REACTION OF AROYL CHLORIDES WITH 1,4-DIPHENYLTHIOSEMICARBAZIDE: FORMATION OF BOTH 1,3,4-THIADIAZOLIUM-2-AMINIDES AND 1,3,4-TRIAZOLIUM-2-THIOLATE

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Abstract: The reaction of aroyl chlorides with 1,4-diphenylthiosemicarbazide has been re-studied and is now shown to constitute a useful route for producing derivatives of the 1,3,4-thiadiazolium-2-aminide system as well as derivatives of the 1,3,4-triazolium-2-thiolate system.Conditions for obtaining both systems in good yield; for their inter-conversion of the 1,3,4-thiadiazolium-2-aminide derivatives to the corresponding 1,3,4-triazolium-2-thiolate derivatives and for isolating the intermediate aroyl-1,4-diphenylthiosemicarbazides are presented.

Introduction

Mesoionic compounds belonging to the 1,3,4-triazolium-2-thiolate system **2** were prepared by Busch *et al.*(1-7) by the reactions of1,3,4-thiadiazolium-2-thiolates **3** (**Figure 1**) with primary amines and by the reactions of 1,4-diphenylthiosemicarbazide 4 with carboxylic acid chlorides **5**.

Schönberg (8), on the basis of theoretical studies, suggested that Busch's second method produced a pair of compounds involving the interconversion of isomeric systems **1** and **2**.

The products prepared by Busch's second method were re-investigated somewhat later (9,10) and those studies indicated that the products formed are 1,3,4-triazolium-2-thiolates **2**. Furthermore, Ollis and Ramsden (10) synthesized derivatives of the 1,3,4-thiadiazolium-2-aminide system **1** by reactions of suitable hydrazines with nitriles. The two studies (9,10) utilized data such as mp, elemental analysis, IR, UV and ^{1}H NMR spectroscopy for purposes of structural characterization.

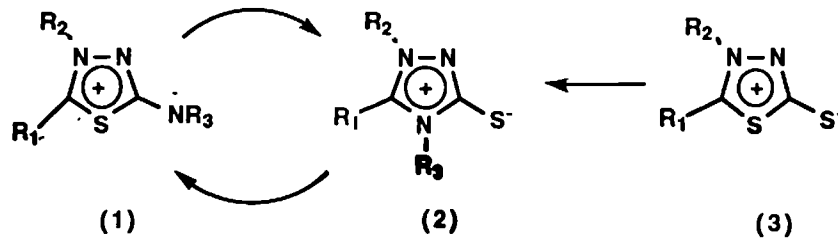


Figure 1: Mesoionic compounds prepared by Busch

Our studies of the reaction of 1,4-diphenylthiosemicarbazide with aroyl chlorides, which also included ^{13}C NMR spectroscopy, indicate that the derivatives of the 1,3,4-thiadiazolium-2-aminide system **1** are the kinetic products and that the derivatives of the 1,3,4-triazolium-2-thiolate system **2** are the thermodynamic products and that both can be readily isolated. In addition, we have been able to confirm the structure of one derivative of each system by X-Ray diffraction studies (11,12). These enabled us to deduce experimentally-based Bird aromaticity indices (13) to support our calculations of the greater aromaticity of the 1,3,4-triazolium-2-thiolate system **2**.

Experimental

Melting points were determined on a Kofler hot-stage apparatus and are uncorrected. The IR spectra were recorded on a Perkin-Elmer 1240 spectrometer. The ^{13}C NMR spectra were recorded on a Bruker AC-200 NMR spectrometer operating at 50.3 MHz with 16 K data points. Saturated solutions in DMSO-d_6 in 5 mm tubes were prepared using the center of the DMSO-d_6 septet as reference (DMSO-d_6 = 39.6 ppm). Mass spectra were obtained on a Hewlett Packard 5987A spectrometer. Column chromatography was carried out using Merck Kieselgel 60.

Compounds of system 6:

42 Mmoles of aromatic carboxylic acid chloride (5a-c) in 20 ml of dry 1,4-dioxan were added slowly, with magnetic stirring, at room temperature to a suspension of 42 mmoles of 1,4-diphenyl-thiosemicarbazide 4 in 20 ml of dry 1,4-dioxan. The reaction mixture, protected from humidity, was allowed to stand for 24 h (5a), 24 h (5b) and 12 h (5c). After these periods, the reaction mixtures were chromatographed (silica gel column). In this way compounds 6a and 6b were obtained as pale-yellow crystals and compound 6c was obtained as intense yellow crystals.

