Pergamon

Tetrahedron Letters, Vol. 35, No. 3, pp. 477-480, 1994
Elsevier Science Ltd
Printed in Great Britain
0040-4039/94 $6.00+0.00

0040-4039(93)E0251-E

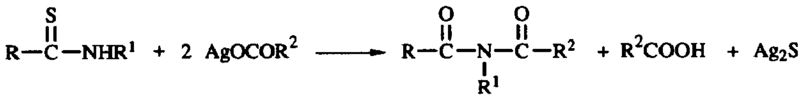
Reaction of Thioamides with Silver Carboxylates in Aprotic Media. A Nucleophilic Approach to the Synthesis of Imides, Amides, and Nitriles

Martín Avalos, Reyes Babiano, Carlos J. Durán, José L. Jiménez, and Juan C. Palacios
Departamento de Química Orgánica, Universidad de Extremadura, 06071-Badajoz (Spain)

Abstract: Syntheses of nitriles, imides, and amides by reaction of silver carboxylates with unsubstituted, *N*-substituted, and *N,N*-disubstituted thioamides in aprotic media are described.

Thioamides have attracted considerable attention in organic synthesis as versatile intermediates[1-4] as well as ligands of remarkable donor character.[5] Thus, some transition-metal-promoted reactions have emerged as an useful tool in the conversion of thioamides into amides,[1a,4,6] amidines,[6a,7] nitriles,[4] and heterocycles[8] among others. In this paper, we report on a new and efficient synthesis of nitriles, imides, and amides[9] by reaction of thioamides with silver carboxylates in organic solvents.

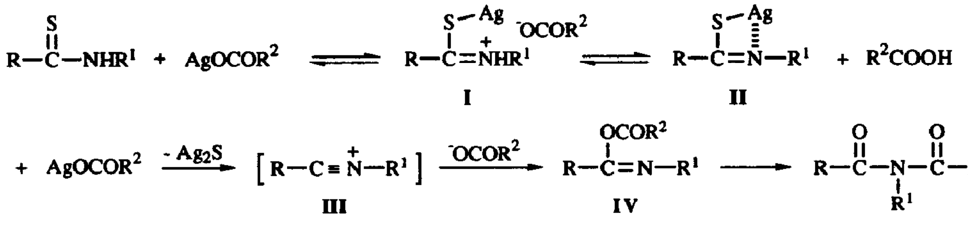
N-Alkyl or aryl thioamides react with silver carboxylates at room temperature to give *N*-alkyl or aryl imides. This process involves an O/S interchange and subsequent *N*-acylation with the acyl group coming from the carboxylate used. Reactions were monitored by NMR and results are summarised in Table 1.



$$R{-}\overset{\displaystyle S}{\overset{\|}{C}}{-}NHR^1 + 2\ AgOCOR^2 \longrightarrow R{-}\overset{\displaystyle O}{\overset{\|}{C}}{-}\underset{\displaystyle R^1}{\underset{|}{N}}{-}\overset{\displaystyle O}{\overset{\|}{C}}{-}R^2 + R^2COOH + Ag_2S$$

Scheme 1 shows a likely pathway for the formation of the imide.

Scheme 1

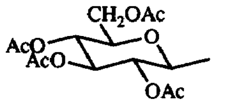
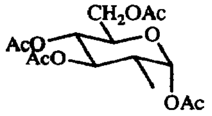


The ambident nucleophilic character of thioamides[5] must favour a rapid coordination which would result in a silver thioimidate (**II**). This complex must then undergo an elimination-addition process promoted by a second molecule of silver acetate. In the last step, the Mumm rearrangement[10] of the *O*-acylisoimide (**IV**) into the imide occurs.

Although several methods for both, O/S interchange[11] and acylation of *N*-substituted thioamides[1c] have been described, the conversion of thioamides into imides in one-step procedure have no precedents in the literature. This protocol can be useful for the preparation of unsymmetrical *N*-substituted imides that are often synthesised by *N*-acylation of amides.[12] Moreover, unlike the strong electrophilic character of the conventional acylation reagents, carboxylates react as nucleophiles and they can be utilised in a different synthetic strategy.

