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Synthesis of 6,7-dihydro-1,5,8-trimethylnaphtho(2,1-b) furan from 2,5-dimethyl-7-hvdroxy-1-tetralone

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ABSTRACT: 6,7-dihydro-1,5,8-trimethylnaphtho(2,1-b)furan was reported to be the first furocadinanesesquiterpenoid was isolated from rhizomes of *Curcuma zedoaria* Roscoe. Here, we have attempted the synthesis of 6,7-dihydro-1,5,8-trimethylnaphtho(2,1-b)furan, an important natural product by different way from the synthesis given by Vishwanalh and Krishna Rao. Synthesis of natural products is always a challenging work because of multi-steps involvement and purification after each step. The starting compound used was 2,5-dimethyl-7-hydroxy-1-tetralone which was de-methylated by using pyridine hydrochloride and also by aluminium iodide to yield 2,5-dimethyl-7-acetonyloxy-1-tetralone. This tetralone on cyclisation with trifluoracetic acid and also with polyphosphoric acid gave 1,5,8-trimethyl-7,8-tetrahydronaphtho(2,1-b)furan(6H) one. Reduction of naphthofuranone with sodium borohydride followed by dehydration with para-toluene sulphonic acid as well as with iodine gave desired 6,7-dihydro-1,5,8-trimethylnaphtho(2,1-b)furan. The compounds synthesized were characterized by infra-red and nuclear magnetic resonance spectroscopy techniques.

Key words: Sesquiterpenoid, Tetralone, De-methylation, Terpene.

INTRODUCTION

From the vast number of naturally occurring compounds, terpenes forms the largest group having plant origin. Most of the natural terpene hydrocarbons have the molecular formula $(C_5H_8)n$. Depending on the value of n, terpenes have been categorized into mono($C_{10}H_{16}$), sesquiterpenes ($C_{15}H_{25}$), diterpenes ($C_{20}H_{30}$), triterpenes ($C_{30}H_{48}$), tetraterpenes ($C_{40}H_{64}$) and polyterpenes. Mono and sesquiterpenes are obtained from sap and tissues of plants while di and tri terpenes are obtained from gums and resins of the plants. All the classes of terpenes have one common feature that, most of them obey a well-known follow isoprene rule. All naturally occurring terpenes consists of isoprene units. This has been proved by the thermal decomposition terpenes. Thus, divisibility into isoprene units may be regarded as an essential condition to be satisfied by the structure of any plant synthesized terpene. However, there is a class of sesquiterpenes namely eremophilanes which don't follow isoprene rule hence it is considered as first naturally occurring non-isoterpenoid. Wide investigation of this class of compounds has earlier been carried out by Pinder [1] and Sorm [2].

Present work reports the synthesis of 6,7-dihydro-1,5,8-trimethylnaphtho(2,1-b)furan(pyrocurzerenone) from 2,5-dimethyl-7-methoxy-1-tetralone. The structure of pyrocurzerenone and its pyrolytic disproportionation products dihydropyrocurzerenone and furocadalene was substantiated by its synthesis by Vishwanath and Rao [2]. The second total synthesis of curzerenone, its epimer and pyrocurzerenone has also been reported via 2-methyl furan annulation reaction using 1-nitro-l (phenylthio) propene. Pyrocurzerenone is structurally related to furanoeremophilane, 1-oxo-9-desoxycacalol, cacalol and cacalone isolated from the leaf extract of Bolivian Senecioserralifolis [3] and Mexican shrub Cacaliadecomposita [4] respectively. Our earlier studies on the synthesis of l-oxo-9-desoxycacaIol using p-benzoyl propionic acid as a starting material tempted us to undertake the synthesis of pyrocurzerenone.

EXPERIMENTAL PROCEDURE

A. Synthesis of 2.5-Dimethyl-7-hvdroxy-1-tetralone

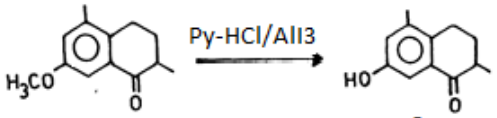
a. Using pyridine hydrochloride. 2,5-Dimethyl-7-methoxy-1-tetralone (1.4 g) was de-methylated by heating with pyridine hydrochloride (15 g) at 180-190°C for three hours. On cooling, the reaction mixture was diluted with water and then extracted with ether. The ether extracted was washed repeatedly with water, dried over anhydrous sodium sulfate and ether removed to yield the impure phenolic tetralone (1.320 g). The material on chromatography over silica gel (60 g) gave pure phenolic tetralone (0.620 g), m. p, 168°C (Lit. m. p, 171 – 172°C).