4,5-Diphenyl-1,3,4-thiadiazolium-2-phenylamine chloride, 6a 68% yield. Mp 358°C; IR (KBr)(cm^{-1}): 3280, 3150 (N-H); 3080, 3050 (aromatic C-H); 1730 (exocyclic C-N); 1600, 1540, 1515, 1495 (aromatic C-C); 1365, 1350 (C-S); 1310 (C-N); ms, m/z (%): 329 ($M^{+\cdot}$, 54), 212 (23), 180 (27), 121 (70), 77 (100), 55 (43); ^{13}C NMR see **Table 1**.

4-Phenyl-5-(4-methoxyphenyl)-1,3,4-thiadiazolium-2-phenylamine chloride, 6b 57% yield. Mp 238°C; IR(KBr) (cm^{-1}): 3270, 3180 (N-H); 2939, 2841 (CH_3); 1698 (exocyclic C-N); 1600, 1570,

1541, 1500 (aromatic C-C); 1360 (C-S); 1305 (C-N); ms, m/z (%): 359 ($M^{+\cdot}$, 63), 242 (24), 210 (18), 151 (100), 77 (60), 51 (22); ^{13}C NMR, see Table 1.

4-Phenyl-5-(4-nitrophenyl)-1,3,4-thiadiazolium-2-phenylamine chloride, 6c 67% yield. Mp.138-139°C; IR (KBr) (cm^{-1}): 3028 (aromatic C-H); 1603, 1569 (aromatic C-C); ms, m/z (%): 374 ($M^{+\cdot}$, 37), 328 (2), 225 (23), 211 (21), 179 (19), 166 (12),120 (48),77 (100), 65 (21), 51 (23); ^{13}C NMR, see **Table1**.

Compounds of system 7:

(1) Under humid conditions: 42 mmoles of aroyl chloride (5a-c) in 20 ml of 1,4-dioxan were added slowly, with magnetic stirring, at room temperature to a suspension of 42 mmoles of 1,4-diphenyl-thiosemicarbazide 4 in 20 ml of humid 1,4-dioxan (5% water).The reactions were carried out in an open system and reaction mixtures were allowed to stand for 30 h (for 7a); 54 h (for 7b) and 20 h (for 7c). After these periods, the reaction mixtures were chromatographed (silica gel columns). In this way, compound 7a was obtained as golden-yellow crystals in 35% yield; compound 7b was obtained as bright yellow crystals in 34% yield and compound 7c was obtained as brick-red crystals in 39% yield.

(2) With addition of pyridine to reaction mixtures: 42 mmoles of aromatic carboxylic chlorides (5a-c) in 20 ml of 1,4-dioxan were added slowly, with magnetic stirring, to a suspension of 42 mmoles of 1,4-diphenylthiosemicarbazide 4 in 1,4-dioxan,42 mmoles of pyridine were then added.The reaction mixtures were allowed to stand in a freezer for 48 h (7a);96h (7b) and 24 h (7c). The precipitates formed were filtered off and recrystallized from chloroform/ether. Compound 7a was obtained as golden-yellow crystals in 87% yield; compound 7b was obtained as bright yellow crystals in 84% yield and compound 7c was obtained as brick-red crystals in 89% yield.

(3) By addition of pyridine to compounds of system **6**: Pyridine (24 mmoles) in 20 ml of dichloromethane was added to 24 mmoles of compounds 6a and 6b respectively, with magnetic stirring. The reaction mixtures were then allowed to stand in a freezer for 48 h (6a) and 96 h (6b). Compound 7a was obtained as golden-yellow crystals in 86% yield and compound 7b was obtained as bright pale-yiellow crystals in 62% yield. Compounds 6a-c are also obtained.

1,4,5-Triphenyl-1,3,4-triazolium-2-thiol chloride, (7a). Mp 280°C; IR (KBr) (cm^{-1}): 3190 (N-H);3060, 3015 (aromatic C-H); 2760 (S-H); 1600, 1570, 1540, 1510, 1495, 1475 (aromatic C-C); 1455, 1450, 1441, 1320 (C-N); ms, m/z (%): 320 ($M^{+\cdot}$, 27), 180 (58), 77(100), 51(35); ^{13}C NMR, see **Table 1**.

1,4-Diphenyl-5-(4-methoxyphenyl)-1,3,4-triazolium-2-thiol chloride, (7b). Mp268°C; IR (KBr) (cm^{-1}): 3045 (aromatic C-H); 2981, 2945 (CH3); 2660 (S-H); 1600, 1560, 1540, 1490, 1470 (aromatic C-C); 1449, 1431, 1335 (C-S); 1320, 1310, 1260, 1220 (C-N); ms, m/z (%): 359 ($M^{+\cdot}$, 56), 210 (75), 135 (23), 77 (100), 51 (17); ^{13}C NMR, see Table 1.

