Communications to the Editor

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NEW ASPECTS OF THE 1,3-DIPOLAR CYCLOADDITION OF THIAZOLIUM N-IMINES WITH DIMETHYL ACETYLENEDICARBOXYLATE(DMAD)

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The reaction of thiazolium N-imines with DMAD in methanol was studied. 4-Methylthiazolium N-imine (1a) reacted with DMAD to give three products, dimethyl [2-(3',4'-bismethoxycarbonyl-1-pyrazolyl)-propenylthio]fumarate (4, 1:2 adduct)[1b], dimethyl 2,3-bis[2'-(3",4"-bismethoxycarbonyl-1"-pyrazolyl)-propenylthio]succinate (5, 2:3 adduct), and 3-methyl-6-methoxycarbonyl-8-oxidothiazolo[3,2-b]pyridazinium (6a). The structure of 6a was established by X-ray analysis and infrared (IR) spectral data. In a similar reaction with 4,5-dimethylthiazolium N-imine (1b), 2,3-dimethyl-6,7-bismethoxycarbonyl-7,7a-dihydro-4H-thiazolo[3,2-b]pyrazole (2'b, 1:1 adduct) was isolated, and this compound, when heated in ethanol, underwent ring expansion to be converted into an 8-oxidothiazolo[3,2-b]pyridazinium derivative (6b), an analog of 6a.

KEYWORDS——1,3-dipolar cycloaddition; thiazolium N-imine; dimethyl 2,3-bis[2'-(3",4"-bismethoxycarbonyl-1"-pyrazolyl)-propenylthio]succinate; 2,3-dimethyl-6,7-bismethoxycarbonyl-7,7a-dihydro-4H-thiazolo[3,2-b]pyrazole; 8-oxidothiazolo[3,2-b]pyridazinium betaine; ring expansion; X-ray analysis; IR spectrum

It has been thought that the 1,3-dipolar cycloaddition of five-membered heteroaromatic N-imines with suitable dipolarophiles is generally followed by cleavage of heterocyclic rings in postulated primary adducts differently from the similar reaction of six-membered heteroaromatic N-imines such as pyridinium N-imines and isoquinolinium N-imines[1a,b] Furthermore, Potts et al.[1b] reported that 4-methylthiazolium N-imine (1a) reacted with DMAD in dimethylformamide (DMF) to give a 1:2 adduct, N^1-substituted pyrazole compound (4) which was formed by the addition of the intermediate vinyl sulfide (3), produced by fission of the C-S bond in the postulated primary adduct (1:1), to a second molecule of DMAD. We attempted a similar reaction using methanol instead of DMF, because the reaction of thiazolium N-phenylimine with acrylonitrile[2] produced quite different products when the two solvents, DMF and methanol, were used. The reaction was carried out by adding triethylamine to a mixture of 3-amino-4-methylthiazolium chloride and DMAD in methanol with cooling. Three compounds were produced: A (mp 95-105°C),[3] B (mp 194°C) and C (mp 195-197°C), isolated in 4%, 10.8% and 21.5% yields, respectively. Compound A was identified as 4 by comparison with the authentic sample prepared according

to the Potts's procedure.[4] The proton nuclear magnetic resonance (^{1}H-NMR) spectral data[5] of B showed that methyls in the methoxycarbonyl groups and a methyl adjacent to a double bond exist in a ratio of 3:1. As the methoxycarbonyl groups are thought to come from those of DMAD, it is considered that this compound has six methoxycarbonyls rising from three molecules of DMAD, and they exist as three equivalent pairs. Accordingly, it was concluded that a signal due to methyl group adja-