Fig. 1(a) IR (nujol): 3400 (phenolic -OH), 1670 (C=0) cm^{-1}.

Fig. 1(b) PMR ($CDC1_3$,): 1.25 (3H,d, J=7 Hz, Ar-CO-CH-CH_3), 1.8 (2H,q, J=7 Hz, Ar-CH_2-CH_2), 2.2 (2H, m, Ar-CH_2) 2.3 (3H, s, Ar-CH_3), 2.9 (1H, sextet, J=7 Hz, Ar-CO-CH-CH_3), 5.7 (1H, bs, Ar-OH), 7.0 (HI, bs, Ar-H ortho to -CH_3) and 7.60 (1H, bs, Ar-H para to -CH_3).

b. Using aluminium iodide. To a stirred solution of methylated ketone (1) (3.8 g) in dry acetonitrile (60 ml) was added in small amounts aluminium iodide (7.0 g) and the mixture was refluxed on water bath for four hours. Completion of reaction was monitored by thin layer chromatography (TLC). The reaction mixture was poured into ice-water. The solution was decolorized by addition of aqueous sodium thiosulphate and then extracted with dilute sodium hydroxide (3×30 ml). Acidification of alkaline phase gave desired phenolic tetralone (2) which was re-extracted with ether. The routine work up yielded the phenol (3.3 g).

The compound so prepared was identical in every respect with the one prepared using pyridine hydrochloride and the yield of phenol obtained by de-melhylation with aluminium iodide was found to be far superior. The phenol so obtained was used as such for the next step.



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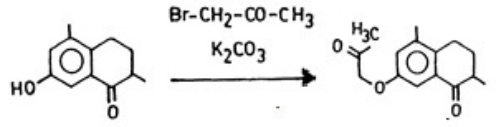
B. Synthesis of 2,5-Dimethyl-7-acetonyloxy-1-tetralone

To the phenolic tetralone (2) (3.1 g) and freshly distilled bromoacetone [5] (5.0 ml) in dry acetone (50 ml) were refluxed in presence of anhydrous potassium carbonate (4 g) on a water bath for eight hours. The completion of reaction was monitored by TLC. After completion, reaction mixture was diluted with water and extracted with ether. Ether extract was washed with water, dilute sodium hydroxide, again with water, dried and ether removed to get a gummy solid (3.7 g) which was chromatographed over silica gel (80 g). Elution with benzene gave the pure acetonyloxytetralone (3) (1.8 g) which solidified on cooling; m. p. 71°C (Lit. m. p. 72-73°C).

Fig. 2(a) IR (nujol): 1735 (CH_3C=O) and 1685 (C=0) cm^{-1}.

Fig. 2(b) PMR ($CDC1_3$): 1.25 (3H, d, J=7 Hz, -CH-CH_3),1.95(2H, m, Ar-CH_2-CH_2), 2.9 (1H, sextet, J=7Hz,-CH-CH_3), 2.2 (6H,s, Ar-CH_3 and CO-CH_3), 4.65 (2H, s, Ar-O-CH_2), 7.1 (1H, bs, Ar-H ortho to -CH_3) and 7.35 (1H, bs, Ar-H para to CH_3)



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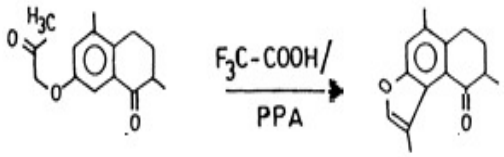
C. Synthesis of 1,5,8-Trimethyl-7,8-tetrahydronaphtho(2,1-b) furan(6H)one

a. Using polyphosphoric acid. To a solution of polyphosphoric acid [prepared from phosphorous pentoxide (31.0 g) and ortho-phosphoric acid (21 ml)] was added the above acetonyloxytetralone (3) (1.0 g) and reaction mixture was stirred at room 64 °C temperature for two hours. It was decomposed using ice water and extracted with ether. The ether extract was washed with water, dilute sodium hydroxide, water, dried and ether removed to yield a gummy product (1.050 g). This was chromatographed over silica gel (30 g). Elution with petroleum ether gave the pure naphthofuranone (4) (0.360 g), m. p. 76°C (Lit. m. p. 78- 79°C).

Fig. 3(a) IR (nujol): 1685 (ketone) cm^{-1}.

