## Communications to the Editor

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# A NEW RING TRANSFORMATION OF THIAZOLO[4,5-g]QUINAZOLINE 3-OXIDES INTO [1,4]THIAZINO[3,2-g]QUINAZOLINES BY THE 1,3-DIPOLAR CYCLOADDITION REACTION

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1,3-Dipolar cycloaddition reaction of thiazolo[4,5-g]quinazoline 3-oxides with ethyl phenylpropiolate resulted in a ring transformation of the thiazole nucleus to give [1,4]thiazino[3,2-g]quinazolines, a new class of heterocycles.

KEYWORDS — thiazolo[4,5-g]quinazoline 3-oxide; ethyl phenylpropiolate; 1,3-dipolar cycloaddition reaction; ring transformation; [1,4]thiazino[3,2-g]quinazoline

We have recently reported that the 1,3-dipolar cycloaddition reaction of a thiazolo[5,4-d]pyrimidine 3-oxide with acetylenic dipolarophiles causes a new ring transformation of the thiazole nucleus to give pyrimido[4,5-b][1,4]thiazines as primary reaction products.[1] In connection with these findings and with current stimulated medicinal interest in benzologs of purine and pteridine,[2] we have now investigated the reaction of the laterally extended benzolog of thiazolo[5,4-d]-pyrimidine, i.e., 2-substituted 6,8-dimethylthiazolo[4,5-g]quinazoline-5,7(6H,8H)-dione 3-oxides (1a,b),[3] with ethyl phenylpropiolate (EPP).

As shown in Chart 1, heating 1a (0.8 mmol) with EPP (1.6 mmol) in toluene (10 ml) at 130°C for 50 h gave the expected [1,4]thiazino[3,2-g]quinazoline (6a; 34%),[4] along with the deoxygenation product of 1a (13%)[5] after chromatographic separation on activated alumina with $CHCl_3$. The characterization of 6a was based on satisfactory analytical and spectral data (IR, $^1$H-NMR, MS). Of particularly interest is the occurrence of a secondary amino group in both the IR (3280 $cm^{-1}$) and the $^1$H-NMR ($\delta$ 9.41, $D_2O$ exchangeable) spectra, which indicates the formation of a 1,4-thiazine nucleus.

On the other hand, heating of 1b (0.5 mmol) with EPP (1.5 mmol) in toluene (50 ml) at 130°C for 25 h afforded not only the thiazinoquinazoline (6b; 16%)[6] corresponding to 6a but also the 4-benzoylthiazinoquinazoline (5b; 25%)[7] together with the deoxygenation product of 1b (12%).[3] The structure of 6b was supported by its spectral analogy to 6a, while that of 5b was indicated by the lack of a secondary amino group in both the IR and the $^1$H-NMR spectra and by the presence of a characteristic $M^+$-105 fragment ion due to the liberation of a benzoyl radical. The structure was confirmed by hydrolytic conversion to 6b (55%) with ethanolic HCl.

