Kinetics and mechanism of condensation reactions of thiobenzamides and *N*-substituted thioureas

Luciano Forlani* and Carla Boga

Dipartimento di Chimica Organica "A. Mangini", Viale Risorgimento 4, 40136 Bologna, Italy. E-mail: forlani@ms.fci.unibo.it; Fax: +390512093654; Tel: +390512093641

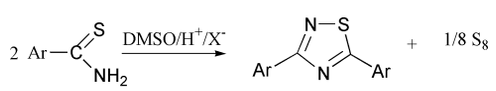
Received (in Cambridge, UK) 18th December 2001, Accepted 29th January 2002
First published as an Advance Article on the web 19th February 2002

The condensation reaction of thiobenzamides and of *N*-substituted thioureas in dimethyl sulfoxide or in methanol, in the presence of the mixture DMSO–H^+–X^- (X = Cl, Br) produces 1,2,4-thiadiazole derivatives. Kinetic investigation emphasizes the importance of the presence of dimethyl sulfoxide, of halide ions and of an acidic catalyst. For reactions of thiobenzamide, the bromide ion increases the reaction rate 150 times more than the chloride ion. The presence of electron-donating groups on the starting thioamidic group enhances the reactivity. Reported data indicate that the mixture DMSO–H^+–X^- produces a positive halogen species. The proposed mechanism involves the formation of the *N*-halogenated thioamides (or *N*-substituted thioureas) in the rate-determining step. The reactivity of thionicotinamide *S*-oxide is also reported and discussed.

Introduction

Even if DMSO is mainly used as a solvent, there are a number of reactions where DMSO is a reacting species.[1] Our interest concerns the use of DMSO as a reagent/solvent in cyclization reactions of thioamides or substituted thioureas producing heterocycles containing both nitrogen and sulfur atoms in the heterocyclic ring.[2]

Previously, we reported that the condensation reaction of thioamides in the presence of DMSO and an acid affords[2] 1,2,4-thiadiazole derivatives, as shown in Scheme 1. The

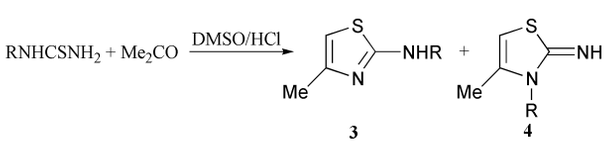


1 **2**

X = Cl, Br; Ar = phenyl (**a**), 3-pyridyl (**b**)

Scheme 1

DMSO–HCl mixture acts as a condensation reagent also in the reaction of thiourea and carbonyl compounds to yield 2-aminothiazole **3** and thiazol-2-imine derivatives[3]



3 **4**

Scheme 2

4 (Scheme 2). These reactions involve the DMSO both as a solvent and as a reacting species.

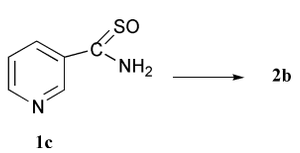
In the reactions considered here, the separation of elemental sulfur is an indication of the presence of an oxidizing process. It is known that DMSO is an oxidizing species in the presence of acids[4] and apparently, the reactions shown in Scheme 1 are examples of this ability of DMSO. The oxidation reactions of alcohols to ketones occur with DMSO activated by dicyclohexylcarbodiimide[5] or by other activating reagents.[6] With the aim of learning more about the role of DMSO in the condensation shown in Scheme 1 and, in particular, to investigate the mechanism of the formation of elemental sulfur, we carried out some kinetic measures on the condensation reactions of thiobenzamide (**1a**), thionicotinamide (**1b**), thionicotinamide *S*-oxide (**1c**), *N*-phenylthiourea (**5a**) and *N*-benzylthiourea (**5b**).

Results

Products and experimental conditions

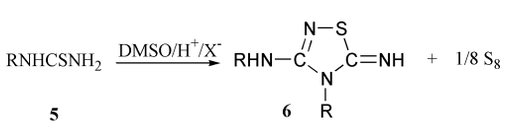
The presence of hydrogen chloride (or hydrogen bromide) is essential to the reaction of Scheme 1. In fact, sulfuric, perchloric or methanesulfonic acids are unable to catalyze the reaction. When the latter acids are used, compounds **2** may be obtained after addition of chloride or bromide salts to the reaction mixtures.

