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Reactions of Thioamides with Metal Carboxylates in Organic Media

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Abstract: Reactions of thioamides with metal carboxylates in organic solvents are described. These processes enable the selective preparation of nitriles, imides or amides depending on the substitution pattern of the starting material. Mechanistic hypotheses supported by experimental evidences, including the unequivocal synthesis of bis(thioacetanilide)mercury(II) as a key reaction intermediate, are also proposed. © 1997 Elsevier Science Ltd.

Key Words: Amides, imides, metal carboxylates, nitriles, thioamides.

INTRODUCTION

Functional group manipulations are of paramount importance to synthetic organic chemists and hence, the development of novel transformations still remains of great interest. Organosulfur compounds have largely demonstrated their versatility as precursors and synthons to accomplish a wide variety of reactions and functional group interconversions.[1] Numerous processes require the presence of a soft metal ion which ultimately activates the organosulfur substrate.[2-4] The role of the metal reagent has been the subject of a certain controversy, although it is believed that the ion generates a transient complex which further releases the product. In fact, our research group has found some evidences about the intermediacy of coordination complexes in the reaction of thioamides, amines, and mercury(II) oxide to yield amidines.[3] These metal promoted reactions,[2] however, are markedly influenced by the solvent and thus, in an aqueous environment, products resulting from hydrolytic cleavage are prevalent.[2,5,6] It is therefore hoped that the inertness of most organic solvents enables

useful transformations, albeit this approach has been scarcely exploited to date.[3,4]

An in-depth understanding of metal-promoted reactions in organic solvents is hampered by the existence of numerous and competing coordination equilibria in which the metal ion can complex to reagents, products, or the solvent. Likewise, since most metal salts are poorly soluble in organic media the counterion is often a source of problems.[3]

Metal carboxylates derived from transition and main group elements have long been utilized in organic synthesis[7] and many of them are now commercially available. Thioamides can be converted into amides,[1,2,4] amidines,[3,8] nitriles,[2,9] and heterocyclic derivatives[10] by means of transition metals.

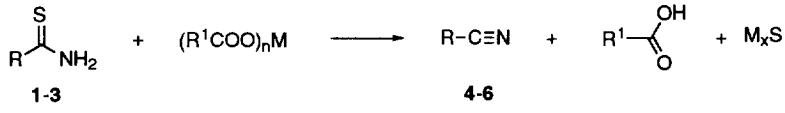
In this work we describe the simplified and convenient utilization of silver(I) and mercury(II) carboxylates for inducing the transformation of thioamides in organic solvents. Herein we describe the selective conversion of unsubstituted, *N*-substituted, and *N,N*-disubstituted thioamides into nitriles, imides, and amides, respectively. A portion of this research has been previously reported as a preliminary communication.[11]

RESULTS

Reaction with unsubstituted thioamides. Synthesis of nitriles. Unsubstituted thioamides **1-3** were reacted with several metal carboxylates in dichloromethane solution to afford exclusively the nitriles **4-6** in moderate to good yields (Scheme 1, Table 1).

Although there are numerous literature citations on the conversion of thioamides into nitriles,[2,5,6,9,12] to the best of our knowledge the usefulness of metal carboxylates had not been documented.

The stoichiometry of the process involves a 2:1 carboxylate/thioamide ratio. Under these conditions the transformation of the starting thioamide into nitrile was generally complete, with the sole exception of the less thiophilic metals (see Table 1), as evidenced by NMR analysis of crude samples after removal of the metal sulfide. The NMR monitoring also reveals the concomitant formation of the corresponding carboxylic acid

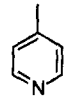


1-3 **4-6**

Scheme 1

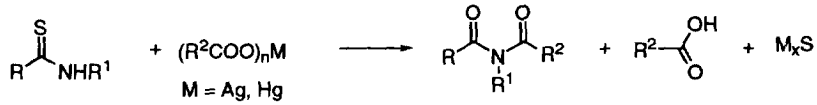
Table 1 also illustrates the influence of metal carboxylate on reaction rates. Silver(I), mercury(II), and copper(II) carboxylates gave fast reactions (entries 1-3, 5-7 and 9), affording the corresponding nitriles with 100% conversion and in moderate to good isolated yields. On the contrary, reactions with the less thiophilic thallium(I) formiate and lead(II) acetate proceeded very slowly and gave little or no reaction product (entries 4 and 8).

Table 1. Reaction of unsubstituted thioamides with metal carboxylates.

Entry	R	Thioamide	$(R^1COO)_nM$	Time (h)	Conversion (%)[a]	Nitrile (%)
1	Ph	**1**	AcOAg	1	100	**4** (72)
2	Ph	**1**	$(AcO)_2Hg$	1	100	**4** (83)
3	Ph	**1**	$(AcO)_2Cu.H_2O$	1	100	**4** (85)
4	Ph	**1**	HCOOTl	250	0	—
5	Ph	**1**	PhCOOAg	1	100	**4** (49)
6		**2**	AcOAg	1	100	**5** (46)
7		**2**	$(AcO)_2Hg$	1	100	**5** (49)
8		**2**	$(AcO)_2Pb.3H_2O$	160	12	**5**[b]
9		**3**	AcOAg	1	100	**6** (39)

[a]Determined by ^1H NMR. [b]Not isolated.

