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THE 1:2 MOLAR ADDUCTS IN THE REACTION OF 5-PHENYLTHIAZOLE AND DIMETHYL ACETYLENEDICARBOXYLATE

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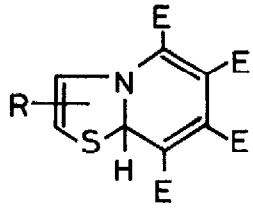
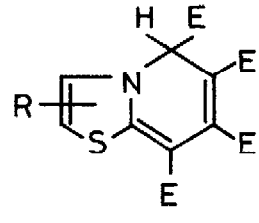
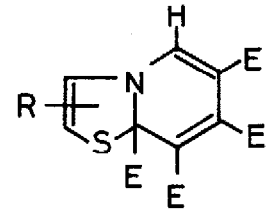
Recently cycloadditions of thiazoles with dimethyl acetylenedicarboxylate (DMAD) have been extensively studied.[1-3] In these reactions 1:2 molar adducts of type (B) and (C) have been isolated except type (A). The formation of isolable adducts (B and C) has been interpreted as proceeding by way of a [1,5]-sigmatropic shift or by a molecular rearrangement of normal adduct (A) formed initially. However, there is no conclusive evidence to show that (C) is formed only at the expense of (A).[4] We now report on the first example of the isolation of three isomeric 1:2 molar adducts from 5-phenylthiazole (1) with DMAD, which indicates strongly the necessity of reconsideration on the mechanism of the characteristic cyclization in the related systems.



(A)



(B)



(C) E:$COOCH_3$

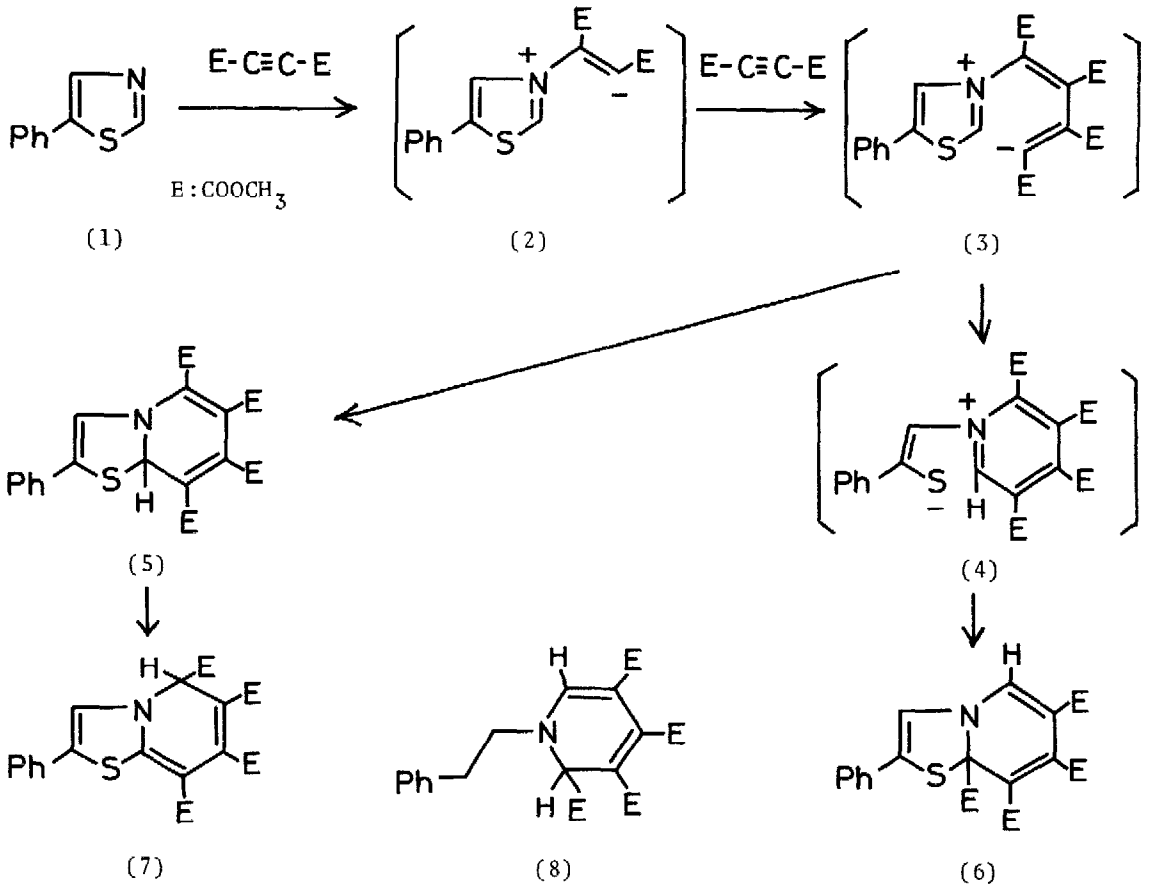
5-Phenylthiazole (1) reacts with DMAD in 1:2 molar ratio at 60° without solvent for 2hr, followed by silica gel chromatography, to give three isomeric products, tetramethyl 6-phenyl-4aH-pyrido[2,1-b]thiazole-1,2,3,4-tetracarboxylate (5)[yellow needles, m.p. 193-195°, 1.3%], tetramethyl 6-phenyl-1H-pyrido[2,1-b] thiazole-2,3,4,4a-tetracarboxylate (6)[red granules, m.p. 169°, 30.6%] and tetramethyl 6-phenyl- 1H-pyrido[2,1-b]thiazole-1,2,3,4-tetracarboxylate (7) [fluorescent yellow needles, m.p. 189°, 3.6%].[5]