Thioamides *S*-oxide, such as thionicotinamide *S*-oxide[7] (**1c**), produce the same thiadiazoles, as shown in Scheme 3.



1c

Scheme 3



5 **6**

X = Cl, Br; R = phenyl (**a**), benzyl (**b**)

Scheme 4

Scheme 4 shows the cyclization reactions of *N*-substituted thioureas. In the cases of thioureas **5a** and **5b**, the substituted nitrogen is preferred in the ring closure reaction, in spite of possible steric hindrance. With more hindered groups (2-butyl) the ring closure occurs on the unsubstituted nitrogen.[2]

All the reactions produce the indicated compounds in almost quantitative yields (≥90%) as tested by product isolation from the reaction mixtures,[2,7] or by UV/vis spectrophotometric analysis at 'infinite' reaction times. Small amounts of Me_2S were recovered from the reaction mixtures by trapping it in a bath at −70 °C.

 DOI: 10.1039/b111538n

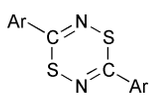
Table 1 Kinetic data for the cyclization reaction of thiobenzamide (**1a**) to thiadiazole derivative (**2a**) in MeOH (H_2O 7 vol%) and in the presence of hydrogen chloride (0.21 mol dm^{-3}) at 25 °C

$[\mathbf{1a}]_0 = 1.7 \times 10^{-4}$ mol dm^{-3}					
$[DMSO]_0$/mol dm^{-3}	0.0100	0.0200	0.0400	0.0500	0.0780
$10^2 k_{obs}$/ s^{-1}	0.025	0.055	0.095	0.120	0.178

Table 2 Kinetic data for the cyclization reaction of thionicotinamide *S*-oxide (**1c**) to thiadiazole derivative (**2b**) in DMSO at 25 °C

[Thionicotinamide *S*-oxide]$_0 = 1.9 \times 10^{-4}$ mol dm^{-3}							
$[TBABr] = 4.0 \times 10^{-3}$ mol dm^{-3}							
$[MeSO_3H]_0$/mol dm^{-3}	0.0508	0.102	0.127	0.153	0.182	0.203	0.254
$10^4 k_{obs}$/ s^{-1}	0.267	0.462	0.617	0.945	1.33	1.57	2.08
$[MeSO_3H]_0 = 0.26$ mol dm^{-3}							
$10^3[TBABr]$/ mol dm^{-3}	1.06	1.59	2.12	2.65	3.18		
$10^4 k_{obs}$/ s^{-1}	0.718	1.11	1.39	1.59	1.94		

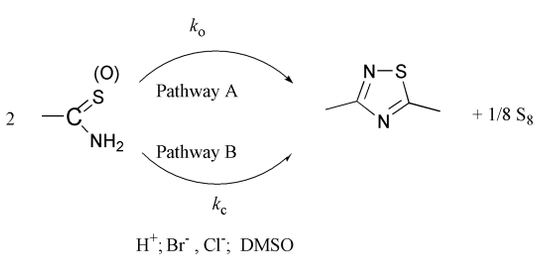
Formation of sulfinic derivatives was observed from thioamides or from thioureas in the presence of oxidizing reagents.[4] Under our experimental conditions, we did not observe the presence in the reaction mixtures of 1,4,2,5-dithiadiazines **7** which are the main products of reactions of amino sulfines and $Et_3O^+BF_4^-$, probably *via* chlorosulfenate group **8**.[8]



7

8

From previous and present data, it can be shown that the formation of thiadiazole derivatives from thiobenzamides or *N*-substituted thioureas or their *S*-oxides, may occur by two main pathways: i) the spontaneous cyclization reaction; ii) a cyclization reaction catalyzed by acids, halide ions, or an oxidant reagent which may be DMSO. Both reaction pathways are reported in Scheme 5.



