Proc. Indian Acad. Sci., Vol. 85 A, No. 6, 1977, pp, 524–530

Synthesis of benzodipyrandiones

J. R. MERCHANT, S. S. SHIRALI, M. S. KAMAT AND S. Y. DIKE

Department of Organic Chemistry, Institute of Science, Bombay 400032

MS received 18 November 1976; in revised form 3 January 1977

ABSTRACT

The reaction of hydroxycoumarins, flavones, isoflavones and chromones with α, β-unsaturated acids, in the presence of PPA has been found to give a number of compounds whose structures have been elucidated on the basis of spectral data and the formation of 2, 4–DNP derivatives.

1. INTRODUCTION

IN our previous publications we have reported that hydroxy coumarins,[1, 2] flavones, isoflavones and chromones with acrylonitrile in the presence of basic catalysts afford the corresponding O-propionitriles. Hydrolysis of the latter with conc. hydrochloric acid yields the respective O-propionic acids, which could be cyclised with PPA to give the appropriate benzodipyrandiones.

The above method apart from being elaborate is not suitable for the syntnesis of benzodipyrandiones having alkyl substituents in the pyranone ring as the corresponding acrylonitriles are not easily available. Hence a shorter and convenient route described here for this synthesis is to heat directly the hydroxybenzopyrone with the appropriate α, β-unsaturated acid in the presence of PPA to yield the corresponding benzopyrandione in about $15 \sim 30\%$ yields.

6-Hydroxy-4-methylcoumarin[3] (A) was heated with acrylic acid in the presence of PPA at 100–120°, when a brown mass was isolated which was chromatographed over alumina. Elution with benzene afforded an orange crystalline solid ($C_{13}H_{10}O_4$), m.p. 210–12°, which was assigned the linear structure I[1] on the basis of its NMR ($CDCl_3$)which showed two singlets at δ 7·29 and δ 7·46 for C_5 and C_{10} protons respectively. 2, 4–DNP, m.p.

298–300°. The second compound eluted with chloroforms was a yellow crystalline solid having the molecular formula $C_{13}H_{10}O_4$, m.p. 235–37° was assigned the ester structure (II *a*).

The reaction of (A) with α-methylacrylic acid in the presence of PPA afforded a single compound (II *b*) m.p. 105–07°, which was found to be the corresponding acrylate.

Crotonic acid reacted with (A) under identical conditions to give a yellowish-brown solid, m.p. 142–43°. Its structure (II *c*) was consistent with its spectral data.

β, β-Dimethylacrylic acid with (A) gave a yellow oil, b.p. 135–36°/3–3·5 mm. which was found to be the corresponding acrylate (II *d*).

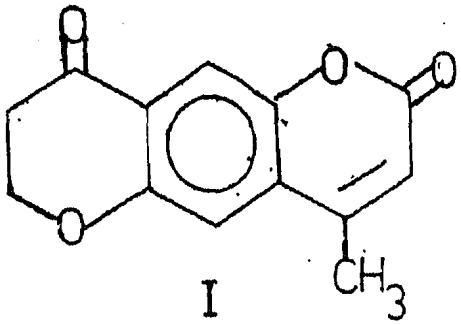
The reaction of 7-hydroxycoumarin[4] (B) with acrylic acid in the presence of PPA yielded two compounds which were separated by column chromatography over alumina.

The first compound eluted with benzene, m.p. 207–09°, was assigned the linear structure (III *a*)[1], 2, 4-DNP, m.p. 291–92°. The second compound eluted with benzene-ether (1 :1), m.p. 216–18°, was assigned the angular structure (IV *a*)[1], 2, 4-DNP, m.p. 286–88°. Under identical conditions (B) reacted with α-methylacrylic acid to give a white solid, m.p. 125–28° (II *e*). Attempts to cyclise the latter resulted in the hydrolysis of the ester group.