The structure (5) was deduced by the great spectral similarities [^{1}H-n.m.r. ($CDCl_3$); δ 5.00 (s, 1H, 4a-H) and 6.80 (s, 1H, 7-H)] to the analogous type of adducts obtained from quinoline, isoquinoline[6] and quinazoline[7] series. The structure (6) was determined by the appearance of ^{1}H-n.m.r. (CD_3COCD_3) signals at δ 8.18 (s, 1H, 1-H) and 6.92 (s, 1H, 7-H) and the resonance of an sp^3 carbon atom, not attached to any hydrogen atom, at 70.5 ppm in the ^{13}C-n.m.r. (DMSO) spectrum, similar to those of closely related compounds.[2,7] The adduct (7), which had the expected spectral similarities to tetramethyl 1H-pyrido[2,1-b]benzothiazole-1,2,3,4-tetracarboxylate,[2] showed singlets at δ 7.97 (1H, 7-H) and 6.38 (1H, 1-H) in the ^{1}H-n.m.r. ($CDCl_3$) spectrum, and indicated an sp^3 carbon atom, attached to one hydrogen atom, at 59.0 ppm in the ^{13}C-n.m.r. ($CHCl_3$) spectrum. Additional proof of structures (6) and (7) was given by their desulfurizations with Raney-Ni to give the same compound, tetramethyl 1-phenethyl-1,2-dihydropyridine-2,3,4,5-tetracarboxylate (8). The structure (8) was confirmed by its spectral properties [δ ($CDCl_3$); 5.14 (d, 1H, J=1.5 Hz) and 7.63 (d, 1H, J=1.5 Hz), λ_{max}^{EtOH}; 279 nm (log ε 4.92) and 376 nm (log ε 3.78)] which show the presence of 1,2-dihydropyridine system.[8]

Heating of (6) in benzene at 130° for 12hr led to the formation of (5) (7.7%) and (7)(32%). On the other hand, the adduct (5) was gradually isomerized to (7) either by standing in a $CDCl_3$ solution in a n.m.r. sample tube at room temperature, or by heating in benzene at 130°, conceivably proceeding via a [1,5]-sigmatropic shift. The adduct (7) had a good thermal stability.

The most characteristic on the reactivity of the adduct (5) is the complete lack of the conversion into (6), even heating in benzene, or in each ethanol solution including 5-phenylthiazole (1), DMAD or acetic acid.[9] Therefore, the previous proposal seems to encounter considerable difficulty in the present study. Furthermore, the facts that adduct (5) rearranges only to (7), and that no subsequent isomerization of (7) is observed under the above reaction conditions, rigorously also rule out the operation of the successive [1,5]-shift of hydrogen and ester group for the formation of (6).

The our results strongly require that (5) as well as (6) are the initial addition products. Thus the reaction of (1) with DMAD follows an alternative



course of the cycloaddition, which is considered to reflect a general feature of thiazole system. One attractive pathway leading to the direct formation of (6) would involve the vinyl sulfide intermediate (4) which might be formed by the opening of the thiazole ring in the second zwitterion (3)[10] competitively with normal cyclization leading to the adduct (5). This species (4) would be expected to undergo ring closure to give the adduct (6). Although it is generally recognized that the ring opening of thiamine or related system arises through a pseudobase, similar to the type of (5), formed by addition of an internal or external nucleophile to the thiazolium ring,[11] this mechanistic consideration is not accommodated for the present system due to the complete lack of the formation of (6) from (5). The ring opening step postulated here is conceivably possible because any driving force for this reaction may derive from some special property of sulfur in such a system, especially the C_2-S bond in (3) is supposed to be the

weakest bond in the ring. Moreover, it may be argued that the thermal isomerization of (6) to (5) also proceeds through the same intermediate (4).

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References and Footnotes.

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