Scheme 5

Kinetic measurements

Even if the reactions considered clearly follow multi-step pathways, the UV/vis spectrophotometric analysis at variable reaction times indicates the presence of only starting materials and final reaction products (see Experimental section). In solvents of high polarity such as dimethylformamide, the presence of DMSO (or H_2O_2) is necessary. In the case of the use of H_2O_2, **2** and **6** are probably obtained *via* S-oxide derivatives.[2,7]

The kinetic data of reactions in Schemes 1 and 3 are obtained by the UV/vis spectrophotometric method by following the appearance of the thiadiazole derivatives. In the presence of methanesulfonic acid (without Cl^-, Br^- ions) in DMSO, no formation of thiadiazoles was observed even for long reaction times (1 week). It is evident that the reaction needs an acid catalyst bearing particular counter ions, *i.e.* halides.

We performed kinetic runs at a constant initial concentration of all components with the exception of the initial concentration of one component (**Z**) present in large excess. In this way, the importance of **Z** may be quantitatively measured.

For example, Table 1 reports the kinetic data obtained in CH_3OH (with 7% H_2O) for the cyclization reaction of thiobenzamide in the presence of constant amounts of HCl and with variable amounts of DMSO. The plot of k_{obs} *versus* $[\mathbf{Z}]_0$ is linear and may be algebraically expressed by eqn. (1) where $[\mathbf{Z}]_0$

$$k_{obs} = k_o + k_C [\mathbf{Z}]_0 \quad (1)$$

is the initial concentration value of the component of the reaction mixture with variable initial concentration. In the case reported in Table 1, **Z** = DMSO.

The k_o (in s^{-1}) and k_C (in dm^3 mol^{-1} s^{-1}) values are related to the uncatalyzed pathway A and to the catalyzed pathway B of Scheme 5, respectively. This procedure was repeated for other reagents. The k_o and k_C values are reported in Table 3 together with some statistical parameters.

Discussion

Catalyzed and uncatalyzed pathways

Firstly, we consider the k_o values (see Table 3) which represent the reaction rate in the absence of the considered (variable) component **Z**. In most cases, k_o is very close to zero, consequently the reactions in the absence of **Z** do not occur or the rate of formation of products is very low. For example the ratio $k_C[DMSO]_o : k_o$ is from 3–24 for the reaction of **1a** (entry 1 in Table 3): the presence of DMSO is very important in obtaining **2a**.

The presence of acid is also essential in obtaining compounds **2** and **4**, as indicated by k_o values which are insignificant with respect to $k_C[\mathbf{Z}]_0$ values (entries 2, 3, 7, 8, 10, 12).

Thionicotinamide *S*-oxide (**1c**) represents an exception: the catalysis by acid (see Table 2 and entry 13 of Table 3) enhances the reaction rate, but the spontaneous cyclization reaction was also observed in the absence of acid.[7] Previously, we reported the reaction of **1c** to **2b** by simple heating a methanolic solution of **1c**.[7] Probably **1c** reacts by two different reaction pathways (catalyzed and uncatalyzed). $k_C[TBABr]_o > k_o$ (entry 14) and it emphasizes the importance of the presence of the bromide ion for the cyclization reaction of **1c** (see entry 14 *versus* entry 13).

Change of substrate

The k_C values, shown in Table 3, enable a comparison of the reactivity of the different thioamidic substrates used. When **Z** is tetrabutylammonium bromide (TBABr) (entries 4,6,9) the reactivity ratios **5b** : **1a** : **1b** are 23 : 15 : 1, respectively. In G–$CSNH_2$, when G is an electron-donating group (G = BnNH in **5b**) the reaction is faster than when G is the phenyl group (**1a**) or an electron-withdrawing group such as the 3-pyridyl group of **1b**. The reported ratios indicate that in the reaction pathway there is an important step which involves the attack of an electrophilic reagent on the substrate.

The thionicotinamide *S*-oxide (**1c**) reacts slightly faster than thionicotinamide **1b**, (entries 6, 7, 13, 14). This fact does not, however, discriminate if **1c** is on the reaction pathway of **1b** to yield **2b** or if it is involved in a parallel process.

