Proc. Indian Acad. Sci., Vol. 81 A, No. 1, pp. 38 - 41

Synthesis of phenyl substituted furanobenzopyrones*

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MS received 12 August 1974; after revision 23 November 1974

ABSTRACT

The syntheses of 1, 2-diphenyl-6-methyl-8-oxo-8H-furo-[2, 3-*h*] (1) benzopyran, 2, 3-diphenyl-5-methyl-7-oxo-7H-furo [2, 3-*g*] (1) benzopyran and 1, 2-diphenyl-4-methyl-6-oxo-6H-furo [2, 3-*f*] (1) benzopyran are described, and uv and ir data of the compounds reported. The compounds were found to be devoid of anti-implantation activity when tested on albino rats.

BASED on the work of Chawla *et al.*[1] on benzofurans possessing antifertility activity, we have synthesised simple and condensed 2′, 3′-diphenylbenzofurans as possible antifertility agents.[2] Lednicer *et al.*[3] have shown that a few of the 3, 4-diarylcoumarins synthesised by them on structural analogy with potent 2, 3-diphenylindenes have antifertility activity at a dose of 0·1 mg/kg/rat/day. Hence, it seemed of interest to synthesise diphenyl substituted furanobenzo-α-pyrones wherein the two phenyl nuclei are on the furan ring constituting a modified version of the triarylethylene structure associated with antifertility activity and with a hetero atom as in benzofuran and an α-pyrone ring fused with the benzene ring. Such compounds can be expected to have antifertility activity. Further the observations of Pomshehenko[4] that the well-known furanocoumarins, psoralen and isopsoralen, prevent pregnancy in rats at a dose of 100 mg/kg lend further support to this work. As model experiments 7-hydroxy-4-methylcoumarin[5] and 7-hydroxy-4, 8-dimethylcoumarin[6] besides 5-hydroxy-4, 7-dimethylcoumarin[7] have been condensed with benzoin in the presence of polyphosphoric acid (PPA) to yield the angular or the linear furanobenzo-α-pyrones as the case may be (chart 1). Further a comparative study of the effectiveness of PPA as against other reagents like 73% H_2SO_4,[8] HCl in dioxan[9] for such condensation has now been made and the superiority of PPA is clearly established. By employing 73% H_2SO_4 charring is observed and a dark mass

* This paper is Part XXIII of a series entitled "Furano Compounds".

of the cyclised product is obtained from which the pure substance could be obtained in only 8% yield. With dioxan-HCl, the reaction does not proceed probably due to the poor reactivity of the phenol and only benzil due to oxidation of benzoin is obtained. Employing PPA and a temperature of 100–110° the diphenyl substituted furanobenzo-α-pyrones could be obtained in 16% yield. The required coumarins have been obtained by the Pechmann reaction of resorcinol, 2-methylresorcinol or orcinol with acetoacetic ester.

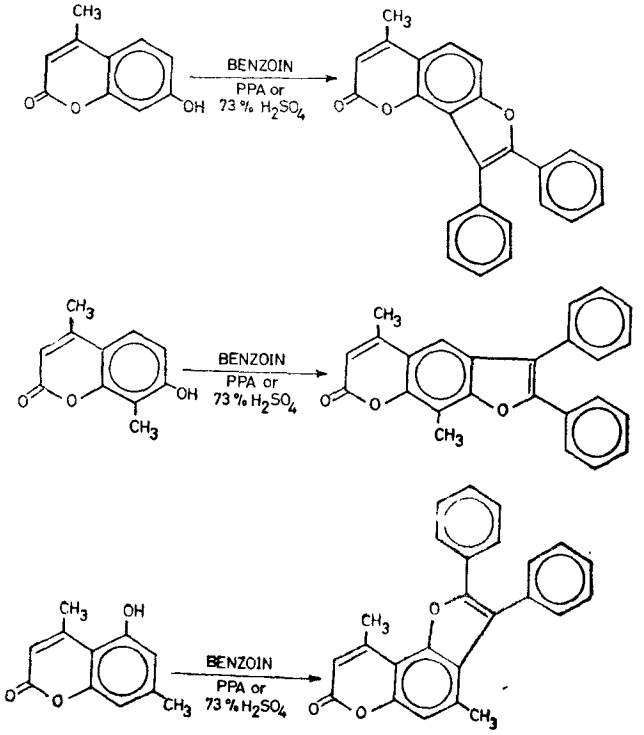

Chart I

Biological activity.—All the compounds were tested for their anti-implantation activity in pregnant female albino rats by the method described by Kar *et al.*[10] at the Central Drug Research Institute, Lucknow. None of the compounds was found to be active at a dose of 10 mg/kg in a 5-day schedule when given orally.

Experimental

Infrared spectra were determined on a Perkin Elmer Model-157 Spectrophotometer with sodium chloride prism in KBr-disc. UV spectra were determined on Beckmann DB Spectrophotometer.

TLC of the compounds reported was carried out using benzene-ethyl acetate (4·6 + 4 ml). In all cases single spots were obtained establishing the purity of the compounds.