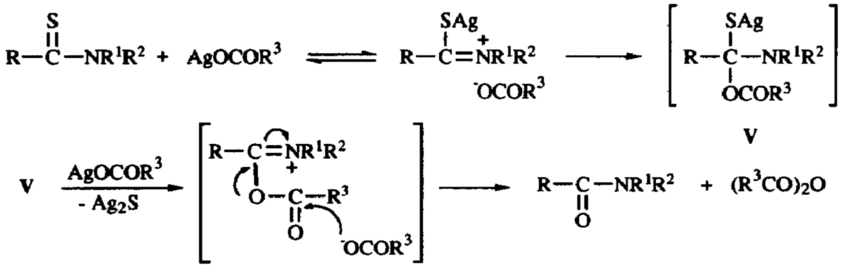
Remarkably, caprolactame was also obtained when thiocaprolactame was used as starting material (see Table 1, entries 5 and 6). In this case, the cyclic structure obstructs the elimination reaction leading to the *N*-alkylnitrilium ion **III**, and presumably the alternative pathway outlined in Scheme 2 (with R^2=H) should be involved.

Table 1. Reaction of *N*-substituted thioamides with silver carboxylates

Entry	R	R^1	R^2	Solvent	% Conversion[a]		Isolation[b]
					Imide	Amide	Yield(%) of Imide
1	CH_3	Ph	CH_3	CH_2Cl_2	100	0	70
2	CH_3	Ph	Ph	CH_2Cl_2	100	0	39
3	CH_3		CH_3	CH_2Cl_2	100	0	83
4	CH_3		CH_3	CH_2Cl_2	100	0	84
5	—$(CH_2)_5$—		CH_3	CH_2Cl_2	58	42	c
6	—$(CH_2)_5$—		CH_3	ether	86	14	53

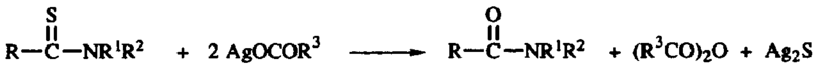
[a] Determined by NMR measurements. Unreacted thioamides were not observed. [b] Yields were calculated after purification by crystallisation or flash chromatography. [c] Not isolated.

Scheme 2



The presence of anhydride was confirmed by NMR experiments.

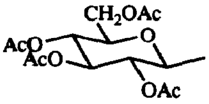
When the reaction was carried out with *N*,*N*-dialkyl thioamides in the same conditions mentioned above, the corresponding amides were the only products detected and isolated (see Table 2).



$$R-\overset{\overset{\large S}{\|}}{C}-NR^1R^2 + 2\,AgOCOR^3 \longrightarrow R-\overset{\overset{\large O}{\|}}{C}-NR^1R^2 + (R^3CO)_2O + Ag_2S$$

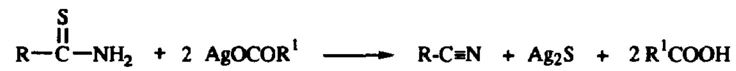
The presence of a second *N*-alkyl group prevents the formation of complex **II**, and the tetrahedral intermediate (**V**) undergoes the attack of the second molecule of silver acetate as depicted in Scheme 2. This is the first reaction in which a silver salt has been used to provoke the O/S interchange in non-aqueous solvents.[13]

Table 2. Reaction of *N*,*N*-disubstituted thioamides with silver carboxylates[a]

Entry	R	R^1	R^2	R^3	Yield (%)[b]
1	CH_3	CH_3	$PhCH_2$	CH_3	74 [90]
2	H	CH_3	CH_3	Ph	[55]
3	CH_3		C_3H_7	CH_3	81
4	CH_3	—$(CH_2)_4$—		CH_3	80 [82]

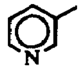
[a] In dichloromethane. [b] Calculated yields from NMR measurements are given in brackets.

Finally, unsubstituted thioamides were converted into nitriles[9] by treatment with silver carboxylates in dichloromethane (Table 3). This metal-promoted dehydrosulphurisation was previously described[4] in aqueous solution using Ag(I), Hg(II), Cu(I), etc., as reagents.



$$R-\overset{\overset{S}{\|}}{C}-NH_2 + 2\ AgOCOR^1 \longrightarrow R\text{-}C{\equiv}N + Ag_2S + 2\,R^1COOH$$

Table 3. Reaction of unsubstituted thioamides with silver carboxylates[a]

Entry	R	R^1	Yield (%)
1	Ph	CH_3	71
2		CH_3	39
3		CH_3	46
4	Ph	Ph	49

[a] In dichloromethane

In conclusion, new procedures for the synthesis of nitriles, imides, and amides by reaction of silver carboxylates with unsubstituted, *N*-substituted, and *N*,*N*-disubstituted thioamides, respectively, are now described. With this methodology, acylating electrophilic reagents are replaced by nucleophilic reagents in organic media to give the aforementioned compounds with moderate to good yields under mild conditions.

