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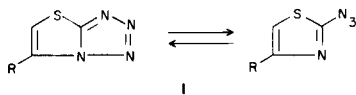
2-Phenyltetrazolo[4,5-*a*]-1,3,4-thiadiazole (**4**), in its azido form, reacted with diethyl fumarate and diethyl maleate to give 2-phenyl-7-carbethoxy-5*H*-1,3,4-thiadiazolo[2,3-*a*]pyrimidin-5-one (**5**). To assign the structure of compound **5**, 2-phenyl-5-carbethoxy-7*H*-1,3,4-thiadiazolo[2,3-*a*]pyrimidin-7-one (**6**) was prepared from the reaction of 2-amino-5-phenyl-1,3,4-thiadiazole (**7**) with diethylacetylene dicarboxylate. Physical properties and spectral data of compound **6** were different from compound **5**. Theoretical and experimental aspects are discussed.

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The azido-tetrazole tautomerism in fused tetrazole derivatives is an interesting phenomenon, concerning which a lot of articles and reviews have been published. For example, Tisler (2) in a review explained some aspects of azido-tetrazole isomerization, and Elguero, *et al.* (3) also discussed the same phenomenon in detail. Depending on the structure and physical state of the molecule, these derivatives may possess the azido or tetrazole form. The conversion of a tetrazole form into an azido form is an endothermic process. In most cases, azido-tetrazole equilibria were observed in solutions, in some cases, however this phenomenon has also been observed in the melts (4). The factors that control the azido-tetrazole isomerization are as follows: (a) electron donating capacity of the heterocycles to which the tetrazole ring is fused; (b) polarity of the solvents used; and (c) temperature.

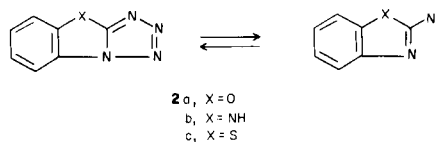
There have been many reports concerning the structure and reactivity of tetrazoles fused with six-membered heterocycles, most of which explain the azido form in solutions and tetrazole form in the solid state, depending on the substituents and the type of heterocycles (2). Tetrazoles fused with five-membered heterocycles have been reported to be generally in the azido form. For example, Elguero, *et al.* (5) reported the predominance of the azido form in thiazolo[2,3-*e*]tetrazole (**1**, R = H), while in the 3-methyl analog (**1**, R = Me), the tetrazole form is predominant (Figure I). Reynolds, *et al.* (6), also reported

Figure I



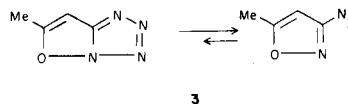
that in the case of tetrazolo[5,1-*b*]benzoxazole (**2a**) and tetrazolo[5,1-*b*]benzimidazole (**2b**), the azido form is predominant, while in tetrazolo[5,1-*b*]benzothiazole (**2c**), the predominant form is the tetrazole form (Figure II).

Figure II



The same result was published by Faure, *et al.* (7), in the case of tetrazolo[5,1-*b*]benzothiazole (**2c**). These authors also reported the predominance of the azido form in 2-methyltetrazolo[2,3-*e*]isoxazole (**3**) (Figure III).

Figure III



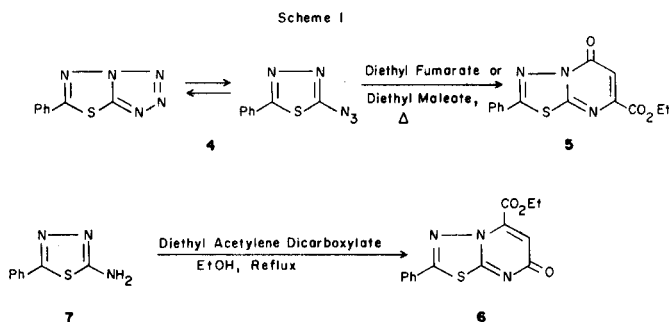
Considering the above data, one can imagine the effect of azido-tetrazole isomerization on the chemical reactivity of these compounds. Depending on structure and reaction condition, these compounds can usually undergo nitrene addition, nitrene insertion, cycloaddition, and rearrangement reactions with appropriate reagents (8-12).

