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REACTION OF 4-AMINO-3-METHYLTHIO-5-OXO-6-R-4,5-DIHYDRO-1,2,4-TRIAZINES WITH SULFONYLACETIC ACID NITRILES

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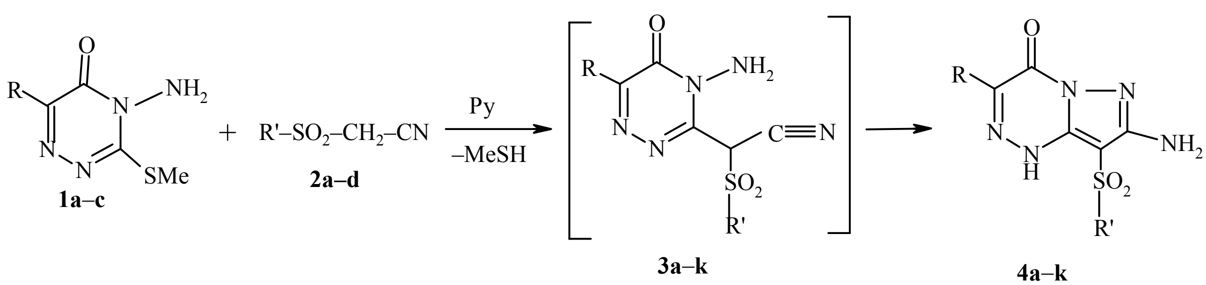
The reactions of 4-amino-3-methylthio-5-oxo-6-R-4,5-dihydro-1,2,4-triazines with arylsulfonylacetonitriles and with dinitriles of sulfonyldiacetic acid and methylenebis(sulfonylacetic) acid have been studied. 7-Amino-3-R-8-(R'-sulfonyl)-1,4-dihydropyrazolo[5,1-c][1,2,4]triazin-4-ones have been synthesized and these are the first representatives of geminal sulfones in which the heterocyclic ring is bound directly to the sulfur atoms of the sulfonyl groups.

Keywords: 4-amino-3-methylthio-5-oxo-6-R-4,5-dihydro-1,2,4-triazines, 7-amino-3-R-8-(R'-sulfonyl)-1,4-dihydropyrazolo[5,1-*c*][1,2,4]triazin-4-ones, arylsulfonylacetonitriles, dinitriles of sulfonyldiacetic and methylenebis(sulfonylacetic) acids.

Heterocyclic compounds which contain a 1,2,4-triazine ring show a high degree of pesticidal activity [1, 2]. Continuing a study of the heterocyclization reaction of 1,2,4-triazines with arylsulfonylacetonitriles [3, 4] we have examined the interaction of the 4-amino-3-methylthio-5-oxo-6-R-4,5-dihydro-1,2,4-triazines **1a-c** with compounds containing an active methylene group, i.e. the arylsulfonylacetonitriles **2a-c** and sulfonyldiacetic acid dinitrile (**2d**). The reaction was carried out in refluxing pyridine with the evolution of methyl mercaptan. It is likely that the intermediate nitriles **3a-k** are initially formed and these undergo intramolecular cyclization (addition of the NH_2 group to the CN group [5]) to give the 7-amino-3-R-8-(R'-sulfonyl)-1,4-dihydropyrazolo-[5,1-*c*][1,2,4]triazin-4-ones **4a-k** in 35-67% yields.



1 a R = Me, **b** R = *t*-Bu, **c** R = Ph; **2 a** R' = Ph, **b** R' = *p*-MeC_6H_4, **c** R' = *p*-ClC_6H_4, **d** R' = $NCCH_2$; **3**, **4 a**, **d**, **g**, **j** R = Me, **b**, **e**, **h** R = *t*-Bu; **c**, **f**, **i**, **k** R = Ph, **a-c** R' = Ph, **d-f** R' = *p*-MeC_6H_4, **g-i** R' = *p*-ClC_6H_4; **j**, **k** R' = $NCCH_2$