Fig. 3(b) PMR ($CDC1_3$) : 1.25 (3H,d, J=7 Hz Ar-CO-$CHCH_3$), 2.25 (2H, q, J=7 Hz, Ar-CH_2 – CH_2), 2.30 (3H,s, Ar-CH_3), 2.40 (3H,s, furan CH_3), 2.7 (2H,m, Ar-CH_2), 2.9 (1H, sextet, J=7 Hz - CO-CH-CH_3), 7.5 (2H, bs, Ar-H, and furan H).

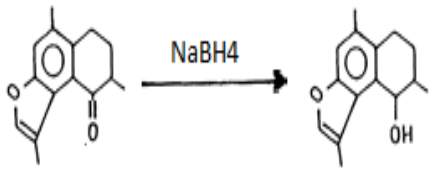
b. Using trifluoroacetic acid. To a solution of trifluoroacetic acid (15 ml) was added acetonyloxy product (0.400 g) slowly with stirring. The reaction mixture was refluxed for eight hours. After cooling, trifluoroacetic acid was removed under vacuum and the residue was extracted with ether. It was then washed with water, aqueous sodium carbonate, water, dried and ether removed to yield the naphthofuranone (0.300 g) identical in all respects (m.p., TLC and PMR) to that obtained by PPA cyclisation. During cyclization, the presence of keto group at position 1must be responsible for exclusive formation of product as there are reports in the literature [6].



3 4

D. Synthesis of l,5,8-Trimethvl-6,7-dihydronaphtho[2,1-b] furanol

To the stirred solution of above naphthofuranone (4) (0.300 g) in alcohol (15 ml) was added sodium borohydride (0.300 g) and reaction mixture left overnight. It was decomposed by pouring into saturated solution of ammonium chloride and then extracted with ether. Ether extract was repeatedly washed with water, dried and ether removed to yield the naphthofuranol (5) (0.270 g) as a liquid. The alcohol being almost pure, it was used as such for the next step. Fig. 4 IR ($CHCl_3$: 3450 cm^{-1})



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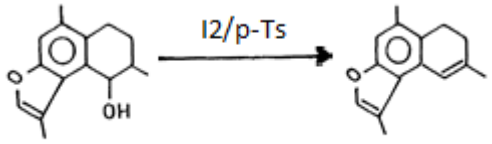
E. l,5,8-Trimethvl-6,7-dihydronaphtho[2,1-b] furan (Pyrocurzernone)

a. Using p-toluenesulphonic acid. To a solution of above naphthofuranol (5) (0.250 g) in benzene (10 ml), p-toluenesulphonic acid (0.050 g) was added and mixture refluxed for thirty minutes. The reaction was monitored by TLC and on completion, the reaction mixture was diluted with ether and ether extract was washed with aqueous sodium carbonate, dried and ether removed to yield a gummy material (0.220 g). This was purified over four preparative TLC plates, using petroleum ether as mobile phase, to yield pure pyrocurzerenone (6) (0.06g), m. p. 73-74°C (Lit. m. p. 77-78°C);

Fig. 5. PMR ($CDCl_3$): 2.0(3H, s, allylic CH_3), 2.38 (6H,s, Ar-CH_3& furan -CH_3), 6.65 (1H, bs, olefinicH), 6.90 (1H, bs, Ar-H) and 7.1(1H, bs, furan-H). This spectral data is in complete agreement with that reported earlier [1, 2] for pyrocurzerenone.

b. Using iodine. To the solution of above alcohol 7.5 in benzene was added a small crystal of iodine and refluxed for four hours on water bath. It was decomposed by pouring into ice-water and extracted with ether. Ether extract was washed with water, with very dilute sodium thiosulfate, water, dried and ether removed to yield a sticky material. The examination of TLC and PMR spectrum showed it to be identical with the pyrocurzerenone prepared by dehydration of alcohol with para-toluenesulphonic acid (p-Ts).



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RESULTS AND DISCUSSION

Synthesis of pyrocurzerenone was carried out in different steps starting from 2.5-dimethyl-7-hvdroxy-1-tetralone. The product obtained in every step was purified by using thin layer chromatography and also column chromatography and their melting points were recorded which values are in close proximity of the literature data. Further, the compounds so obtained were characterized by infrared and proton magnetic resonance spectroscopic techniques for their structure confirmation.

