Conversion of a Polypyrone into Phenolic Compounds

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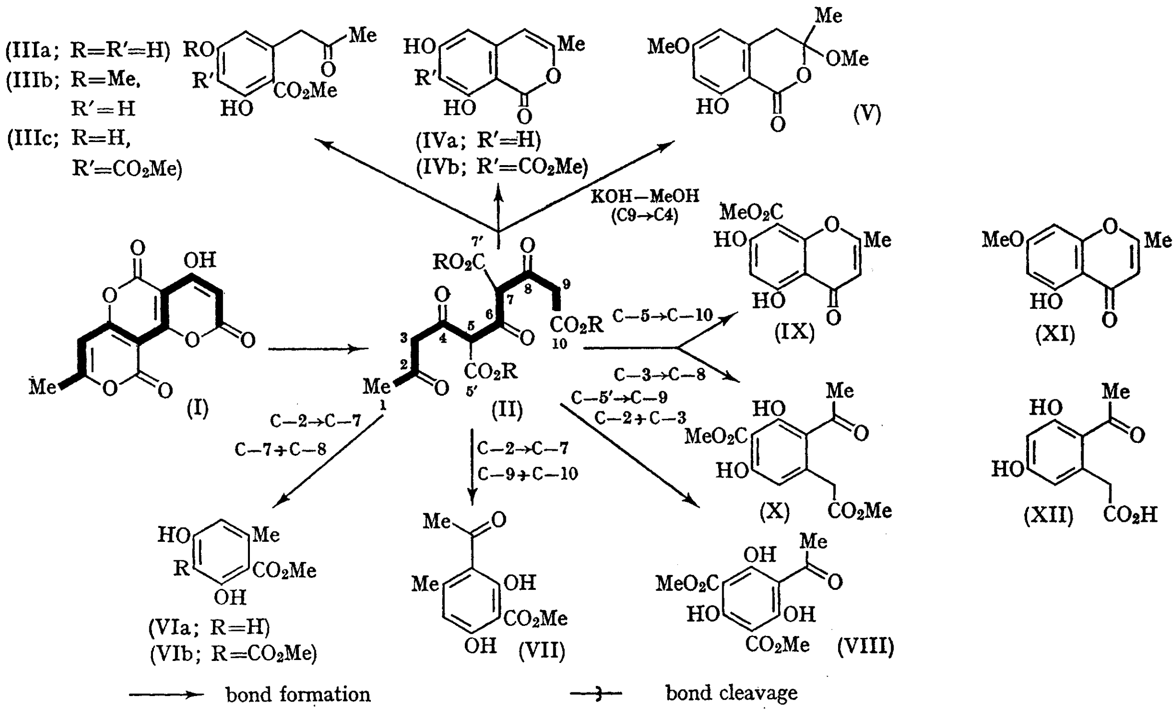
FOR synthetic purposes the tripyrone (I) can be regarded as the masked form of a C_{10}-polyacetate chain (thickened lines in I and II) and it has been shown[1,2] that treatment of (I) with methanolic potassium hydroxide yields the aromatic compounds (IIIa—c) (IVa, b) and (V). The products represent one possible condensation mode (C-9—C-4) of the intermediate β-tetraketo-ester (II; R = H and/or Me), although five other carbon–carbon bond formation processes are available to the intermediate (II). Here we show that at least two of these (C-3, C-8; C-5, C-10) occur when methanolic magnesium methoxide is used as base.

Treatment of the tripyrone (I) with 1M-methanolic magnesium methoxide at 25° for two days under nitrogen yielded a mixture of aromatic compounds (10—15% yield) which were separated by preparative thin-layer chromatography (silica gel G).

