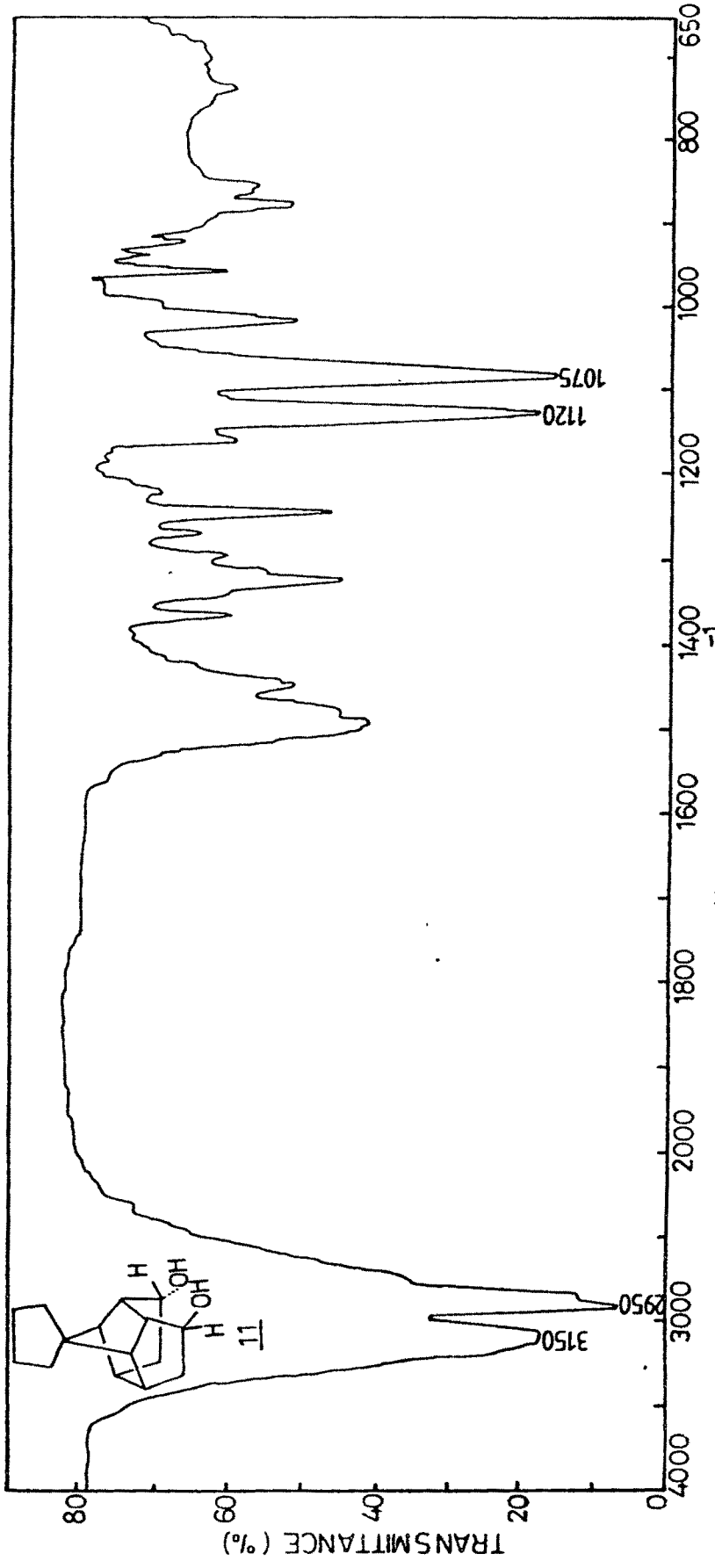


Fig. V.13 : IR (KBr) spectrum of compound 11