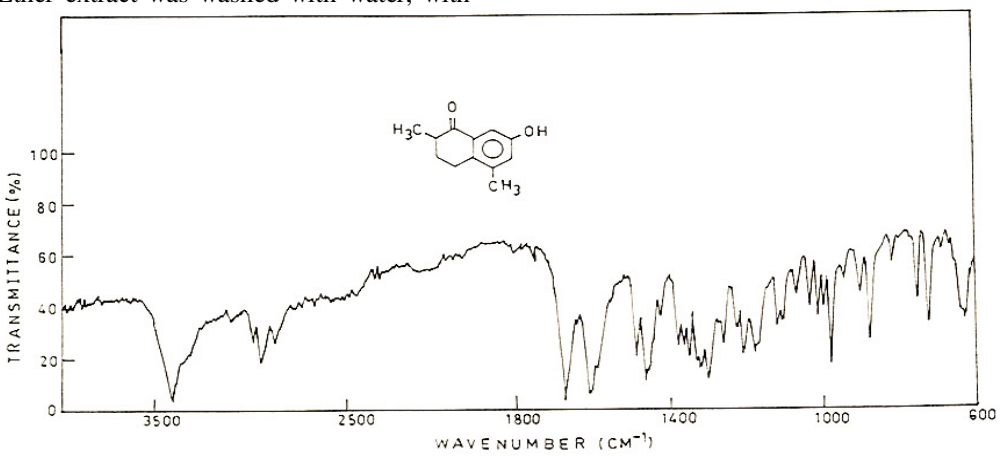

Fig. 1(a) Infrared Spectrum.

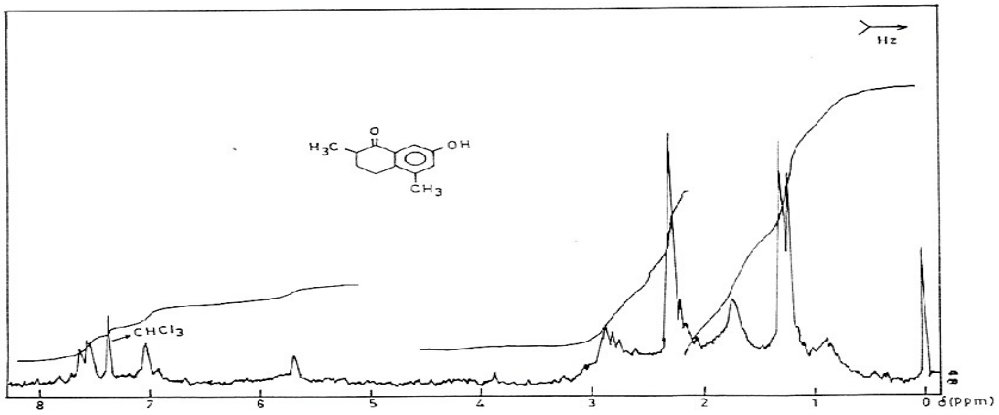

Fig. 1(b) PMR Spectrum.