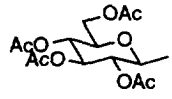
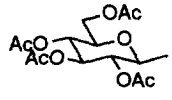
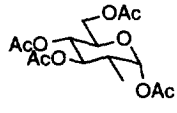
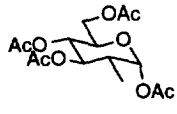
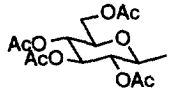
Reaction with *N*-substituted thioamides. Preparation of imides. Thioamides **7-12** were reacted with metal carboxylates in dichloromethane to give imides (**13-18**) (Scheme 2, Table 2). Again the stoichiometry of the process involves a 2:1 carboxylate/thioamide ratio. Under these conditions the transformation of the starting thioamide was always complete on the NMR basis. The unequivocal formation of one mole of carboxylic acid as by-product was also detected.



7-12 **13-18**

Scheme 2

Table 2. Reaction of *N*-substituted thioamides with metal carboxylates.

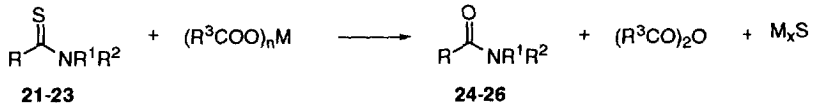
Entry	R	R^1	Thioamide	$(R^2COO)_nM$	Time (h)	Conversion (%)[a]	Imide (%)
1	Me	Ph	**7**	AcOAg	12	100	**13** (70)
2	Me	Ph	**7**	$(AcO)_2Hg$	12	100)	**13** (67)
3	Me	Ph	**7**	$(AcO)_2Cu.H_2O$	720	52[b]	**13**[c]
4	Me	Ph	**7**	HCOOTl	100	0	—
5	Et	$4\text{-}ClC_6H_4$	**8**	AcOAg	12	100	**14** (60)
6	Me		**9**	AcOAg	12	100	**15** (83)
7	Me		**9**	$(AcO)_2Hg$	12	100	**15** (88)
8	Me		**10**	AcOAg	12	100	**16** (84)
9	Me		**10**	$(AcO)_2Cu.H_2O$	700	53[d]	**16**[c]
10	Me	Ph	**11**	PhCOOAg	12	100	**17** (39)
11	Me		**12**	PhCOOAg	12	100	**18** (46)

[a]Evaluated by ^1H NMR. [b]Acetanilide (**19**, 48% conversion) was also detected. [c]Not isolated. [d]2-Acetamido-1,3,4,6-tetra-*O*-acetyl-2-deoxy-α-D-glucopyranose (**20**, 47% conversion) was also observed.

Data of Table 2 show the influence of metal carboxylate on both the reaction rate and selectivety. Only silver(I) and mercury(II) carboxylates are of practical importance giving selectively imides in good yields. Reactions with copper(II) acetate gave moderate conversions (entries 3 and 9) and thallium(I) formiate did not react at all (entry 4). The methodology is mild enough tolerating the presence of other functional groups. Thus it is worth pointing out the extension of this protocol to protected sugar thioamides (entries 6-9 and 11) which may find interesting aplications in carbohydrate chemistry.

The unprecedented procedure described above enables the preparation of symmetrical and unsymmetrical imides under mild conditions. The overall process involves a tandem reaction of S/O exchange and *N*-acylation, the latter provided by the carboxylate reagent. Remarkably, our methodology is based on nucleophilic reagents instead of electrophilic ones, which are employed in the classical syntheses of imides by acylation of amides and amines.[13]

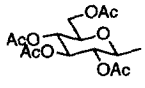
Reaction with *N,N*-disubstituted thioamides. Preparation of amides. Thioamides **21-23** reacted with metal carboxylates to give amides **24-26** (Scheme 3, Table 3).



21-23 **24-26**

Scheme 3

Table 3. Reaction of *N,N*-disubstituted thioamides with metal carboxylates.

Entry	R	R¹	R²	Thioamide	$(R^3COO)_xM_y$	Time (h)	Conversion (%)[a]	Amide (%)
1	Me	Bn	Me	**21**	AcOAg	3	100	**24** (74)
2	Me	Bn	Me	**21**	PhCOOAg	3	100	**24** (55)
3	Me	Bn	Me	**21**	$(AcO)_2Hg$	3	100	**24** (52)
4	Me	Bn	Me	**21**	$(AcO)_2Cu.H_2O$	500	35[b]	**24**[c]
5	Me	Bn	Me	**21**	HCOOTl	500	0	—
6	Me	Pr		**22**	AcOAg	3	100	**25** (82)
7	Me		$-(CH_2)_4-$	**23**	AcOAg	3	100	**26** (80)

[a]Evaluated by ^1H NMR. [b]The starting thioamide **21** was recovered in 65% yield. [c]Not isolated.

