Concerning the "synthesis of 2-amino-5-aryl-5*H*-thiazolo[4,3-*b*]-1,3,4-thiadiazoles"

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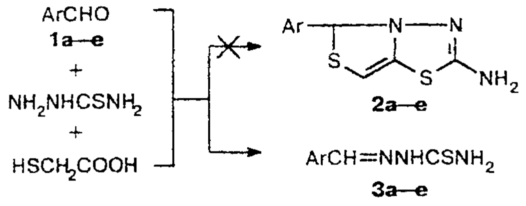
Compounds described previously as 2-amino-5-aryl-5*H*-thiazolo[4,3-*b*]-1,3,4-thiadiazoles were found to be thiosemicarbazones of aromatic aldehydes.

Key words: 2-amino-5-aryl-5*H*-thiazolo[4,3-*b*]-1,3,4-thiadiazoles, thiosemicarbazones of aromatic aldehydes.

In a work published recently[1] it was claimed that the reaction of equimolar amounts of aromatic aldehyde **1a—e**, thioglycolic acid, and thiosemicarbazide yields 2-amino-5-aryl-5*H*-thiazolo[4,3-*b*]-1,3,4-thiadiozoles (**2a—e**).

In an attempt to involve anisaldehyde in the reaction, we succeeded only in isolating the anisaldehyde thiosemicarbazone in a high yield. Then, we reproduced the conditions of the syntheses of **2a,b** described previously[1] and obtained compounds in a high yield whose melting points and ^{1}H NMR spectra agree with those reported for **2a,b**. However, these compounds were found to be the thiosemicarbazones **3a,b**. This fact is supported by ^{1}H and ^{13}C NMR and mass spectral data as well as by the values of melting points of mixtures with authentic samples of **3a,b**.



Ar = Ph (**a**), 4-$O_2NC_6H_4$ (**b**), 4-FC_6H_4 (**c**), 2-OH-5-BrC_6H_3 (**d**), 4-$Me_2NC_6H_4$ (**e**)

Analysis of the published data revealed that all compounds described earlier[1] as heterocycles **2a—e** are in fact the thiosemicarbazones of aromatic aldehydes **3a—e** (Table 1). Thus, the ^{1}H NMR spectra published previously[1] correspond to the structure of thiosemicarbazones **3a—e** but are inconsistent with structures **2a—e**, *e.g.*, the chemical shifts of a proton at δ 11.09—11.22 can not arise from a proton attached to an sp^3 hybridized C atom. The IR spectra (see Ref. 7) and melting points of the compounds obtained (see Table 1) agree almost exactly with the literature data for **3a—e**.

In conclusion, the report published previously[1] on the synthesis of heterocycles **2a—e** is not correct.

Table 1. Melting points of **2a—e** and **3a—e**

Compound	M.p./°C	
	2, literature data[1]	3, literature data
a	158—160; 159—161	159—160[2]
b	245—247	262; 255; 232—233; 230—231[3]
c	188—190	180[4]
d	247—250	~250[5]
e	210—212	214—215; 208—209; 207—208[6]

Experimental

Melting points were measured on a Boetius heating table. ^{1}H and ^{13}C NMR spectra were registered on a Bruker AM-300 spectrometer in DMSO-d_6, and mass spectra were registered on a Finnigan MAT INCOS-50 (EI, 70 eV) chromato mass spectrometer.

Attempt to synthesize 2-amino-5-aryl-5*H*-thiazolo[4,3-*b*]-1,3,4-thiadiazoles (2a,b). Following the known procedure,[1] 0.04 mol of aldehyde **1a,b**, 3.68 g (0.04 mol) of freshly-distilled thioglycolic acid, 4.00 g (0.044 mol) of thiosemicarbazide ("pure for analysis" grade), and 20 ml of concentrated H_2SO_4 (*d* 1.84) were allowed to react. During and after the addition of H_2SO_4 a considerable amount of SO_2 was liberated. Light yellow crystals of **3a,b** were obtained after the work-up.

