α-Thiocyanation of Ketones and Esters Using (Dichloroiodo)benzene-Lead(II) Thiocyanate

Om Prakash,*[a] Neena Rani,[a] Vijay Sharma,[b] and Robert M. Moriarty*[a]

[a]Department of Chemistry, University of Illinois at Chicago, 845-W. Taylor, Chicago, IL. 60607, USA; Fax: (312) 996 5242

[b]Chemistry Department, Kurukshetra University, Kurukshetra, Haryana, 136119, INDIA

Received 11 July 1997

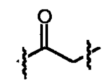
Abstract: Reaction of enol silyl ethers of acetophenone, 2-acetylfuran, 2-acetylthiophene, 2-acetylpyridine, cyclopentanone and cyclohexanone, and ketene silyl acetals of arylacetic esters with a combination of lead(II) thiocyanate and (dichloroiodo)benzene affords the corresponding α-thiocyanated ketones and esters.

The thiocyanato group has merged as an important functionality in certain anti-cancer natural products formed in the decomposition of glucosinolates derived from cruciferous vegetables.[1,2] α-Carbonyl thiocyanates[3,4] are of interest as synthetic precursors for heterocyclic ring systems and a facile synthesis of this class of compounds is desirable.

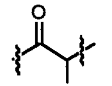
In recent years, the use of organohypervalent iodine compounds as oxidizing agents has gained attention in synthetic organic chemistry.[5] Our previous studies in this area have shown that the organoiodine(III) reagents, iodobenzene diacetate (IBD) and [hydroxy(tosyloxy)iodo]benzene (HTIB) are extremely useful for introduction of oxygen containing functionalities at the alpha position of carbonyl compounds.[6] In this paper, we report on the α-thiocyanation of ketones and esters *via* oxidation of enol silyl ethers and ketene silyl acetals with dichloroiodobenzene-lead(II) thiocyanate.[7-10]

The synthetic strategy adopted in this work is based on the fact that a combination of (dichloroiodo)benzene and lead(II) thiocyanate is expected to generate *in situ* hypervalent iodine compound, [bis(thiocyanato)iodo]benzene (**1**) (Eq. 1), which in analogy with HTIB might convert **2** to I(III) intermediate **3** containing the thiocyanato ligand. Intermediate **3** eventually might lead to α-thiocyanato derivative **4**.

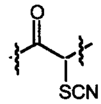
$$\mathrm{PhICl_2} + \mathrm{Pb(SCN)_2} \xrightarrow[0^\circ\mathrm{C},\ 20\ \mathrm{min.}]{\mathrm{dry\ CH_2Cl_2}} \underset{\mathbf{1}}{\mathrm{PhI(SCN)_2}} \qquad \text{(Eq. 1)}$$



2

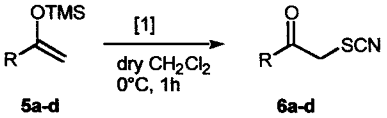


3



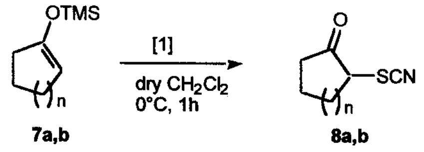
4

Reagent **1**, generated *in situ* according to the procedure recently described by Kita *et al.*,[9] did not show any reaction with ketones such as acetophenones and cyclohexanone in dichloromethane at 0°C. These observations led us to use enol silyl ethers which have been employed effectively in the hypervalent iodine mediated functionalization of ketones.[11-14] This strategy, indeed, afforded α-thiocyanato ketones not only in the case of acetophenone (**5a** to **6a**), but also in other cases namely, 2-acetylfuran (**5b** to **6b**), 2-acetylthiophene (**5c** to **6c**) and 2-acetylpyridine (**5d** to **6d**) (Scheme 1), cyclopentanone (**7a** to **8a**) and cyclohexanone (**7b** to **8b**) (Scheme 2).