1,4-Diphenyl-5-(4-nitrophenyl)-1,3,4-triazolium-2-thiol chloride, (7c). Mp 320°C; IR(KBr) (cm^{-1}): 3060 (aromatic C-H); 1595, 1527 (aromatic C-C); 1346 (C-S); ms, m/z (%): 374 (M+., 100), 327 (18), 225 (76), 179 (33), 135 (24); ^{13}C NMR, see **Table 1**.

Table 1: ^{13}C NMR chemical shifts[a] for the mesoionic carbon atoms in systems **6** and **7**.

Compound	6a	6b	6c	7a	7b	7c
R	**H**	**OCH_3**	**NO_2**	**H**	**OCH_3**	**NO_2**
C 2	160.7	162.9	162.2	169.8	169.9	170.4
C 5	164.7	164.1	163.1	148.2	149.6	146.9

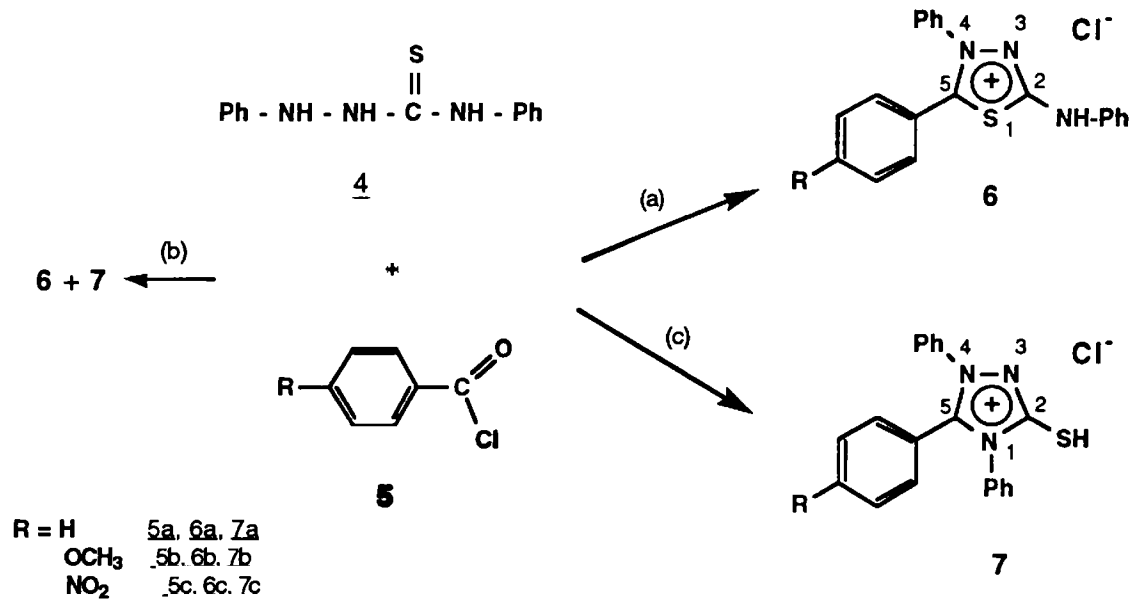
[a] δ ppm, in DMSO-d_6.

Results and Discussion

Our theoretical studies relevant to this work, recently reported in part at scientific meetings (14,15) indicate that derivatives of the 1,3,4-thiadiazolium-2-aminide system (**1**) are the kinetic products of the reactions of aroyl chlorides with 1,4-diphenylthiosemicarbazide-cyclization of the intermediate aroyl derivatives via the sulphur being favoured by about 35 kJ/mol; whereas the 1,3,4-triazolium-2-thiolate derivatives (**2**) are the thermodynamic products, being more stable by about 25 kJ/mol. The greater aromaticity of the system is further shown by comparing their experimentally based (11,12) Bird indices (13).Values are 57.4 for the 1,3,4-thiadiazolium-2-aminide system (**1**) and 66.3 for the 1,3,4-triazolium-2-thiolate system (**2**).

Interestingly, Bird (13a) included 19 mesoionic systems in his survey. While all are different from ours, it is noteworthy that only 5 of them have aromaticity indices higher than the 1,3,4-triazolium-2-thiolate system (**2**); 9 of them have lower aromaticity indices than the 1,3,4-thiadiazolium-2-aminide system (**1**); and 5 of them have aromaticity indices in the range of our two systems, viz., 57.4 to 66.3. It is relevant to compare these values with aromaticity indices for some standard 5-membered ring compounds, which we took from a more recent study by Katritzky *et al.* (16). We cite from their compilation pyrrole 69; thiophene 66 and furan 43.