In this paper we wish to report an interesting approach to the synthesis of 2-phenyl-7-carbethoxy-5*H*-1,3,4-thiadiazolo[2,3-*a*]pyrimidin-5-one (**5**), using 2-phenyltetrazolo[4,5-*a*]-1,3,4-thiadiazole (**4**).

Compound **4**, which was synthesized by Kanaoka (13), was shown to have the tetrazole structure in solid state, and azide structure in solution. The ir spectrum of this compound in the solid state (potassium bromide disk) showed no absorption in the region of 2120-2160 cm^{-1} (typical of $-\text{N}_3$ band), but in chloroform solution it showed an absorption at 2130 cm^{-1} , indicating the existence of the azido form. Considering the effect of temperature on this isomerism, our attention was focused on the reaction of this compound with diethyl fumarate and diethyl maleate at elevated temperature to observe which isomer would be

involved in this reaction.

When compound **4** was heated with diethyl fumarate at 120° for 1.5 hours, pale yellow prisms of m.p. 211-213° were obtained in 50% yield. On the basis of spectral data, the structure of the product was assigned as **5** or **6**. To determine the exact structure, 2-phenyl-5-carbomethoxy-7*H*-1,3,4-thiadiazolo[2,3-*a*]pyrimidin-7-one (**6**) was prepared by refluxing a mixture of 2-amino-5-phenyl-1,3,4-thiadiazole (**7**) and diethyl acetylenedicarboxylate in ethanol, according to the method of the preparation of 5-carbomethoxy analog of **6** (14). Physical properties and spectral data of this compound was completely different from the product obtained from the above reaction. The structure of the product was comparatively assigned as 2-phenyl-7-carbomethoxy-5*H*-1,3,4-thiadiazolo[2,3-*a*]pyrimidin-5-one (**5**) (Scheme I).



The physical properties and spectral data of compounds **5** and **6** are summarized in Table I.

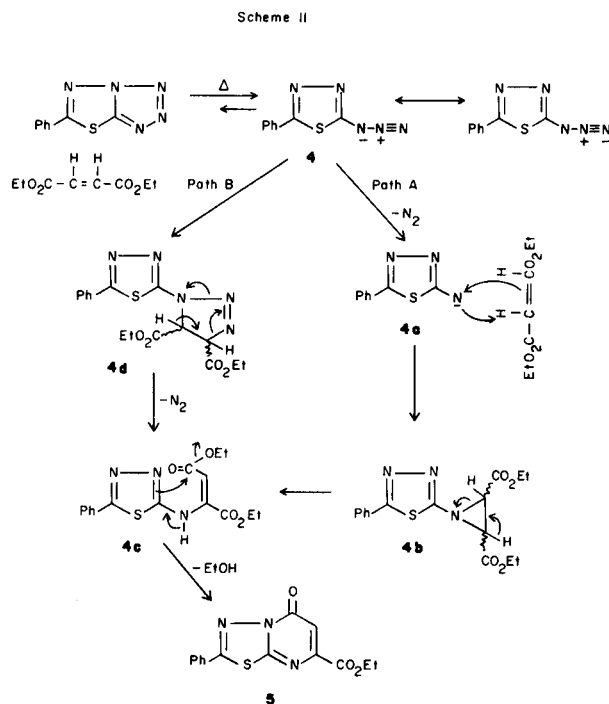
Table I

The Properties of Compounds **5** and **6**

Compound No.	C=O in ir cm^{-1}	H-6 in nmr ppm	M.p., C°
5	C-5, 1715	7.25	211-213
6	C-7, 1655	6.8	168

The same product was obtained from the reaction of **4** with diethyl maleate in lower yield and longer reaction time, in comparison with diethyl fumarate. A likely mechanism for this reaction is shown in Scheme II.