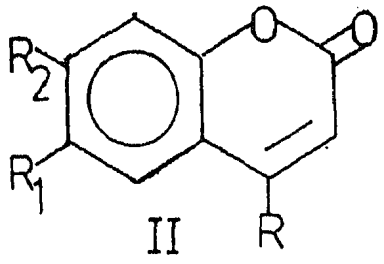
With crotonic acid, the coumarin (B) reacted in the presence of PPA to afford a single compound, m.p. 92–94°, which was purified by chromatography over alumina. The structure (IV *b*) was assigned to it from its analytical and spectral data and the formation of 2, 4-DNP (m.p. 265–67°).

Condensation of (B) with β, β-dimethylacrylic acid in the presence of PPA failed to yield a pure substance. However, when (B) was reacted with β, β-dimethylacrylic acid in the presence of zinc chloride and phosphorus oxychloride at room temperature for 48 hr., a white solid having the molecular composition $C_{14}H_{12}O_4$ was isolated in 35% yield. Its NMR ($CDCl_3$) showed a singlet at δ 3·05 for methylene protons. Its i.r. did not show a keto band around 1680 cm^{-1}, but a band at 1740 cm^{-1} was observed. It did not give a 2, 4-DNP. From the above data the compound was assigned the dihydrocoumarin structure (V).

The reaction of 7-hdroxy-4-methylcoumarin (C)[5] with acrylic acid in the presence of PPA yielded three compounds which were separated by chromatography over alumina.

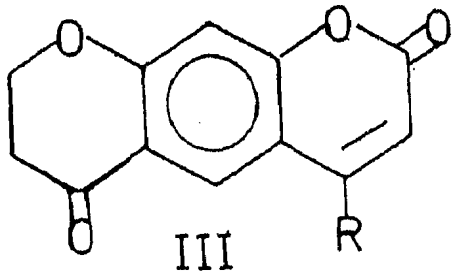


I



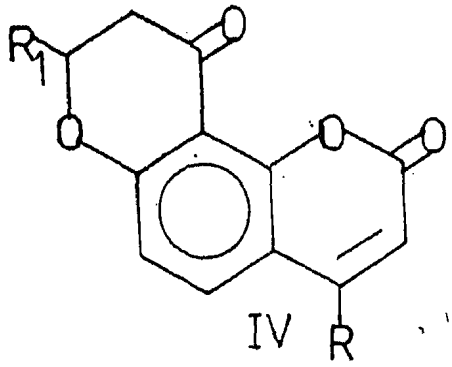
II

(*a*) R = CH_3; R_1 = O.COCH = CH_2; R_2 = H.
(*b*) R = CH_3; R_1 = O.COC(CH_3) = CH_2; R_2 = H
(*c*) R = CH_3; R_1 = O.CO.CH(CH_3) = CH; R_2 = H.
(*d*) R = CH_3; R_1 = O.CO.CH = C(CH_3)(CH_3); R_2 = H.
(*e*) R = R_1 = H; R_2 = O.CO.C(CH_3) = CH_2
(*f*) R = CH_3; R_1 = H; R_2 = O.CO.CH = CH_2.
(*g*) R = CH_3; R_1 = H; R_2 = O.CO.C(CH_3) = CH_2
(*h*) R = CH_3; R_1 = H; R_2 = O.CO.CH(CH_2) = CH
(*i*) R = CH_3; R_1 = H; R_2 = O.CO.CH = C(CH_3)(CH_3)



III

(*a*) R = H
(*b*) R = CH_3



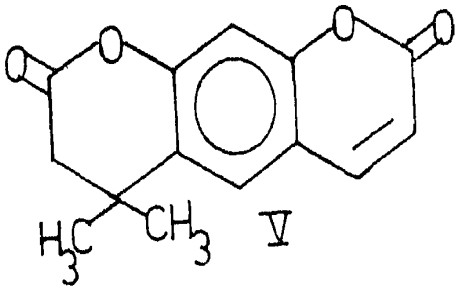
IV

(*a*) R = R_1 = H.
(*b*) R = H; R = CH_3
(*c*) R = CH_3; R_1 = H
(*d*) R = R_1 = CH_3.

