Preparation of 4*H*-1,3,4-Thiadiazolo[2,3-*c*]-1,2,4-triazin-4-one Derivatives

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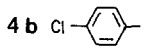
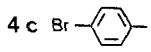
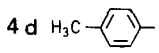
We have aimed at the synthesis of fused heterocycles which contain the 1,3,4-thiadiazole moiety e.g. 1,3,4-thiadiazolo[3,2-*a*]pyridines[1,2] and *s*-triazolo[3,4-*b*]-1,3,4-thiadiazole derivatives[3]. We now describe a new synthesis of derivatives of 4*H*-1,3,4-thiadiazolo[2,3-c]-1,2,4-triazin-4-ones which contain the 1,3,4-thiadiazole and 1,2,4-triazine moieties. The methods described for the preparation of 4*H*-1,3,4-thiadiazolo[2,3-*c*]-1,2,4-triazin-4-ones can be classified in three groups, all of them using 4-amino-6-methyl-5-oxo-3-thioxo-2,3,4,5-tetrahydro-1,2,4-triazine **(1)** as starting material. The first involves cyclization under basic conditions with cyanogen bromide to give the corresponding 2-amino derivatives[4]; the second involves cyclization with carbon disulfide of the appropriate 3-methylthio[5] or 3-hydroxylamino[6] derivative to give the corresponding 2-mercapto derivative. Finally, reaction of com-

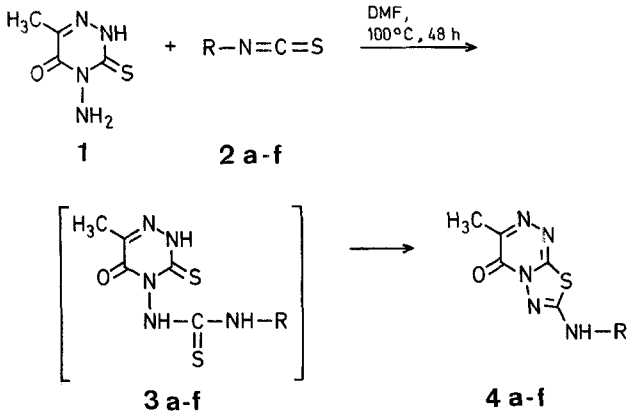
Table. 4*H*-1,3,4-Thiadiazolo[2,3-*c*]-1,2,4-triazin-4-ones **4** prepared

Compound No	R	Yield[a] [%]	m.p.[b] [°C]	Molecular formula[c]	I.R. (Nujol)[d] υ [cm^{-1}]	M.S.[e] *m/e* (%)
4 a		77	291–293	$C_{11}H_9N_5OS$ (259.3)	3240, 3190, 3060, 1680, 1620, 1600, 1560, 1480, 1320, 1300, 1260, 1230, 1200, 1070, 900, 760, 750, 690	259 (100), 231 (76), 161 (47), 136 (40), 135 (70), 104 (35), 77 (86)
4 b		84	324–326	$C_{11}H_8ClN_5OS$ (293.7)	3240, 3190, 1680, 1620, 1560, 1490, 1320, 1230, 1080, 830, 750	295 (20), 293 (60), 267 (25), 265 (45), 195 (25), 171 (50), 169 (100), 152 (25), 138 (45), 111 (50), 99 (25), 90 (20)
4 c		76	326–328	$C_{11}H_8BrN_5OS$ (338.2)	3250, 3190, 3020, 1680, 1620, 1560, 1540, 1400, 1330, 1310, 1260, 1230, 1200, 1075, 1010, 840, 830, 820, 760, 750	340 (60), 338 (60), 312 (55), 310 (60), 214 (100), 197 (20), 156 (50)
4 d		79	320–321	$C_{12}H_{11}N_5OS$ (273.3)	3240, 3200, 1690, 1620, 1560, 1480, 1320, 1200, 1080, 840, 820, 750	273 (35), 245 (20), 151 (25), 135 (20), 118 (100), 105 (20), 91 (30)
4 e		87	274–276	$C_{12}H_{11}N_5OS$ (273.3)	3240, 3200, 1690, 1600, 1580, 1490, 1470, 1320, 1210, 1080, 770, 760	273 (31), 245 (15), 151 (20), 135 (15), 118 (100), 117 (25), 105 (15), 91 (20)
4 f		80	327–329	$C_{12}H_9N_5O_2S$ (287.3)	3240, 3220, 1710, 1670, 1570, 1490, 1465, 1300, 1220, 1200, 1070, 890, 720, 710, 690	287 (50), 259 (15), 236 (10), 143 (12), 129 (12), 105 (100), 77 (85)

[a] Yield of isolated, pure product.
[b] Uncorrected.
[c] Microanalyses were in good agreement with the calculated values: C ±0.22, H ±0.12, N ±0.26, S ±0.09.
[d] Recorded on a Perkin-Elmer spectrometer.
[e] Recorded at 70 eV with a Hewlett-Packard 5980A instrument.

pound **1** with aromatic carboxylic acids in the presence of phosphoryl chloride leads to the corresponding 2-aryl derivatives[7].

We report here a convenient one-pot preparation of 7-arylamino-3-methyl-4*H*-1,3,4-thiadiazolo[2,3-*c*]-1,2,4-triazin-4-ones **4** in synthetically useful yields by reaction of 4-amino-6-methyl-5-oxo-3-thioxo-2,3,4,5-tetrahydro-1,2,4-triazine (**1**; readily available from thiocarbohydrazide and pyruvic acid[8]) with aryl isothiocyanates **2** under neutral conditions.



When treated with one equivalent of aryl isothiocyanate **2** in dimethylformamide at 100 °C for 48 h, the *N*-aminoheterocycle **1** is directly converted into the corresponding bicyclic derivative **4**, which is isolated as a crystalline solid in high yield. Structural elucidation of **4** was accomplished on the basis of spectral data and microanalysis. Compounds **4** display in the I.R. spectra absorptions at 3240 cm^{-1}, assigned to the N—H stretching vibration, at 1690–1670 cm^{-1}, attributable to the carbonyl group of the triazinone moiety, and in the region of C=N stretching vibration (1620–1600 cm^{-1}). In addition, compound **4f** shows an absorption at 1710 cm^{-1} due to the benzoyl group. The ^{1}H-N.M.R. spectra of all bicyclic compounds **4** show a singlet at $\delta = 2.38$ ppm attributable to the methyl group attached at the triazine ring.

The reaction seems to be quite general for the aromatic series, however, attempts with aliphatic isothiocyanates failed to give **4**. We believe that the mechanism of this conversion involves the initial formation of *N,N'*-disubstituted thioureas **3** which under the reaction conditions undergo cyclodehydrosulfurization to give **4**.

7-Arylamino-3-methyl-4*H*-1,3,4-thiadiazolo[2,3-*c*]-1,2,4-triazin-4-ones 4; General Procedure:

To a solution of 4-amino-6-methyl-5-oxo-3-thioxo-2,3,4,5-tetrahydro-1,2,4-triazine (**1**; 0.5 g, 3.16 mmol) in dry dimethylformamide (15 ml), an equimolecular amount of the appropriate aryl isothiocyanate **2** is added. The mixture is heated at 100 °C for 48 h. After cooling, the resultant solution is poured into ice/water (70 ml) and the precipitated solid is separated by filtration and recrystallized from ethanol/chloroform (1 : 1, w : w) to give **4** as a crystalline solid (Table).

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