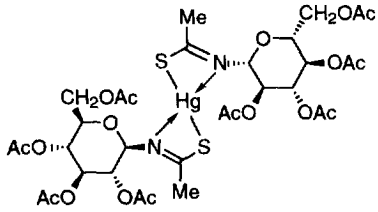
Again, only silver(I) and mercury(II) carboxylates were useful giving rapid and high-yielding reactions. The stoichiometry and reaction conditions are coincidental with those of *N*-substituted thioamides described above. The formation of amides was monitored by NMR spectroscopy which also revealed the formation of one mole of acid anhydride.

There has been an increasing interest in synthetic protocols involving the transformation of C=S into C=O groups.[4d,14] Mercury(II) acetate has been successfully employed for this purpose with thiocarbonyl compounds such as imidazolidine-2-thiones[15] and thioaldehydes.[16] This work also demonstrates its utility for the desulfurization of *N*, *N*-disubstituted thioamides.

DISCUSSION

Thioamides reacted quantitatively, in a selective fashion, in dichloromethane solution with two equivalents of metal carboxylates. Although reaction times depicted in Tables are not optimized, the reactions were rapid for silver(I) and mercury(II) carboxylates and, with some exceptions, essentially complete within a few hours. The reactions of thioamide **7** (Table 2, entries 1 and 2) were conducted either with a radical promotor (AIBN) or a radical inhibitor (hydroquinone), which had no influence on reaction rates at all. This fact seems to rule out a radical pathway in favor of an ionic one.

In a previous paper[3] we have proposed the intermediacy of species such as **27** or **28** in the reaction of thioamidosugars with amines in the presence of mercury(II) oxide.



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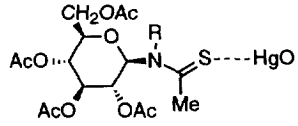


28

The preparation of neutral metal complexes derived from thioamides may be particularly difficult and strong bases are usually required for NH-proton abstraction.[17] Metal acetylides have a characteristic reactivity profile. They are only moderately basic, but the well-known alkali metal acetylides are relatively nucleophilic owing to the high polarity of the carbon-metal bond, which obviously decreases with the less electropositive metals. Thus, mercury(II) acetylides can be therefore considered as mild nucleophiles for the preparation of metal complexes, since these reagents are suitable bases for deprotonation and provide a thiophilic cation for metal complexation. One of these complexes (**29**) could be synthesized when thioamide **7** was allowed to react with

mercury(II)-1-butynide in diethyl ether. The only side product, the volatile 1-butyne, does not interfere in the reaction outcome (Scheme 4).

Scheme 4

Figure 1 depicts the solid state structure of **29** determined by X-ray diffraction analysis.[18] It is noteworthy that the C=N bonds exhibit different *E* and *Z* configurations in the crystal. The ambident nucleophilic character of thioamides[19] enables a coordination at sulfur and nitrogen atoms which leads to a mercury thioimidate. The resulting configuration[3] is a consequence of the anchorage provided by such a coordination. The distance of 2.919(8) Å between Hg(1) and N(1) of the *E* configuration suggests a certain interaction of such atoms.[20] Alternatively, the *Z* configuration adopted by the S(2)-C(9)-N(2) moiety facilitates a significant interaction with the electron cloud of an aromatic ring,[21] with a perpendicular distance Hg-phenyl of 2.94 Å.

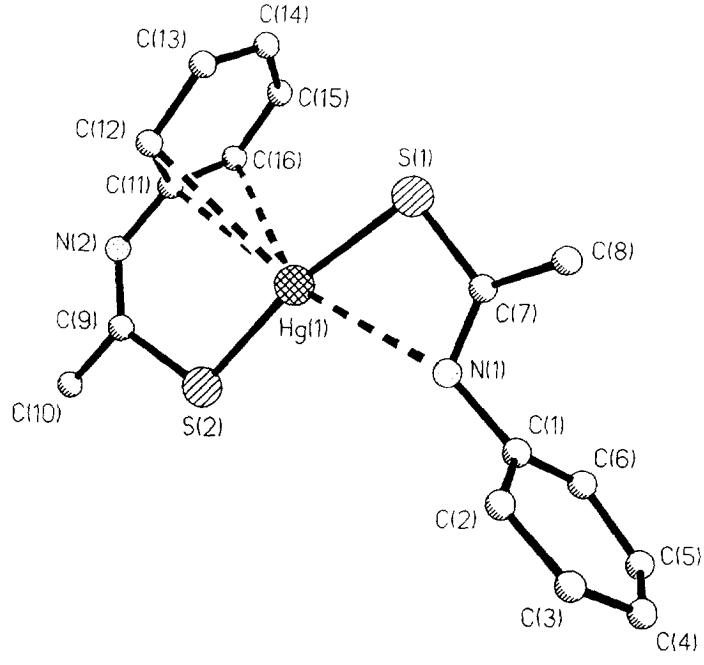
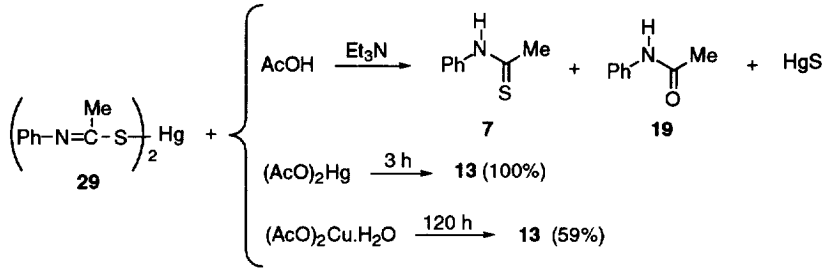