Acknowledgements: The authors are indebted to the University of Extremadura for a predoctoral fellowship (C. J. D.) and to DGICYT (PB92-0525-C02-01) for financial support. We are also grateful to Dr. P. Cintas foı his helpful discussions.

References and notes:

1. a) Hurd, R. N. and DeLaMater, G., *Chem. Rev.*, **1961**, *61*, 45. b) Walter, W. and Bode K.-D., *Angew. Chem., Int. Ed. Engl.*, **1966**, *5*, 447. c) Walter, W. and Voss, J. Chemistry of Thioamides in *The Chemistry of Amides*, Zabicky, J., Ed.; Interscience: London, 1970, pp. 383-475.
2. a) DeBruin, K. E. and Boros, E. E., *J. Org. Chem.*, **1990**, *55*, 6091. b) Avalos, M., Babiano, R., García-Verdugo, C., Jiménez, J. L., and Palacios, J. C., *Tetrahedron Lett.*, **1990**, *31*, 2467. c) Avalos, M., Babiano, R., Durán, C. J., Jiménez, J. L., and Palacios, J. C., *J. Chem. Soc., Perkin Trans. 2*, **1992**, 2205.
3. Michael, J. P. and Jungmann, C. M., *Tetrahedron*, **1992**, *48*, 10211.
4. Satchell, D. P. N., *Chem. Soc. Rev.*, **1977**, *3*, 345.
5. a) Raper, E. S., *Coord. Chem. Rev.*, **1985**, *65*, 115. b) Vagg, R. S. Bidentate Ligands, in *Comprehensive Coordination Chemistry*, Wilkinson, G, Guillard, A. D., and McCleverty, J. A., Eds.; Pergamon Press: Oxford, 1987, Vol. 2, pp. 793-812. c) Ali, M. A. and Livingstone, S. E., *Coord. Chem. Rev.*, **1974**, *13*, 101.
6. a) Foloppe, M. P., Rault, S., and Robba, M., *Tetrahedron Lett.*, **1992**, *33*, 2803. b) Hall, A. J. and Satchell, D. P. N., *J. Chem. Soc., Perkin Trans. 2*, **1975**, 778.
7. a) Marchand-Brynaert, J., Moya-Portuguez, M., Huber, I., and Ghosez, L., *J. Chem. Soc., Chem. Commun.*, **1983**, 818. b) Avalos, M., Babiano, R., Durán, C. J., Jiménez, J. L., and Palacios, J. C., unpublished results.
8. a) Kjaer, A., *Acta Chem. Scand.*, **1952**, *6*, 1374. b) El Khadem, H. S., Kawai, J, and Swartz, D. L., *Carbohydr. Res.*, **1989**, *189*, 149.
9. All new compounds showed correct analytical and spectroscopic data.
10. a) Mumm, O., Hesse, H., and Volquartz, H., *Ber.*, **1915**, *48*, 379. b) Schulemberg, J. W. and Archer, S. The Chapman Rearrangement, in *Organic Reactions*, Cope, A. C., Ed.; John Wiley & Sons, Inc.: New York, 1965, Vol. 14, pp. 1-51. c) Brady, K. and Hegarty, A. F., *J. Chem. Soc., Perkin Trans. 2*, **1980**, 121.
11. a) Narasimhamurthy, N. and Samuelson, A. G., *Tetrahedron Lett.*, **1986**, *27*, 3911. b) Rani, B. R., Rahman, M. F., and Bhalerao, U. T., *Tetrahedron*, **1992**, *48*, 1953.
12. Challis, B. C. and Challis, J. A. Amides and Related Compounds, in *Comprehensive Organic Chemistry. The Synthesis and Reactions of Organic Compounds*, Barton, D. and Ollis, D., Eds.; Pergamon Press: Oxford, 1979, Vol.2, pp. 957-1065.
13. Mercury(II) acetate has been employed to achieve an analogous transformation on the 1,3-diacylimidazolidines-2-thione[14] and *N*-substituted thioamides[8a]. However, the low yieds described in this last case suggest that *N*-substituted amides could be minor reaction products as we have found (see Table 1, entries 5 and 6).
14. Davies, S. G. and Mortlock, A. A., *Tetrahedron Lett.*, **1991**, *32*, 4791.

(*Received in UK* 25 *October* 1993; *accepted* 19 *November* 1993)