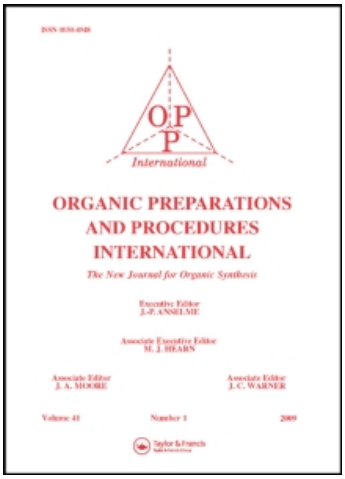


Organic Preparations and Procedures International
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t902189982

SYNTHESIS OF FURANO BENZOSUBERONES AND FURANO TETRALONES *via* CLAISEN REARRANGEMENT

V. Peesapati[a]; N. Lingaiah[a]
[a] Department of Chemistry, Osmania University, Hyderabad, India

To cite this Article Peesapati, V. and Lingaiah, N.(1992) 'SYNTHESIS OF FURANO BENZOSUBERONES AND FURANO TETRALONES *via* CLAISEN REARRANGEMENT', Organic Preparations and Procedures International, 24: 1, 27 — 32
To link to this Article: DOI: 10.1080/00304949209356692
URL: http://dx.doi.org/10.1080/00304949209356692

ORGANIC PREPARATIONS AND PROCEDURES INT., 24 (1), 27-32 (1992)

SYNTHESIS OF FURANO BENZOSUBERONES AND FURANO TETRALONES *via* CLAISEN REARRANGEMENT

V. Peesapati* and N. Lingaiah

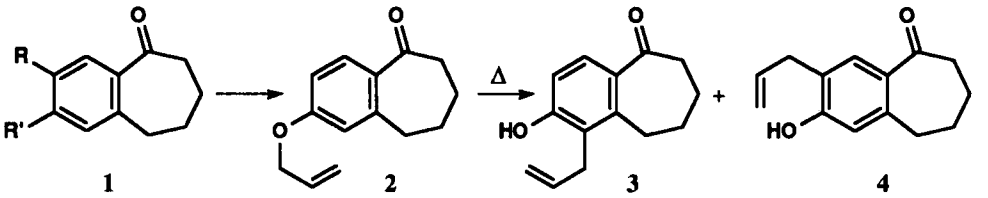
Department of Chemistry
Osmania University, Hyderabad 500 007, INDIA

Since the benzosuberone (**1**) showed anti-tumor activity in murine P 388 tests,[1] it was of interest to obtain heterocyclic fused benzosuberones for biological activity evaluation. In continuation of our earlier work[2] on the synthesis of fused heterocyclic systems, we now report convenient preparations of furanobenzocycloheptenone and tetralones.

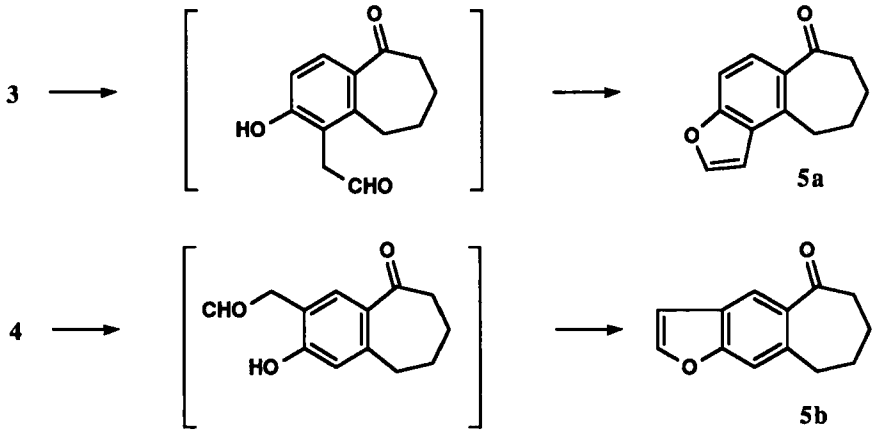
Alkylation of 6,7,8,9-tetrahydro-2-hydroxybenzocyclohepten-5-one[3] (**1b**) with 2,3-dichloropropene or allyl bromide gave the corresponding allyl ethers by the Claisen rearrangement. The resulting C-allyl derivatives were then cyclized in good yield to furanobenzosuberones with polyphosphoric acid. Thus, the allyl ether **2** obtained from the hydroxy benzocycloheptenone **1b** by treatment with allyl bromide was rearranged by heating under reduced pressure and gave two isomeric products **3** and **4.** These were separated on a neutral alumina column followed by preparative tlc gave a major (more polar) and a minor (less polar) product. The structures of these isomers **3** and **4** were assigned on the basis of their ^{1}H NMR spectra. The ^{1}H spectrum of the major component **3** showed the presence of *ortho* coupled aryl protons. This is possible only when the allyl group had migrated to C-1 rather than to the C-3 position as expected. On the other hand, the NMR spectrum of the minor product indicates that the allyl group in this case had migrated to the C-3 position, since two singlet aryl proton signals were observed.