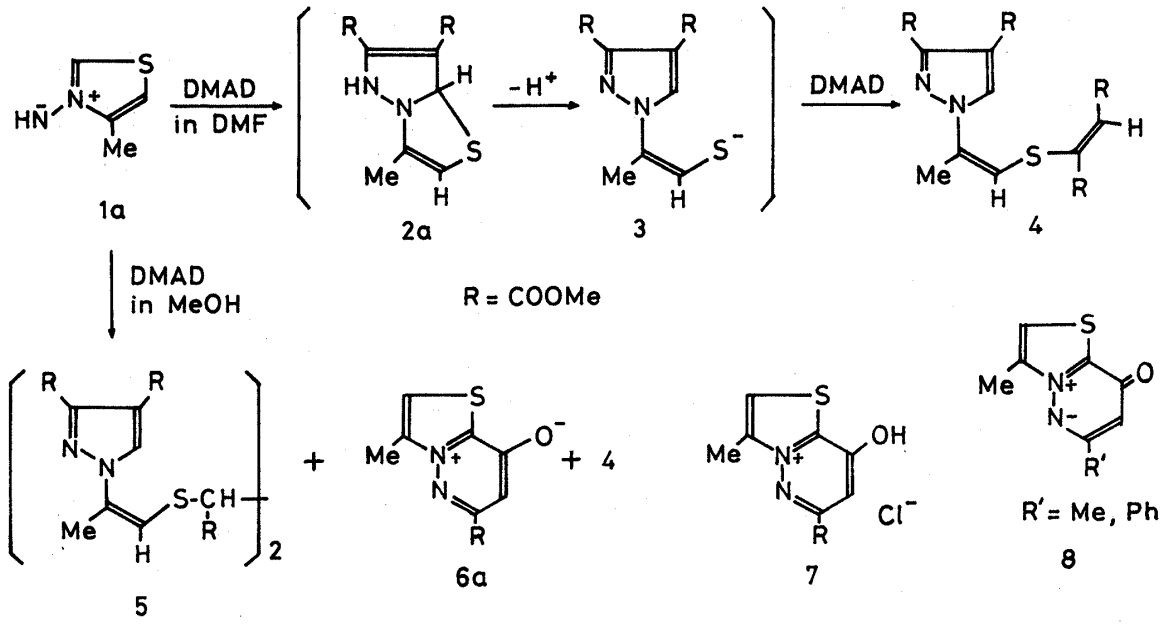

Chart 1

cent to the double bond appeares as a singlet due to the overlaping of two equivalent methyl groups. From these observations and the result of microanalysis, compound B was determined to be dimethyl 2,3-bis[2'-(3",4"-bismethoxycarbonyl-1"-pyrazolyl)-propenylthio]succinate (5), which may be obtained by adding the intermediate 3 to 4. Treatment of 5 with Raney Ni afforded 3,4-bismethoxycarbonyl-1-isopropylpyrazole[1b] and dimethyl succinate.

The mass (MS) spectral data and microanalysis of compound C agreed with the molecular formula $C_9H_8N_2O_3S$, which corresponds to the formulation resulting from the elimination of CH_3OH from a 1:1 adduct of 1a with DMAD. The ^{1}H-NMR spectral data[6] showed only two aromatic protons besides two methyl groups, one assigned as a methyl on the aromatic ring and the other on the methoxycarbonyl group, respectively. It is thought that the elimination of CH_3OH was due to removal of a methoxy group in either of two methoxycarbonyl groups, and the residual carbonyl group was incorporated in an aromatic ring. From these observations, it was deduced that this compound may be a thiazolo[3,2-b]pyridazine derivative, but could not obtain definitive evidence for the structure. So an X-ray crystallographic analysis was carried out.

Crystals of compound C were obtained from the methanol solution. X-ray intensity data were collected on a Rigaku AFC-5 diffractometer to a resolution of $2\underline{\theta}$=130°C with Cu K$\underline{\alpha}$ radiation monochromated by a graphite plate and 1838 independent reflections [Fo> σ(Fo)] were employed for the structure determination. The

diffractometer measurements indicate space group $P2_1/c$ with unit cell dimensions: $a = 4.497(3)$, $b = 16.579(9)$, $c = 15.559(14)$ Å, $\beta = 111.48(10)°$, $V = 1079(1)$ Å^3, $Z = 4$, $D_x = 1.380$ Mg·m^{-3}. The structure was solved by the direct method with program MALTAN[7] using 160 reflections with $|E|>1.720$. Fifteen atoms out of 16 nonhydrogen atoms were obtained from the E-map with the highest absolute figure of merit(2.890). The remaining atom was located by weighted Fourier synthesis. The positional parameters of these nonhydrogen atoms in the asymmetric unit were refined by the block-diagonal least-squares method with anisotropic thermal parameters. All the H atoms were found by a difference Fourier synthesis. Further refinement was carried out including H atoms with isotropic thermal parameters and the final R-value was 0.059. As a result, the structure of C was established as 3-methyl-6-methoxycarbonyl-8-oxidothiazolo[3,2-b]pyridazinium (6a), whose molecular structure is shown in Fig. 1.

