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REACTION OF BENZIMIDAZOLE-2(2H)-THIONE WITH DIMETHYL ACETYLENEDICARBOXYLATE

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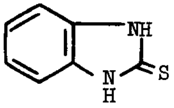
Reaction of benzimidazole-2(2H)-thione 1 with dimethyl acetylenedicarboxylate (DMAD) has been reported by Grinblat and Postovskii to give the thiazolo[3,2-a]benzimidazole 2.[1] On mechanistic grounds, however, condensation of 1 with DMAD can give rise to one or more of at least four products 2, 3, 4a and 5, depending on whether (a) nitrogen or sulphur participates in the initial conjugate addition reaction, and (b) ring closure results in the formation of a 5- or 6-membered ring. As there is no clear mechanistic basis



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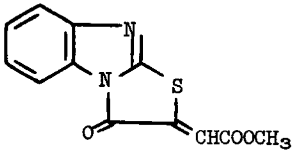

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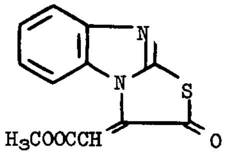

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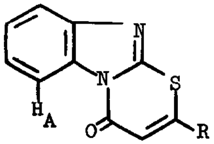
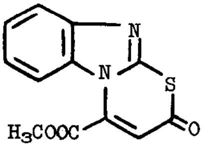


4, a $R = COOCH_3$
b $R = H$



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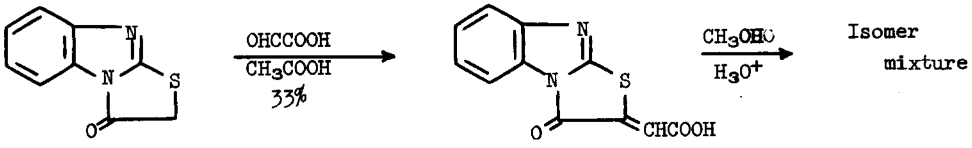
for exclusive formation of 2 we have reinvestigated this reaction and now provide conclusive evidence that Grinblat and Postovskii's structural assignment is correct.

Reaction of 1 with DMAD in either glacial acetic acid or methanol gave a mixture (mp 150-155°) of two isomers[2] which could not be separated chromatographically; ^{1}H nmr analysis (COOC$\underline{H}_3$) showed that the isomers were produced in 1:1 and 2:1 relative amounts in acetic acid and methanol respectively. One of the isomers was obtained analytically pure by careful fractional crystallisation from either benzene-hexane (1:1) or acetone, and had mp 192-193°; the product obtained by Grinblat and Postovskii, and assigned structure 2, was reported to have mp 190-192°.

Spectroscopic data (ir, uv, nmr) for the isomer mp 192-193° did not provide unambiguous evidence of structure; consequently, compound 2 was synthesised independently. In a first approach, condensation of 6 with glyoxylic acid[3] gave the expected product 7,[4] but attempted acid-catalysed esterification of 7 with methanol resulted in partial isomerisation and formation of a mixture of isomers (nmr) similar to that obtained from the condensation of 1 with DMAD.[5] Compound 2 was, however, obtained in the following way. Condensation of 1 with maleic anhydride in glyme at 160° gave 8,[4] which was smoothly converted into 2 by treatment first with diazomethane in THF[4] followed by bromine in acetic acid. The physical and spectroscopic properties of



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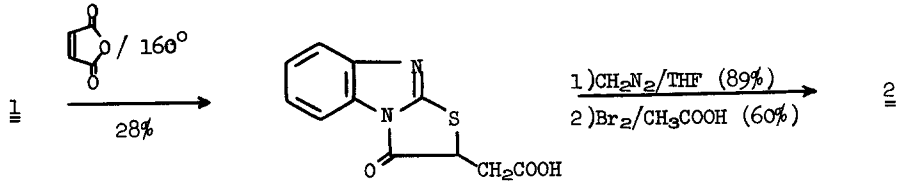

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synthetic 2 were identical to those of the single isomer mp 192-193° obtained from the 1/DMAD reaction mixture.