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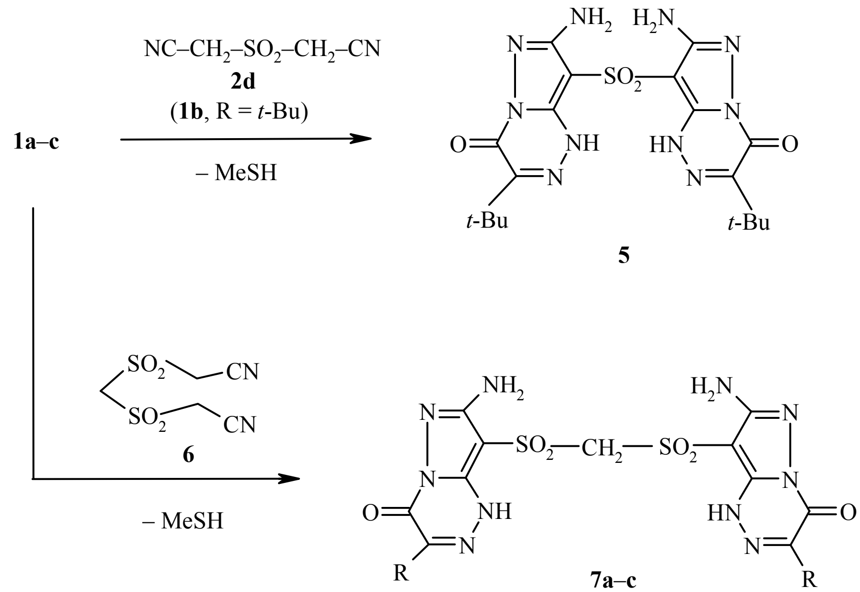
In the reaction with the *tert*-butyl substituted triazine **1b** both CN groups of the dinitrile **2d** take part to form the bis[7-amino-3-*tert*-butyl-4-oxo-1,4-dihydropyrazolo[5,1-*c*][1,2,4]triazin-8-yl]sulfone (**5**) in 36% yield. The formation of the latter is probably associated with the increased solubility of the initial cyclization product thanks to the presence of the *tert*-butyl substitutent.

We have previously synthesized the methylenebis(sulfonylacetic) acid dinitrile (**6**) and showed that, depending on the reaction conditions, two of the three methylene groups in it are active [6]. In this work we have shown that the reaction of the dinitrile **6** with the triazines **1a-c** gives the bis(7-amino-3-R-4-oxo-1,4-dihydropyrazolo[5,1-*c*][1,2,4]triazin-8-ylsulfonyl)methanes **7a-c** in 28-49% yields.



7 **a** R = Me, **b** R = *t*-Bu; **c** R = Ph

The result obtained can be explained by the fact that the methylene group situated between the sulfonyl groups in the dinitrile **6** is of low reactivity (apparently due to steric factors) and this agrees with our results in [6, 7].

The synthesized compounds **4, 5, 7** are colorless, high melting materials which are poorly soluble in polar organic solvents (see Table 2). The ^{1}H NMR spectra of **4, 5, 7** are characterized by singlet signals for the NH_2 and NH groups in the regions 6.23-6.40 and 13.02-13.98 ppm respectively and compounds **4j-k** and **7a-c** by singlets for the CH_2 groups at 5.06-5.10 and 5.53-5.66 ppm respectively. The IR spectra of all of the compounds show stretching vibrations for an S=O type group at 1300-1330 and 1150-1170 cm^{-1}, C=O at 1680-1700 cm^{-1}, and NH at 2900-3300 cm^{-1}. The IR spectra of compounds **4j-k** also show an absorption band for the CN group at 2200-2280 cm^{-1}.

Overall, the studied reaction can be regarded as a method for introducing a hetaryl substituent into a sulfonyl containing CH-acid. The synthesized compounds **7a-c** are the first representatives of geminal sulfones in which the $–SO_2–CH_2–SO_2–$ grouping is bonded to the heterocyclic nuclei.

EXPERIMENTAL

^{1}H NMR spectra were recorded on a Varian-300 instrument (300 MHz) using DMSO-d$_6$ and TMS internal standard. IR spectra were taken on a UR-20 instrument for KBr tablets. Mass spectra were recorded on an MX-1303 instrument.