Figure 1. X-ray structure of complex **29**

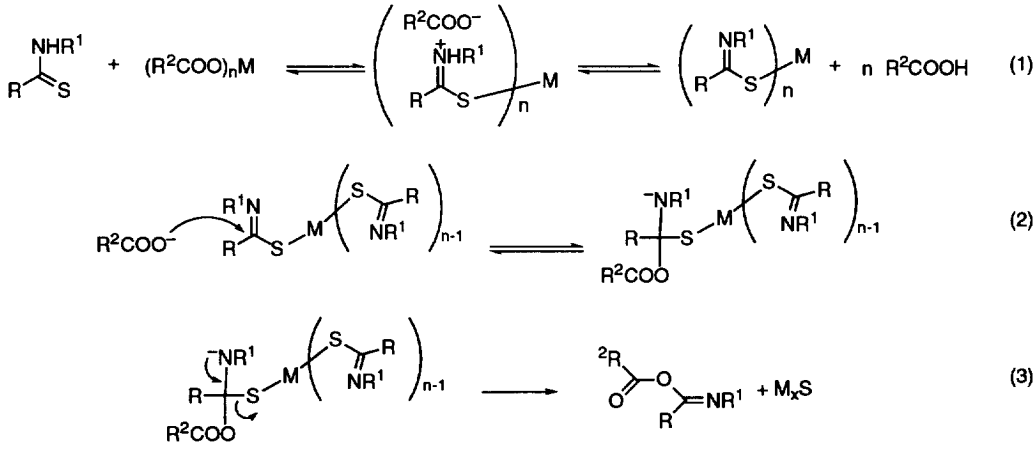
In solution, however, two signal sets are observed in ^1H NMR spectra of **29** showing different proportions in $CDCl_3$ (72:28) and DMSO-d_6 (59:41) without further evolution for 48 h. Such signal sets cannot therefore be attributed to *E* and *Z* configurations of an unique structure, and both conformational and complexation-dissociation equilibria are possible.

The treatment of **29** with acetic acid in the presence of triethylamine yielded a mixture of thioamide **7** and amide **19** with concomitant demercuriation. With carboxylates derived from late transition metals, **29** was converted into imide **13**. This transformation was rapid and quantitative with mercury(II) acetate while a slow and partial conversion was observed with copper(II) acetate (Scheme 5). The selectivity of these processes contrasts with those of entries 3 and 9 in Table 2.



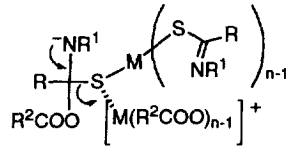
Scheme 5

The above observations are consistent with the intermediacy of species like **29** in the transformation of *N*-substituted thioamides into imides. It is possible to anticipate a series of equilibria *via* an addition-elimination mechanism (Scheme 6), which has already been proposed in the reaction of thioamides with amines.[3] The remarkable metal influence on reactivity evidences that metal complexation (or chelate formation) should be a driving force in steps 2 and 3.



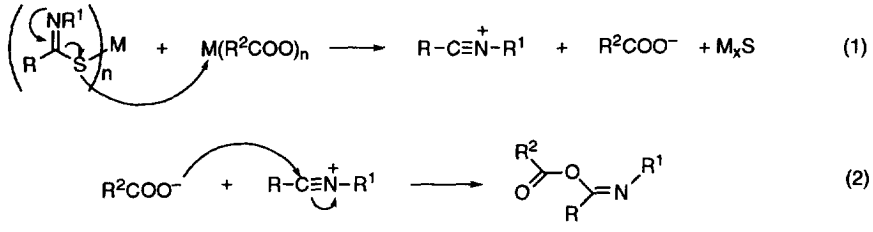
Scheme 6. Addition-elimination mechanism.

The experimental results of Scheme 5, also suggets that a second molecule of metal carboxylate could be coordinated to give an intermediate such as **30**, thus facilitating the extrusion of the sulfur atom.



30

An alternative elimination-addition pathway (Scheme 7) can also be invoked to explain the reaction outcome. The product forms through an intermediate nitrilium ion, suggested by Mumm and his associates as early as 1915, and it is also thought to be the true intermediate in processes such as the Chapman rearrangement.[22a]



Scheme 7. Elimination-addition mechanism.

In order to ascertain the feasibility of this hypothesis, we carried out the reactions of thiocaprolactam (**31**) with silver(I) and mercury(II) acetates (Scheme 8). Mixtures of *N*-acetylcaprolactam (**32**) and caprolactam (**33**) were obtained with a poor selectivity in dichloromethane (~1:1), that could be improved in ether (Table 4).