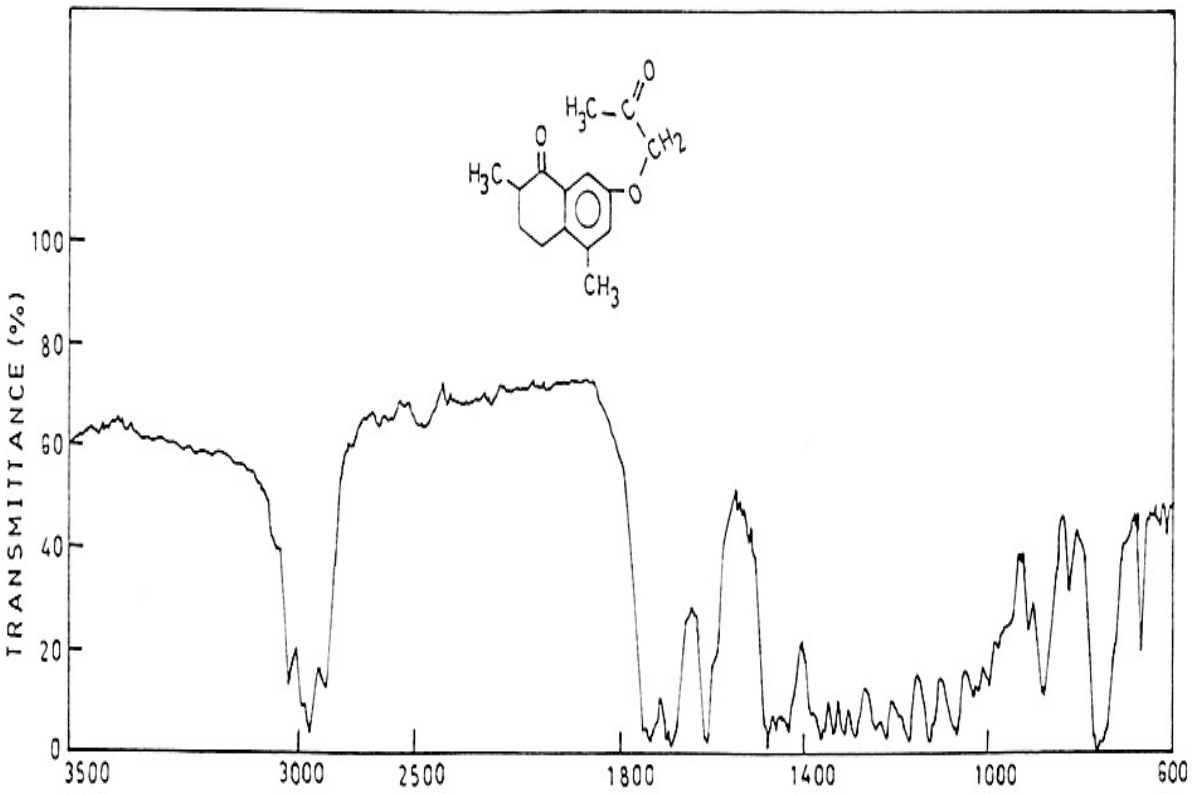

Fig. 2(a) Infrared Spectrum.

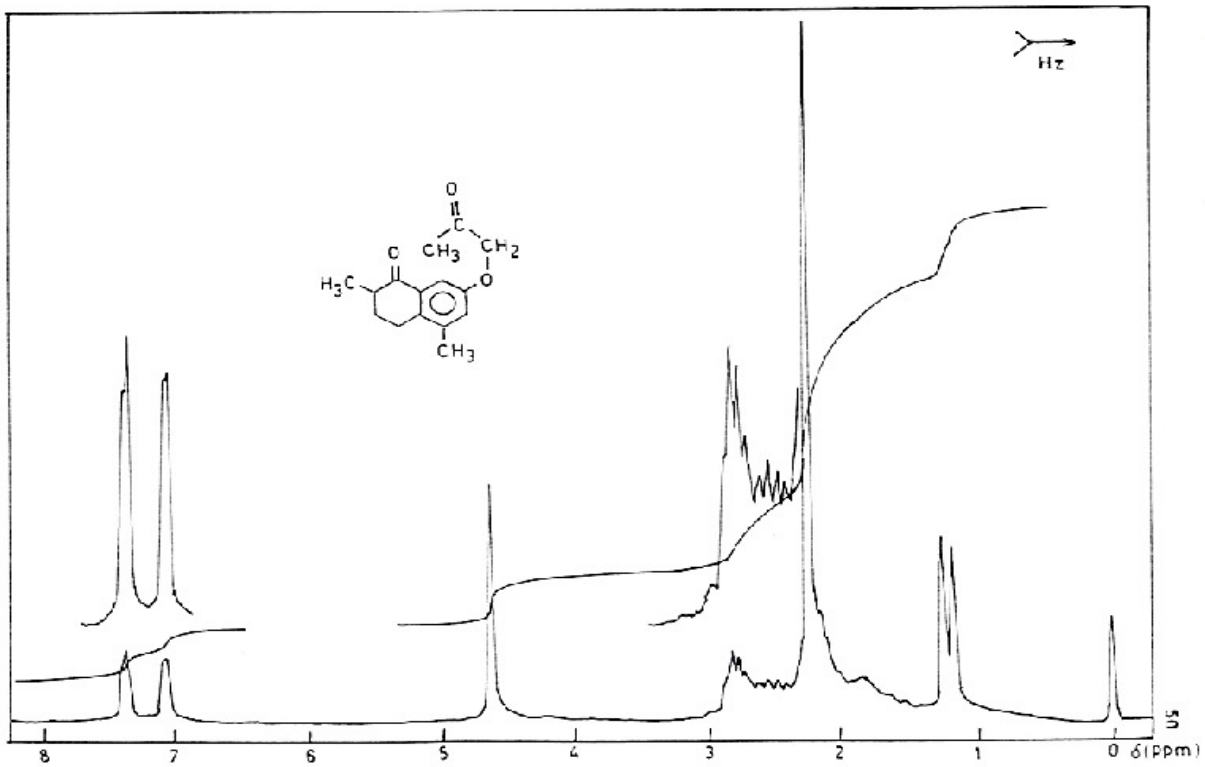

Fig. 2(b) PMR Spectrum.