The major product **3** was subjected to ozonolysis and the resulting aldehyde cyclized with freshly prepared polyphosphoric acid to give the furanobenzocycloheptenone (**5a**) in good yield. The ^{1}H NMR spectrum of **5a** shows a furan α-proton (δ 7.60) and β-proton (δ 6.40) with a coupling of 3 Hz, characteristic of a α- and β-unsubstituted furan structure. Mass and elemental analysis also confirm the structure. The minor component **4** was cyclized using the same procedure as before and gave isomer **5b** only in a small amount.

Using the same procedure, phenolic ketone **1b** was allylated with 2,3-dichloropropene and the resulting ether **6** rearranged by heating in N,N-dimethylaniline. Of the two products formed on Claisen rearrangement, the structure of major isomer (**7**) was again confirmed on the basis of its ^{1}H NMR spectra. The presence of two singlets (δ 6.62) and (δ 7.65) in the NMR spectrum of the minor



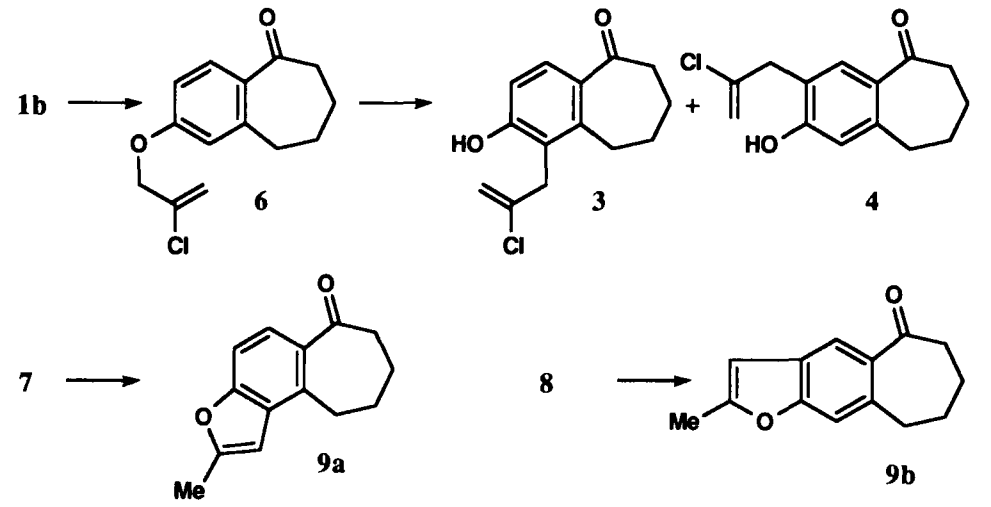
a) R = OH, R' = OME
b) R = H, R' = OH



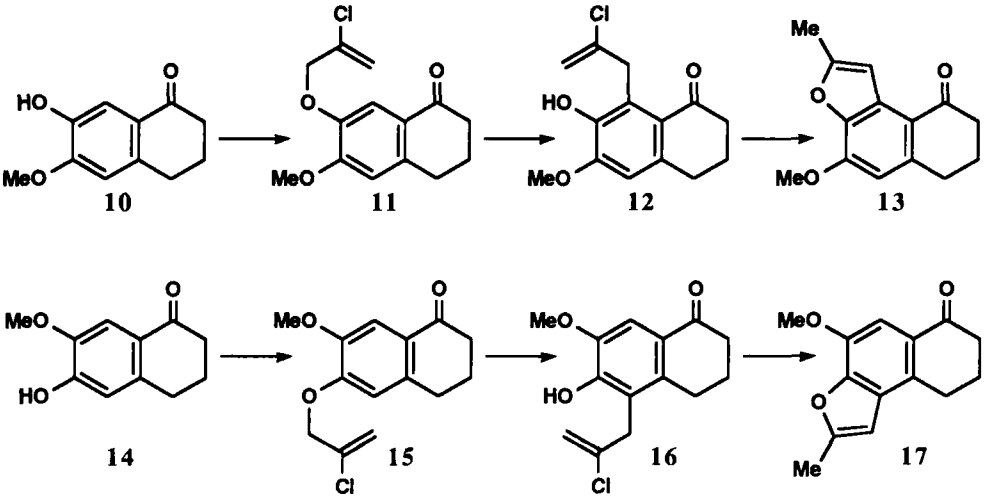
component from the rearrangement of **6** clearly shows the other minor product is isomer **8**; the infrared spectra confirms the presence of the hydroxy group in both cases Mass spectra analysis showed significant M^+ peaks with appropriate fragment ions.

