An Interesting Synthesis of Thieno[2,3-*d*][1,2,3]thiadiazole *via* Decomposition/Recyclization of 3-Methoxycarbonyl-1*H*-thieno-[2,3-*e*][1,3,4]thiadiazine 4,4-Dioxide

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Attempted hydrolysis of the ester of 3-methoxycarbonyl-1*H*-thieno[2,3-*e*][1,3,4]thiadiazine 4,4-dioxide (**I**) under acidic conditions gave the ring-contracted thieno[2,3-*d*][1,2,3]thiadiazole (**V**) instead of the expected carboxylic acid. In addition to a discussion of the reaction, a plausible mechanism is presented.

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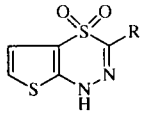
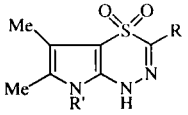
In previous papers [2-4], we have described the synthesis of certain thieno- and pyrrolo-fused thiadiazine 4,4-dioxides containing either a methoxycarbonyl or cyano group at the 3-position and corresponding to general structures **I-IV**.



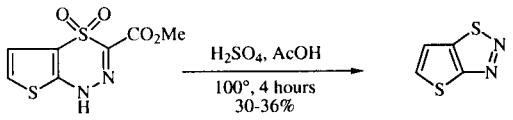
I R = CO_2Me
II R = CN



III R = CO_2Me
IV R = CN

As indicated in those papers, our attempted hydrolysis of the ester or cyano group of these compounds, as well as that of the corresponding 1,4-thiazine derivatives [2-3, 5-6], has to this point been unsuccessful, with standard hydrolysis conditions generally leading to recovery of starting material or decomposition to intractable tars depending upon reaction severity. During the course of more recent work with these compounds, however, we have been able to isolate in modest yield a new compound arising from the attempted acid-hydrolysis of ester-substituted thienothiadiazine **I**. The unexpected physical properties of this new compound (*i.e.*, low melting point and high solubility) quickly suggested that it was not the targeted carboxylic acid. Structural assignment was therefore pursued, which resulted in our identification of the product as thienothiadiazole **V**. Thus, under the acidic conditions employed, the thiadiazine ring of **I** underwent a decomposition/recyclization reaction with loss of the ester group, a ring carbon, and two oxygens from sulfur to give the ring-contracted thiadiazole. In this note, we describe this interesting reaction and present a plausible mechanism by which it might proceed.

As shown in Equation 1, when a suspension of thienothiadiazine **I** in a mixture of acetic acid:sulfuric acid:water (2:1:1 by volume) was heated at 100° for 4 hours and then neutralized with aqueous sodium hydroxide, thienothiadiazole **V** was obtained as off-white fluffy needles in yields ranging from 30-36% [7].



Eq. 1

I **V**

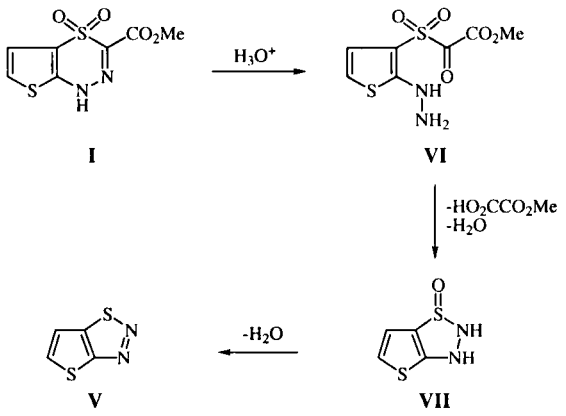
Our characterization of the product is based on detailed spectral analysis, with all data being consistent with the assigned structure. Thus, the high-resolution mass spectrum indicates a molecular weight of 141.9656 [M^+], which corresponds to the molecular formula of $C_4H_2N_2S_2$. The mass spectrum also shows fragments which are ascribed to [M^+-N_2] (*m/z* 114), [M^+-N_2-CS] (*m/z* 70), and [M^+-N_2-CS-H] (*m/z* 69), a pattern which is common to 1,2,3-thiadiazoles [8-9]. The ^1H nmr spectrum has just a pair of doublets in the aromatic region (δ 7.35 and 7.83, J = 5.5 Hz), indicative of the two adjacent thiophene protons, while the ^{13}C nmr shows just four signals, each again in the aromatic region. This carbon data, in particular, is consistent with the extrusion of the methyl ester and ring carbon from the starting thiadiazine, as well as the established molecular formula. The ir spectrum, being relatively non-descript in the high-frequency region, lacks both the N-H and C=O absorption that were present in the starting thiadiazine. Final confirmation of structure is based on the melting point of the product (78.5-79°), which is practically identical to that reported in the literature (78-79°) [10].