Table 3 Dependence of rate (k_{obs}/s^{-1}) of formation of thiadiazoles with variable amount of reagent **Z** [eqn. (1)]

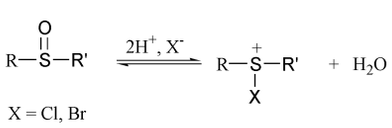
Entry	$[S]_0$ [a]	Solvent	$[Acid]_0$ [b]	**Z** [b]	$[Salt]_0$ [b]	n [c]	k_0/s^{-1} [d]	$k_C/dm^3\ mol^{-1}\ s^{-1}$ [d]	r [e]
1	**[1a]$_0$** (1.7)	MeOH[f]	HCl (0.21)	DMSO (from 1–8 × 10^{-2})	—	5	(7 ± 3) × 10^{-5}	(2.22 ± 0.1) × 10^{-2}	0.999
2	**[1a]$_0$** (1.7)	MeOH–DMSO[f]	HCl	HCl (from 0.1–0.4)	—	5	(2 ± 5) × 10^{-3}	(4.80 ± 0.2) × 10^{-2}	0.998
3	**[1a]$_0$** (1.1)	DMSO[f]	$MeSO_3H$	$MeSO_3H$ (from 0.5–3.5 × 10^{-1})	KBr (4.4 × 10^{-3})	6	(2 ± 5) × 10^{-5}	(2.98 ± 0.3) × 10^{-3}	0.985
4	**[1a]$_0$** (0.98)	DMSO	$MeSO_3H$ (0.26)	KBr (TBABr[h]) (from 1–6 × 10^{-3})	KBr	7	(−3 ± 3) × 10^{-5}	0.284 ± 0.08	0.998
5	**[1a]$_0$** (1.1)	DMSO	$MeSO_3H$ (0.26)	TEACl[g] (from 0.2–1.5 × 10^{-1})	TEACl[g]	4	(4 ± 1) × 10^{-5}	(1.83 ± 0.1) × 10^{-3}	0.997
6	**[1b]$_0$** (1.1)	DMSO	$MeSO_3H$ (0.26)	TBABr[h] (from 1–6 × 10^{-3})	TBABr[h]	9	(4.8 ± 0.3) × 10^{-5}	(1.93 ± 0.08) × 10^{-2}	0.993
7	**[1b]$_0$** (1.1)	DMSO	$MeSO_3H$	$MeSO_3H$ (from 0.1–0.5)	TBABr[h] (4.1 × 10^{-3})	6	(−5 ± 6) × 10^{-6}	(4.83 ± 0.2) × 10^{-4}	0.997
8	**[5b]$_0$** (1.1)	DMSO[f]	$MeSO_3H$	$MeSO_3H$ (from 0.1–1)	TBABr[h] (2.7 × 10^{-3})	5	(−6 ± 1) × 10^{-4}	(5.95 ± 0.4) × 10^{-3}	0.993
9	**[5b]$_0$** (1.2)	DMSO[f]	$MeSO_3H$ (0.26)	TBABr[h] (from 0.5–3 × 10^{-3})	TBABr[h]	9	(−2 ± 0.4) × 10^{-4}	(0.437 ± 0.02)	0.995
10	**[5b]$_0$** (1.4)	DMSO[f]	$MeSO_3H$	$MeSO_3H$ (from 0.5–3 × 10^{-1})	KBr (4.5 × 10^{-3})	5	(−2 ± 1) × 10^{-4}	(4.25 ± 0.4) × 10^{-3}	0.986
11	**[5b]$_0$** (1.1)	DMSO[f]	$MeSO_3H$ (0.26)	TEACl[g] (from 0.05–0.3)	TEACl[g]	8	(−4 ± 3) × 10^{-5}	(5.2 ± 0.1) × 10^{-3}	0.999
12	**[5b]$_0$** (1.4)	MeOH[f]–DMSO	HCl	HCl (from 0.5–3 × 10^{-1})	—	8	(−8 ± 2) × 10^{-4}	(4.30 ± 0.1) × 10^{-2}	0.995
13	**[1c]$_0$** (1.9)	DMSO[f]	$MeSO_3H$	$MeSO_3H$ (from 0.05–0.25)	TEABr[h] (4.5 × 10^{-3})	7	(4 ± 1) × 10^{-5}	(9.5 ± 0.8) × 10^{-4}	0.981
14	**[1c]$_0$** (1.9)	DMSO[f]	$MeSO_3H$ (0.26)	TBABr[h] (from 1–3 × 10^{-3})	TBABr[h]	8	(1.8 ± 0.7) × 10^{-5}	(5.5 ± 0.3) × 10^{-2}	0.996