The details of the reaction conditions leading to the formation of each of the two systems and of the rearrangements are set out in **Figure 2.**



(a) 1,4-Dioxan;RT; anhydrous conditions
(b) 1,4-Dioxan;RT; 5% water
(c) 1,4-Dioxan;RT; pyridine

Figure 2: Reaction conditions for obtaining salts of mesoionic systems **6** and **7**.

The 4,5-diaryl-1,3,4-thiadiazolium-2-phenyl aminide derivatives (6a-c) were obtained in both anhydrous conditions and in 5% aqueous solvent. The molecular structure of the hydrochloride 4-phenyl-5-(4-methoxyphenyl)-1,3,4-thiadiazolium-2-phenylamine chloride (6b) as derived from the X-ray crystallographic analysis (11) is given in **Figure 3**.

In the presence of pyridine the hydrochlorides of the mesoionic 4,5-diaryl-1,3,4-thiadiazolium-2-phenylaminides (6a-c) isomerize to the hydrochlorides of the corresponding 1,4,5-triaryl-1,3,4-triazolium-2-thiolates (7a-c). In humid conditions (5% water) a mixture of the hydrochlorides is obtained.

The molecular structure of 1,4,5-triphenyl-1,3,4-triazolium-2-thiolate (7a), as derived from X-ray crystallographic analysis is given in **Figure 4** (12).

The ^{13}C NMR spectra serve to discriminate well between the two systems **6** and **7**. In system **6**, C-2 is more shielded than is C-5, whereas in system **7**, C-2 is less shielded than is C-5. The ^{13}C NMR chemical shifts for C-2 and C-5 of the mesoionic rings are shown in **Table 1**.

The mass spectra also present characteristic differences. As shown in **Figure 5**, the characteristic fragments of system **6** are the ions 4-R-C_6H_4-C(=S)-N^+-C_6H_5 (m/z = 212 and R=H) and 4-R-$C_6H_4C{\equiv}S^+$ (m/z=121 and R=H).

For system **7**, the characteristic fragments are ions 4-R-$C_6H_4C{\equiv}N^+$-C_6H_5 (m/z=180 and R=H) and $C_6H_5N{=}C{=}S^+$ (m/z =135 and R=H).

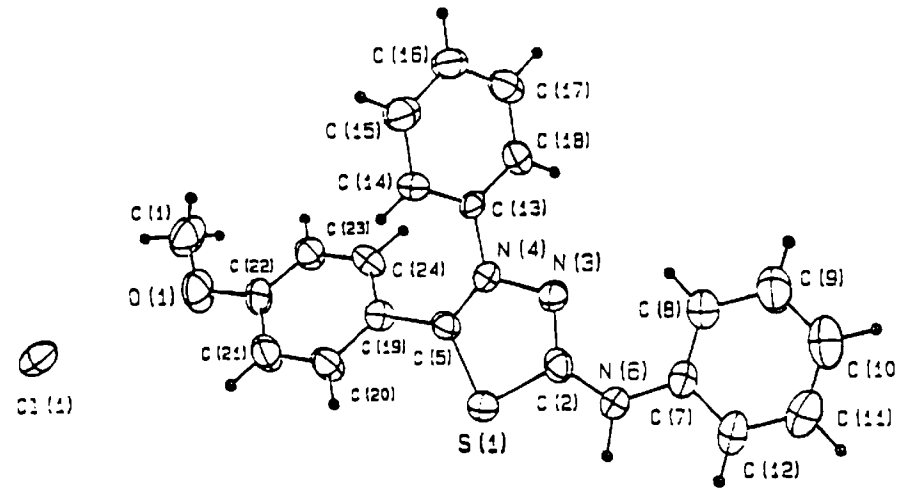


Figure 3: ORTEP drawing of the molecular structure of 4-phenyl-5-(4-methoxyphenyl)-1,3,4-thiadiazolium-2-phenylaminide hydrochloride 6b as determined by X-ray crystallographic analysis.