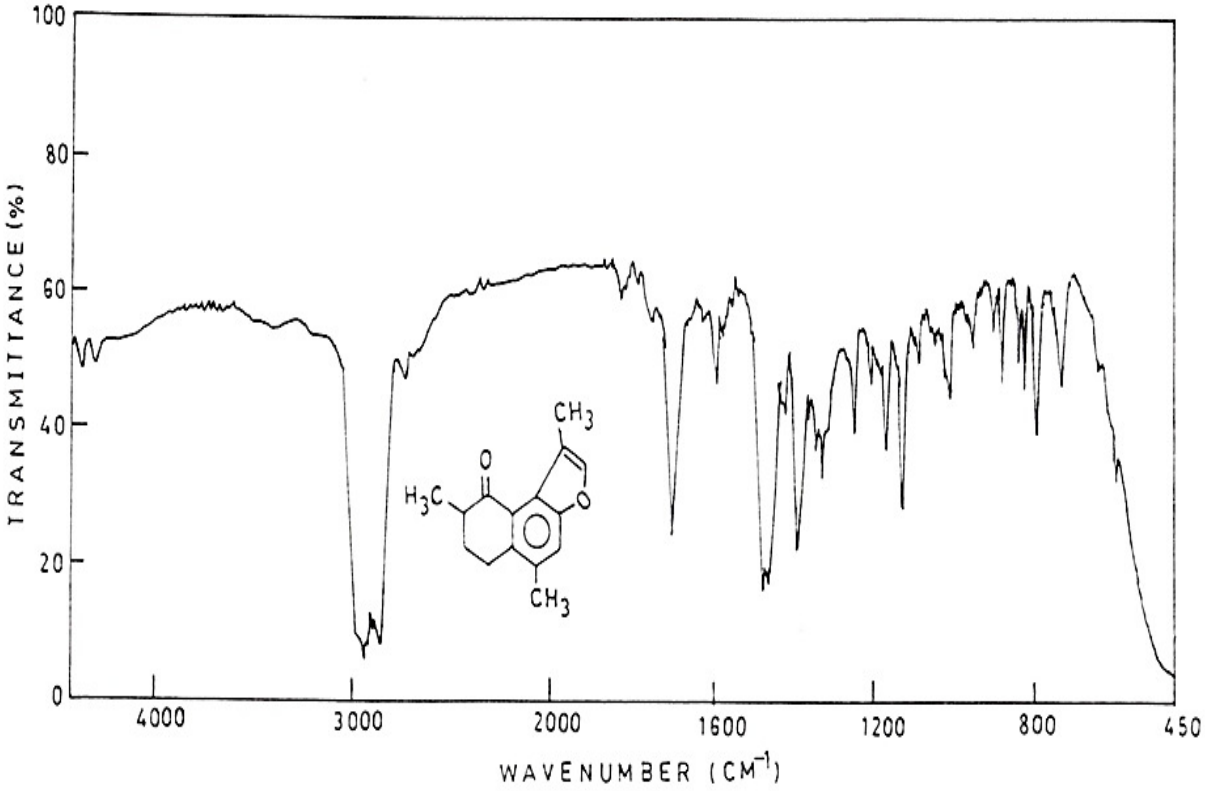

Fig. 3(a) Infrared Spectrum.