[a] S = substrate; in brackets, the concentration value used (× 10^4 mol dm^{-3}). [b] In brackets, the concentration value (or the range of concentrations) in mol dm^{-3}. [c] Number of points. [d] Errors are standard deviations. [e] Correlation coefficient. [f] 7% H_2O; in the mixtures MeOH–DMSO, $[DMSO]_0$ = 2.34 mol dm^{-3}. [g] TEACl = tetraethylammonium chloride. [h] TBABr = tetrabutylammonium bromide.

Change of halide ion

The k_C value is affected by the type of halide ion. The presence of bromide ion enhances the reaction rate more than the chloride ion. The $k_{C\ Br}/k_{C\ Cl}$ ratios are 153 and 84 for **1a** and **5b** respectively (entries 4, 5, 9, 11); **5b** is more reactive and consequently less selective than **1a**. The counter ion of the bromide salt (potassium or tetrabutylammonium) does not affect the reactivity (see entries 8 and 10).

The racemization reactions of sulfoxides catalyzed by halide ions[9] in the presence of an acid have been explained by a mechanism involving the presence of a species bearing an electrophilic halogen, as depicted in Scheme 6. In the racemization reactions, the formation of halosulfonium ion was shown to be the rate determining step.

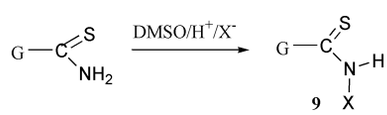


Scheme 6

The relative reactivity of racemization of sulfoxides catalyzed by halide ions[9] was k_{Br}/k_{Cl} = 3, a value far from that reported here. The difference in the k_{Br}/k_{Cl} ratio is an indication that the rate determining step of these cyclization reactions hardly involves the simple oxidation of halide ions by the DMSO–H^+ mixture.

It is known[10] that the mixture DMSO–HX forms the electrophilic halogen, either as the halosulfonium ion or the molecular halogen. Both species are able to produce *N*-halogenated thioamides **9** as depicted in Scheme 7.

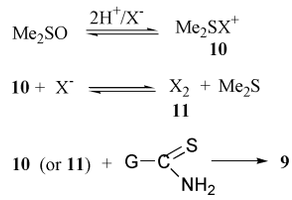
A possible explanation for the higher k_C value of bromide compared with the k_C value of chloride is the fact that bromide ion is oxidised more easily to the positive bromonium ion (or bromine) than chloride, if the chloro- or bromosulfonium cation[11] is the 'activated' DMSO species that leads to oxidation



X = Cl, Br; G = Ar, PhNH, BnNH

Scheme 7

reactions. Consequently the reaction pathway involves the formation of a halonium ion which may attack the nitrogen atom of the thioamido group, producing *N*-bromo (-chloro) derivatives **9** which spontaneously evolve to thiadiazole derivatives[3] (Scheme 8).



Scheme 8

The reaction mechanism

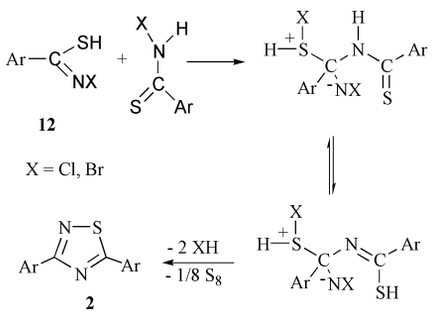
The rate determining step of the reaction may be the activation of thioamides or thioureines by the DMSO–HX mixtures. In effect, this pathway is a process complicated by several steps.

Compounds **9** (G = BnNH, X = Cl, Br) were previously isolated from the reaction mixtures of **5a**, **5b** in DMSO–HCl or HBr in acetone.[3] Compounds **9** spontaneously produce **2** by moderate heating (to have complete solubilisation of **9**) of their solutions in methanol. The reaction of **9** to **2** is much faster than the overall reaction of **1** to **2**.

