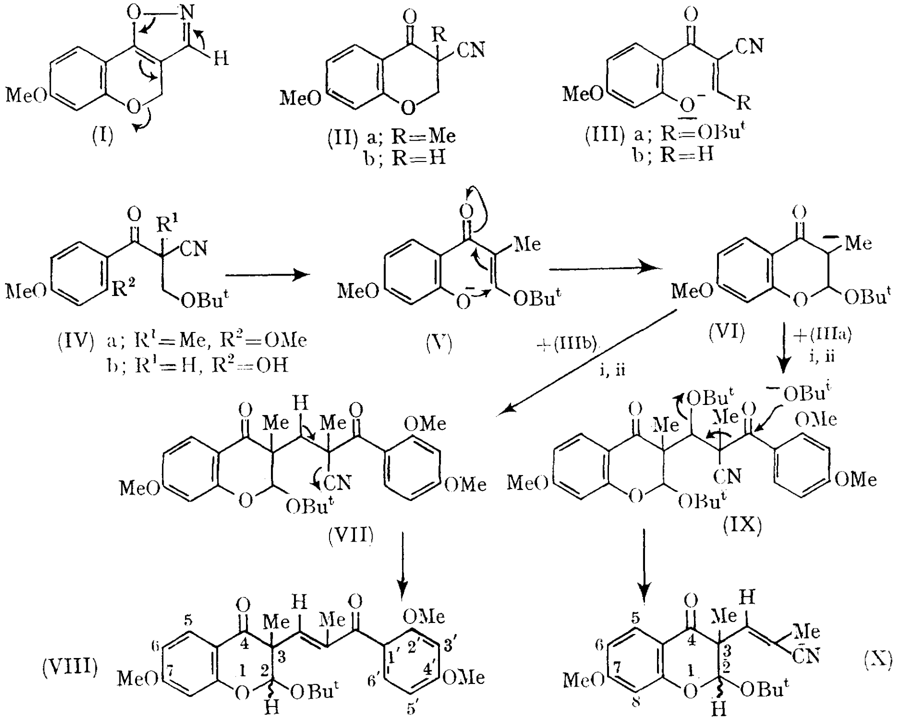
Structure of Abnormal Products isolated from the Isomerization of 7-Methoxychromano[3,4-*d*]isoxazole[1]

By T. R. KASTURI,* K. M. DAMODARAN, G. SUBRAHMANYAM, P. BROWN, and G. R. PETTIT
(*Department of Organic Chemistry, Indian Institute of Science, Bangalore* 12, *India*)

WE have discussed[1] the structure of an abnormal product (IVa) obtained during isomerization of 7-methoxychromano[3,4-*d*]isoxazole (I) with potassium t-butoxide in t-butanol followed by alkylation with methyl iodide.[2] The expected cyanomethyl ketone (IIa) was also obtained by the inverse addition of 1·2 M of alkoxide to the isoxazole (I) with excess methyl iodide in the respective alcohol. We have reinvestigated these reactions, and with the help of rigorous column chromatography and t.l.c., have isolated some novel 'abnormal' products.

The crude neutral product,[1] isolated from the reaction of isoxazole (I) under Johnson's condition,[2] was chromatographed on activated alumina. The purified fraction eluted with 1 : 1 petroleum