In this way six aromatic compounds were characterised and assigned the structures (VI)—(X) on the basis of spectroscopic and analytical properties. Two of the compounds, methyl



orsellinate (VIa) and 2,4-dimethoxycarbonylorcinol (VIb), were easily characterised since they had previously been obtained from base treatment of a dipyrone.[2] Although the exact sequence is unknown the formation of (VIa) and (VIb) can be explained by aldol condensation (C-2—C-7) of the β-tetraketone intermediate (II) followed by cleavage between C-7 and C-8. Aldol condensation between C-3 and C-8 before or after cleavage of the C-9—C-10 bond accounts for the formation of acetyl-4-methoxycarbonylorcinol (VII), m.p. 96—98°; Gibb's test; positive. λ_{max}(EtOH) 249 (14,200); 265 sh (8100); 325 (3900); ν_{max}(Nujol) 3420, 1675, 1570, 1245, 1165, 800 cm.$^{-1}$; τ ($CDCl_3$) −1·35 (1H, hydrogen-bonded hydroxyl), −0·10 (1H, hydrogen-bonded hydroxyl), 3·68 (1H, aromatic), 5·95 (3H, ester methyl), 7·47 (3H, aromatic methyl), 7·70 (3H, methyl); mass spectrum, *m/e* 224 (parent). An alternative aldol condensation (C-5—C-8) without concomitant cleavage of the C_{10}-chain yields methyl 4-methoxycarbonylcurvulinate (X), m.p. 110—112° λ_{max}(EtOH) 236 sh, 259, 265 sh, 327 mμ (ϵ 16,000, 19,200, 11,400, 5650); τ ($CDCl_3$) −0·66 (1H hydrogen-bonded hydroxyl), 0·34 (1H, hydrogen-bonded hydroxyl), 3·61 (1H, aromatic), 5·90 (3H, ester methyl), 6·29 (2H, methylene), 6·31 (3H, ester methyl), 7·44 (3H, methyl ketone): ν_{max}(Nujol) 3400, 1725, 1680, 1645, 1565 cm.$^{-1}$; molecular ion *m/e* 282 (parent); positive ferric chloride and Gibb's test.

The two remaining aromatic compounds were characterised as acylphloroglucinol derivatives and obviously arose by Claisen condensation of the intermediate β-polyketo-ester chain (II). Thus the formation of 3,5-dimethoxycarbonylacetylphloroglucinol (VIII), m.p. 172—173°, can be explained by Claisen condensation (C-5′—C-9) and bond cleavage C-2—C-3 and exhibited the following spectroscpic properties: λ_{max} 256, 270 sh mμ (ϵ 41,700, 20,100); ν_{max} 1640, 1570, 1320, 1240, 980, 970, 955, 910 cm.$^{-1}$; τ ($CDCl_3$), −5·38 (2H, hydrogen-bonded hydroxyls), −4·08 (1H, hydrogen-bonded hydroxyl), 6·02 (6H, methoxyl), 1·29 (methyl); molecular ion, *m/e* 284; positive ferric chloride and negative Gibb's test.

Claisen condensation (C-5—C-10) or (C-5′—C-9) of the intact chain accounts for the formation of 5,7-dihydroxy-8-methoxycarbonyl-2-methylchromone (IX), m.p. 178° (decomp.); λ_{max}(EtOH) 225, 257, 280 sh mμ (ϵ 17,300, 26,000, 8000); ν_{max} (Nujol) 3200, 1675, 1620, 1585, 1330, 1180, 1130 cm.$^{-1}$; τ ($CDCl_3$) −3·71 (1H, hydrogen-bonded hydroxyl), −2·42 (1H, hydrogen-bonded hydroxyl), 3·68 (1H, aromatic), 3·88 (1H, vinyl), 6·01 (ester methyl), 7·60 (methyl); molecular ion *m/e* 250; positive ferric chloride and negative Gibb's test.

In previous studies[3,4,7] with dipyrones, it was shown that the use of magnesium methoxide resulted in Claisen condensation products (phloroglucinols) while aqueous or alcoholic potassium hydroxide produced aldol condensation products (orsellinates). With the more complex tripyrone structure, it is evident that this control over the direction of cyclisation is somewhat diminished and we find that magnesium methoxide produces a mixture of Claisen and aldol condensation product.

The present results when considered with those previously reported[1,2] show that from the base treatment of (I) four structural types of aromatic compound can be obtained. These correspond to the carbon skeletons of *C*-acetylorsellinic acid (IIIa; as acid), 6,8-dihydroxy-3-methylisocoumarin (IVa), curvulinic acid (XII), and eugenin (XI). All of these compounds occur naturally[5] and the polyacetate theory[6] predicts that they are derived by those cyclisation modes of a common C_{10}-β-polyketo-acid precursor, corresponding to Claisen and aldol mechanisms illustrated in the reactions of (II).

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