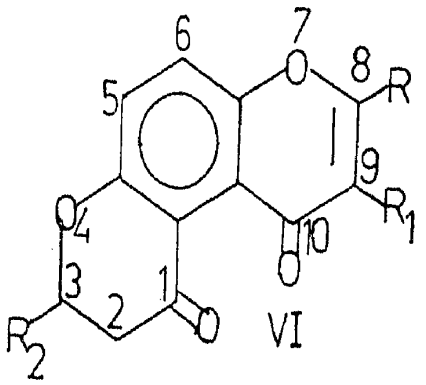
Elution with benzene gave the previously reported linear benzodipyrandione (III *b*)[2], m.p. 235–37°, 2, 4-DNP, m.p. 297–98°, whilst the benzene-chloroform fraction (4:3), yielded the known angular isomer (IV *c*)[2], m.p. 244–46°, 2, 4-DNP, m.p. 292°. From the chloroform fraction, the acrylate (II *f*), m.p. 312–13°, was isolated in 15% yield.

Under identical conditions (C) with α-methylacrylic acid gave an acrylate (II g), m.p. 177–80°.

Crotonic acid reacted with (C) under identical conditions to give two compounds which were separated by column chromatography over alumina

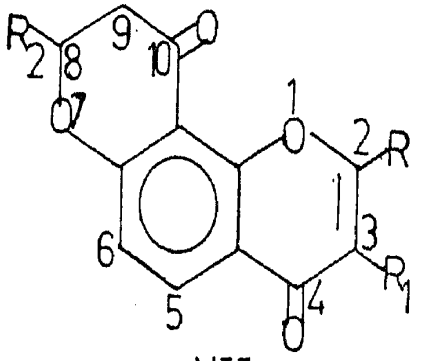


V



VI

(*a*) R = Ph; $R_1 = R_2 = H$.
(*b*) R = Ph; $R_1 = H$; $R_2 = CH_3$.
(*c*) R = CH_3; $R_1 = R_2 = H$.
(*d*) R = $R_2 = CH_3$; $R_1 = H$.



VII

(*a*) R = Ph; $R_1 = R_2 = H$.
(*b*) R = Ph; $R_1 = H$; $R_2 = CH_3$
(*c*) R = CH_3; R_1 = Ph, $R_2 = H$.
(*d*) R = $R_2 = CH_3$; R_1 = Ph.
(*e*) R = R_1 = Ph; $R_2 = H$.
(*f*) R = R_1 = Ph; $R_2 = CH_3$.
(*g*) R = CH_3; $R_1 = R_2 = H$.
(*h*) R = $R_2 = CH_3$; $R_1 = H$

The first compound eluted with benezne-chloroform (19:1 formed colourless needles, m.p. 196–98°, having the molecular composition $C_{14}H_{12}O_4$. The structure (IV *d*) was assigned to it from its analytical and spectral data and the formation of 2, 4-DNP, m.p. 290–91°. NMR (CF_3COOH) showed an AB pattern of two doublets at δ 7·3 and 8·1 corresponding to the two aromatic protons.

The second compound eluted with chloroform, m.p. > 280° was found to be the acrylate (II *h*).

β, β-Dimethylacrylic acid with (C) gave a yellow oil, b.p. 215–20°/3–3·5 mm, which was found to be the corresponding acrylate (II *i*).

From the mechanistic point of view, two competing reactions seem to take place in the above synthesis. The first is the Michael addition of the α, β-unsaturated acid to the phenolic – OH followed by ring closure to give a benzodipyrandione. Alternatively, it is also possible that a

Friedel-Craft acylation occurs first at a favourable position and is followed by ring closure. The second is the formation of acrylates (these are isolated in many cases) which would be expected to undergo a Fries rearrangement followed by cyclisation to give a coumarin derivative.

Thus, hydroxycoumarins with acrylic and crotonic acids afford the benzodipyrandiones as well as the acrylates in some cases, but α-methylacrylic- and β, β-dimethylacrylic-acids yield only the acrylates.