31 **32** **33**

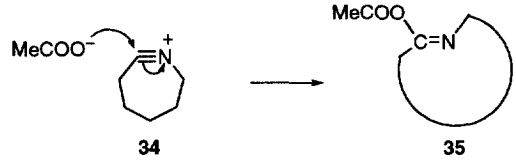
Scheme 8

Table 4. Conversions of thiocaprolactam.[a]

Entry	$(RCOO)_xM$	Solvent	Time (h)	Imide (%)	Amide (%)
1	AcOAg	Et_2O	3	**32** (86)	**33** (14)
2	AcOAg	CH_2Cl_2	3	**32** (58)[b]	**33** (42)
3	$(AcO)_2Hg$	CH_2Cl_2	3	**32** (59)	**33** (41)

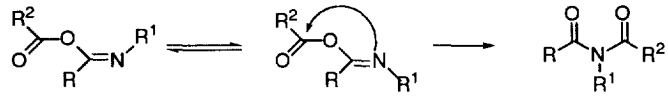
[a]Evaluated by ^1H NMR. [b]Isolated in 53% yield.

The mechanistic hypothesis of elimination-addition cannot be favored since it is very unlikely the intermediacy of a nitrilium ion in the conversion of thiocaprolactam **31** into the imide **32**. The formation of such an intermediate (**34**) should involve a considerable strain. Moreover the transformation of **34** into the isoimide **35**, by subsequent attack of acetate (Scheme 9), will be impeded because the *O*-acyl group and the substituent at the nitrogen atom must adopt a *Z* disposition, as in acyclic nitrilium ions.[22b]



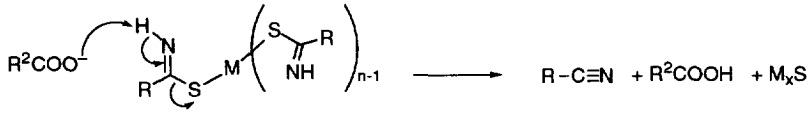
Scheme 9

Either by a preliminary addition or by the nitrilium mechanism, the final rearrangement of *O*-acylisoimides into imides will take place by an intramolecular nucleophilic displacement of the *E* isomers (Scheme 10).[22b]



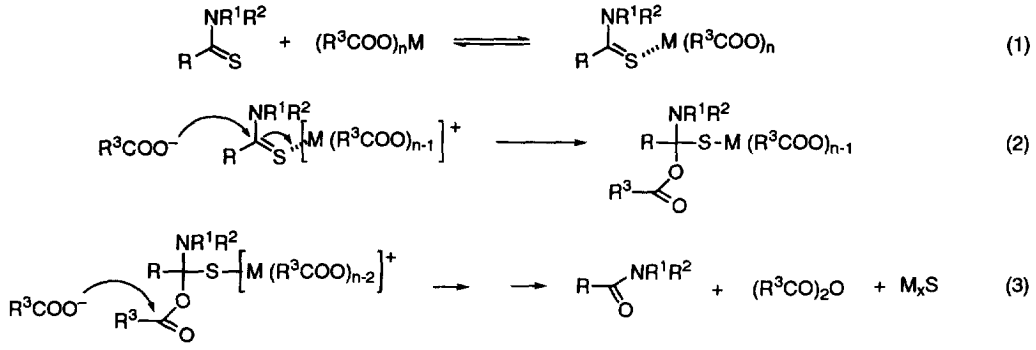
Scheme 10

Assuming the participation of intermediates like **29**, the formation of nitriles from unsubstituted thioamides appears to be consistent with a further step in which the carboxylate anion captures the thioamide proton (Scheme 11).



Scheme 11

How does the metal carboxylate steer the S/O exchange in *N*,*N*-disubstituted thioamides?. In this case, it is possible a simple metal-sulfur complexation that facilitates the nucleophilic attack of the anion to the thiocarbonyl group (Scheme 12). Acyl migration to the nitrogen atom will be unlikely as it would lead to an unstable acylammonium ion. Therefore the products, amide plus acid anhydride emerge from a feasible acylation of the carboxylate moiety followed by cleavage.



Scheme 12

The latter mechanism may also become operative for thiocaprolactam **31** and the acyclic *N*-substituted thioamides **7** and **10**, which are partially transformed into amides by treatment with copper(II) acetate (Table 2, entries 3 and 9). On the one hand, proton abstraction in **31** should be more difficult than in its acyclic counterparts due to steric hindrance. On the other hand, the weaker copper-sulfur interaction does not enhance enough acidity of thioamides **7** and **10** (Scheme 6, equation 1) nor facilitates the heterolytic cleavage of C-S bonds (Scheme 6, equations 2 and 3).

In conclusion, this paper describes novel transformations of unsubstituted, *N*-substituted, and *N,N*-disubstituted thioamides in organic media. The cooperative effect of the carboxylate anion and the thiophilicity of silver(I) or mercury(II) cations enables the formation of: 1) nitriles by means of a protocol in which the carboxylate anion serves as a base, 2) imides without the requirement of the classical electrophilic acylating agents, and 3) amides avoiding oxidizing reagents for achieving the S/O exchange. Moreover, this work also evidences how some thiophilic metal carboxylates can be harnessed for the desulfurization of organics, a topic of current research in the search of more environmentally benign industrial processes, such as the treatment of fuel or waste residues.