Thiosemicarbazone of benzaldehyde (3a), yield 78%, m.p. 159—161 °C (from aqueous MeOH), no depression of melting point of a mixture with an authentic sample of **3a** is observed. ^{1}H NMR, δ: 7.40 (m, 3 H, Ph); 7.75 (m, 2 H, Ph); 7.90 and 8.15 (2 H, NH_2); 8.10 (s, 1 H, CH); 11.40 (s, 1 H, N=NH). ^{13}C NMR, δ: 127.7 (*o*-C); 128.5 (*m*-C); 129.7 (*p*-C); 134.0 (quat. arom.); 142.4 (CH=N); 178.1 (C=S). MS, *m/z*: [M]$^+$ 179.

Thiosemicarbazone of *p*-nitrobenzaldehyde (3b), yield 85%, m.p. 250—255 °C (from aqueous DMF). No depression of melting point of a mixture of the product with an authentic sample of **3b** is observed. ^{1}H NMR, δ: 8.07 (d, 2 H arom.);

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8.12 (s, 1 H, CH=N); 8.20 (d, 2 H arom.); 8.37 (NH$_2$); 11.7 (s, 1 H, N=NH). ^{13}C NMR, δ: 123.6 ($\underline{C}$H—C—NO$_2$); 128.0 ($\underline{C}$H—C—CH=N); 139.5 (CH=N); 140.6 ($\underline{C}$—CH=N); 147.5 ($\underline{C}$—NO$_2$); 178.6 (C=S). MS, *m/z*: [M]$^+$ 224.

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Comparison of α- and β-trifluoromethylsubstituted acrylic acids in their reactions with thiols

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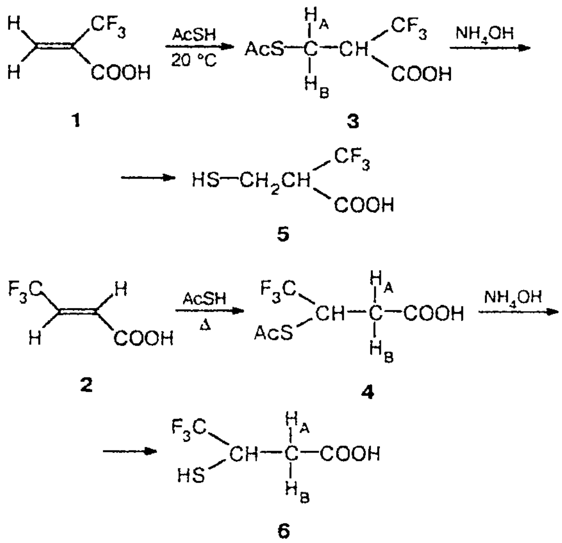
α-(Trifluoromethyl)acrylic acid (**1**) and γ,γ,γ-trifluorocrotonic acid (**2**) add AcSH (exothermally and at 100 °C, respectively) in the absence of a catalyst to form products of β-thiolation, which can be easily hydrolyzed to the corresponding β-mercaptoalkanoic acids. Thiols also add regiospecifically to acids **1** (in the absence of a catalyst) and **2** (only in the presence of trifluoromethanesulfonic acid as the catalyst) when heated.

Key words: α-(trifluoromethyl)acrylic acid, γ,γ,γ-trifluorocrotonic acid, thiolacetic acid; thiols, thiolation.

There are few reports on the addition of nucleophiles to the C=C bond of α-(trifluoromethyl)acrylic (**1**) and γ,γ,γ-trifluorocrotonic (**2**) acids. In the presence of enzymes, acid **1** reacts with water, diethylamine, and thiophenol and does not react with ethanol or phenol.[1,2] Addition of ammonia to acid **2** occurs under drastic conditions.[3] The reactions of compounds **1** and **2** with thiols and thiolcarboxylic acids were not studied. Acid **1** was found to react exothermally with AcSH to form only the product of β-thiolation (**3**). Acid **2** reacts regiospecifically with AcSH to give the β-(acetylthio) derivative **4**, but only when heated. The presence of air oxygen does not affect the direction of these reactions. The synthesized β-(acetylthio)substituted acids **3** and **4** were converted to β-mercaptoacids **5** and **6** by treating them with aqueous ammonia (Scheme 1).

The addition of thiols to acids **1** and **2** is much more difficult. For example, the reaction of acid **1** with α-toluenethiol occurs at a reasonable rate only at 100 °C to give exclusively benzyl sulfide **7** in a high yield. Under these conditions, acid **2** does not form any addi-

Scheme 1



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