Formation of **9** may be due to the presence of a positively charged halogen (or molecular halogen) in a way similar to that indicated for the racemization reaction of sulfoxides by halide ions in the presence of acid.[12] Scheme 8 reports a possible way

to the formation of **9**, and represents the 'slow part' of the reaction pathway.

In DMSO, the formation of **9** is followed by the cyclization reaction as reported in Scheme 9. Probably, the tautomeric form



Scheme 9

of **9** (**12**) is the reactive species. The two steps in Scheme 9 may be simultaneous. Anyway, all of the steps of Scheme 8 may be the rate limiting part of the reaction.

Our data indicate that compounds **9** are intermediates of the cyclization reaction and their formation is a complicated rate determining pathway of the whole reaction. The cyclization reaction of Scheme 9 may occur without catalysts and is probably a fast step.

In DMSO, the formation of **2** from **9** is a spontaneous process, while in acetone the reaction may be stopped at **9** because of their insolubility in this solvent.

In acetone, **1** reacts with acetone in the presence of HCl–DMSO mixtures affording 1,3-thiazole derivatives **3** and **4**.[3] This reaction cannot be ascribed to the intermediate **9**. Compound **3** and **4** probably result from other thioamide activations, while **9** is the intermediate in reactions leading to thiadiazole derivatives.

In Scheme 9, the formation of elemental sulfur arises from the departure of thiohypochlorous acid HSCl[13] during the cyclization step.

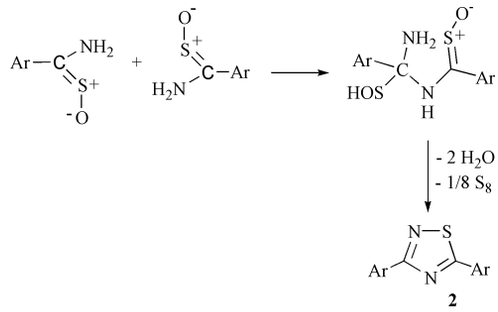
Cyclization reactions of *S*-oxides

Some interesting points are observed from the reaction of thionicotinamide *S*-oxide (**1c**).[2] The oxidation of the sulfur atom of the amides may occur using the DMSO–HX mixture. Even if we cannot rule out that thioamide *S*-oxides such as **1c** are intermediates of the reactions in Schemes 1 and 4, we consider this hypothesis to be improbable. The behaviour of thionicotinamide *S*-oxide **1c** (entries 13 and 14 of Table 3) partially parallels that of thionicotinamide **1b** (entries 6 and 7). Both substrates cyclize by catalysis of the acid ($MeSO_3H$) and of the bromide ion. However, the acid catalysis of the cyclization reaction of **1c** is less important than the catalysis of the cyclization of **1b**; the low ratio of $k_C[MeSO_3H]_o/k_o$ is from 1–6 (entry 13) in agreement with the fact that **1c** may cyclize spontaneously by moderate heating of its solutions. The very large catalytic effect of bromide ion on the cyclization reaction of **1c** ($k_C[TBABr]_o/k_o$ is from 3–9, entry 14) may be considered an indication that the *S*-oxide **1c** cyclizes by a direct reaction pathway,[2] as reported in Scheme 10, and by another reaction pathway in which the catalytic effect of H^+ and of Br^- is similar to that reported above for thioamides and thioureine, and therefore is scarcely affected by the presence of the oxygen atom on the sulfur atom.

This hypothesis agrees with the finding that k_C values are similar for both substrates: k_C**1c**/k_C**1b** = 2, entries 13 and 7; k_C**1c**/k_C**1b** = 3, entries 14 and 6.

Conclusion

In conclusion, the reported data confirm that the mixture DMSO–H^+–X^- produces a positive halogenic species. There



Scheme 10

are strong indications that the *N*-halogenated thioamides or thioureas are intermediates of the cyclization reaction of thioamides and thioureas. The cyclization reaction of thioamide *S*-oxides follow an uncatalyzed pathway in competition with another reaction pathway, probably *via* a *N*-halogenated derivative. The separation of elemental sulfur arises from the oxidative power of DMSO–H^+ mixtures: the probable pathway involves the departure and successive decomposition of the HSX species (X = Cl, Br) in the cyclization step.