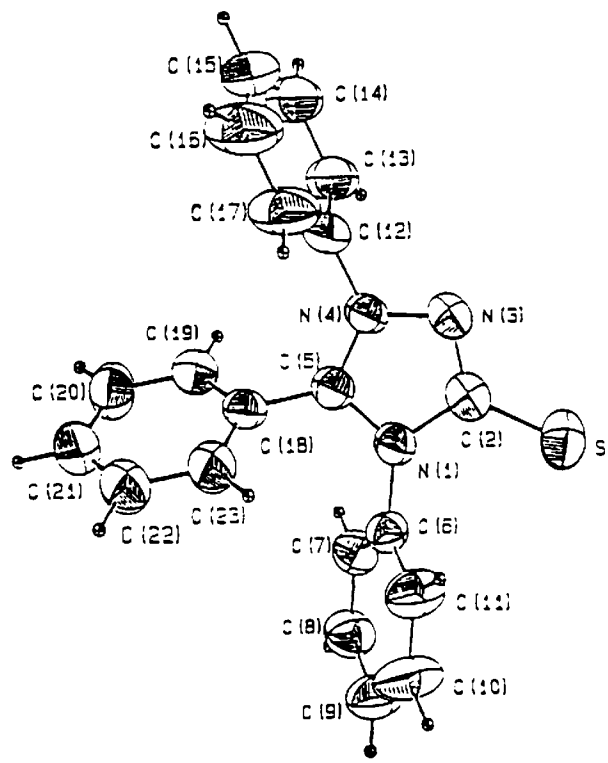


Figure 4: ORTEP drawing of the molecular structure of 1,4,5-tnphenyl-1,3,4-triazolium-2-thiolate 7a as determined by X-ray crystallographic analysis.

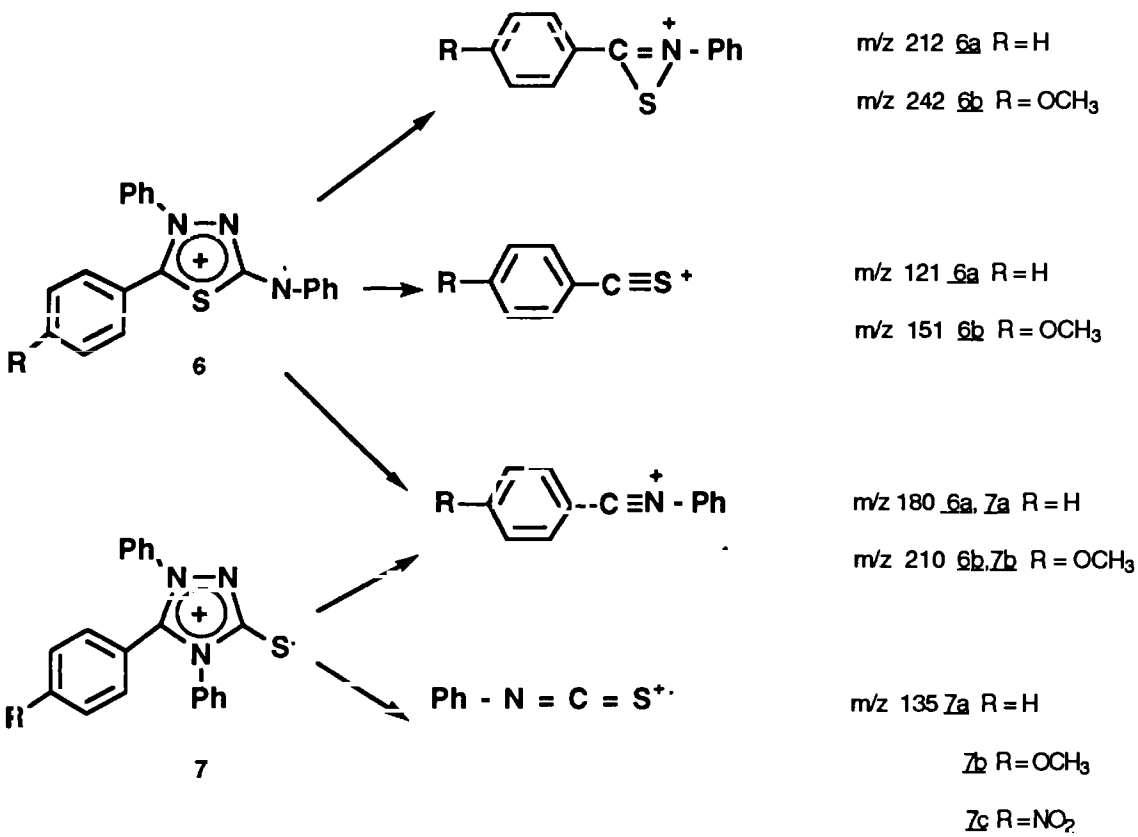


Figure 5: Characteristic fragments in the mass spectra of mesoionic systems **6** and **7.**

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