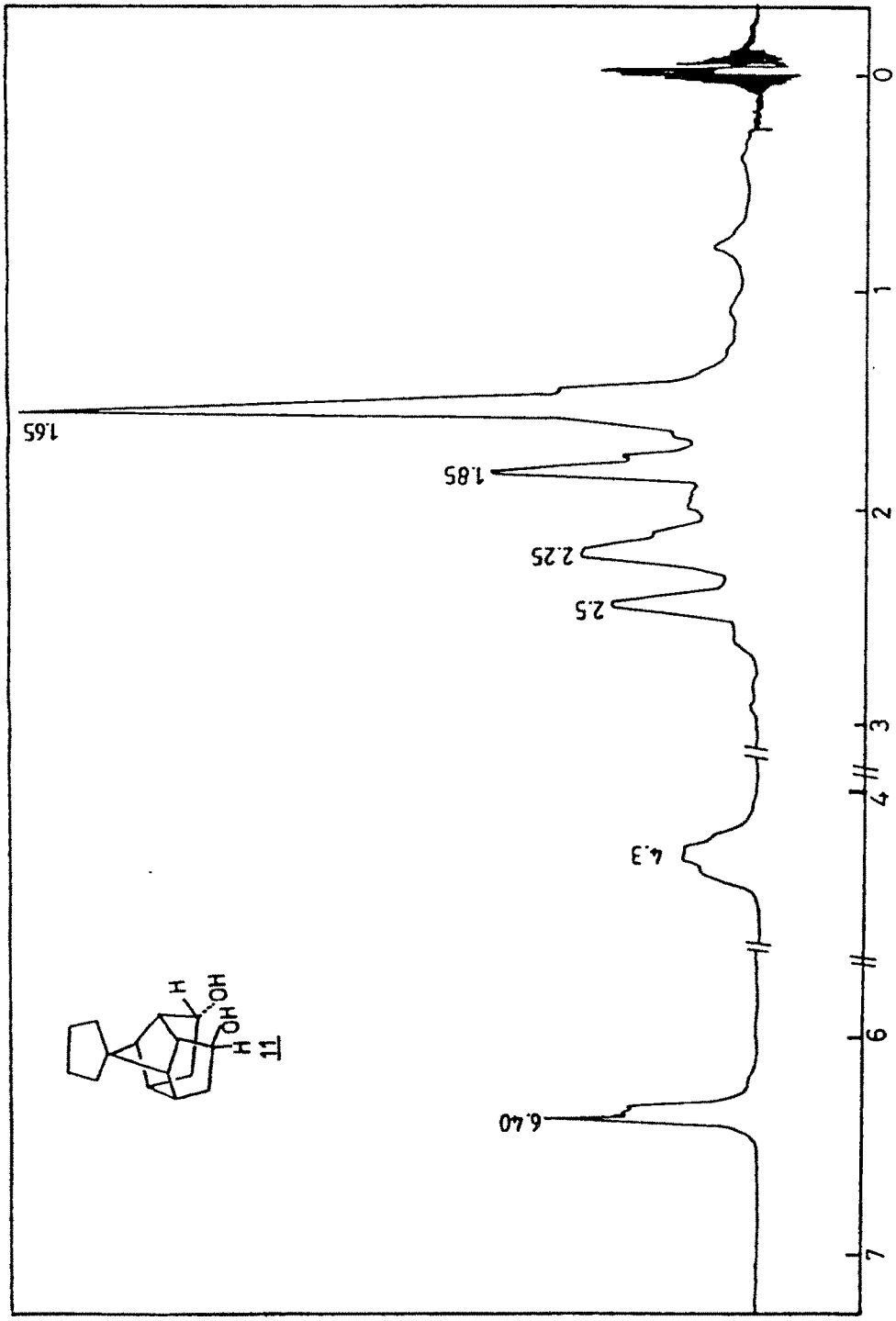


Fig. V.14 : NMR ($CDCl_3$, 90 MHz) spectrum of compound 11

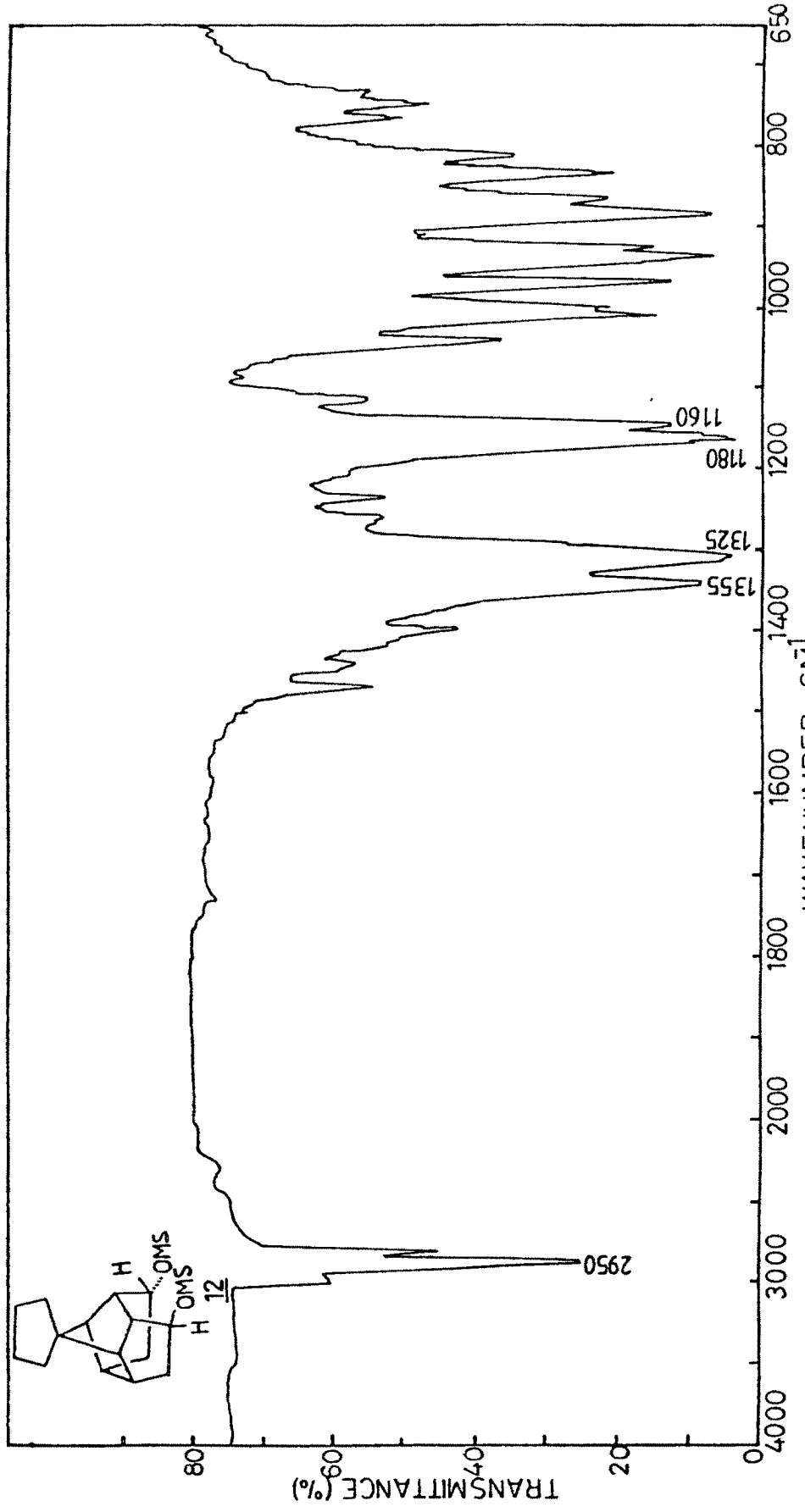