Experimental

Uv/vis spectrophotometric data were recorded on a Perkin Elmer (model Lambda 5) spectrophotometer.

Under the reported experimental conditions, UV/vis spectrophotometric analysis (as well as TLC analysis) did not show evidence for the presence of the *S*-oxide **1c** in the reaction mixture of **1b**. In the same way, no evidence of the presence of compounds **9** was observed. Fig. 1 reports the UV/vis spectra

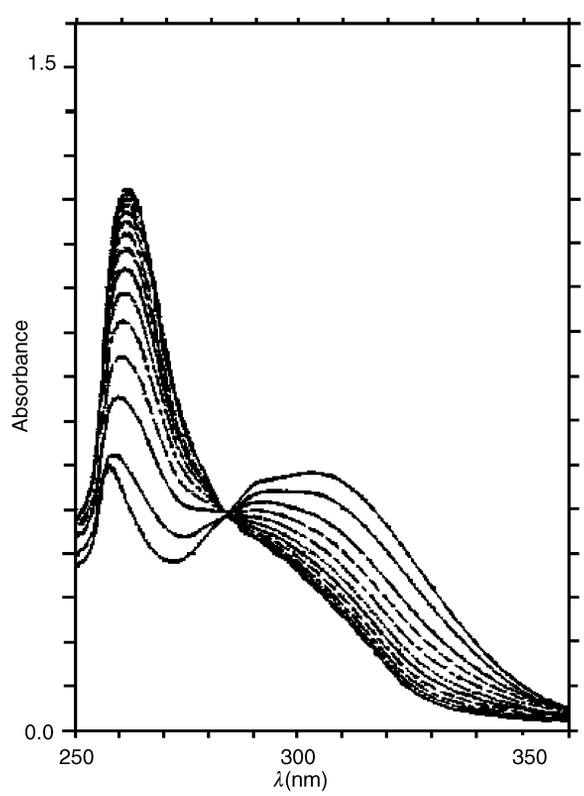


Fig. 1 Typical run for the cyclization reaction of thiobenzamide (**1a**) to thiadiazole (**2a**).

for a typical run. The same behaviour was observed for the reactions of *S*-oxides.

Starting materials and reaction products were as previously described.[2] To avoid difficulties with the solubility of chloride

and bromide salts, some reactions were carried out in the presence of small amounts of water (5 or 7% by vol). The presence of water slightly depresses the rate of the condensation reaction. For example, for $[\mathbf{1a}]_0 = 1.5 \times 10^{-4}$ mol dm^{-3}, $[TBABr]_0 = 1.5 \times 10^{-3}$ mol dm^{-3}, $[MeSO_3H]_0 = 0.25$ mol dm^{-3} and $[H_2O] = 0.12$ and 2.7 mol dm^{-3}; k_{obs} were 6.7×10^{-4} and 2.8×10^{-4} s^{-1} respectively.

Kinetic runs were performed by the usual procedures, at 25 °C, by following the appearance of the reaction products until high percent of conversion. Compounds **2a**, **2b**, **4a**, **4b** show, in DMSO with 5% (by vol.) of water λ_{max}/nm ($\varepsilon \times 10^{-4}$ dm^3 mol^{-1} cm^{-1} = 254(3.20), 260(1.41), 262(12.0), 260(0.700), respectively. All the reactions were performed under pseudo first order kinetic conditions. Reproducibility of k_{obs} was ±2%.

In some cases, the same k_{obs} values are obtained by following the disappearance of starting materials. Compounds **1a**, **1b**, **5a**, **5b**, **1c** show, in DMSO with 5% (by vol.) of water λ_{max}/nm ($\varepsilon \times 10^{-3}$ dm^3 mol^{-1} cm^{-1}) = 302 (7.35), 301(0.614), 274(16.4), 259(0.665), 360(16.6), respectively.

Acknowledgements

The authors thank the Ministero dell'Università e della Ricerca Scientifica e Tecnologica, the Consiglio Nazionale delle Ricerche (CNR, Roma) and the University of Bologna (funds for selected research topics 1999–2001).

