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LETTERS TO THE EDITOR

Cycloaddition with Nitriles of an Active Methylene Group to Substituted 1,2,4-Thiadiazol-5(2*H*)-imines

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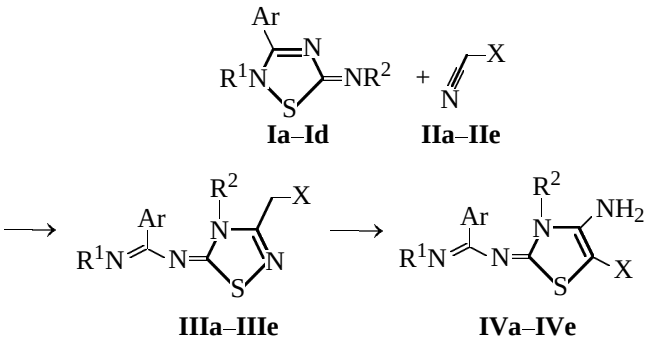
An important property of substituted 1,2,4-thiadiazol-5(2*H*)-imines (**I**) is their ability to participate in in [3 + 2]-cycloaddition reactions as 1,3 dipoles [1–4]. Heating on acetonitrile results in directed addition of the C≡N group to the N=C–S triad with heteroring cleavage [1].

We performed reactions of accessible reagents **I** [1, 5] with substituted acetonitriles **II** containing an active methylene group and revealed an unusual reaction direction, since expected cycloaddition products **III** underwent rearrangement into thiazol derivatives **IV**.



Ia–Id **IIa–IIe**

IIIa–IIIe **IVa–IVe**

R^1 = Ph (**a, b, e**), $PhCH_2$ (**c**), 4-MeC_6H_4 (**d**); R^2 = Ph (**a–c, e**), Me (**d**); Ar = 4-MeC_6H_4 (**a, e**), 4-$MeOC_6H_4$ (**b**), Ph (**c, d**); X = CO_2Et (**a**), NO_2 (**b**), $P(O)Ph_2$ (**c**), Ts (**d**), CN (**e**).

The yields of compounds **IV** are much dependent on the nature of substituent X in reagents **II**. Thus, if nitriles contain strong electron-acceptor groups X (NO_2, Ts, or CN), cycloadducts **IIIb**, **IIId**, and **IIIe** cannot be isolated, and the yields of recyclization products are mostly high. At the same time, the major products of the reaction of compounds **Ia** and **Ic** with cyanoacetic ester and diphenylphosphinoylacetonitrile at room temperature are compounds **IIIa** and **IIIc**, which can be converted into corresponding compounds **IV** by heating.

The structure of recyclization products **IV** was proved by ^{1}H NMR and IR spectra. Moreover, the presence of the enaminonitrile fragment in compound **IVe** and its analogs was proved by annelation reactions which will be described in further publications.

Ethyl [5-(4-methyl-*N*-phenylbenzimidoyl)imino-4-phenyl-4,5-dihydro-1,2,4-thiadiazol-3-yl]acetate (IIIa). A solution of 2.5 mmol of compound **Ia** and 2.5 mmol of ethyl cyanoacetate in 10 ml of CH_2Cl_2 was allowed to stand at 20–25°C for 24 h. The solvent was removed in a vacuum, the residue was treated with ethanol, and the precipitate that formed was filtered off. Yield 75%, mp 148°C. IR spectrum (CH_2Cl_2), ν, cm^{-1}: 1740 (C=O). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.18 t (CH_3CH_2), 2.24 s ($CH_3C_6H_4$), 3.67 s (CH_2CO), 4.08 q (CH_3CH_2), 6.85–7.60 m ($2C_6H_5$, C_6H_4). Found, %: N 12.38; S 7.10. $C_{26}H_{24}N_4O_2S$. Calculated, %: N 12.27; S 7.02.

Ethyl 4-amino-2-(4-methyl-*N*-phenylbenzimidoyl)imino-3-phenyl-2,3-dihydrothiazol-5-carboxylate (IVa). A solution of 0.5 mmol of compound **IIIa** in 15 ml of ethanol was heated under reflux for 25 h and then allowed to stand at 20–25°C for 48 h. The precipitate that formed was filtered off. Yield 69%, mp 182°C (EtOH). IR spectrum (CH_2Cl_2), ν, cm^{-1}: 1660 (C=O), 3350, 3460 (NH_2). ^{1}H NMR spectrum ($CDCl_3$; stereoisomeric mixture), δ, ppm: 1.33 t (CH_3CH_2), 2.21 s, 2.38 s (6:1, $CH_3C_6H_4$), 4.26 q (CH_3CH_2), 5.71 s (NH_2), 6.80–7.76 m ($2C_6H_5$, C_6H_4). Found, %: N 12.41; S 7.12. $C_{26}H_{24}N_4O_2S$. Calculated, %: N 12.27; S 7.02.

