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A NOVEL CONVERSION OF CHROMONE-3-CARBOXALDEHYDE TO 5-NITRO-2,3-BENZOFURANDIONE-(Z)-2-OXIME

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Summary: The conversion of chromone-3-carboxaldehyde to 5-nitro-2,3-benzofurandione-(Z)-2-oxime under nitrating conditions is reported.

The nitration of chromone-3-carboxaldehyde (1) using fuming nitric acid and concentrated sulfuric acid in an ice bath to afford 6-nitro-chromone-3-carboxaldehyde has been reported by Nohara et al.[1] We report here nitration of compound 1 using red fuming nitric acid to give 5-nitro-2,3-benzofurandione-(Z)-2-oxime(2).

Chromone 1 (10.0g., 0.057 mol.) was dissolved in 50 ml. of concentrated sulfuric acid and chilled in an ice bath. Red fuming nitric acid (50 ml.) was added over a period of 30 min. with stirring. The reaction mixture was stirred at room temperature for two hours then poured onto ice. The mixture was allowed to stand at room temperature overnight and the light yellow crystals were collected, washed with water and dried to afford 5.7 g (48%) of compound 2; m.p. 168-170° dec; IR(KBr) $\bar{\nu}$5.75 and 6.05 μ (C=N); NMR(CDCl$_3$/d$_6$DMSO) δ 7.66(d,j=9 Hz,1,7-H), 8.47(d,j=2Hz,1,4-H), 8.60(dd,j=2Hz, and 9Hz,1,6-H), 12.66(s,1,OH); MS m/e 208(M+). The complete structure of this product, including stereochemistry was established by X-ray analysis (vide infra).

1 2

The reaction of chromone-3-carboxylic acid [2] under the same conditions also produced compound 2. Thus the more vigorous reaction conditions employed in this communication, compared with the previous report[1], result in further nitration.

A plausible route for this process involves the conversion of chromone-3-carboxaldehyde (1) or the corresponding carboxylic acid to 6-nitrochromone-3-carboxylic acid (3). The reaction of compound 3 with nitronium ion could proceed through carbonium ion 4 which after

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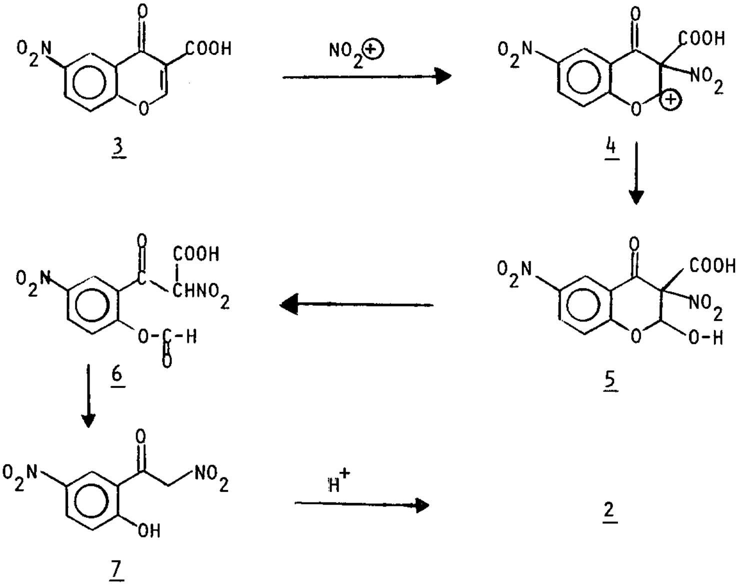

hydration to 5 and a retroaldol process lead to compound 6 which could readily hydrolyze and decarboxylate to give the nitroketone 7. Compound 7 could ring close under acid conditions.