a, R = Ph; b, R = 2-furyl; c, R = 2-thienyl; d, R = 2-pyridyl

Scheme 1

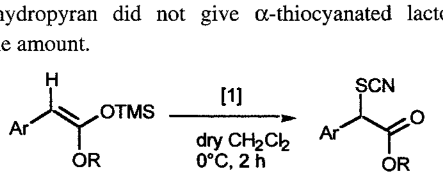


a, n = 1; b, n = 2

Scheme 2

In a typical procedure, (dichloroiodo)benzene (660 mg, 2.4 mmol) was added to a suspension of lead(II) thiocyanate (930 mg, 3 mmol) in dry dichloromethane (20 mL) at 0°C. The mixture was stirred for 15-20 min. at the same temperature and then a solution of acetophenone silyl enol ether (384 mg, 2 mmol) in dry dichloromethane (10 mL) was added. After stirring the resulting mixture for about 2 h, it was filtered. Silica gel (4 g) was added to the filtrate, which was then filtered and concentrated *in vacuo*. Purification of crude residue by column chromatography on silica gel using ethyl acetate-hexanes gave α-thiocyanatoacetophenone (**6a**, 60%) as a colorless oil.

The method was successful in effecting α-thiocyanation of esters *via* their silyl ketene acetals (Scheme 3). However, this method when applied to ketene silyl acetals derived from lactones such as 2-oxotetrahydropyran did not give α-thiocyanated lactones even in detectable amount.



a, Ar = Ph, R = Me; b, Ar = p-ClC$_6$H$_4$, R = Me; c, Ar = p-MeC$_6$H$_4$, R = Et; d, Ar = p-OMeC$_6$H$_4$, R = Me

Scheme 3

The mechanisic pathway for this thiocyanation process is probably analogous to that previously reported α-tosyloxylation of enol silyl ethers and ketene silyl acetals.[12] Physical data of the products is summarized in Table 1.

This study offers a convenient method for α-thiocyanation of ketones and esters. The ready availabilty of α-thiocyanato carbonyl compounds which are important precursors in the synthesis of heterocyclic compounds can be useful in the heterocyclic chemistry. The results also indicate that a combination of Pb(SCN)$_2$ and PhICl$_2$ [equivalent to PhI(SCN)$_2$] is effective on relatively more reactive substrates because of instability of the *in situ* generated reagent even at room temperature.

Acknowledgement: We thank National Science Foundation (Grant No 9520157) for financial support.

Downloaded by: University of Southern California. Copyrighted material.

Table 1. **α-Thiocyanatoketones and α-Thiocyanatoesters**

Product	Yield (%)	Physical state/mp °C (lit. mp °C)	Mol. Formula
6a	60	oil[15]	*b*
6b	46	colorless crystals, 101-103	$C_7H_5NO_2S^{b,c}$
6c	64	light brown solid, 89-91 (88)[16]	*b*
6d	65	oil (unstable)	*b,d*
8a	66	pale yellow oil[17]	*b*
8b	66	light yellow oil[17]	*b*
10a	70	oil[18]	*b*
10b	57	oil	$C_{10}H_8ClNO_2S^{b,c}$
10c	75	oil	$C_{12}H_{13}NO_2S^{b,c}$
10d	85	oil	$C_{11}H_{11}NO_3S^{b,c}$

a Yields of isolated products with respect to the quantity of enol silyl ether

b Spectral properties (IR, ^{1}HNMR and MS) were in total agreement with those previously reported or required. IR spectra of the products showed a characteristic band at ~ 2160 cm^{-1} (indicative of thiocyanato) in addition to the carbonyl bands.

c Elemental analyses (C, H, N, S) were satisfactory.

d Elemental analyses results and mass spectral data were not satisfactory because product is prone to decomposition

References and Notes

(1) Shahidi, F. in *Sulfur Compounds in Foods*, Mussinan, C. J.; Keelan, M. E., Eds.; American Chemical Society, Washington, DC, 1994, Chapter 9, p 106.

(2) Mehta, R. G.; Liu, J.; Constantinou, A.; Thomas, C. F.; Hawthorne, M.; You, M.; Gerhaeuser, C.; Pezzuto, J. M.: Moon, R. C.; Moriarty, R. M. *Carcinogenesis* **1995**, *16*, 399.