TABLE 1. Characteristics of Compounds **4, 5, 7**

Compound	Empirical formula	Found, % / Calculated, % C	H	N	mp, °C (dec.)	Yield, %
4a	$C_{12}H_{11}N_5O_3S$	47.51 / 47.21	3.54 / 3.63	22.68 / 22.94	350-355	44
4b	$C_{15}H_{17}N_5O_3S$	50.62 / 51.86	4.98 / 4.93	20.11 / 20.16	280-285	52
4c	$C_{17}H_{13}N_5O_3S$	55.28 / 55.58	3.75 / 3.57	19.28 / 19.06	285-290	41
4d	$C_{13}H_{13}N_5O_3S$	48.61 / 48.90	4.31 / 4.10	21.80 / 21.93	355-360	43
4e	$C_{16}H_{19}N_5O_3S$	52.89 / 53.17	5.22 / 5.30	19.36 / 19.38	265-268	57
4f	$C_{18}H_{15}N_5O_3S$	56.40 / 56.68	3.91 / 3.96	18.42 / 18.36	285-290	60
4g	$C_{12}H_{10}ClN_5O_3S$	42.30 / 42.42	2.68 / 2.97	20.82 / 20.61	345-350	35
4h	$C_{15}H_{16}ClN_5O_3S$	47.36 / 47.18	4.39 / 4.22	18.42 / 18.34	245-250	67
4i	$C_{17}H_{12}ClN_5O_3S$	50.55 / 50.81	3.16 / 3.01	17.53 / 17.43	295-300	49
4j	$C_8H_8N_6O_3S$	35.76 / 35.82	3.19 / 3.01	31.45 / 31.33	310-320	58
4k	$C_{13}H_{10}N_6O_3S$	47.36 / 47.27	3.17 / 3.05	25.71 / 25.44	280-285	62
5	$C_{18}H_{24}N_{10}O_4S$	45.60 / 45.37	5.22 / 5.08	29.61 / 29.39	345-350	36
7a	$C_{13}H_{14}N_{10}O_6S_2$	33.26 / 33.19	3.09 / 3.00	29.66 / 29.77	340-345	29
7b	$C_{19}H_{26}N_{10}O_6S_2$	41.28 / 41.15	4.79 / 4.73	25.45 / 25.26	335-340	49
7c	$C_{23}H_{18}N_{10}O_6S_2$	46.75 / 46.46	3.20 / 3.05	23.45 / 23.56	350-355	28

TABLE 2. Spectroscopic Characteristics of Compounds **4, 5, 7**

Compound	IR spectum, ν, cm^{-1}	^1H NMR spectrum, δ, ppm (*J*, Hz)	$[M]^+$
1	2	3	4
4a	3300-3100 (NH_2), 1700 (C=O), 1600 (C=N), 1510, 1470, 1440, 1310 and 1160 (S=O)	2.21 (3H, s, CH_3); 6.31 (2H, s, NH_2); 7.64 (3H, m, *m*- and *p*-H_{Ph}); 8.15 (2H, d, *J* = 5.9, *o*-H_{Ph}); 13.48 (1H, br. s, NH)	305
4b	3300–3100 (NH_2), 2900, 1700 (C=O), 1620 (C=N), 1540, 1480, 1450, 1320 and 1160 (S=O)	1.34 (9H, s, $(CH_3)_3C$); 6.33 (2H, s, NH_2); 7.63 (3H, m, *m*- and *p*-H_{Ph}); 8.17 (2H, d, *J* = 6.2, *o*-H_{Ph}); 13.60 (1H, br. s, NH)	347
4c	3300-3100 (NH_2), 1700 (C=O), 1610 (C=N), 1520, 1430, 1310 and 1150 (S=O)	6.36 (2H, s, NH_2); 7.42-8.19 (10H, m, $2C_6H_5$); 13.98 (1H, br. s, NH)	367
4d	3300-3100 (NH_2), 2900, 1700 (C=O), 1610 (C=N), 1530, 1480, 1440, 1330 and 1170 (S=O)	2.19 (3H, s, CH_3); 2.28 (3H, s, CH_3); 6.23 (2H, s, NH_2); 7.41 (2H, d, *J* = 6.8, *m*-H_{Ar}); 7.99 (2H, d, *J* = 6.8, *o*-H_{Ar}); 13.19 (1H, br. s, NH)	319
4e	3300-3100 (NH_2), 2900, 1690 (C=O), 1600 (C=N), 1530, 1490, 1310 and 1150 (S=O)	1.34 (9H, s, $(CH_3)_3C$); 6.32 (2H, s, NH_2); 7.45 (2H, d, *J* = 6.6, *m*-H_{Ar}); 8.06 (2H, d, *J* = 6.6, *o*-H_{Ar}); 13.63 (1H, br. s, NH)	361
4f	3300-3100 (NH_2), 2950, 1700 (C=O), 1610 (C=N), 1530, 1490, 1440, 1300 and 1160 (S=O)	2.23 (3H, s, CH_3); 6.36 (2H, s, NH_2); 7.45 (5H, m, C_6H_5); 7.90 (2H, d, *J* = 6.5, *m*-H_{Ar}); 8.05 (2H, d, *J* = 6.5, *o*-H_{Ar}); 13.98 (1H, br. s, NH)	381