In support of this we have synthesized the nitroketone 7,[3] and found that it readily cyclizes to afford compound 2 by treatment with concentrated sulfuric acid.[4]

Crystals of 2 grown from ethyl acetate/hexane solution are monoclinic, space group $P2_1/c$, $Z=4$, $a=8.241(9)$, $b=6.422(9)$, $c=15.484(16)$Å, $\beta=91.52(7)°$. The measured density is 1.669 gm cm $^{-3}$ (by flotation in $C_2H_2Br_4/CCL_4$ mixture) which agrees with the calculated value 1.686 gm cm^{-3} based on one molecule, $C_8H_4N_2O_5$, in the asymmetric unit. A crystal approximately .10 x .18 x .68mm was used for three dimensional data collection on an Enraf-Nonius computer controlled diffractometer. The $\theta/2\theta$ scan method was used with Ni-filtered CuKα radiation. In the range $3<\theta<60$, 1222 independent reflections were measured of which 1035 were classified as observed ($I>2.0\sigma(I)$); no absorption corrections were applied.

A trial structure containing all nonhydrogen atoms was obtained using the MULTAN direct phase determination program.[5] After preliminary block-diagonal, isotropic least-squares refinement[6] of the trial structure nitrogen and oxygen atoms were assigned on the basis of individual temperature parameter values and the proposed chemical structure. Further anisotropic refinement led to a final discrepancy factor of R = .046 for the observed reflections.[7] The molecule obtained is shown in Fig. 1; the average estimated standard deviation in the bond lengths is .002Å. There are no unusual bond lengths or angles in the molecule. Except for the oxygen atoms of the $-NO_2$ group the ring system and its substituents are coplanar within experimental error. There is a twist of 19° around the C-N bond of the nitro group that displaces the oxygen atoms by ±.34Å from the mean plane of the molecule. In the crystal the N-OH bond is cis with respect to the adjacent endocyclic C-O bond. Molecules are arranged in layers perpendicular to the b-axis; within a layer symmetry related pairs of molecules are linked by a hydrogen bond between the hydroxyl group of one and an oxygen of the nitro group of the other (O-H...O=2.81Å, OH...O=176° H...O=2.03Å).

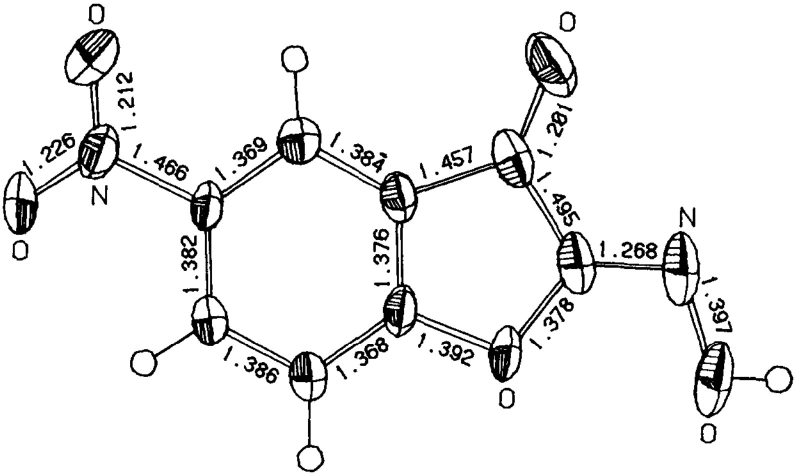

Figure 1

References and Footnotes

1. A. Nohara, T. Umetani and Y. Sanno, Tetrahedron, 30, 3553 (1974).
2. A. Nohara, T. Umetani, K. Ukawa, and Y. Sanno, Chem, Pharm. Bull., 22, 2959 (1974).
3. G. O. P. Becket and G. P. Ellis, Tetrahedron Letters, 719 (1976).
4. Reference 3 describes a similar ring-closure to give the unsubstituted 2,3-benzofurandione-2-oxime using ethyl oxalyl chloride in pyridine.
5. G. Germain, P. Main and M. M. Woolfson, Acta Cryst. A27, 368-376 (1971).
6. All calculations were made on a DEC-10 computer using the X-RAY SYSTEM (1976) system of programs (Technical Report TR-446, The Computer Science Center, University of Maryland, College Park, Maryland). The atomic scattering factors were taken from International Tables for Crystallography (1968), Vol. III Birmingham: Kynoch Press.
7. Final atomic coordinates and a list of structure factors may be obtained from the authors.

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