Treatment of the major component phenol (**7**) with polyphosphoric acid led to the methyl furanobenzosuberone (**9a**). The single proton signal (δ 6.45) in the NMR spectrum is in agreement with the β-unsubstituted furan structure assigned and the methyl proton at the α-position of the furan appeared at δ 2.50. The first fraction (minor product **8**) was cyclized in the same way and gave the other furano isomer (**9b**) in low yield. ^{1}H NMR and mass spectral data confirm the above structures.

For comparison with the benzosuberone homologue (**1b**), the synthesis of furanotetralones was studied. Thus, the allyl ether **11**, obtained from 7-hydroxy-6-methoxy-1-tetralone (**10**),[4] gave the Claisen rearrangement product **12** in nearly quantitative yield. Infrared and ^{1}H NMR spectra of **12** confirms the presence of an hydroxyl group. Treatment of phenol **12** with polyphosphoric acid led to the furanotetralone **13.** The ^{1}H NMR spectrum of **13** includes a β-proton signal (δ 6.40) and α-methyl proton signal (δ 2.45). The isomeric β-chloroallyl ether **15** obtained from the corresponding 6-hydroxy-7-methoxy-1-tetralone (**14**)[4] gave the phenol **16** on Claisen rearrangement, which on treatment with acid yielded the furanotetralone **17.** The single proton signal (δ 6.30) in the ^{1}H NMR spectrum of **17** is in agreement with β-unsubstituted furan structure assigned.



The structure of various compounds could be deduced from their IR, ^{1}H NMR, MS spectra and elemental analysis.



EXPERIMENTAL SECTION

Melting points were determined in open glass capillaries on a Mettler FP5 melting point apparatus and are uncorrected. ^{1}H NMR spectra were recorded in $CDCl_3$ on a Varian FT-80A spectrometer. IR spectra were recorded with a Shimadzu 337 spectrophotometer. Mass spectra were taken on VG micromass 7070H and Finnigan Met 1020B mass spectrometers. Elemental analysis were performed by Physical Chemistry Department of the Indian Institute of Chemical Technology, Hyderabad, India.

2-Allyloxy-6,7,8,9-tetrahydrobenzocyclohepten-5-one (2).- A mixture of the hydroxyketone (**1b,** R = H, R' = OH) (2 g, 0.011 mol),[3] allyl bromide (2 mL, 0.023 mol), anhydrous potassium carbonate (20 g, 0.145 mol) and dry acetone (200 mL) was refluxed for 6 hrs. After filtration and evaporation,

the residual oil was extracted into ethyl acetate, washed with aq. NaOH (0.8%, w/v), with brine to neutrality, dried and evaporated. The product was chromatographed on silica gel. Elution with benzene-light petroleum (1:9) gave a pale yellow liquid (2.2 g, 89%), bp. 204-205°/2 mm Hg. IR .(KBr): 1655 (CO) cm^{-1}. ^1H NMR: δ 7.47 (1H, d, J = 9Hz, 4H) 6.88 (1H, d, J = 9Hz, 3H), 6.50 (1H, s, 1H), 5.85 (1H, dd), 5.30-5.05 (2H, m), 4.55 (2H, d), 2.90 (2H, t, J = 6Hz, 9H), 2.72 (2H, t, J = 6Hz, 6H), 1.85-1.65 (4H, m).