References

1 (*a*) T. Durst, *Adv. Org. Chem.*, 1969, 285; (*b*) H. H. Szmont, in *Dimethylsulfoxide*, eds. S. Jacoo, E. Rosenbaum and D. Wood, Marcel Dekker, New York, 1971.
2 (*a*) Y. Takikawa, K. Shimada, K. Sato, S. Sato and S. Takizawa, *Bull. Chem. Soc. Jpn.*, 1985, **58**, 995; (*b*) L. Forlani, A. Lugli, C. Boga, A. B. Corradi and P. Sgarabotto, *J. Heterocycl. Chem.*, 2000, **37**, 63.
3 C. Boga, L. Forlani, C. Silvestroni, A. B. Corradi and P. Sgarabotto, *J. Chem. Soc., Perkin Trans. 1*, 1999, 1363.
4 U. Miotti, *J. Chem. Soc., Perkin Trans. 2*, 1991, 617.
5 (*a*) C. R. Johnson and W. G. Phillips, *Tetrahedron Lett.*, 1965, 2101; (*b*) K. Torsell, *Tetrahedron Lett.*, 1966, 4445; (*c*) K. Torsell, *Acta Chem. Scand.*, 1967, **21**, 1.
6 (*a*) T. Tidwell, *Synthesis*, 1990, 857; (*b*) K. E. Pfitzner and J. G. Moffatt, *J. Am. Chem. Soc.*, 1965, **87**, 5661; (*c*) U. Lerch and J. G. Moffatt, *J. Org. Chem.*, 1971, **36**, 3391; (*d*) C. R. Johnson and W. G. Phillips, *J. Org. Chem.*, 1967, **32**, 1926.
7 A. B. Corradi, C. Boga, L. Forlani and P. Sgarabotto, *J. Chem. Crystallogr.*, 1999, **29**, 113.
8 G. Lenz and B. Zwanenburg, *J. Chem. Soc., Chem. Commun.*, 1984, 1386.
9 (*a*) D. Landini, G. Modena, F. Montanari and G. Scorrano, *J. Am. Chem. Soc.*, 1970, **92**, 7168; (*b*) G. Modena, *Int. J. Sulfur Chem. C*, 1972, **7**, 95.
10 (*a*) S. K. Srivastava, P. M. S. Chauhan and A. P. Bhaduri, *J. Chem. Soc., Chem. Commun.*, 1996, 2679; (*b*) G. Majetich, R. Hicks and S. Reister, *J. Org. Chem.*, 1997, **62**, 4321.
11 (*a*) A. Bovio and U. Miotti, *J. Chem. Soc., Perkin Trans. 2*, 1978, 172; (*b*) B. Zwanenburg, *Recl. Trav. Chim. Pay-Bas*, 1982, **101**, 1.
12 (*a*) K. Mislow, T. Simmons, J. T. Melillo and A. L. Ternay, *J. Am. Chem. Soc.*, 1964, **86**, 1452; (*b*) D. Landini and F. Montanari, *J. Chem. Soc., Chem. Commun.*, 1968, 86; (*c*) M. Cioni, E. Ciuffarin, S. Gambarotta, M. Isola and L. Senatore, *J. Chem. Res. (S)*, 1978, 270; M. Cioni, E. Ciuffarin, S. Gambarotta, M. Isola and L. Senatore, *J. Chem. Res. (M)*, 1978, 3429; (*d*) E. Ciuffarin, S. Gambarotta, M. Isola and L. Senatore, *J. Chem. Res. (S)*, 1978, 272; E. Ciuffarin, S. Gambarotta, M. Isola and L. Senatore, *J. Chem. Res. (M)*, 1978, 3442; (*e*) E. Ciuffarin and S. Gambarotta, *J. Chem. Res. (S)*, 1978, 274; E. Ciuffarin and S. Gambarotta, *J. Chem. Res. (M)*, 1978, 3454.
13 (*a*) J. Eberhard, W.-C. Chen, C. Yu, Y.-P. Lee and B.-M. Cheng, *J. Chem Phys.*, 1998, **108**, 6197; (*b*) F. R. Ornellas, *Theor. Chem. Acc.*, 2000, **103**, 469.