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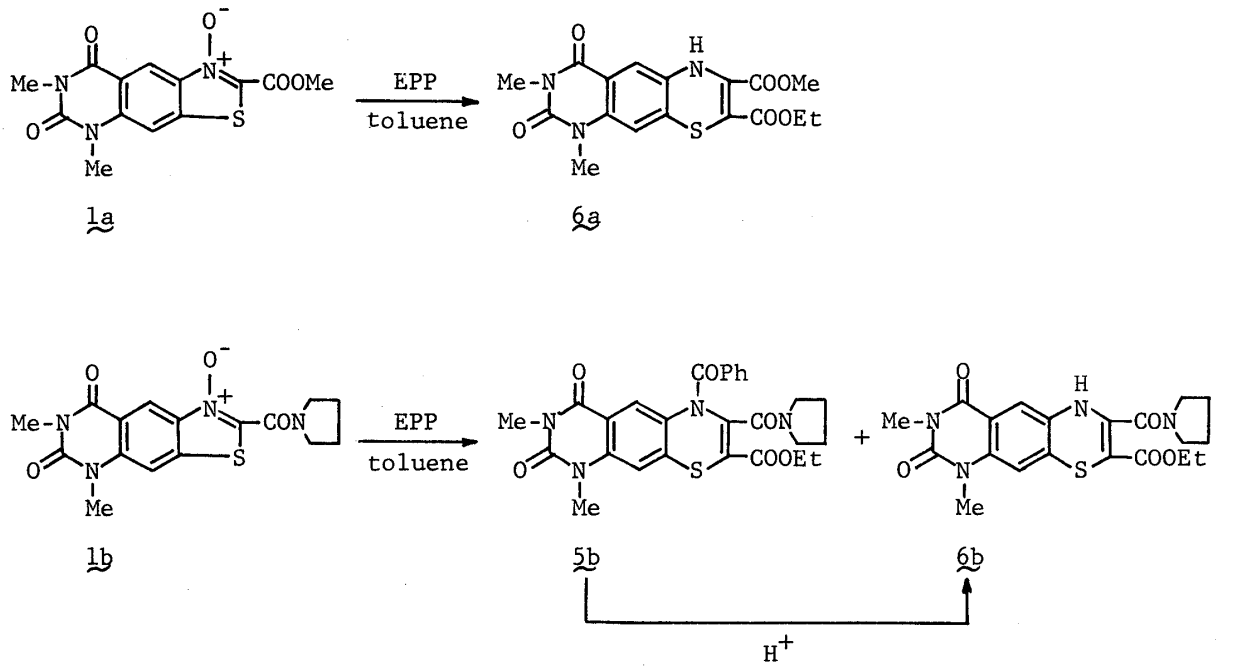
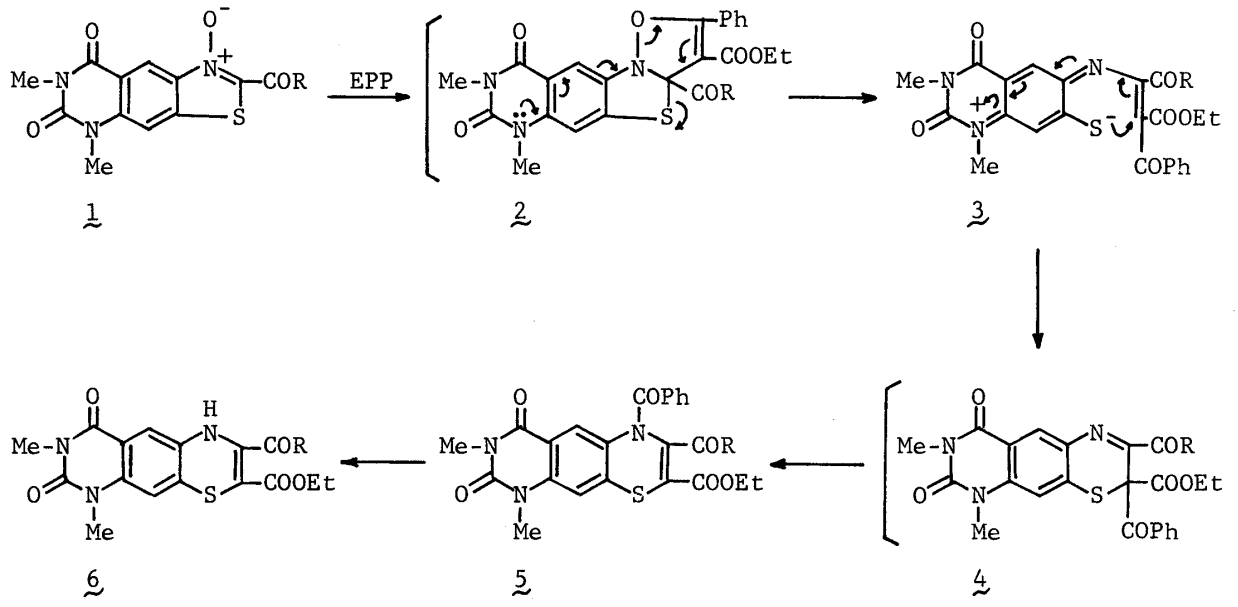