As shown in Scheme 1, a plausible mechanism for this reaction begins with the acid-catalyzed hydrolysis of the imine double bond of **I** to give hydrazino intermediate **VI**. From here, hydrolytic loss of the oxalate group from sulfur and condensation of the hydrazine with the resulting sulfinic acid could give hydrated thienothiadiazole **VII**. In the presence of mineral acid [11], this intermediate could then undergo a Pummerer-type dehydration [11-13] similar to that found in Hurd and Mori's monocyclic thiadiazole synthesis [14] to give the final product. While such a mechanism appears reasonable, we do note that we have made no investigation into its validity.

Surprisingly, when this decomposition/recyclization reaction was extended to ester-substituted pyrrolothiadiazine **III** [R' = -$(CH_2)_2$Ph], no trace of the expected pyrrolothiadiazole was obtained. In this case, only a dark, intractable residue was recovered. A possible explanation for this result may be that the pyrrole nucleus of an intermediate such as **VI** is susceptible to acid-mediated ring decomposition. In a similar manner, cyano-substituted thiadiazines **II** and **IV** also failed to give the expected thiadiazoles.

In conclusion, we have described an interesting synthesis of thieno[2,3-*d*][1,2,3]thiadiazole (**V**) by way of acid-catalyzed decomposition/recyclization of ester-substituted thienothiadiazine **I**. As the only other reported synthesis [10] for thienothiadiazole **V** involves eight steps, with the last step requiring the chromatographic separation of two major reaction products [15], this may be an attractive route to this bicyclic heterocycle.

Scheme 1



EXPERIMENTAL

General analytical details are as previously described [2-3].

Thieno[2,3-*d*][1,2,3]thiadiazole (**V**).

To a suspension of thienothiadiazine **I** (0.36 g, 1.46 mmole) in acetic acid (7 ml) was added concentrated sulfuric acid:water (1:1 by volume, 7 ml) and the mixture was stirred at 100° (oil bath) for 4 hours. The resulting solution was poured over ice and neutralized with concentrated sodium hydroxide solution. The resulting precipitate was collected, rinsed with water, and air dried to give off-white fluffy needles (0.075 g, 36%), mp 77.5-78°. An analytical sample recrystallized from hexanes had mp 78.5-79°; lit mp 78-79° [10]; ir (potassium bromide): ν 3095, 3065, 1385, 1270, 1215, 1180, 960, 765, 725, 645 cm^{-1}; ^1H nmr (300 MHz, deuteriochloroform): δ 7.35 (d, *J* = 5.5 Hz, 1H), 7.83 (d, *J* = 5.5 Hz, 1H); ^{13}C nmr (100 MHz, deuteriochloroform): δ 165.0, 147.1, 135.4, 115.2; ms (ei): *m/z* (relative intensity) 142 (M^+, 100), 114 (43), 88 (39), 70 (49), 69 (100), 57 (10); hrms (ei): calcd. for $C_4H_2N_2S_2$: 141.9659. Found: 141.9656; hrms (ei): calcd. for $C_4H_2S_2$ ($M^+ - N_2$): 113.9589. Found: 113.9591.

Anal. Calcd. for $C_4H_2N_2S_2$: C, 33.78; H, 1.42; N, 19.70; S, 45.10. Found: C, 33.87; H, 1.49; N, 19.64; S, 45.14.

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[7] The reaction was run three different times, with the only difference being a slight change in scale. The yield is thus unoptimized.

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[15] The final step of the literature synthesis gives the 5-chloro derivative along with the unsubstituted thienothiadiazole. Yields for the reaction were not given.