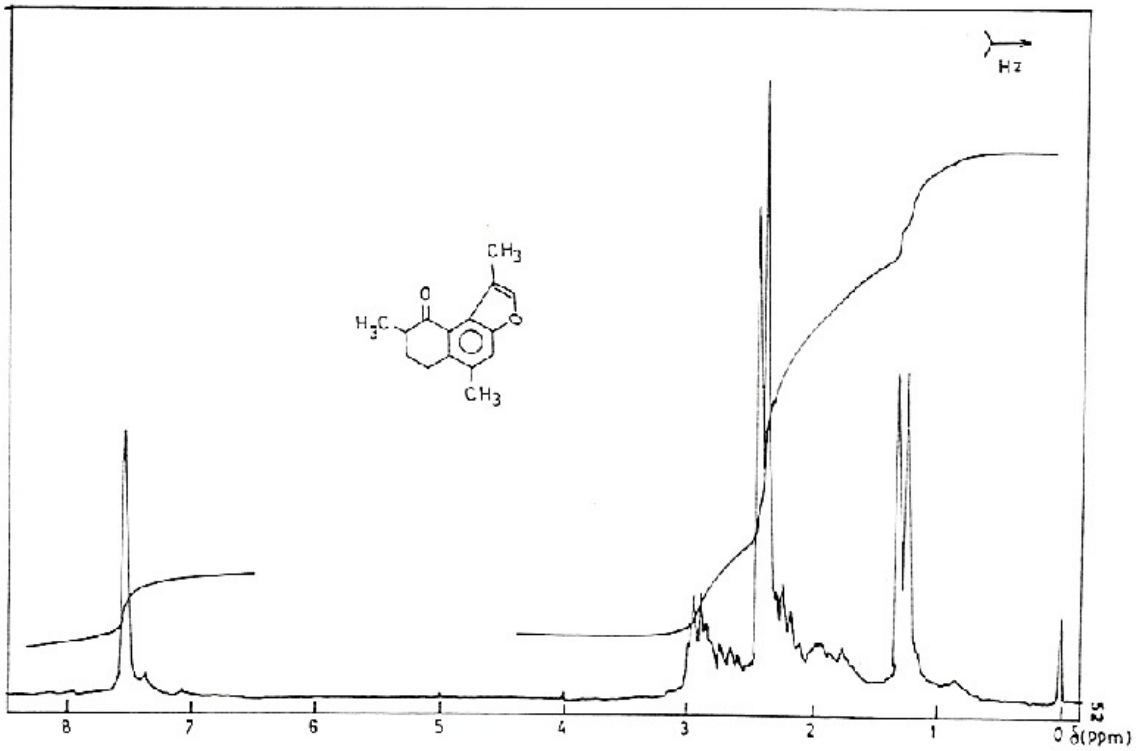

Fig. 3(b) PMR Spectrum.

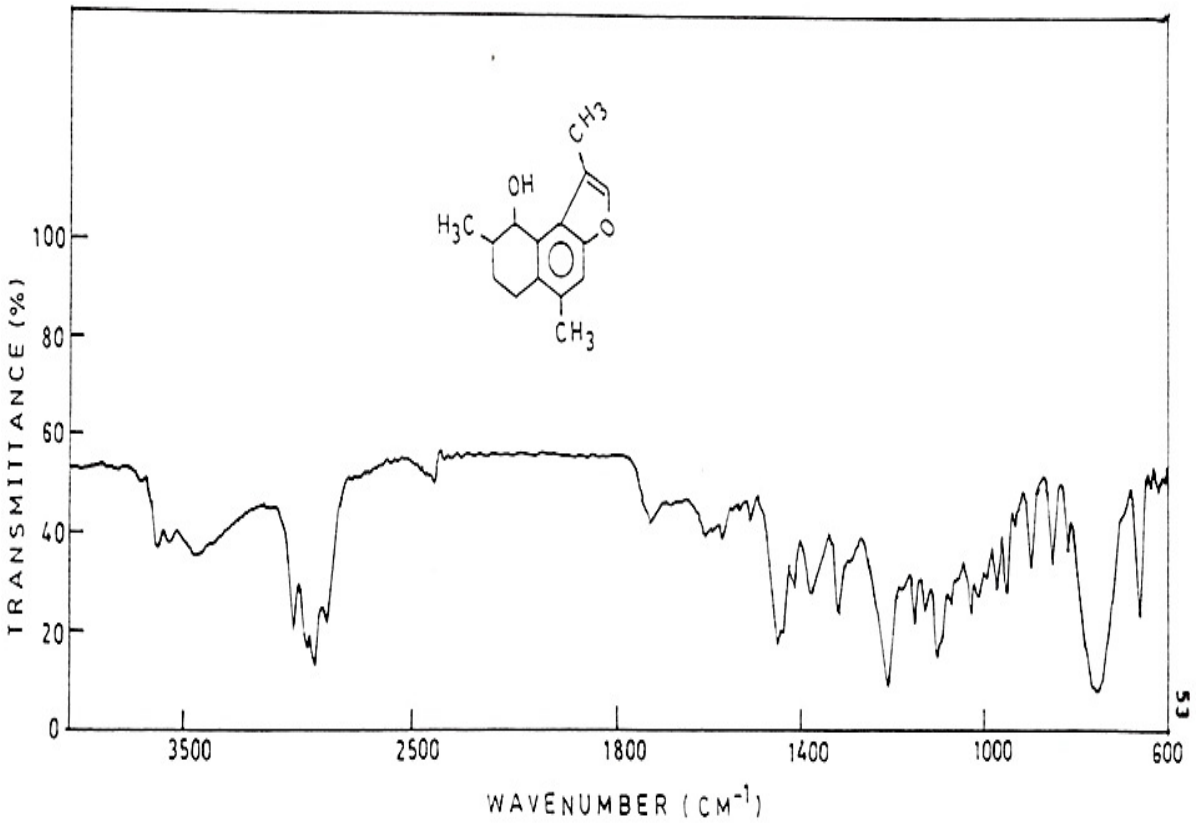

Fig. 4. Infrared Spectrum.