This reaction of α, β-unsaturated acids in presence of PPA was further extended to 6-hydroxy-,[6] 7-hydroxy-,[7–10] 5-hydroxy-[5,11–14] flavones; 7-hydroxy-2-methyl-,[15–17] and 7-hydroxy-2-phenylisoflavones[17] and 6-hydroxy-2-methyl-,[18, 19] 7-hydroxy-2-methyl-,[20, 21] and 5-hydroxy-2-methyl-[5, 11, 12, 22, 23] chromones. However, the reaction of acrylic acid with 5-hydroxy-flavone and 5-hydroxy-2-methylchromone gave compounds in poor yields (2, 4-DNP, m.p. 250–52° and 270–72° respectively). The structures of these were based on spectral and analytical data, and the formation of 2, 4-DNP derivatives. Surprisingly, the reaction of the above compounds failed with α-methyl- and β, β-dimethyl-acrylic acids and the original substances were recovered unchanged.

2. EXPERIMENTAL

All m.ps are uncorrected. I.R. spectra were recorded on a Perkin-Elmer 421 spectrophotometer, 60 MHz NMR spectra were recorded on a Varian instrument. The homogeneity of compounds were ascertained by T.L.C. on silica gel G plates using petrolether-ethyl acetate (95 : 5) as the solvent system. The spots were developed in an iodine chamber. Neutral alumina was used for column chromatography.

REACTION OF HYDROXYBENZOPYRONE WITH α-β-UNSATURATED ACID IN THE PRESENCE OF PPA

To a mixture of phosphorus pentoxide (50 g) and phosphoric acid (25 ml) preheated at 100° for 0·5 hr was added the hydroxybenzopyrone (0·1 mole) and the α, β-unsaturated acid (0·1 mole). The heating was continued for 4·5 hr more at 100–120 with occasional shaking. The mixture was poured in water (500 ml), then extracted with chlorofrom, washed with sodium hydroxide solution (10%), water and dried. Removal of the solvent left behind a dark semi-solid which was purified by column chromatography.

REACTION OF 7-HYDROXYCOUMARIN WITH β, β-DIMETHYLACRYLIC ACID IN THE PRESENCE OF ZINC CHLORIDE AND PHOSPHORUS OXYCHLORIDE

A mixture of 7-hydroxycoumarin (1·6 g), β, β-dimethylacrylic acid (1·5 g), zinc chloride (4 g) and phosphorus oxychloride (15 ml) was shaken

well and kept at room temperature for 48 hr. It was then decopmosed with ice, when a brownish-yellow solid separated. It was filtered, washed well with sodium hydroxide solution (10%), water and dried. A pinkish-white solid (V) (600 mg) was obtained, m.p. 123–25°.

(VI *a*): m.p. 180–82°** (benzene-pet. ether*); 2, 4-DNP; m.p. 254–56°.

(VII *a*)[24]: m.p. 218–19°**** (benzene-pet. ether); 2, 4-DNP; m.p. 250–51°.

(VII *c*)[24]: m.p. 189–91°**** (ethyl acetate-pet. ether); 2, 4-DNP; m.p. 268–70°.

(VII *e*): m.p. 250–52°**** (benzene-pet. ether); 2, 4-DNP; m.p. 285–87°.

(VI *c*): m.p. 189–90°*** (ethyl acetate-pet. ether); 2, 4-DNP; m.p. 247–49°.

(VII *g*)[24]: m.p. 183–85°**** (ethyl acetate-pet. ether); 2, 4-DNP; m.p. 288–89°.

(VI *b*): m.p. 205–07°** (benzene-pet. ether); 2, 4-DNP; m.p. 219–20°. I.R. ($CHCl_3$) 1685 (>C=O chromanone), 1630 (>C=O flavone) cm^{-1}; NMR (δ, $CDCl_3$): 1·74 (3H, d, C_3CH-CH_3), 3·1 (2H, s, C_2CH_2); 4·9 (1H, m, C_3CH), 7·0 (1H, s, C_9H), 7·4 ~ 7·9 (5H, m of C_6H_5 at C_8), 7·98 (1H, d, C_5H, J = 10Hz), 8·34 (1H, d, C_6H, J = 10Hz).