(3) For a review, see: Guy, R. G. in *The Chemistry of the Cyanates and Their Thio Derivatives*, Patai, S. ed: Wiley-Interscience; New York, 1977, p 819.

(4) For recent examples of α-thiocyanation of carbonyl compounds, see: Atkins, E. F.; Dabbs, S.; Guy, R. G.; Mahomed, A. A.; Mountford, P. *Tetrahedron* **1994**, *50*, 7253; Tanabe, Y.; Makita, T.; Mori, K. *Chem. Lett.* **1994**, 2275.

(5) Varvoglis, A. *The Organic Chemistry of Polycoordinted Iodine*; VCH Publishers, Inc.; New York, 1992; Varvoglis, A. *Hypervalent Iodine in Organic Synthesis*; Academic Press, New York, 1996; Varvoglis, A. *Tettrahedron* **1997**, *53*, 1179; Stang, P. J.; Zhdankin, V. V. *Chem. Rev.* **1996**, 96, 1123; Koser, G. F. in *The Chemistry of Halides, Pseudo-Halides and Azides Suppl D2*; Patai, S.; Rappoprt Z., Eds.; Wiley-Interscience: Chichester, 1995; Chapter 21, p 1173.

(6) Moriarty, R. M.; Prakash, O. *Acc. Chem. Res.* **1986**, *19*, 244; Moriarty, R. M.; Vaid, R. M.; Koser, G. F. *Synthesis* **1990**, 431; Prakash, O.; Rani, N.; Tanwar, M. P.; Moriarty, R. M. *Cont. Org. Synth.* **1995**, *2*, 121; Moriarty, R. M.; Prakash, O. in *Organic Reactions* (In Press).

(7) Only one general synthetic application of [(dithiocyanato)iodo]benzene (generated *in situ* by using a mixture of $PhICl_2$ and $Pb(SCN)_2$) reported in literature[6,7] is the thiocyanation of phenols and anilines.

(8) Neu, R. *Ber.* **1939**, *72*, 1505.

(9) Kita, Y. Okuno, T.; Masahiro, E.; Iio, K.; Takeda, Y.; Akai, S. *Synlett* **1994**, 1039.

(10) For an example of α-thiocyantion of enol silyl ether using a combination of $PhICl_2$ and $Pb(SCN)_2$, see: Back, T. G.; Brian, P. D.; Parvez, M. *J. Org. Chem.* **1995**, *60*, 703.

(11) Moriarty, R. M.; Prakash, O.; Duncan, M. P.; Musallam, H. A. *J. Org. Chem.* **1987**, *52*, 150; Moriarty, R. M.; Duncan, M. P. *J. Chem. Soc., Perkin Trans.1* **1987**, 1781.

(12) Moriarty, R. M.; Penmasta, R.; Awasthi, A.; Epa, E. W.; Prakash, I. *J. Org. Chem.* **1989**, *54*, 1101.

(13) Zhdankin, V. V.; Mullikin, M.; Tykwinski, R.; Berglund, B.; Caple, R.; Zefirov, N. S.; Kozmin, A. S. *J. Org. Chem.* **1989**, *54*, 2605; Zefirov, N. S.; Samoniya, N. S.; Kutateladze, T. G.; Zhdankin, V. V. *J. Org. Chem. USSR (Engl. Transl.)* **1991**, 27, 220.

(14) Chen, K.; Koser, G. F. *J. Org. Chem.* **1991**, *56*, 5764; Koser, G. F.; Chen, K.; Huang, Y.; Summers, C. A. *J. Chem. Soc., Perkin Trans.1* **1994**, 1375.

(15) Prakash, O.; Saini, N. *Synth. Commun.* **1993**, *23*, 1455.

(16) Singh, S. P.; Sehgal, S.; Singh, L.; Dhawan, S. N. *Indian J. Chem.* **1987**, *26B*, 154.

(17) Morrison, G. A. *J. Chem Res. (M)* **1981**, 2901.

(18) Gagnon, P. E.; Boivin, J. L.; Brown, J. L. *Can. J. Chem.* **1959**, *37*, 1597.

Downloaded by: University of Southern California. Copyrighted material.