The sequence 1 → 8 → 2 does not, however, provide unambiguous proof of structure; as with the DMAD reaction, either nitrogen or sulphur can in principle participate in conjugate addition to the maleic anhydride.[6] Consequently, a single crystal X-ray study was undertaken; this demonstrated that the original assignment[1] of structure of the adduct as 2 is correct.

Crystal data: $C_{12}H_8N_2O_3S$, M = 260.2. Monoclinic, a = 8.212(3), b = 6.101(2), c = 22.428(5)Å, β = 95.3(1)°, U = 1119Å^3, Z = 4, D_c = 1.548, D_m = 1.54 g.cm^{-3}, F(000) = 536. Space group $P2_1/n$ (from systematic absences). Mo-Kα radiation (graphite monochromator) λ = 0.71069 Å, μ = 2.9 cm^{-1}.

The cell parameters were initially found from oscillation and Weissenberg photographs and then refined by least-squares from the setting angles of 23 reflections on a Hilger/Watt four-circle diffractometer. Photography (four different crystals) also showed twinning to be present and it was correctly inferred that it would not be possible to collect a complete set of data free from interference from the minor twin.

Reflections were scanned (ω-2θ mode) for $\theta \leq 25°$ giving a total of 2155 measurable reflections. 1415 of these had a net count $\geq 3\sigma$ but of these 145 were recorded by the diffractometer as having large uneven backgrounds and large setting errors and were disregarded. The refinement was therefore carried out with the remaining 1270 intensities. Lorentz and polarisation but not absorption errors were applied.

The structure was solved using the centro-symmetric direct methods routine of SHELX,[7] which automatically found all the non-hydrogen atoms in the molecule. Refinement proceeded by full-matrix least-squares and hydrogen atoms were found from a difference map and were subsequently included in the computations in fixed calculated positions. At anisotropic convergence the maximum shift/standard deviation was 0.02 and R was 6.2%; bond lengths and angles were all close to expected values.

We have so far been unable to obtain unambiguous evidence for the structure of the isomer of 2 which is also formed in the DMAD reaction. The lowest field aromatic (H_A) ^{1}H nmr resonance at δ 8.84 is close to the value reported (δ 8.50) for 4b[8] and on this basis we tentatively assign structure 4a to the second isomer. Structure 5 cannot be excluded, however, as anisotropic deshielding of the corresponding aromatic proton would also be anticipated in this case.

Acknowledgement

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References and Notes

1. E. I. Grinblat and I. Ya. Postovskii, *Zhur. Obsch. Khim.*, **31**, 394 (1961); *Engl. Trans.*, **31**, 357 (1961).

2. Analytical and mass spectroscopic data indicated molecular formulae $C_{12}H_8N_2O_3S$.

3. c.f. R. B. Blackshire and C. J. Sharpe, *J. Chem. Soc.* (*C*), 3062 (1971); G. F. Duffin and J. D. Kendall, *J. Chem. Soc.*, 361 (1956).

4. Satisfactory analytical and spectroscopic data were obtained for all new compounds.

5. In an independent control experiment it was shown that a sample of pure **2** was converted into a 1:2 mixture of isomers when heated under reflux with CH_3OH/conc.H_2SO_4 (5:1/vv) for 8 hr.

6. Condensation of **1** with acrylonitrile gives 1,3-dihydro-1,3-bis(2-cyanoethyl)-2*H*-benzimidazole-2-thione (A. Davidson, Ph.D. Thesis, Heriot-Watt University, Edinburgh (1977)).

7. G. M. Sheldrick, private communication.

8. L. V. Zavyalva, N. K. Razhova, and K. L. Seitanidi, *Khim. Geterotsikl Soedin*, 47 (1975); *Chem. Abstr.*, **83**, 9441d (1975).