TABLE 2 (continued)

1	2	3	4
4g	3300-3000 (NH_2), 1700 (C=O), 1610 (C=N), 1530, 1480, 1440, 1310 and 1170 (S=O)	2.18 (3H, s, CH_3); 6.31 (2H, s, NH_2); 7.71 (2H, d, J = 8.0, m-H_{Ar}); 8.12 (2H, d, J = 8.0, o-H_{Ar}); 13.54 (1H, br. s, NH)	340
4h	3300-3100 (NH_2), 2950, 1680 (C=O), 1600 (C=N), 1540, 1470, 1320 and 1150 (S=O)	1.32 (9H, s, $(CH_3)_3C$); 6.36 (2H, s, NH_2); 7.72 (2H, d, J = 8.2, m-H_{Ar}); 8.18 (2H, d, J = 8.2, o-H_{Ar}); 13.63 (1H, br. s, NH)	382
4i	3300-3100 (NH_2), 1700 (C=O), 1600 (C=N), 1530, 1480, 1440, 1310 and 1150 (S=O)	6.40 (2H, s, NH_2); 7.47-7.80 (5H, m, C_6H_5); 7.95 (2H, d, J = 8.3, m-H_{Ar}); 8.18 (2H, d, J = 8.3, o-H_{Ar}); 13.94 (1H, br. s, NH)	402
4j	3300-3100 (NH_2), 2900, 2280 (C≡N), 1700 (C=O), 1610 (C=N), 1520, 1480, 1310 and 1170 (S=O)	2.15 (3H, s, CH_3); 5.06 (2H, s, CH_2CN); 6.33 (2H, s, NH_2); 13.02 (1H, br. s, NH)	268
4k	3300-3000 (NH_2), 2900, 2200 (C≡N), 1700 (C=O), 1610 (C=N), 1530, 1430, 1320 and 1160 (S=O)	5.10 (2H, s, CH_2CN); 6.40 (2H, s, NH_2); 7.51-7.98 (5H, m, C_6H_5); 13.11 (1H, br. s, NH)	330
5	3300-2900 (NH_2), 1700 (C=O), 1600 (C=N), 1550, 1450, 1330 and 1170 (S=O)	1.30 (18H, s, $2(CH_3)_3C$); 6.51 (4H, s, $2NH_2$); 13.32 (2H, br. s, 2NH)	476
7a	3400-3100 (NH_2), 2900, 1700 (C=O), 1600 (C=N), 1570, 1470, 1430, 1310 and 1160 (S=O)	2.15 (6H, s, $2CH_3$); 5.60 (2H, s, $-CH_2-$); 6.25 (4H, s, $2NH_2$); 13.23 (2H, br. s, 2NH)	470
7b	3300-3100 (NH_2), 2900, 1700 (C=O), 1620 (C=N), 1540, 1470, 1430, 1320 and 1150 (S=O)	1.36 (18H, s, $2(CH_3)_3C$); 5.53 (2H, s, $-CH_2-$); 6.24 (4H, s, $2NH_2$); 13.31 (2H, br. s, 2NH)	555
7c	3300-3100 (NH_2), 2900, 1700 (C=O), 1610 (C=N), 1530, 1490, 1450, 1310 and 1160 (S=O)	5.66 (2H, s, $-CH_2-$); 6.36 (4H, s, $2NH_2$); 7.47-8.00 (10H, m, $2C_6H_5$); 13.20 (2H, br. s, 2NH)	594

Arylsulfonylacetonitriles were prepared by a known method [8] and sulfonyldiacetic acid dinitrile, methylenebis(sulfonylacetic) acid dinitrile, and 4-amino-3-methylthio-5-oxo-6-R-4,5-dihydro-1,2,4-triazines by methods [9], [6], and [10] respectively.

Reaction of Triazines 1a-c with Sulfonylacetic Acid Nitriles 2a-d. (General Method). A mixture of triazine **1** (20 mmol), the methylene-active nitrile or dinitrile **2** (25 mmol) and pyridine (1 ml) was refluxed for 4 h. After cooling, the precipitated product **4**, **5** or **7** was filtered off, washed with ethanol (2 × 10 ml), recrystallized from DMSO, and dried.

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