Reagents: i, Bu^{t}O$^-$; ii, MeI

SCHEME 1

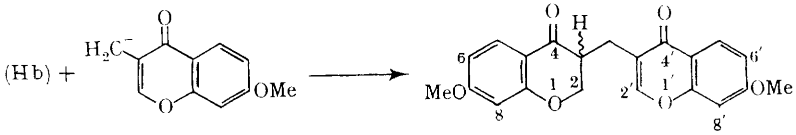
ether–benzene gave in addition to (IVa), a solid† (X) (5%), m.p. 156—158°, M (by mass spectrometry) 329, λ_{max} (ϵ 17,000), 274 (15,990), and 309 mμ (8,500), ν_{max} (Nujol) 2242 (C≡N), 1684 (C=O), 1383, 1366, 1253, 1245 (t-butyl), 1025, 1000, 890, and 862 cm.$^{-1}$ (t-butoxy), δ 1·22 (9H, t-butyl), 1·62 (3H, 3-methyl), 2·05 (3H,d,$J_{allylic}$ 1·7 Hz, vinyl methyl), 3·87 (3H, 7-methoxy), 5·87 (1H, 2-H), 6·4 (1H,d,$J_{H\ 8,6}$ 2·5 Hz, 8-H), 6·63 (1H, pair of doublets, $J_{H\ 6,5}$ 9 Hz, $J_{H\ 6,8}$ 2·5 Hz, 6-H), 6·83 (1H,d,$J_{allylic}$ 1·7 Hz, vinyl H), and 7·89 (1H,d, $J_{H\ 5,6}$ 9 Hz, 5-H),(m/e), 329 (M), 274, 256 ($M - C_4H_9O$), 228, 191, and 151. The fraction eluted with benzene–ether gave the cyanomethyl ketone (IIa) and also two more products.‡ The fraction eluted with methanol gave a white crystalline solid (VIII), (< 10%), m.p. 150—152°, M (by mass spectrometry) 468, λ_{max} 234 (ϵ 25,360), 274 (20,030), and 308 mμ (12,150), ν_{max} (Nujol) 1678 (C=O), 1639 (C=C), 1387, 1366, 1238 (t-butyl), 1025, 1000 (t-butoxy), and 839 cm.$^{-1}$ (trisubstituted double bond), δ 1·15 (9H, t-butyl), 1·42 (3H, 3-methyl), 1·95 (3H, d, $J_{allylic}$ 1·7 Hz, vinyl methyl), 3·63 (3H,7-methoxy), 3·79(6H,2′,4′-methoxyls), 5·34 (1H,2-H), 6·2—6·7 (5H,m,6,8,3′,5′- and vinyl-H), 7·23 (1H,d,$J_{H\ 5,6}$ 9 Hz,5-H) and 7·82 (1H,d, $J_{H\ 6',5'}$ 8·5 Hz, 6′-H), (m/e), 468(M), 395($M - C_4H_9O$), 245, 191, 165, and 151.

The neutral product,[1] isolated from the reaction of isoxazole (I) with alkoxide and methyl iodide in alcohol under the modified condition,[1] on chromatography gave (IIa) and a pale yellow solid (XII) (< 10%), m.p. 174—175°, M (by mass spectrometry) 366, λ_{max} 249 (ϵ 20,810), 276 (20,840), and 305 mμ (17,570), ν_{max} (Nujol) 1675 (C=O), 1631 (=C–O–), and 834 cm.$^{-1}$ (trisubstituted double bond), δ 2·41—3·41 (3H, m, 3-H and allylic methylene), 3·78 (3H, 7-methoxy), 3·87 (3H, 7′-methoxy), 3·92—4·83 (2H, m, 2-methylene), 6·3—7·08 (4H, m, 6,8,6′,8′-H), 7·82 (1H,d,J_{ortho} 9 Hz,

---

† 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 tetramethylsilane as internal standard) and mass spectra were taken on an Atlas CH-4 spectrometer equipped with a molecular beam inlet system.

‡ Structures of these two products are under investigation.



(XI) (XII)

SCHEME 2

5 or 5′-H), 7·9 (1H, 2-H) and 8·12 (1H,d,J_{ortho} 9 Hz, 5′ or 5-H), (*m/e*) 366 (*M*), 215, 190, 189, and 177 ($M - C_{11}H_9O_3$). Formation of the product (X) occurs *via* Michael addition of chromanone (VI) to the unsaturated keto-nitrile (IIIa) followed by methylation and expulsion of butoxide ion with β-keto-nitrile cleavage (Scheme 1). Presumably, the unsaturated keto-nitrile (IIIa) originates either by the autoxidation of the keto-nitrile (IVb) or by disproportionation of (IVb) with a molecule of keto-nitrile (IIIb). Addition of the cleavage product (IIIb) to the chromanone (VI) to give (VII) followed by elimination of hydrogen cyanide furnishes the unsaturated ketone (VIII). The anion of the chromone (XI), initially formed from the keto-nitrile (IIa) with elimination of hydrogen cyanide, probably expels the cyanide ion from the unmethylated keto-nitrile (IIb) to produce (XII) (Scheme 2).

(*Received, May* 10*th*, 1968; *Com.* 588.)

---

[1] Part I, T. R. Kasturi and K. M. Damodaran, *Tetrahedron*, 1966, **22**, 1027.

[2] W. S. Johnson, J. W. Peterson, and C. D. Gutsche, *J. Amer. Chem. Soc.*, 1945, **67**, 2274; 1947, **69**, 2942.