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RING-SELECTIVE PHOTOREARRANGEMENT OF BITHIAZOLES[1]

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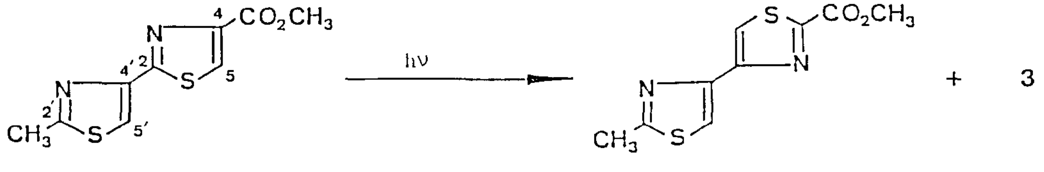
Summary: Photoirradiation of methyl 2'-methyl-2,4'-bithiazole-4-carboxylate (**1**) leads predominantly to 4,4'-bithiazole **2** with the formation of a small amount of isothiazole **3**. The ring-selective photorearrangement is interpreted in terms of LUMO bond index.

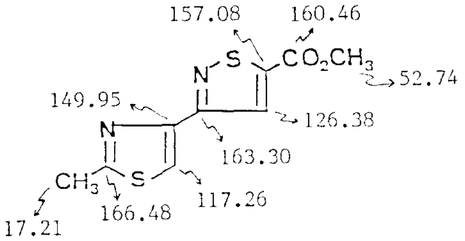
Photochemistry of polychromophoric molecules leading to a site-selective transformation is an important and interesting subject in organic photochemistry. Such investigations would provide useful information on the intramolecular excitation transfer within a complex polychromophoric molecule.[2] In this context photochemistry of dimeric, trimeric or polymeric five-membered heterocycles such as polypyrroles and polythiazoles seems to be quite attractive, since each component of the molecule has the capability of photochemical ring-atom transposition in its excited state.[3] In connection with our recent work on the phototransformed bleomycin antibiotics,[4] we have examined the photoreaction of a 2,4'-bithiazole system as a simplest case. We report herein a unique phototransformation of 2,4'-bithiazole leading to a selective ring-atom transposition at only one of the thiazole rings.

External irradiation of methyl 2'-methyl-2,4'-bithiazole-4-carboxylate (**1**) (1.8 mM) in acetonitrile with a 60 W transilluminator (302 nm)[5] gave 4,4'-bithiazole **2**[4] in 95% yield as determined by HPLC. *A more careful examination of the photolysate by HPLC* revealed the presence of an another isomer, **3** (2%); no product derived from the photorearrangement of the methyl-substituted thiazole ring was detected. The structure of **3** was assigned by spectroscopic data (high-resolution MS, ^{1}H- and ^{13}C NMR).[6] In particular, all the carbon atoms of



1 **2**

3 were rigorously assigned by means of long-range enhanced ^{1}H-^{13}C 2D NMR in comparison with the 2D NMR of **1**. Further support on the structure was obtained by mass spectral fragmentations (Chart 1). The appearance of the fragment ions at m/e 199 ($C_7H_5NO_2S_2$), 168 ($C_6H_2NOS_2$) and 140 ($C_5H_2NS_2$) indicates the existence of a partial structure of 2-methyl-4-substituted thiazole, whereas the distinct ion at m/e (C_3HNS) is consistent with the 3-(4-thiazolyl)-isothiazole skeleton.[7] The substitution pattern on the isothiazole ring was further confirmed by ^{1}H NMR NOE difference spectrum of the reduction product **4**[6] obtained by reduction with $LiAlH_4$.



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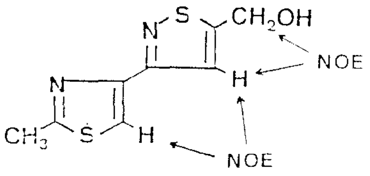

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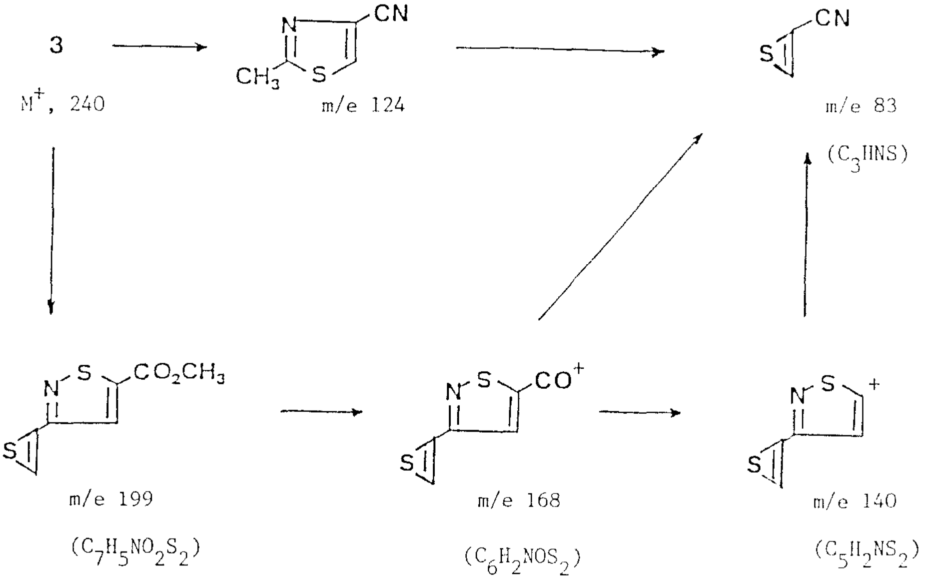
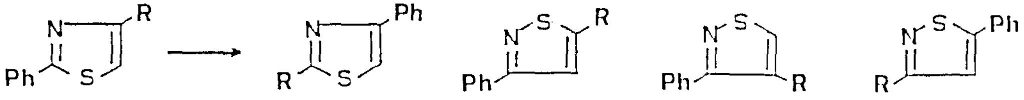
Chart 1