Anal. Calcd. for $C_{14}H_{16}O_2$: C, 77.77; H, 7.40. Found : C, 77.75; H, 7.37

Claisen Rearrangement of 2.- The above O-allyl ether (1 g, 0.004 mol) was heated at 200° *in vacuo* (1 mm Hg) for 3 hrs. After cooling, the solid was dissolved in chloroform and shown to contain two compounds by tlc. These were separated by chromatography over alumina using petroleum ether as the eluent. Final purification was achieved by preparative tlc (chloroform). The first fraction (R_f 0.25) was phenol **4** (100 mg, 10%), mp. 90°. IR (KBr): 3300-3200 (OH), 1650 (C=O) cm^{-1}. ^1H NMR: δ 6.62 (1H, s), 7.57 (1H, s), 5.91 (1H, m), 5.55 (1H, s, OH), 5.05 (2H, d), 3.44 (2H, d).

Anal. Calcd. for $C_{14}H_{16}O_2$: C, 77.77; H, 7.40. Found : C, 77.76; H, 7.20

The second fraction (R_f 0.17) was the phenolic isomer (**3**) (400 mg, 40%), mp. 126-130°. IR (nujol): 3250 (OH), 1655 (C=O) cm^{-1}. ^1H NMR: δ 7.45 (1H, d, J = 9Hz, 4H), 6.70 (1H, d, J = 9Hz, 3H), 5.94 (1H, m), 5.55 (1H, s, OH), 5.05 (2H, d), 3.45 (2H, d).

Anal. Calcd. for $C_{14}H_{16}O2$: C, 77.77; H, 7.40. Found : C, 77.70; H, 7.19

Furano-(1,2:2',3')-6,7,8,9-tetrahydrobenzocyclohepten-5-one (5a).- Ozonized oxygen was bubbled into a suspension of C-allyl compound (**3**) (400 mg, 1.85 mmol) in dichloromethane until tlc showed the absence of (**3**) (~ 45 minutes). The ozone was displaced by nitrogen and dimethyl sulfoxide (1 mL) was added. After evaporation of the solvent the residue was treated with polyphosphoric acid (8 mL) at 950 for 45 minutes and poured into ice water. After extraction with chloroform followed by column chromatography on alumina, elution with ethyl acetate/ benzene (3:7) gave the final product (**5a**) (100 mg, 27%), mp. 92-94°, (from benzene): IR (nujol) : 1660 (C=O) cm^{-1}. ^1H NMR: δ 7.45 (1H, d), 6.85 (1H, d), 7.60 (1H, d, J = 3Hz), 6.40 (1H, d, J = 3Hz). MS, m/e: 200 (M^+).

Anal. Calcd. for $C_{13}H_{12}O_2$: C, 78.00; H, 6.00. Found : C, 78.02; H, 5.85

Furano-(2,3:2',3')-6,7,8,9-tetrahydrobenzocyclohepten-5-one (5b).- The furano compound **5b** was prepared under conditions similar to those described for the synthesis of **5a** starting from **4** (75 mg, 0.34 mmol) and yielded (25 mg, 35%), mp. 105-107°; IR (KBr): 1655 (C=O) cm^{-1}. ^1H NMR: δ 7.75 (1H, d, J = 3Hz), 6.80 (1H, d, J = 3Hz), 6.70 (1H, s), 7.25 (1H, s). MS, m/e: 200 (M^+, 100).

Anal. Calcd. for $C_{13}H_{12}O_2$: C, 78.00; H, 6.00. Found : C, 78.20; H, 5.96

2-(2-Chloroallyloxy)-6,7,8,9-tetrahydrobenzocyclohepten-5-one (6).- The hydroxyketone (**1b**, R = H; R' = OH) (2 g, 0.011 mol), 2,3-dichloropropene (4 mL, 0.043 mol), potassium iodide (2 g, 0.012 mol), anhydrous potassium carbonate (20 g, 0.145 mol), and dry acetone (200 mL) were refluxed for 10 hrs. The usual work up gave a liquid 2.1 g, 87%), bp. 207-208°/2 mm Hg; ^1H NMR: δ 7.75 (1H, d, J = 9Hz, 4H), 6.80 (1H, d, J = 9Hz, 3H), 6.60 (2H, s), 5.30-5.45 (2H, 2d), 4.60 (2H, d), 2.90 (2H, t), 2.69 (2H, t), 1.90-1.75 (4H, m). MS, m/e (rel. intensity, %): 250 (M^+ 38), 215 (100), 175 (45), 145 (75), 75 (70).