EXPERIMENTAL

Melting points were measured by a Electrothermal 8100 apparatus and are uncorrected. ^1H and ^{13}C NMR spectra were recorded with Bruker AC 200-E and Bruker 400 AC/PC spectrometers. Assignments were confirmed by homo- and hetero-nuclear double-resonance, and DEPT experiments. TMS was used as the internal standard (δ = 0.00 ppm) and all *J* values are given in Hz. $CDCl_3$, DMSO-d_6, and $(CD_3)_2CO$ were used as deuterated solvents (99.9% D). IR spectra were run on Perkin-Elmer 399 and FT Midac Co. spectrophotometers in the range of 4000-600 cm^{-1}. Solid samples were recorded on KBr pellets (Merck). Optical rotations were measured at 20 ± 2 °C with a Perkin-Elmer 241 polarimeter. Organic solutions were dried

over anhydrous $MgSO_4$ or Na_2SO_4 and the solvents were evaporated on a rotary evaporator. Analytical thin layer chromatography (TLC) was performed on silica gel-coated plastic sheets (Merck silica gel 60 GF_{254}) with the indicated solvent systems. Chromatographic purification refers to flash chromatography[23] and dry-column flash chromatography[24] using Merck silica gel 60 (230-400 mesh). Microanalyses were determined by the *Servei de Microanàlisi del Centre d'Investigació i Desenvolupament del CSIC*, Barcelona.

Reaction of thioamides with metal carboxylates. General procedure. To a solution of the starting thioamide in dichloromethane (1 g/10 mL) was added the metal carboxylate [two moles of silver(I) acetate or benzoate, or of thallium(I) formiate, or one mole of mercury(II) acetate, or of copper(II) acetate monohydrate, or of lead(II) acetate trihydrate]. The suspension was stirred at room temperature and the reaction time was monitored by TLC (toluene:acetone, 7:3). The reaction mixture was filtered on barium sulfide or Celite® 521 and evaporated to dryness. Reactions in other solvents (see Tables) were conducted in following this protocol as well. Crude samples were dissolved in the appropriate deuterated solvent (usually $CDCl_3$) and conversions were determined by ^1H NMR.

Benzonitrile (4). Table 1, entries 1-3, and 5: the residue was treated with ethanol, evaporated and the process was repeated 3 times. The oil was purified by distillation to afford **4**, b.p. 193 °C (lit.[25] 190-191 °C).

3-Cyanopyridine (5). Table 1, entries 6-8: in following the general protocol the final residue was crystallized from petroleum ether to afford **5**; m.p. 51-53 °C (lit.[26] 50 °C).

4-Cyanopyridine (6). Table 1, entry 9: according to the general procedure, the title compound was crystallized from diethyl ether-petroleum ether; m.p. 81-82 °C (lit.[27] 83 °C).

Diacetanilide (13). According to the general procedure, the reaction was conducted either with silver(I) or mercury(II) acetate (Table 2, entries 1 and 2). The reaction mixture was concentrated *in vacuo*, treated with ethanol, and again concentrated *in vacuo* (this procedure was repeated 3 times). The residue was crystallized from CCl_4-petroleum ether, m.p. 40-41 °C (lit.[28] 38 °C).

***N*-Acetyl-*N*-(4-chlorophenyl)propanamide (14).** Table 2, entry 5: in following the general procedure, the title compound was crystallized from petroleum ether. An analytical sample was obtained after purification by flash chromatography (CH_2Cl_2). M.p. 59-61 °C; ν_{max} 2960, 2920, 2860, 1700, 1480, 1355 and 840-800 cm^{-1}; $\delta_H(CDCl_3)$ 7.44 (d, 2H), 7.09 (d, 2H), 2.48 (q, 2H), 2.37 (s, 3H), and 1,09 (t, 3H); $\delta_C(CDCl_3)$ 176.2, 172.8, 137.6, 134.8, 130.1, 130.0, 31.9, 27.1, and 8.8. Calcd. for $C_{12}H_{14}NO_2Cl$: C, 60.1; H, 5.9; N, 5.8; Found: C, 60.5; H, 5.8; N, 5.6.

***N*,*N*-Diacetyl-2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosylamine (15).** Table 2, entries 6 and 7: the general protocol was applied to thioamide **9**[29] and the resulting residue was crystallized from ethanol to give **15**; m.p. 109-110 °C; $[\alpha]_{589}$ +25 (*c* 0.6, $CHCl_3$); ν_{max} 1753, 1374, and 1235 cm^{-1}; $\delta_H(CDCl_3)$ 6.85 (d, 1H,

H-1, $J_{1,2}$ 9.8), 5.50 (t, 1H, H-2, $J_{2,3}$ 9.0), 5.32 (t, 1H, H-3, $J_{3,4}$ 9.5), 5.16 (t, 1H, H-4, $J_{4,5}$ 9.8), 4.26 (dd, 1H, H-6, $J_{5,6}$ 4.2, $J_{6,6'}$ 12.5), 4.16 (dd, 1H, H-6', $J_{5,6'}$ 2.3), 3.84 (ddd, 1H, H-5), 2.46 (s, 3H, N-Ac); $\delta_C(CDCl_3)$ 173.0, 170.1, 169.5, 169.4, 169.2, 80.3, 74.6, 73.0, 69.0, 67.5, 61.3, 26.0, 20.0, 20.3, 20.0. Calcd. for $C_{18}H_{25}NO_{11}$: C, 50.1; H, 5.8; N, 3.2; Found: C, 50.2; H, 5.8; N, 3.3.