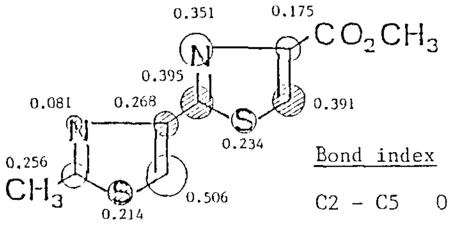
Quantum yields for the formation of **2** and **3** are 0.023 and 0.0005, respectively. Triplet sensitization with benzophenone (E_T = 68.5 kcal) or acetophenone (E_T = 73.5 kcal) did not produce **2** and **3**. Further, the photorearrangement was not quenched by the addition of 1,3-pentadiene. Thus the singlet (π,π^*) state seems to be resposible for the photorearrangement. Most interestingly, the photorearrangement occurs selectively at the thiazole ring substituted by carbomethoxy group. Moreover, the product distribution is quite different from those observed in usual photoisomerization of simple thiazoles, *e.g.*, 2-phenyl-4-methylthiazole (8) which gives four isomers upon photolysis as indicated below.[8,9]

In order to clarify the effect of the carbomethoxy group on the product distribution, we examined the photoreaction of simple mono-thiazole 5. Irradiation of 5 (1.2 mM) in acetonitrile under similar conditions gave 6 (77%) together with a small amount of 7 (7%). The structure of 6 was confirmed by converting it to the known 2-methyl-4-phenylthiazole[8], whereas 7[6] was assigned on the basis of spectral data. The product distribution is very similar to the case of 1. High selectivity was observed for the formation of 2,4-disubstituted thiazole in both cases. Thus the carbomethoxy group has a pronounced effect on the product distribution in the photoreaction of mono- and bithiazoles.



5 : R = CO_2CH_3	6 : 77%	7 : 7%	—	—
8 : R = CH_3	34%	64%	4%	1%

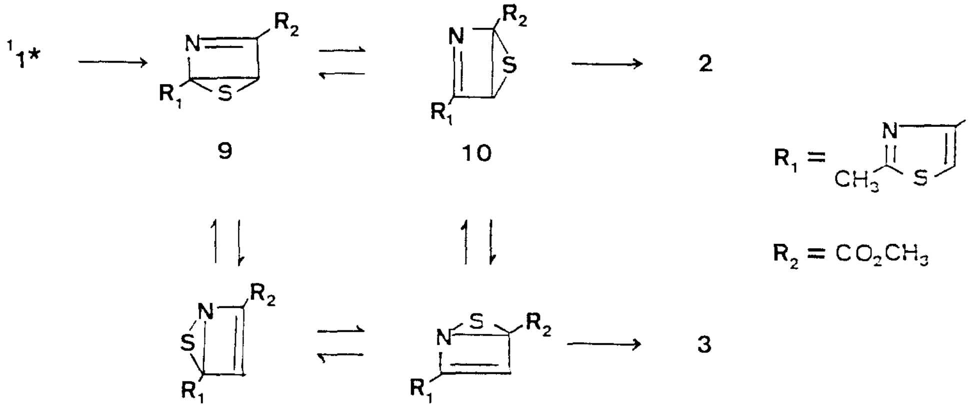
The most important characteristic of the photorearrangement of bithiazole 1 is the remarkably high photoreactivity of the thiazole ring directly attached to the carbomethoxy group. Since the photorearrangement proceeds via the lowest (π,π^*) singlet state, the ring selectivity would be explained in terms of LUMO bond index calculated by INDO SCF method.[10] As shown in Fig. 1, the bond index between C2 and C5 is much larger than that for C2'-C5' bonding in its lowest singlet excited state. It seems therefore reasonable to assume that singlet excitation of 1 would result in an initial disrotatory closure at C2-C5 to Dewar intermediate 9 which rapidly undergoes 1,3-shift of the sulfur atom to give 10. The latter may well be the precursor of 2. Recent low-temperature matrix photolysis of furan and thiophene has indicated the formation of Dewar intermediates as primary products,[11] although several alternative mechanisms including ring contraction-ring expansion routes or tricyclic zwitterionic routes have been proposed for the photorearrangement of thiazoles.[3,8,9]



Bond index

C2 - C5	0.024
C2'-C5'	0.016

Fig. 1 LUMO coefficients calculated by INDO SCF method



Further studies including photoreaction of higher homologues are in progress.

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3. For a review, A. Padwa, in "Rearrangements in Groud and Excited States", vol 3, P. De Mayo Ed., Academic Press, New York, 1980, p. 501.
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5. Irradiation with a high-pressure (Pyrex filter) or low-pressure mercury lamp (Vycol filter) gave the same products but in a slightly different ratio.
6. Consistent spectral data were obtained for all new compounds. Selected data for **3**: UV (acetonitrile) λ_{max} 304 nm (log ε 3.66); 400 MHz ^{1}H NMR ($CDCl_3$) δ 2.77 (s, 3 H), 3.95 (s, 3 H), 7.76 (s, 1 H), 8.25 (s, 1 H).
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10. A similar result was obtained by ab-initio (STO-3G) calculation. The LUMO bond index is represented as follows: bond index ($B_{r,s}$) = (coefficient$_{r,\ LU}$)^2 (coefficient$_{s,\ LU}$)^2.
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