Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry
Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/lsyc20

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Om Prakash [a] & Neena Saini [a]
[a] Department of Chemistry, Kurukshetra University, Kurukshetra, 132119, India
Published online: 23 Sep 2006.

To cite this article: Om Prakash & Neena Saini (1993) Hypervalent Iodine in Organic Synthesis: One Pot Facile Syntheses of α-Thiocyanatoacetophenones, 2-Hydroxy-, and 2-Mercapto-4-arylthiazoles Using [Hydroxy(tosyloxy)iodo]benzene, Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry, 23:10, 1455-1462, DOI: 10.1080/00397919308011236

To link to this article: http://dx.doi.org/10.1080/00397919308011236

SYNTHETIC COMMUNICATIONS, 23(10), 1455-1462 (1993)

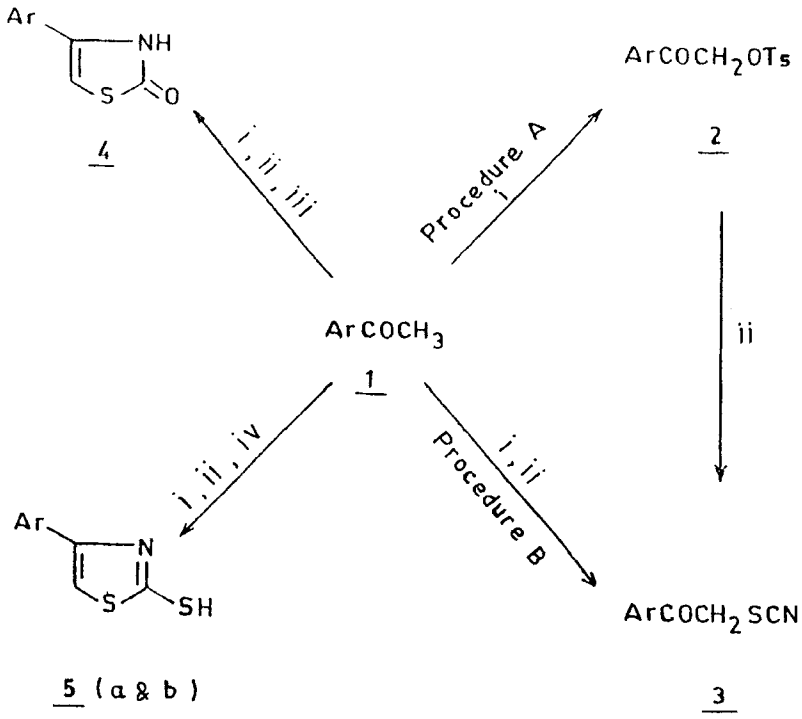
HYPERVALENT IODINE IN ORGANIC SYNTHESIS: ONE POT FACILE SYNTHESES OF α-THIOCYANATOACETOPHENONES, 2-HYDROXY-, AND 2-MERCAPTO-4-ARYLTHIAZOLES USING [HYDROXY (TOSYLOXY)IODO] BENZENE

Om Prakash* and Neena Saini
Department of Chemistry
Kurukshetra University, Kurukshetra-132119, India

Abstract: Hypervalent iodine oxidation of acetophenones (**1a-1e**) with [hydroxy(tosyloxy)iodo]benzene, followed by treatment with potassium thiocyanate offers a new facile synthesis of corresponding α-thiocyanatoacetophenones (**3a-3e**). Cyclization of **3a-3e**, thus generated in situ, using AcOH/H_2O and $H_2NC(S)NH_2$/HCl provides one pot facile syntheses of 2-hydroxy-, and 2-mercapto-4-arylthiazoles (**4** & **5**) respectively.

In our earlier reports[1-5] dealing with hypervalent iodine in organic synthesis, it has been observed that [hydroxy(tosyloxy)iodo]benzene (HTIB)[6] can offer superior and general alternative of existing syntheses which involve the use of lachrymatory and toxic α-halogenoketones. The approach involving HTIB oxidation has particularly been useful in offering convenient syntheses of some heterocycles[1,2,5] and bridgehead heterocyclic compounds[4]. In continuation of these encouraging results, we now report on the one pot facile syntheses of α-thiocyanatoacetophenones (**3**), 2-hydroxy-,

* To whom correspondence should be addressed.



1 – 5	Ar
a	C_6H_5
b	p-Cl C_6H_4
c	p-CH_3 C_6H_4
d	p-OCH_3 C_6H_4
e	p-Br C_6H_4

i = HTIB, CH_3CN

ii = KSCN, CH_3CN or C_2H_5OH

iii = AcOH, H_2O, Conc. H_2SO_4

iv = H_2NCSNH_2, C_2H_5OH, H_2O, HCl

Scheme -1

and 2-mercapto-4-arylthiazoles (**4** & **5**) starting from acetophenones.

Keeping in view that α-halogenoacetophenones and α-tosyloxyacetophenones (**2**) behave analogously, **2(a,b,d,e)**, prepared by the oxidation of **1** with HTIB according to literature procedure[3,7], were treated with potassium thiocyanate in ethanol for 5-10 min. The reaction occurred according to our expectations and **3** were obtained in good yields. The experimental procedure (A) was further simplified by preparing **3a-e** directly from **1a-e** without isolating **2a-e** (procedure **B**).