1,3,4,6-Tetra-*O*-acetyl-2-(*N*,*N*-diacetylamino)-2-deoxy-α-D-glucopyranose (16). Table 2, entry 8: the general protocol was applied to thioamide **10**[29] and the residue was crystallized from ethanol to give **16**; m.p. 113-114 °C (lit.[30] 111-112 °C).

***N*-Acetyl-*N*-phenylbenzamide (17).** Table 2, entry 10: in following the general protocol the residue was treated with petroleum ether to afford a mixture of **17** and benzoic acid. This mixture was dissolved in CH_2Cl_2 (30 mL), washed twice with a saturated solution of $NaHCO_3$, water, dried, and evaporated. Te title compound crystallized from petroleum ether: m.p. 68-70 °C (lit.[31] 67-68 °C).

***N*-Acetyl-*N*-benzoyl-2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosylamine (18).** Table 2, entry 11: in following the general protocol the residue was dissolved in CH_2Cl_2 (30 mL), washed twice with a saturated solution of $NaHCO_3$, water, dried, and evaporated. The title compound crystallized from ethanol: m.p. 145-146 °C; $[\alpha]_{589}$ −25 (*c* 0.5, $CHCl_3$); ν_{max} 1753, 1373, and 1240 cm^{-1}; $\delta_H(CDCl_3)$ 7.81 (d, 2H, *J* 7.0), 7.65 (t, 2H, *J* 7.4), 7.50 (t, 2H, *J* 7.4), 5.75 (t, 1H, H-2, $J_{2,3}$ 8.8), 5.48 (d, 1H, H-1, $J_{1,2}$ 9.5), 5.20 (t, 1H, H-3, $J_{3,4}$ 8.4), 5.11 (t, 1H, H-4, $J_{4,5}$ 9.7), 4.21 (bd, 2H, H-6, H-6', $J_{5,6}$ 3.8), 3.75 (dt, 1H, H-5), 2.12 (s, 3H, N-Ac); $\delta_C(CDCl_3)$ 172.8, 171.5, 170.3, 169.9, 169.1, 168.9, 134.1, 133.6, 129.3, 128.7, 82.6, 74.3, 73.5, 68.7, 67.6, 61.6, 25.8, 20.5, 20.3, 20.2. Calcd. for $C_{23}H_{27}NO_{11}$: C, 56.0; H, 5.5; N, 2.8; Found: C, 55.9; H, 5.4; N, 2.9.

Acetanilide (19). Table 2, entry 3: the residue was purified by flash chromatography by using a gradient of toluene-acetone to yield **26** that was crystallized from water; m.p. 113-115 °C (lit.[32] 115-116 °C).

***N*-Benzyl-*N*-methylacetamide (24).** Table 3, entries 1-4: the resulting residue was treated with ethanol and evaporated; **24** crystallized from diethyl ether-petroleum ether, m.p. 47-48 °C (lit.[33] 48 °C).

***N*-acetyl-2,3,4,6-tetra-*O*-acetyl-*N*-propyl-β-D-glucopyranosylamine (25).** Table 3, entry 6: the general protocol was applied to thioamide **22**[29] and the resulting residue was crystallized from ethanol; m.p. 101 °C (lit.[34] 101 °C).

***N*-acetylpyrrolidine (26).** Table 3, entry 7: the oily residue was purified by distillation to give amide **26**, b.p. 224 °C (lit.[35] 224-225 °C).

Reaction of thioacetanilide (7) with silver(I) acetate in the presence of AIBN or hydroquinone. Two solutions of thioacetanilide (**7**) (0.045 g, 0.3 mmol) in dichloromethane (5 mL) were treated with silver(I) acetate (0.1 g, 0.6 mmol) and hydroquinone (3 mg), respectively. Two additional

solutions of **7** were treated in a similar way but replacing the hydroquinone by AIBN (3 mg). Finally, two solutions of **7** were equally treated but without adding AIBN or hydroquinone. The suspensions were stirred at room temperature, filtered, and analyzed by ^{1}H NMR. In all cases, the conversions into diacetanilide (**13**) were ~23% after 10 min and ~30% after 25 min.