Anal. Calcd. for $C_{14}H_{15}ClO_2$: C, 67.20; H, 6.00. Found : C, 67.08; H, 6.10

Claisen Rearrangement of 6.- Chloroallyl ether **6** (1 g, 0.004 mol) was heated in N,N-dimethylaniline (2 mL, 0.015 mol) at 200° for 3 hrs under nitrogen. The resulting solution was shaken with ice and dilute hydrochloric acid and extracted with chloroform. Upon evaporation, the organic layer gave a mixture of two components (tlc) which were separated by preparative tlc [SiO_2-Chloroform], the first fraction (R_f 0.25) was the minor component **8** (70 mg, 7%). An analytical sample, mp. 126° was obtained as colorless crystals by crystallization, 10% ethyl acetate/benzene. ^{1}H NMR: δ 7.65 (1H, s), 6.62 (1H, s), 5.25 and 5.15 (2H, 2d, J = 2Hz), 3.65 (2H, s), 4.75 (1H, br, s,OH).

Anal. Calcd. for $C_{14}H_{15}ClO_2$: C, 67.20; H, 6.00. Found : C, 67.15; H, 5.94

The second fraction (R_f 0.17) on crystallization from 10% ethyl acetate/benzene gave **7** (300 mg, 30%), mp. 190°; IR (nujol) : 3350-3200 (OH), 1670 (C=O) cm^{-1}. ^{1}H NMR: δ 7.65 (1H, d, J = 9Hz, 4Hz), 6.72 (1H,d , J = 9Hz, 3H), 5.55 (1H, br, OH), 5.15 and 4.80 (2H, 2d, J = 2Hz), 3.70 (2H, s), 2.89 (2H, t, J = 6Hz, 9H), 2.70 (2H, t, J = 6Hz, 6H), 1.90-1.60 (4H, m). MS, m/e: 250 (M^+), 145 (M-105, base peak).

Anal. Calcd. for $C_{14}H_{15}ClO_2$: C, 67.20; H, 6.00. Found : C, 67.05; H, 5.96

Furano-(1,2:2'-methyl,3')-6,7,8,9-tetrahydrobenzocyclohepten-5-one (9a).- C-Allyl compound **7** (200 mg, 0.78 mmol) was stirred in polyphosphoric acid for 45 min at 100°. The usual work up followed by preparative tlc [SiO_2-chloroform] gave the crystalline product **9a** (75 mg, 44%), mp. 80-82° (from benzene-ethyl acetate). IR (KBr) : 1660 (CO) cm^{-1}. ^{1}H NMR: δ 7.70 (2H, d), 7.35 (2H, d), 6.45 (1H, s), 2.50 (3H, s). MS, m/e: 214 (M^+ base peak).

Anal. Calcd. for $C_{14}H_{14}O_2$: C, 78.50; H, 6.54. Found : C, 78.35; H, 6.50

C-Allyl derivative **8** (70 mg, 0.32 mmol) was cyclized in the same way as before and gave the isomeric product **9b** (20 mg, 12%), mp. 87°. ^{1}H NMR: δ 7.75 (1H, s), 7.10 (1H, s), 6.40 (1H, s), 2.40 (3H, s). MS, m/e: 214 (M^+, 100 base peak).

Anal. Calcd. for $C_{14}H_{14}O_2$: C, 78.50; H, 6.54. Found : C, 78.46; H, 6.52

7-(2-Chloroallyloxy)-3,4-dihydro-6-methoxynaphthalen-1(2H)-one (11).- Hydroxy tetralone **10** (1 g, 0.005 mol),[4] anhydrous potassium carbonate (10 g, 0.072 mol), potassium iodide (1 g, 0.006 mol), 2,3-dichloropropene (2 mL, 0.021 mol) and dry acetone (100 mL) were refluxed for 6 hrs Work-up as before followed by crystallization from light petroleum-benzene gave **11** as colorless crystals (1.2 g, 87%), mp. 92-93°. ^{1}H NMR: δ 7.45 (1H, s), 6.75 (1H, s), 3.75 (3H, s), 5.50 (2H, 3d), 4.60 (2H, br, s), 2.85 (2H, t), 2.55 (2H, t), 2.2-1.95 (2H, m).

Anal. Calcd. for $C_{14}H_{15}ClO_3$: C, 63.15; H, 5.63. Found : C, 63.10; H, 5.60

8-2(-Chloroallyl)-3,4-dihydro-7-hydroxy-6-methoxynaphthalen-1(2H)-one (12).- Chloroallyl ether **11** (1 g, 0.003 mol) was treated with N,N-dimethylaniline (2 mL, 0.015 mol) at 200° for 3 hrs under nitrogen. Work-up as before yielded **12** as a crystalline product (0.75 g, 75%), mp. 121-123° (from benzene-light petroleum). IR (KBr) : 3300-3400 (OH), 3030 (C=CH_2), 1660 (C=O), 890 (>C=CH_2), 610, 650, 660 (-ClC=C) cm^{-1}. ^{1}H NMR: δ 6.50 (1H, s), 5.20 (2H, d), 3.65 (2H, br, s), 3.75 (3H, s). MS. m/e: 266 (M^+).