(VII *b*): m.p. 226–27°***** (alcohol); 2, 4-DNP; m.p. 264–65°. I.R. ($CHCl_3$) 1680 (>C=O chromanone), 1630 (>C=O flavone); NMR (δ, $CDCl_3$), 1·6 (3H, d, C_8, CH-CH_3), 2·75 (2H, d, C_9, CH_2), 4·8 (1H, m, C_8 CH), 7·0 (1H, d, C_6H, J = 9Hz), 7·5 ~ 7·9 (5H, m of C_6H_5 at C_2), 8–33 (1H, d, C_5H, J = 9Hz).

(VII *d*): m.p. 216–17°**** (alcohol) 2, 4-DNP, m.p. 279–80°.

(VII *f*): m.p. 235–37°**** (alcohol); 2, 4-DNP; m.p. 281–83°.

(VI *d*): m.p. 192–93°** (benzene-pet. ether); 2, 4-DNP; m.p. 279–80°.

(VII *h*): m.p. 180–82°***** (benzene-pet. ether); 2, 4-DNP; m.p. 274–76°.

---

* Pet. ether used throughout had b.p. 40–60°.

** Yellow needles.

*** Orange needles.

**** Colourless needles.

***** Brown needles.

ACKNOWLEDGEMENTS

The authors are grateful to Dr. K. Nagarajan, Dr. S. Selvavinayakam (Ciba-Geigy Research Centre, Bombay) and Mr. V. M. Paradkar for IR and NMR spectra. We also thank U.G.C. for the award of Junior Research Fellowship to SSS. and MSK.

REFERENCES

1. Merchant, J. R. and Patell, J. R., *Curr. Sci.* **37** 404 (1968).
2. Merchant, J. R., Patell, J. R. and (Smt.) Barve, N. V., *J. Indian Chem. Soc.* **48** 241 (1971).
3. Borsche, W., *Ber.* **40** 2731 (1907).
4. Bridge, W., Crocker, A. J., Cubin, T. and Robertson, A., *J. Chem. Soc.* 1530 (1937).
5. Pechmann, H. V. and Duisberg, C., *Ber.* **16** 2119 (1883).
6. Pandit, S. and Sethna, S., *J. Indian Chem. Soc.* **27** 3 (1950).
7. Robinson, R. and Shah, R. C., *J. Chem. Soc.* p. 1494 (1934).
8. Baker, W., *J. Chem. Soc.* p. 1386 (1933).
9. Virkar, V. V., *Ph.D. Thesis*, University of Bombay, 1942.
10. Robinson, R. and Venkataraman, K., *J. Chem. Soc.* p. 2345 (1926).
11. Limaye, D. B. *Ber.* **65**, 375 (1932).
12. Limaye, D. B. and Gangal, D. D., *Rasayanam* **1** 64 (1936); *C.A.* **31** 2182 (1937).
13. Baker, W., *J. Chem. Soc.* p. 1954 (1934).
14. Virkar, V. V., *M.SC. Thesis*, University of Bombay (1939).
15. Robinson, R. and Baker, W., *J. Chem. Soc.* p. 127 (1925).
16. Joshi, D. V., *Ph.D. Thesis*, University of Bombay, p. 146 (1951).
17. Nencki, M. and Sieber, N., *J. Prakt. Chemie* **23** 147 (1881).
18. Amin, G. C. and Shah, N. M., *J. Indian Chem. Soc.* **25** 380 (1948).
19. Desai, R. D. and Mavani, C. K., *Proc. Indian Acad. Sci.* **A25** 354 (1947).
20. Kostanecki, St. von and Rozycki, A., *Ber.* **34** 102 (1901).
21. Bloch, M. and Kostanecki, St. von, *Ber.* 33 474 (1900).
22. Limaye, D. B. and Kelkar, G. R., *J. Indian Chem. Soc.* **12** 788 (1935).
23. Limaye, D. B. and Kelkar, G. R., *Rasayanam* **1** 24 (1936); *C.A.* **31** 2213 (1937).
24. Merchant, J. R. and Thakkar, S. M., *Curr. Sci.* **40** 353 (1971).