1a 6a

1b 5b 6b

Chart 1




1 2 3

4 5 6

Chart 2

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As depicted in Chart 2, the ring transformation can be explained theoretically in terms of the initial formation of the adduct (2) by 1,3-dipolar cycloaddition. The cleavage of the N-O and C-S bonds of 2 to form 3, followed by the recyclization, would give 4 as the primary product. It seems likely that 4 is rather unstable and readily converts to the 4-benzoyl derivative 5, although the detailed mechanism is not yet clear. The hydrolytic cleavage of the benzoyl group of 5 would yield 6 as a final product. The deoxygenation of 1 would proceed by the thermal process.[8)]

Further work is in progress to elucidate the mechanism and extend the scope of the reaction.

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## REFERENCES AND NOTES

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2) S.W. Schneller and W.J. Christ, J. Org. Chem., 46, 1699 (1981) and references cited therein.
3) H. Kanazawa, K. Senga, and Z. Tamura, Chem. Pharm. Bull., 33, 618 (1985).
4) Compound 6a: mp 246-247°C. IR (Nujol): 3280 cm$^{-1}$(NH), 1740 (CO), 1695 (CO), 1640 (CO), 1620 (CO). $^1$H-NMR (400 MHz, DMSO-$d_6$) δ: 1.17 (3H, t, Me, J=6 Hz), 3.21 (3H, s, Me), 3.37 (3H, s, Me), 3.77 (3H, s, Me), 4.21 (2H, q, $CH_2$, J=6 Hz), 6.85 (1H, s, 5-H), 7.03 (1H, s, 10-H), 9.42 (1H, s, NH, $D_2O$ exchangeable). MS m/z: 391 ($M^+$), 331, 318, 287, 259.
5) 2-Methoxycarbonyl-6,8-dimethylthiazolo[4,5-g]quinazoline-5,7(6H,8H)-dione: mp 281-282°C. IR (Nujol): 1700cm$^{-1}$(CO), 1660 (CO). MS m/z: 305 ($M^+$), 249, 220, 162, 120.
6) Compound 6b: mp >300°C. IR (Nujol): 3300cm$^{-1}$(NH), 1690 (CO), 1675 (CO), 1620 (CO). $^1$H-NMR (400 MHz, DMSO-$d_6$) δ: 1.14 (3H, t, Me, J=6 Hz), 1.78-1.92 (4H, m, pyrrolidine), 3.23 (3H, s, Me), 3.39 (3H, s, Me), 3.27-3.41 (4H, m, pyrrolidine), 4.03 (2H, q, $CH_2$, J=6 Hz), 9.38 (1H, s, NH, $D_2O$ exchangeable). MS m/z: 430 ($M^+$), 384, 359, 331, 287, 259.
7) Compound 5b: mp 243-245°C. IR (Nujol): 1710sh cm$^{-1}$(CO), 1705 (CO), 1665 (CO), 1640sh (CO). $^1$H-NMR (400 MHz, DMSO-$d_6$) δ: 1.21 (3H, t, Me, J=6 Hz), 1.76-1.84 (4H, m, pyrrolidine), 3.18-3.38 (4H, m, pyrrolidine), 3.21 (3H, s, Me), 3.30 (3H, s, Me), 4.21 (2H, q, $CH_2$, J=6 Hz), 7.35-7.48 (5H, m, Ph), 7.51 (1H, s, 5-H), 7.71 (1H, s, 10-H). MS m/z: 534 ($M^+$), 430, 429, 384, 359, 331, 287, 260, 259.
8) A.R. Katritzky and J.M. Lagowski, "Chemistry of Heterocyclic N-Oxides," Academic Press, London and New York, 1971, p. 229.

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