Since α-thiocyanatoacetophenones are important precursors for the synthesis of various biologically important thiazoles[8,9], it was also considered worthwhile to develop one pot convenient procedure for the synthesis of some of the thiazole derivatives. For example, in the present study, **3a**, generated in situ from acetophenone (**1a**) by the procedure **B**, on treatment with $AcOH/H_2O$ afforded **4a** in 61% yield. Similarly, other substituted acetophenones (**1b-1e**) also underwent smooth one pot transformation to the corresponding **4b-4e**. The another related synthesis, attempted by us, was the conversion of **1** to **5**. The conversion **1** ⟶ **5** was indeed, accomplished by generating **3a** & **3b** in situ, followed by the action of H_2NCSNH_2/HCl. However, the yields of the products **5a** & **5b** are not good. This is because **5** are prone to oxidation to give corresponding bis (4-phenyl-2-thiazolyl)

Table

Compound	m.p.(lit.m.p.)(°C)	Yield[a] (%)[b]
3a	75 (75-6)[13]	71 (55)
3b	137-40 (136)[14,15]	75 (66)
3c	108 (106-7)[14]	52
3d	122-24 (121)[15]	68 (64)
3e	150 (147)[15]	78 (75)
4a	210-12 (208-10)[16]	61
4b	217-20 (223)[16,17]	47
4c	192-93 (197-98)[16,17]	40
4d	250 (250)[16,17]	38
4e	222 (221-3)[16,17]	45
5a	168-72 (172-3)[16]	33
5b	209-11 (210-12)[16]	20

a : % Yield of isolated product obtained from procedure B w.r.t. acetophenones (1).

b : % Yield given in the parentheses represent the overall yield of the isolated product obtained from procedure A w.r.t. acetophenones (1).

sulphides (6) which were actually isolated (15-20%) from the reaction mixture. The synthetic scheme for these conversions are outlined in scheme 1 and data of the products are summarized in table.

Finally, it may be mentioned that hypervalent iodine mediated approach provides new simple syntheses of title compounds and there exists the possibility of using this technique for the large variety of other class of compounds.

Experimental

Melting points were taken in open capillaries in sulphuric acid bath and are uncorrected. I.R. spectra were recorded on IR-20 Beckmen spectrophotometer using nujol mulls. ^{1}H NMR spectra were recorded at 90 MHz on a Perkin-Elmer R-32 machine using TMS as internal standard.

HTIB was prepared by the method of Neiland & Karele[10], and Koser & Wettach[11].

Preparation of α-thiocyanatoacetophenones (3)

Procedure A : Via isolation of α-tosyloxyacetophenones (2): General Procedure

Step I : Preparation of α-tosyloxyacetophenone (2) :

These were prepared by the oxidation of respective acetophenones (2.5 m mol) with HTIB (1 gm, 2.51 m mol) as reported in literature[3,7].

Step II : Preparation of α-thiocyanatoacetophenones (3):

To an α-tosyloxyacetophenone (2, 2.5 m mol) in ethanol (20 ml) was added potassium thiocyanate (0.25 gm, 2.5 m mol) and the reaction mixture refluxed for 5-10 min. On cooling 3 separated out as crystalline solid which was filtered, washed with little ethanol and recrystallized from ethanol.

Procedure B : Direct preparation of α-thiocyanatoacetophenones (3) from acetophenones (1) : General Procedure

To a solution of 1 (2.5 m mol) in acetonitrile (20 ml) was added HTIB (1 gm, 2.51 m mol) and the reaction mixture refluxed for 2 hrs. After cooling, potassium thiocyanate

(0.25 g., 2.5 m mol) was added and the reaction mixture further refluxed for 5-10 min. On dilution with 20 ml water, α-thiocyanatoacetophenone (3) separated out[12] which was filtered and crystallized from ethanol.

Their physical and spectral properties were found to be in agreement with those reported in literature (Table).

One pot synthesis of 2-hydroxy-4-arylthiazoles (4) from acetophenones (1) : General procedure

Acetophenone (1, 2.5 m mol) was treated successively with HTIB (1 gm, 2.51 m mol) and potassium thiocyanate (0.25 gm, 2.5 m mol) according to procedure B. The solvent was distilled off in vacuo. To the remaining residual mass were added glacial acetic acid (5 ml), water (0.25 ml) and conc. H_2SO_4 (0.1 ml). The mixture was heated on a water bath for 1 hr. Dilution with water, followed by crystallization with dilute ethanol afforded 2-hydroxy-4-arylthiazole (4).

One pot synthesis of 2-mercapto-4-phenylthiazole (5a) from acetophenone (1a)

After treating 1a (0.30 gm, 2.5 m mol) with HTIB (1 gm, 2.51 m mol) and potassium thiocyanate (0.25 gm, 2.5 m mol) as in procedure B, the solvent was distilled off in vacuo. Then ethanol (2 ml), water (5 ml), thiourea (0.38 gm, 5 m mol) and conc. HCl (1.25 ml) were added to the remaining residual mass. The mixture was refluxed for 8 hrs. Diluting with water (10ml.), it gave solid which was treated with 5% NaOH and filtered (6a, 20%, m.p. 140°,

lit.[16] m.p. 141°, left in the insoluble portion). Acidification of alkaline solution with dil. HCl gave product **5a**.

Similar treatment with **1b** afforded **5b** (20%) and **6b** (15%, m.p.163-65°, lit.[16] m.p.163°).

Acknowledgements: We are thankful to U.G.C., New Delhi for financial assistance.

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(Received in USA 17 November 1992)