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BENZOPYRONES. PART XII.[1] NOVEL SYNTHESIS OF SOME 3-SUBSTITUTED CHROMONES

G.J.P.Becket and G.P.Ellis*

Department of Chemistry, University of Wales Institute of Science and
Technology, King Edward VII Avenue, Cardiff CF1 3NU, Wales, U.K.

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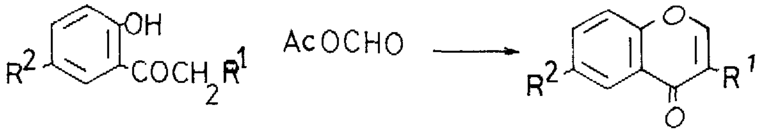
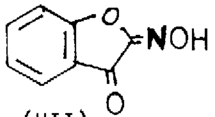
A considerable number of nitrochromones have been described but 3-nitrochromones are almost unknown. A compound which Huebner and Link[2] described as 'probably 2-methyl-3-nitrobenzo-γ-pyrone' was prepared in 18% yield by treatment of 2'-hydroxy-2-nitroacetophenone (I) with acetic anhydride in pyridine.

We describe an efficient synthesis of 3-nitrochromones. 2'-Hydroxy-2-nitroacetophenone[2] (I) reacted with acetic formic anhydride and sodium formate without external heating or cooling to give an almost quantitative yield of 3-nitrochromone (IV), m.p. 151-152° ; ir, 1670, 1620, 1574, 1525, 1462, 1385, 1360 cm^{-1}; nmr, δ [$CDCl_3$] 9.14 (1H, s, 2-H), 8.40 (1H, q, J 8 and 2 Hz, 5-H), 8.10-7.45 (3H, m, 6-, 7- and 8-H). 2,5'-Dinitro-2'-hydroxyacetophenone (II) similarly gave an excellent yield of 3,6-dinitrochromone (V), m.p. 180-182° ir, 1665, 1625, 1555, 1520 cm^{-1}; nmr δ [$(CD_3)_2SO$] 8.68 (1H, d, J 2.5 Hz, 5-H), 8.50(1H, q, J 2.5 and 8.5 Hz,7-H), 8.45 (1H, s, 2-H) 7.67 (1H, d, J 8.5 Hz, 8-H).

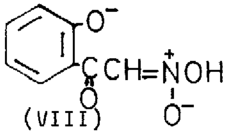


I, $R^1=NO_2$, $R^2=H$
II, $R^1=R^2=NO_2$
III, $R^1=Ac$, $R^2=H$

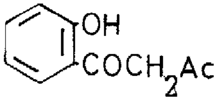
IV, $R^1=NO_2$, $R^2=H$
V, $R^1=R^2=NO_2$
VI, $R^1=Ac$, $R^2=H$



(VII)



(VIII)



(IX)

An attempt to convert the nitroketone(I) into a chromone-2-carboxylic acid or ester by heating with ethyl oxalyl chloride in pyridine[3] gave a high yield of the benzofuranone(VII), m.p.174° (lit.[4] 175°), ir (KBr) 3200 (broad), 1720, 1624, 1520 cm^{-1}; nmr $\delta\,[(CD_3)_2SO]$ 13.52 (1H, s, chelated OH), 7.90-7.35 (4H, m, Ar-H); m/e 163(M), 147(M-O), 120(M-O-HCN). This conversion probably involves the nitronic acid form (VIII) of the nitroketone.

Reduction of 3-nitrochromone with either tin(II) chloride - hydrochloric acid or sodium dithionite gave high yields of 3-aminochromone, m.p. 126-128°, ir, 3400, 3310, 1645, 1625, 1616 cm^{-1}; nmr; $\delta\,[CDCl_3]$ 8.30 (1H, q, J 9 and 2.5 Hz, 5-H), 7.81 (1H, s, 2-H), 7.80-7.20 (3H, m, 6-, 7- and 8-H), 3.55 (2H, s, NH_2). This is the first 3-aminochromone to be isolated as a free base and its properties are similar to those of an arylamine. It is diazotized under normal conditions; the diazonium salt in solution couples with alkaline 2-naphthol and when hydrolysed with sulphuric acid, it gives a high yield of the known 3-hydroxychromone, m.p. and mixed m.p.181°.

Huebner and Link's synthesis[2] of 2-methyl-3-nitrochromone has been confirmed and the yield improved to 81% by treatment of the nitroacetophenone(I) with acetic anhydride-sodium acetate at 20° for 3h followed by heating to 100°.

Chromones unsubstituted at C-2 and with a 3-acyl group are also rare. 3-Acetylchromone(VI) was first prepared in 29% yield from 1-(o-hydroxyphenyl) butan-1,3-dione(IX) and triethyl orthoformate.[5] It has also been formed by acetylation of 3-(o-hydroxyphenyl)-3-oxopropanal.[6]

We find that the dione(IX) is converted into 3-acetylchromone(VI), m.p. 129° [lit.[5] 129°], nmr, $\delta\,[CDCl_3]$ 8.55 (1H, s, 2-H), 8.26 (1H, q, J 8 and 2.5 Hz, 5-H), 7.56-7.17 (3H, m, 6-, 7- and 8-H), 2.78 (3H, s, Me) , in 85% yield under very mild conditions by treatment with acetic formic anhydride and sodium formate.

The compounds prepared gave satisfactory elemental analysis. Work on the synthesis of chromones containing an electron-withdrawing substituent at C-3 is continuing.

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