Anal. Calcd. for $C_{14}H_{15}ClO_3$: C, 63.15; H, 5.63. Found : C, 63.05; H, 5.64

Furano-(7,8:2'-methyl,3')-3,4-dihydro-6-methoxynaphthalen-1(2H)-one (13).- Chloroallyl compound **12** (300 mg, 1 mmol) was stirred in polyphosphoric acid for 45 min at 100°. The usual work-up followed by preparative tlc [SiO_2-chloroform-benzene (7:3)] gave the final product **13** (80 mg, 31%). An analytical sample was obtained as colorless prisms, mp. 145-146°, by crystallization from 5% chloroform-benzene. IR (KBr) : 1665 cm^{-1}. ^1H NMR: δ 6.70 (1H, s), 6.40 (1H, a) 2.45 (3H, s) 3.75 (3H, s). MS, m/e (rel intensity): 230 (100, M^+) 202 (58, M-C_2H_4) 174 (25, M-C_3H_4O).

Anal. Calcd. for $C_{14}H_{14}O_3$: C, 73.04; H, 6.08. Found : C, 73.12; H, 6.00

6-(2-Chloroallyloxy),3,4-dihydro-7-methoxynaphthalen-1(2H)-one (15).- 6-Hydroxy1tetralone **14** (1 g, 0.005 mol) was alkylated using the same procedure as for the preparation of **10**; there was obtained the chloroallyloxy compound **15** (1.1 g, 80%), mp 86-88° (from benzene-petroleum). IR (KBr): 1668 (C=O), 920, 910, 850 (C=CH_2) cm^{-1}. ^1H NMR: δ 7.45 (1H, s), 6.70 (1H, s), 5.55 (2H, d), 4.60 (2H, s), 3.83 (3H, s).

Anal. Calcd. for $C_{14}H_{15}ClO_3$: C, 63.15; H, 5.63. Found : C, 63.06; H, 5.54

5-(2-Chloroallyl)-3,4-dihydro-6-hydroxy-7-methoxynaphthalene-1(2H)-one (16).- The same procedure as before was used for the rearrangement of **15** (500 mg, 1 mmol) to give **16** (350 mg, 70%), as a crystalline product, mp. 136-138° (from benzene). IR (KBr): 3300-3400 (OH), 1665 (C=O) cm^{-1}. ^1H NMR: δ 7.40 (1H, s), 3.85 (3H, s), 5.25 (2H, d) 3.64 (2H, s).

Anal. Calcd. for $C_{14}H_{15}ClO_3$: C, 63.15; H, 5.64. Found : C, 63.09; H, 5.58

Furano-(5,6:2'-methyl,3')-3,4-dihydro-7-methoxynaphthalen-1(2H)-one (17).- Using the same procedure as for the preparation of **13**, C-chlorallyl derivative **16** (300 mg, 1 mmol) gave the crystalline furano analogue **17** (150 mg, 58%) (from benzene-ethylacetate), mp. 110-111°. ^1H NMR: δ 7.30 (1H, s), 6.30 (1H, s), 2.40 (3H, s), 3.90 (3H, s), 2.90 (2H, t), 2.55 (2H, t), 1.95-2.20 (2H, m); MS, m/e 230 (100, M^+).

*Anal.*Calcd. for $C_{14}H_{14}O3$: C, 73.04; H, 6.08. Found : C, 73.10; H, 6.03

Acknowledgement.- Helpful discussions with Dr. G. R. Proctor, Strathclyde, University, U. K. is gratefully acknowledged.

REFERENCES

1. National Cancer Institute, Bethesda, MD 24014, USA.

2. J. McLean, V. Peesapati and G. R. Proctor, *J. Chem. Soc., Perkin 1*, 98 (1979); see also, idem., *ibid.*, 450 (1974) and *Bull. Soc. Chim. France*, (2) 793 (1973).

3. G. R. Proctor and A. H. Renfrew, *J. Chem. Soc.* (C), 1187 (1968).

4. P. D. Carpenter, V. Peesapati and G. R. Proctor, J. Chem. Soc., Perkin 1, 103 (1979).

(Received October 14, 1991; in revised form January 7, 1992)