Fig. V.15 : IR (KBr) spectrum of compound 12

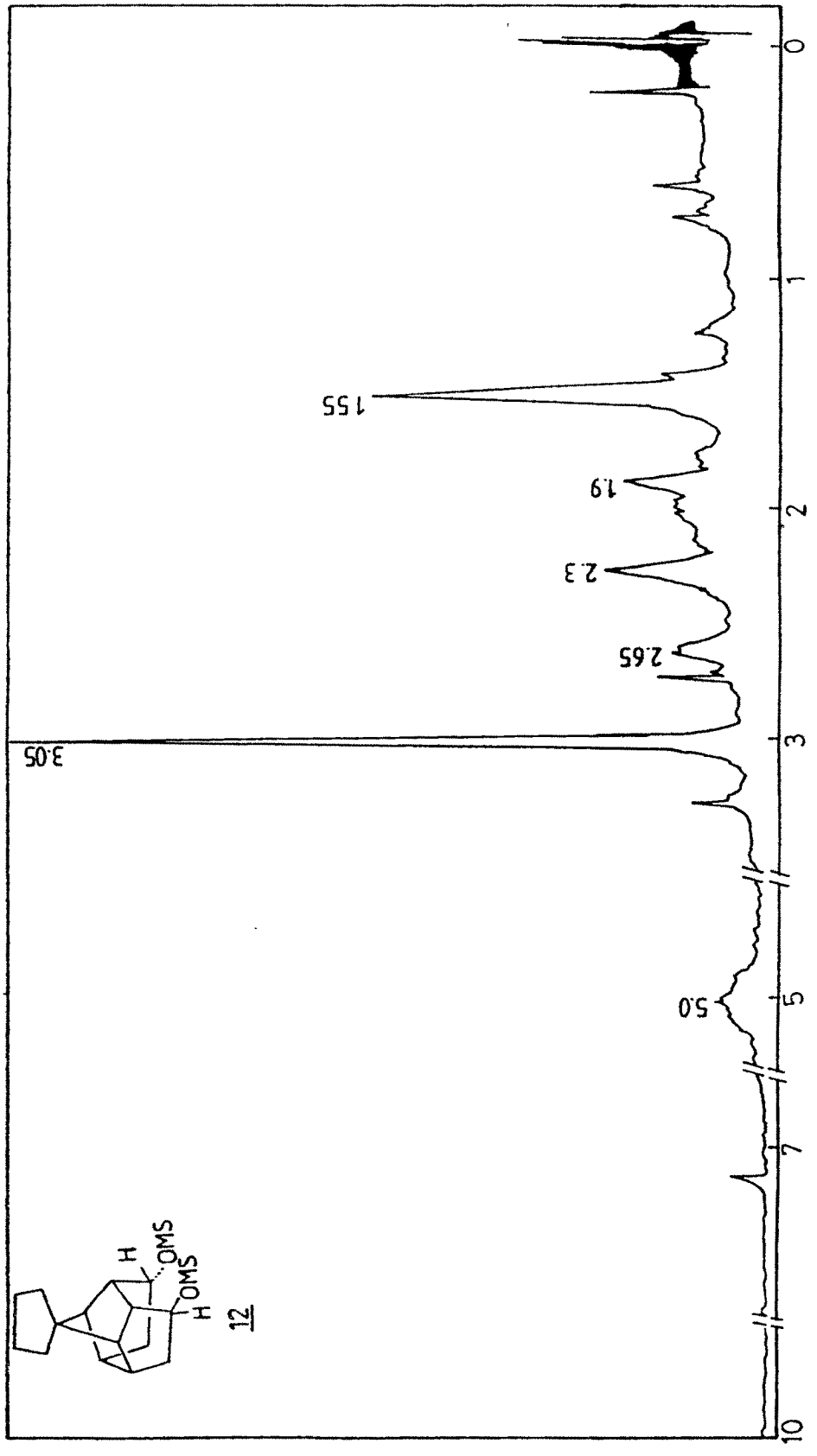


Fig. V.16 : NMR ($CDCl_3$, 90 MHz) spectrum of compound 12

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