Structure of Abnormal Products isolated from the Isomerization of 7-Methoxychromano[3,4-*d*]isoxazole—A Novel Synthesis of One of the Products

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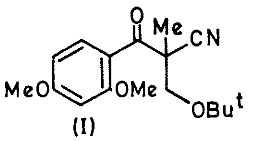
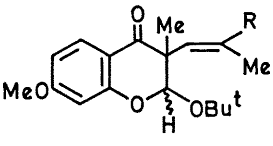
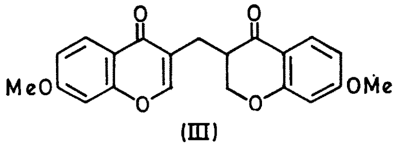
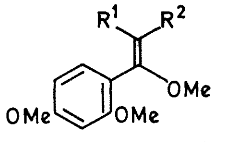
Summary A one-step synthesis of (IIb), an isomerization product of 7-methoxychromano[3,4-*d*]isoxazole, from (III) is reported.

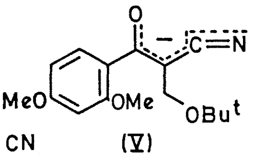
RECENTLY,[1] we have isolated several abnormal products [(I), (IIa), (IIb), and (III)] from the base isomerization of 7-methoxychromano[3,4-*d*] isoxazole. We now report a novel one-step synthesis of (IIb) and structure elucidation of two more products reported earlier in the above reaction.[1]


(I)

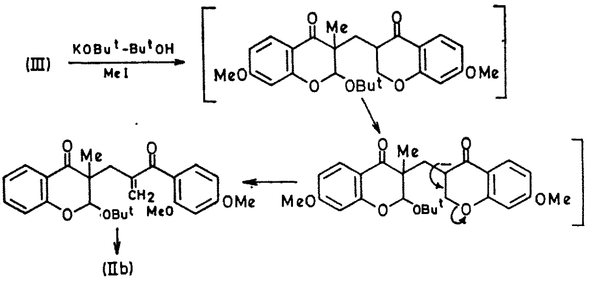

(II)a, R = CN
b, R = CO·C_6H_3·$(OMe)_2$-(2,4)


(III)


(IV)a, R^1 = CH_2·OBu^t; R^2 = CN
b, R^1 = CN; R^2 = CH_2·OBu^t


(V)

An inspection of the chromono-chromanone structure (III)† suggested that it could provide a precursor for the synthesis of (IIb) according to a speculated mechanistic pathway (Scheme). Accordingly, compound (III) was treated with potassium t-butoxide in t-butyl alcohol and methyl iodide at 80° for 40 min. The crude neutral product,‡ after preparative t.l.c., gave the expected diketone (IIb) identical with an authentic sample (t.l.c. and i.r.), in *ca.* 25% yield.



SCHEME

The two compounds, A and B, isolated from the benzene-ether fraction[1] by preparative t.l.c., had very close R_F values. Compound A,§ a colourless oil, λ_{max} 224 (ϵ 21,800), 264 (14,550), 282 (11,730), and 310 nm (3520); ν_{max} (neat)

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† Also obtained as a by-product in the formylation of 7-methoxychroman-4-one.

‡ Structures of other products are under investigation.

§ All new compounds gave satisfactory elemental analyses. U.v. spectra were measured in 95% ethanol solution. N.m.r. spectra were obtained with a Varian A-60 spectrometer ($CDCl_3$ as solvent and Me_4Si as internal standard) and mass spectra were recorded on an Atlas CH-4 spectrometer equipped with a molecular beam inlet system.

2227 (conjugated C≡N); δ 1·1 (s, 4·5 H), 1·28 (s, 4·5 H), 3·55 (s, 3 H), 3·7 (s, 1 H), 3·88, 3·89 (6 H), 4·25 (s, 1 H), 6·4—6·7 (m, 2 H), and 7·26 (d, 1 H, *J* 9 Hz); *m/e*, 305 (*M*), 247 (78%, $M - C_4H_{10}$), and 232 (100%, $M - C_4H_9O$), is assigned the structure (IV). The occurrence of sharp signals at δ 1·1, 1·28, 3·7, and 4·24 in the n.m.r. spectrum of (IV), which is apparently anomalous, is best explained by assuming it to be a mixture¶ of fortuitously equal amounts of geometrical isomers.[3] The isomers could not however be separated either by t.l.c. or by g.l.p.c. The peaks at δ 1·1 and 3·7 may be assigned respectively to the t-butyl and oxymethylene groups shielded[4] by the aromatic ring in the isomer (IVa) and those at δ 1·28 and 4·24 to the t-butyl and oxymethylene groups,** respectively, in the isomer (IVb). The nitrile (IV) is probably formed by *O*-methylation of the intermediate (V) suggested earlier.[1] Compound B, also an oil, was shown by u.v., i.r., n.m.r., and mass spectrometry and also by direct comparison with an authentic sample to be methyl 2,4-dimethoxybenzoate. This could have originated as a by-product during the formation of (IIa) or as a base-cleavage product of (I) or (IIb).

Further utility of the diketone (IIb) in the synthesis of oxasteroids is currently under investigation.

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¶ The possibility of the signals arising from rotational isomers[2] is ruled out on the basis of the intensities of the peaks at δ 1·1 and 1·28.

** t-Butyl group signal occurs at δ 1·22 in (IIa).

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