Bis(thioacetanilide)mercury(II) (29). To a solution of **7** (0.8 g, 5.0 mmol) in diethyl ether (50 mL) was added mercury(II)-1-butynide[36] (0.8 g, 2.5 mmol) and the reaction mixture was stirred at room temperature for 5 days, and then kept at -20 °C until crystallization of the title compound (0.62 g, 50%); m.p. 120 °C (dec.); ν_{max} 3020, 1630, 1575, 1470, 1130, 790, and 605 cm^{-1}; δ_H($CDCl_3$) major isomer: 7.42 (bt, 2H, *J* 7.3, *m*-Ph), 7.19 (t, 1H, *J* 7.3, *p*-Ph), 6.45 (bs, 2H, *o*-Ph), 2.52 (s, 3H); minor isomer: 7.26 (dt, 2H, *J* 7.5, 1.8, *m*-Ph), 7.04 (dt, 1H, *J* 7.2, 0.9, *p*-Ph), 6.64 (dd, 2H, *J* 7.5, 1.1, *o*-Ph), 2.04 (s, 3H); δ_H(DMSO-d_6) major isomer: 7.33 (t, 2H, *J* 7.2, *m*-Ph), 7.06 (m, 1H, *p*-Ph), 6.57 (d, 2H, *J* 7.6, *o*-Ph), 2.41 (s, 3H); minor isomer: 7.29 (t, 2H, *J* 7.2, *m*-Ph), 7.06 (m, 1H, *p*-Ph), 6.68 (dd, 2H, *J* 7.8, *o*-Ph), 2.02 (s, 3H); δ_C($CDCl_3$) major isomer: 163.2 (CN), 151.9 (*ipso*-Ph), 131.0 (*m*-Ph), 120.9 (*p*-Ph), 119.5 (*o*-Ph), 32.3 (Me); minor isomer: 174.5 (CN), 149.0 (*ipso*-Ph), 128.9 (*m*-Ph), 125.1 (*o*-Ph), 123.8 (*p*-Ph), 23.0 (Me). Calcd. for $C_{16}H_{16}N_2S_2Hg$: C, 38.4; H, 3.2; N, 5.6; S 12.8; Found: C, 38.4; H, 3.2; N, 5.6; S 12.6.

Reaction of 29 with acetic acid. To a solution of **29** (0.1 g, 0.2 mmol) in diethyl ether (10 mL) was added acetic acid (0.01 mL, 0.2 mmol) and a catalytic amount of triethylamine (0.004 g, 0.04 mmol). The reaction mixture was monitored by TLC (acetone:petroleum ether, 1:3) for two months. ^{1}H NMR then revealed the complete transformation of **29** into a mixture of acetanilide and thioacetanilide.

Reaction of 29 with mercury(II) acetate. To a solution of **29** (0.05 g, 0.1 mmol) in dichloromethane (5 mL) was added mercury(II) acetate (0.032g, 0.1 mmol). The suspension was stirred at room temperature and after 3 h the analysis by TLC (diethyl ether:petroleum ether, 1:2) evidenced the complete disappearance of **29**. The reaction mixture was filtered and evaporated. ^{1}H NMR of the crude sample revealed the formation of **13** exclusively. The residue was crystallized from diethyl ether-petroleum ether to afford diacetanilide **13** (0.33g, 90%).

Reaction of 29 with copper(II) acetate monohydrate. To a solution of **29** (0.05 g, 0.1 mmol) in dichloromethane (5 mL) was added copper(II) acetate monohydrate (0.02g, 0.1 mmol). The suspension was stirred at room temperature for 5 days, filtered and evaporated. ^{1}H NMR of the crude sample revealed the formation of **29** and acetanilide **13** in a 41:59 ratio.

***N*-acetylcaprolactam (32).** Table 4, entries 1-3: the title compound was obtained after purification by flash chromatography (toluene-CH_2Cl_2, 1:2); b.p. 134 °C at 26 mm (lit.[37] 134-135 °C at 26 mm).

X-ray Structure of 29. A colorless prism with the dimensions 0.30 x 0.24 x 0.14 mm was used for data collection on a Siemens P4 automatic diffractometer at 298 K, using Mo-Kα radiation (λ = 0.71073 Å), monochromatized by a highly oriented graphite crystal. The crystal stability was monitored using three standard reflections every 97 reflections and the data were scaled accordingly. Data were collected employing the 2θ-θ scan technique in the range $2.0^\circ < 2\theta < 60.0^\circ$. The structure was solved by standard Patterson methods followed by Fourier syntheses and refined by full-matrix least squares with anisotropic thermal parameters for Hg(1), S(1), and S(2). Hydrogen atoms were placed at idealized positions (C-H = 0.96 Å) and the coordinate shifts for carbon were applied to the bonded hydrogens. The crystal system was determined to be monoclinic, space group $P2_1$, a = 9.479(1) Å, b = 7.410(1) Å, c = 12.795(1) Å, β = 106.64(1)°, V = 861.1(3) Å^3, Z = 2, δ(calcd) = 1.932 Mg m^{-3}, linear absorption coefficient μ = 9.174 mm^{-1}, and FW = 501.0 for $C_{16}H_{16}HgN_2S_2$, $F(000)$ = 476. The total number of reflections was 3510, 3020 independent [R_i = 0.054], 2198 observed [$F > 4.0\sigma(F)$]. The number of refined parameters was 99. Final R = 0.055, R_w = 0.055.

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