1, 2-*Diphenyl*-6-*methyl*-8-*oxo*-8 *H-furo* [2, 3-*h*] (1) *benzopyran* (I)

(*a*) An intimate mixture of 7-hydroxy-4-methylcoumarin (1·8 g) and benzoin (2·1 g) was added to PPA (25 gms P_2O_5 + 12 ml H_3PO_4) kept at 100–110° and the mixture kept stirred for 6 hr at this temperature. The reaction mixture was decomposed by pouring into ice-cold water and the solid that separated was filtered and crystallised from benzene. The furano-benzo-α-pyrone (I) was obtained as needles. mp 220°. Yield: 0·6 g (16%); uv $\lambda_{max}^{CH_3OH}$: 290 nm (log $\epsilon = 4 \cdot 381$), ir ν_{max}^{KBr}: 1740, 1590, 1520, 1480, 1460, 1440, 880, 870, 825 cm^{-1}. Found: C 81·5, H 4·8; $C_{24}H_{11}O_3$ requires C. 81·8, H 4·5.

(*b*) A mixture of benzoin (2·1 g) and 4-methyl-7-hydroxycoumarin (1·8 g) was heated over direct flame until it melted. Then this was cooled to 60–70°. To this sulfuric acid (73%) (10 ml) was added and heated for 30 min at 120–130° C. The reaction mixture was cooled and poured into ice-cold water. The solid separating was filtered and washed several times with water. On crystallisation from aq. alcohol the furano compound was obtained as colourless needles, mp and mmp 220° C. Yield: 0·3 g (8%).

2, 3-*Diphenyl*-5-*methyl*-7-*oxo*-7 *H-furo*[2, 3-*g*] (1) *benzopyran* (II)

(*a*) 4, 8-Dimethyl-7-hydroxycoumarin (2·0 g) and benzoin (2·2 g) were mixed and added to PPA (25 g P_2O_5 + 12 ml H_3PO_4) kept at 100–110° for 1 hr. The reaction was continued for 6 hr and the reaction product subsequently worked up as in the preceding case. Since all attempts at crystallisation failed the crude furanobenzo-α-pyrone (II) thus obtained was purified by chromatographic adsorption employing silicagel. The benzene eluate gave the pure compound which on further crystallization from benzene-petroleum ether yielded the compound (II) as shining needles. mp 218–219°; yield: 0·58 g (15%); uv $\nu_{max}^{CH_3OH}$ 234–245 nm broad (log $\epsilon = 4 \cdot 339$) 288 nm (log $\epsilon = 4 \cdot 551$); ir ν_{max}^{KBr} 1750, 1600, 1450, 880, 820 cm^{-1}. Found C, 82·5, H. 5·3; $C_{22}H_{18}O_3$ requires C 82·0, H, 4·9.

(*b*) Benzoin (2·2 g) was mixed with 4, 8-dimethyl-7-hydroxycoumarin (2·0 g) and the mixture heated over free flame until it melted. This was then cooled to 60–70° and treated with sulfuric acid (73%) (7 ml) and subsequently heated at 120–140° C for 30 min. After cooling the reaction mixture was poured into ice-cold water and worked up as usual. On crystallisation from alcohol compound (II) was obtained as shining needles, mp

218° C. Yield: 0·3 g (7·5%). (mmp with the sample obtained by the other method showed no depression).

1, 2-*Diphenyl*-4-*methyl*-6-*oxo*-6 *H-furo* [2, 3-*f*] (1) *benzopyran* (III)

(*a*) To a stirred mass of PPA (25 g P_2O_5 + 12 ml H_3PO_4) kept at 100–110° was added a mixture of benzoin (3·3 g) and 4, 7-dimethyl-5-hydroxycoumarin (3·0 g) and the heating was continued for 6 hr. Subsequently the reaction mixture was poured into ice-cold water and worked up as usual. On crystallisation from benzene compound (III) was obtained as rods, mp 239° C; yield: 0·8 g (14%). uv $\lambda_{max}^{CH_3OH}$ 302 nm (log $\epsilon = 4{\cdot}575$); ir ν_{max}^{KBr} 1730, 1640, 1575, 1490, 1450, 885, 810 cm^{-1}. Found: C 80·3, H 5·3. $C_{25}H_{18}O_3$ H_2O requires C 80·2, H 5·3.

(*b*) To a melt of benzoin (3·3 g) and 4, 7-dimethyl-5-hydroxycoumarin (3·0 g) kept at 60–70°, sulfuric acid (73%) (7 ml) was added and the mass heated at 120–140° C for 30 min. After cooling, the reaction mixture was poured into ice-cold water and worked up as usual. Crystallisation from alcohol yielded compound (III) as rods, mp 238° C; yield: 0·45 g (7%) (mmp with the sample obtained by the other method showed no depression).

Acknowledgement

We thank Dr. Nitya Nand, Central Drug Research Institute, for data relating to spectral and elemental analysis and Dr. V. P. Kamboj for the antifertility screening results.

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