***N*^{1}-[4-Amino-5-nitro-3-phenylthiazol-2(3*H*)-ylidene]-4-methoxy-*N*^{2}-phenylbenzamidine (IVb).** Nitroacetonitrile, 5 mmol, was added to a solution of 5 mmol of compound **Ib** in 10 ml of CH_2Cl_2. A precipitate formed immediately and was filtered off. Yield 49%, mp 218°C (decomp.) ($ClCH_2CH_2Cl$). IR spectrum (KBr), ν, cm^{-1}: 3160–3390 (NH_2). ^{1}H NMR

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spectrum (DMSO-d_6; stereisomeric mixture), δ, ppm: 3.67 s, 3.81 s (4:1, CH_3), 6.69–7.79 m ($2C_6H_5$, C_6H_4), 8.21 br.s (NH_2). Found, %: N 15.83; S 7.11. $C_{23}H_{19}N_5O_3S$. Calculated, %: N 15.72; S 7.20.

***N*²-Benzyl-*N*¹-[3-(diphenylphosphinoyl)methyl-4-phenyl-1,2,4-tiadiazol-5(4*H*)-ylidene]benzamidine (IIIc)** and ***N*¹-[4-amino-5-diphenylphosphinoyl-3-phenylthiazol-2(3*H*)-ylidene]-*N*²-benzylbenzamidine (IVc).** *a*. A solution of 5 mmol of compound **Ic** and 5 mmol of diphenylphosphinoylacetonitrile in 10 ml of CH_2Cl_2 was allowed to stand at room temperature for 72 h. The solvent was removed in a vacuum, the residue was treated with 10 ml of ethanol, and the mixture of compounds **IIIc** and **IVc** (2.4:1, by ^{1}H NMR) was filtered off. Recrystallization of this mixture from benzene gave pure compound **IIIc**. Yield 55%, mp 82–85°C. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 3.66 d (CH_2P, J_{HP} 15 Hz), 4.88 s (CH_2N), 7.17–7.73 m ($5C_6H_5$). Found, %: C 70.66; H 5.06; N 9.41; S 5.51. $C_{35}H_{29}N_4OPS$. Calculated, %: C 71.90; H 5.00; N 9.58; S 5.48. The benzene mother liquor was evaporated in a vacuum, the residue was treated with ethanol, and compound **IVc** was filtered off. Yield 10%, mp 163°C (MeCN). IR spectrum (KBr), ν, cm^{-1}: 3340, 3400 (NH_2). ^{1}H NMR spectrum (DMSO-d_6; stereisomeric mixture), δ, ppm: 4.44 s, 4.62 s (1:3, CH_2), 6.05 s, 6.26 s (3:1, NH_2), 7.19–7.77 m ($5C_6H_5$). Found, %: C 71.89; H 4.95; N 9.66; P 5.35. $C_{35}H_{29}N_4OPS$. Calculated, %: C 71.90; H 5.00; N 9.58; P 5.30.

b. A mixture of 0.5 mmol of compound **IIIc**, 3 ml of ethanol, and one drop of triethylamine was heated under reflux for 0.5 h, cooled to 20°C, and compound **IVc** was filtered off. Yield 17%.

***N*¹-[4-Amino-3-methyl-5-tosylthiazol-2(3*H*)-ylidene]-*N*²-*p*-tolylbenzamidine (IVd).** A solution of 5 mmol of triethylamine in 5 ml of ethanol was added dropwise to a solution of 5 mmol of base **Id** hydrobromide and 5 mmol of tosylacetonitrile in 10 ml of CH_2Cl_2. The mixture was allowed to stand at 20–25°C for 24 h, the solvent was removed in a vacuum, and the residue was washed with ethanol and filtered off. Yield 87%, mp 181°C (decomp.) (MeOH/$CHCl_3$). IR spectrum (CH_2Cl_2), ν, cm^{-1}: 3360, 3460 (NH_2). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 2.21 s (CH_3C), 2.25 s (CH_3C), 3.56 s (CH_3N), 6.54 d ($2H_{arom}$), 6.98 s (NH_2), 7.02 d ($2H_{arom}$), 7.24–7.39 m ($7H_{arom}$), 7.78 d ($2H_{arom}$). Found, %: C 62.78; H 5.00; N 11.71; S 13.35. $C_{25}H_{24}N_4O_2S_2$. Calculated, %: C 63.00; H 5.08; N 11.76; S 13.45.

***N*¹-[4-Amino-5-cyano-3-phenyltiazol-2(3*H*)-ylidene]-4-methyl-*N*²-phenylbenzamidine (IVe).** A mixture of 20 mmol of compound Ia, 20 mmol of malonodinitrile, and 10 ml of dioxane was heated under reflux with stirring for 3 h and then cooled to 20°C. The precipitate was filtered off and dried in an oven at 100°C. Yield 76%, mp 215°C (decomp.) (MeCN). IR spectrum (KBr), ν, cm^{-1}: 2200 (C≡N), 3220–3380 (NH_2). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 2.18 s (CH_3), 6.69 d ($2H_{arom}$), 6.84 s (NH_2), 6.92–7.05 m ($5H_{arom}$), 7.17–7.25 m ($2H_{arom}$), 7.47–7.60 m ($5H_{arom}$). Found, %: C 71.48; H 4.80; N 17.41; S 7.87. $C_{24}H_{19}N_5S$. Calculated, %: C 70.39; H 4.67; N 17.10; S 7.83.

The IR spectra were recorded on a Specord IR-71 instrument in CH_2Cl_2 solutions and on a UR-20 instrument in KBr pellets. The ^{1}H NMR spectra were obtained on Varian VXR-300 (compounds **IIIa**, **IIIc**, and **IVa**–**IVd**) and Varian Gemini-200 (compound **IVe**) spectrometers, internal reference TMS.

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