The azido form of **4** in the melt, can react with diethyl fumarate or diethyl maleate by one of two possible pathways. Path A involves the loss of nitrogen and formation of a nitrene intermediate (**4a**), which adds to the C=C double bond of the unsaturated diethyl ester to form an aziridine intermediate (**4b**). Ring cleavage of the aziridine intermediate followed by ring closure with the thiadiazole ring, through the intermediate **4c**, would give rise to compound **5**. In path B, the azide (**4**) undergoes 1,3-dipolar cycloaddition with the unsaturated diethyl ester to form



the triazoline intermediate (**4d**), the ring opening of which followed by the loss of nitrogen results in the formation of intermediate (**4c**). Ring closure of this intermediate with the thiadiazole ring would give rise to the compound **5**.

The formation of compound **5**, under the reaction conditions applied could be a supporting evidence for the formation of the azido form at the expense of the tetrazole form with a rise in temperature.

EXPERIMENTAL

Melting points were determined on a Kofler hot stage microscope and are uncorrected. The nmr spectra were obtained from a Varian T-60 spectrometer, and chemical shifts (δ) are in ppm relative to tetramethylsilane as an internal standard. Ir spectra were obtained from a Unicam SP1000 infrared spectrometer. Mass spectra were determined on a Varian Model Mat CH5 instrument.

Reaction of 2-Phenyltetrazolo[4,5-*a*]-1,3,4-thiadiazole (**4**), with Diethyl Fumarate to Obtain 2-Phenyl-7-carbomethoxy-5*H*-1,3,4-thiadiazolo[2,3-*a*]pyrimidin-5-one (**5**).

A mixture of compound **4** (0.200 g., 0.001 mole) and diethyl fumarate (0.206 g., equivalent to 0.2 ml. of a 98% solution, 0.0012 mole) was heated on an oil bath at 120° for 1.5 hour. After cooling to room temperature, the reaction mixture was treated with petroleum ether followed by ether. The solid which was obtained was purified by recrystallization from acetone to give 0.148 g. (50%) of pale yellow prisms of compound **5**, m.p. 211-213°; ir (potassium bromide): 1755 cm^{-1} (ester carbonyl), 1715 cm^{-1} (C-5 carbonyl); nmr (deuteriochloroform): 1.38 (t, 3H, -CH₃), 4.5 (q, 2H, -CH₂-), 7.26 (s, 1H, H-6), 7.5-8.1 (m, 5H, phenyl protons); ms: *m/e* 301 (M⁺).

Anal. Calcd. for C₁₄H₁₁N₃O₃S: C, 55.80; H, 3.68; N, 13.95; S, 10.14. Found: C, 55.94; H, 3.63; N, 13.82; S, 10.55.

Reaction of Compound 4 with Diethyl Maleate to Obtain Compound 5.

A mixture of compound 4 (0.200 g., 0.001 mole) and diethyl maleate (0.206 g., equivalent to 0.2 ml. of a 98% solution, 0.0012 mole) was heated on an oil bath at 120° for 6 hours. The purification process was the same as above. The physical properties and spectral data of the product were identical in every respect with compound 5, obtained from the above reaction, yield 0.124 g. (42%).

Reaction of 2-Amino-5-phenyl-1,3,4-thiadiazole (7) with Diethyl Acetylene Dicarboxylate to Obtain 2-Phenyl-5-carbomethoxy-7H-1,3,4-thiadiazolo-[2,3-a]pyrimidin-7-one (6).

A mixture of compound 7 (1.77 g., 0.01 mole) and diethyl acetylene dicarboxylate (1.7 g., 0.01 mole) in absolute ethanol (20 ml.) was refluxed for 6 hours. The reaction mixture was cooled, and the crystals obtained were purified by recrystallization from ethyl acetate to give 1.8 g. (60%) of compound 6, as pale yellow prisms, m.p. 168°; ir (potassium bromide): 1755 cm^{-1} (ester carbonyl), 1655 cm^{-1} (C-7 carbonyl); nmr (deuteriochloroform): 1.5 (t, 3H, $-\text{CH}_3$), 4.55 (q, 2H, $-\text{CH}_2-$), 6.8 (s, 1H, H-6), 7.5-8.1 (m, 5H, phenyl protons); ms: m/e 301 (M^+).

Anal. Calcd. for $\text{C}_{14}\text{H}_{11}\text{N}_3\text{O}_3\text{S}$: C, 55.80; H, 3.68; N, 13.95; S, 10.14. Found: C, 55.76; H, 3.82; N, 14.05; S, 10.32.

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