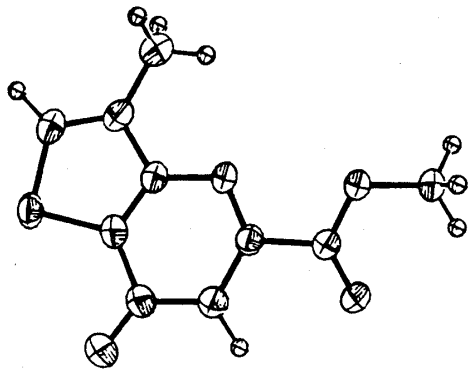

Fig. 1

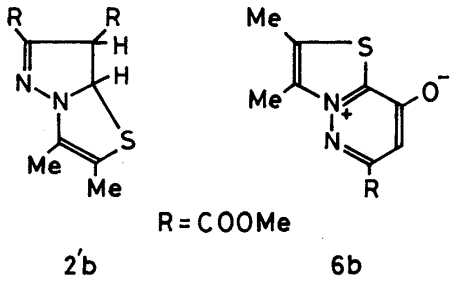

Chart 2

Satoh et al.[8] reported obtaining 8-oxothiazolo[3,2-b]pyridazinium derivatives (8) from thiazolo[3,2-b]pyridazinium perchlorates through four steps. Although 6a may be classified as an analog of 8, it was concluded that 6a exists predominantly in an oxido-ammonium betaine form for the following reasons. Dennis et al.[9] reported that the IR spectra of oxidopyridazinium betaines obtained from the corresponding pyridazinium salts show strong bands at 1550 cm^{-1} which were regarded as the characteristic band for six membered heterocyclic betaines. However, the spectrum of compound 6a showed a strong absorption band at 1590 cm^{-1} ($CHCl_3$) instead of 1550 cm^{-1} and a band at 1735 cm^{-1} due to methoxycarbonyl group. The band at 1590 cm^{-1} showing too low frequency[10] for C=O should be attributed to C-O$^-$ in the oxidopyridazinium betaine 6a. The spectrum of the chloride of 6a did not exibit any ring $\nu_{C=O}$ band nor the band at 1590 cm^{-1}, and therefore, the chloride was identified as 8-hydroxy-3-methyl-6-methoxycarbonylthiazolo[3,2-b]pyridazinium chloride (7).

The reaction of 4,5-dimethylthiazolium N-imine (1b) with DMAD in methanol gave a compound with mp 95°C in 49% yield as insoluble crystals in the reaction mixture. The MS spectral data and the microanalysis of this compound indicated the molecular formula $C_{11}H_{14}N_2O_4S$ corresponding to a 1:1 adduct of 1b and DMAD. The structure was assigned as 2,3-dimethyl-6,7-bismethoxycarbonyl-7,7a-dihydro-4H-thiazolo[3,2-b]pyrazole (2'b) from the ^{1}H-NMR spectral data.[11] In this reaction, we failed to isolate any pyrazole derivatives such as 3 or 4. Heating of 2'b in ethanol gave a thiazolo[3,2-b]pyridazinium derivative (6b, mp 225-6°C),[12] an analog of 6a, by ex-

pansion of the pyrazole ring.

Finally, regarding the production of the 8-oxidothiazolo[3,2-b]pyridazinium betaines (6) resulting from thiazolium N-imines (1) and DMAD, we propose a possible pathway including a 1,2-shift mechanism through intermediates 2' as shown in Chart 3.

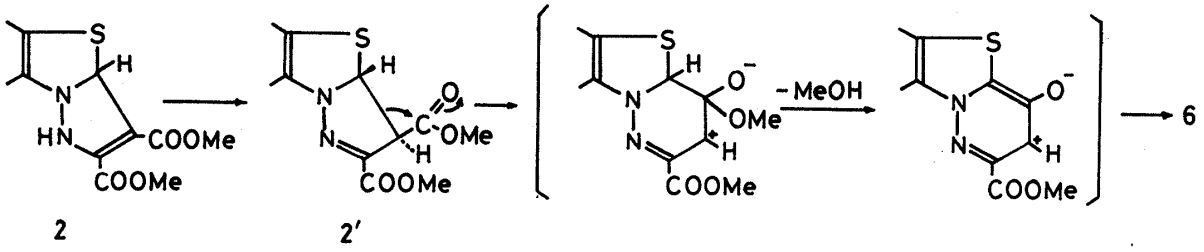

Chart 3

REFERENCES AND NOTES

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2) H. Hirano, K. Sugiyama, M. Yamashita, M. Inoue, and T. Ishida, Chem. Pharm. Bull., 31, 1792 (1983).

3) A mixture containing perhaps a cis-isomer of 4 as a minor product.[1b)]

4) In our experiment carried out according to the Potts's procedure, 5 was obtained in ca. 80% yield, whereas formations of 5 and/or 6a were not observed on TLC of the reaction mixture.

5) ^{1}H-NMR($CDCl_3$) δ: 2.33(6H, s, 2 x CH_3), 3.75, 3.85, 3.96(each 6H, s, 2 x $COOCH_3$), 3.81(2H, s, 2 x -CH), 6.18(2H, s, 2 x -CH=), 8.03(2H, s, 2 x pyrazole-5-H).

6) ^{1}H-NMR($CDCl_3$) δ: 2.78(3H, s, CH_3), 4.02(3H, s, $COOCH_3$), 7.15(1H, s, C_7-H), 7.62(1H, s, C_2-H).

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10) 4-Hydroxypyridazine, existing predominantly in a keto form(1,4-dihydropyridazine-4-one), was reported to show the $\nu_{C=O}$ band at 1662 cm^{-1}($CHCl_3$) in the IR spectrum(S. F. Mason, J. Chem. Soc., 1957, 4874).

11) ^{1}H-NMR($CDCl_3$) δ: 1.87, 2.06(each 3H, s, 2 x CH_3), 3.78, 3.89(each 3H, s, 2 x $COOCH_3$), 4.45(1H, d, J=2.4 Hz, C_7-H), 5.99(1H, d, J=2.4 Hz, C_{7a}-H). The trans configuration was assigned to two vicinal protons at C_7 and C_{7a} from the small coupling constant.

12) IR ν_{max}^{KBr} cm^{-1}: 1600. ^{1}H-NMR($CDCl_3$) δ: 2.66(6H, s, 2 x CH_3), 4.01(3H, s, $COOCH_3$), 7.10(1H, s, C_7-H).

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