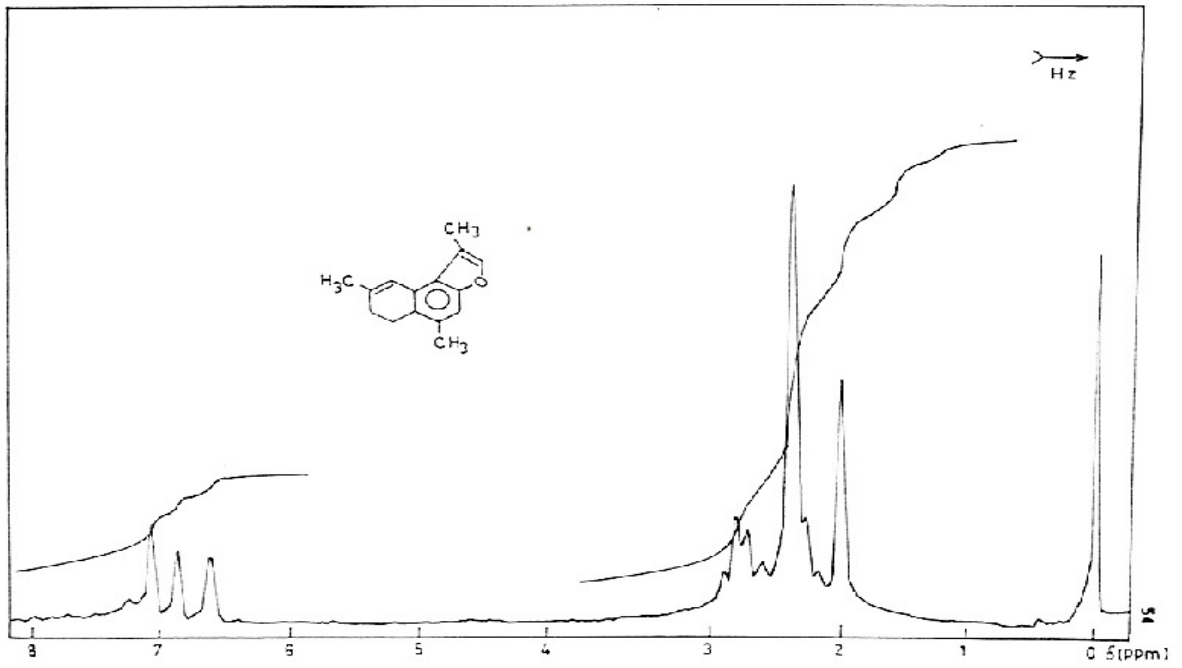

Fig. 5. PMR Spectrum.

CONCLUSIONS

In conclusion, we have successfully synthesized a naturally important terpenoidpyrocurzerenone from 2,5-dimethyl-7-methoxy-1-tetralone by following different steps. Though, it involves little bit extra steps than the synthesis given by V. Vishwanath and G. S. Krishna Rao [2] we have suggested the alternative pathway for the synthesis of pyrocurzerenone. In future, the synthesis of such compounds may attempted by novel techniques that could include minimum steps, less purification work, minimal chemicals and less time for reaction completion. One of the techniques may be by using micro-wave technique.

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REFERENCES

[1]. H. Hikino, K. Agatsuma, C. Kono and T. Takemoto (1968). *Tetrahedron Lett*., 4417.
[2]. V. Vishwanalh and G. S. Krishna Rao (1974). *J. Chem. Soc., (Perkin Trans-I)*, 450.
[3]. F. Bohlmann, C. Zedro and R. King, (1979). *Phytochemistry*, **18**: 125.
[4]. J. Romo and P.J. Nathan, (1964). *Tetrahedron*, **20**: 2331.
[5]. A.H. Blatt, (1963). (John Wiley and Sons). *Organic Syntheses*, Coll. Vol. **II**, 88.
[6]. T. P. Velusamy and G. S. K. Rao (1982). *Indian J. Chem*., **21B**: 291.