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POLY[4-DIACETOXYIODO] STYRENE-PROMOTED THIOCYANATION OF AROMATIC ETHERS, ANILINES, AND INDOLES

Liqiang Wu,¹ Shujun Chao,² Xiao Wang,¹ and Fulin Yan¹

¹School of Pharmacy, Xinxiang Medical University, Xinxiang, Henan, China ²Department of Chemistry, Xinxiang Medical University, Xinxiang, Henan, China



Abstract Thiocyanation of aromatic ethers, anilines, and indoles have been achieved using ammonium thiocyanate in the presence of poly[4-diacetoxyiodo] styrene (PDAIS) in CH_3CN at room temperature.

Keywords Anilines; aromatic ethers; indoles; poly[4-diacetoxyiodo] styrene thiocyanation

INTRODUCTION

The electrophilic thiocyanation of aromatic and hetereoaromatic compounds as a direct method for carbon–sulfur bond formation is a very useful reaction in organic synthesis.¹ Aryl and heteroaryl thiocyanates are important intermediates for the synthesis of sulfurcontaining heterocycles.² The thiocyanate group can also be converted into other sulfurbearing groups.³ Therefore, it is important to find new and fast methods for the synthesis of thiocyanate groups containing aromatic systems. Various methods have been reported

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Address correspondence to Liqiang Wu, School of Pharmacy, Xinxiang Medical University, Xinxiang, Henan 453003, China. E-mail: wliq1974@sohu.com

for the thiocyanation of aromatic systems using ceric ammonium nitrate,^{4a} NaBO₃,^{4b} acidic K10 clay,^{4c} iodine/MeOH,^{4d} FeCl₃^{4e} oxone,^{4f} DDQ,^{4g} SelectfluorTM,^{4h} I₂O₅,⁴ⁱ Mn(OAc)₃,^{4j} 2-iodoxybenzoate,^{4k} Al₂O₃/MeSO₃H,^{4l} *p*-TsOH,^{4m} PhI(OAc)₂,⁴ⁿ HIO₃.^{4o} However, many of the methods utilizing these reagents suffer from various drawbacks, such as the use of excess amounts of strong oxiding agents and expensive reagents, unsatisfactory yield, and high temperatures.

Poly[4-diacetoxyiodo] styrene (PDAIS) is a novel and versatile oxidizing agent, due to its high efficiency, reusability, and mild reaction conditions. PDAIS has been explored as a powerful oxidant for various organic transformations under mild conditions.⁵ In this article, we report a simple, efficient, and practical approach for the thiocyanation of aromatic ethers, anilines, and indoles using ammonium thiocyanate in the presence of PDAIS in CH₃CN at room temperature (Scheme 1).



RESULTS AND DISCUSSION

To choose the optimum conditions, first, the effect of the solvent on the rate of the reaction was studied for the preparation of 1-methoxy-4-thiocyanatobenzene from the reaction of anisole (1 mmol), NH₄SCN (2.5 mmol), and PDAIS (1.2 mmol) in several solvents or under solvent-free conditions at room temperature (Table 1). In CH₃CN, the reaction proceeded smoothly with a short reaction time and high yield.

Next, to determine the optimum amount of PDAIS, the reaction was carried out by varying the amount of the oxidant (Table 2). The maximum yield was obtained with 1.2 equivalents of PDAIS. Further increases in amount of the oxidant in the standard reaction did not have any significant effect on the product yield.

Using these optimized reaction conditions, the scope and efficiency of these procedures were explored for the thiocyanation of a variety of aromatic ethers, anilines, and indoles. The results are summarized in Table 3. As shown in Table 3, aromatic ethers, anilines, and indoles containing electron-donating as well as electron-withdrawing groups were smoothly converted. The reaction is highly regioselective, forming 4-thiocyano aromatic ethers, anilines, and 3-thiocyano indoles as the products. The structures of the thiocyanates

Entry	Solvent	Time (h)	Yield (%) ^a
1	MeOH	1	65
2	H_2O	3	0
3	CH ₂ Cl ₂	1	80
4	DMF	1.5	72
5	CH ₃ CN	1	90
6	neat	1	23

 Table 1 Solvent optimization for the synthesis of 1-methoxy-4-thiocyanatobenzene

^aIsolated yield.

were established from their IR, ¹H NMR, ¹³C NMR, and elemental analyses. This methodology offers significant improvements with regard to the scope of this transformation and simplicity in operation.

After the reaction, PDAIS was converted to polyiodostyrene, which was recovered by simple filtration. The regeneration of PDAIS was achieved by reaction of polyiodostyrene in acetic anhydride with dropwise addition of 32 mL of cold hydrogen peroxide (30% solution) (Scheme 2). The reaction mixture was stirred at room temperature for 16 h. The above reaction mixture was kept overnight at room temperature. The PDAIS product was precipitated with diethyl ether and then dried for use. The recovered PDAIS can be reused at least four additional times in subsequent reactions without significant loss in product yield (Table 4).



Scheme 2

The mechanism of the reaction may involve the initial nucleophilic attack of thiocyanate anion on the fairly electrophilic PDAIS, through a phenomenon of ligand exchange

Entry	PDAIS/equivalent	Time (h)	Yield (%) ^b
1	0	4	0
2	0.5	2	42
3	1.0	1.5	72
4	1.1	1	82
5	1.2	1	90
6	1.3	1	90
7	1.4	1	89
8	1.5	1	88

 Table 2 PDAIS optimization for the synthesis of 1-methoxy-4-thiocyanatobenzene^a

^aReaction conditions: anisole (1 mmol); NH₄SCN (2.5 mmol); rt; CH₃CN. ^bIsolated yield.

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Entry	Substrate	Product ^b	Time (h)	Yield $(\%)^c$	Mp (lit.) ($^{\circ}$ C)
a		SCN	1	90	36–39 (41) ⁴ⁿ
b	MeO	MeO SCN	1	91	Oil (Oil) ⁴ⁿ
с	MeO	MeO	1	86	Oil (Oil) ⁴ⁿ
d	MeO OMe	MeO OMe	1	88	102–104 (104–106) ⁴ 0
		SCN			
e	H ₂ N	SCN	1.5	82	51–53 (51–52) ^{4g}
f	N	N SCN	1.5	85	71–73 (71–72) ^{4g}
g	CI		1.5	88	61–63 (60–61) ^{4g}
h	H ₂ N OMe	H ₂ N OMe SCN	1	82	100–101 (99–100) ^{4g}
i		H ₂ N SCN	1	80	110–112 (105–106) ^{4g}
j			1	89	80-81 (83-84) ^{4g}
k		SCN	1	78	99–101 (99–101) ^{4g}
I	Br		1	76	125–126 (127–129) ⁴ g

Table 3 Thiocyanation of aromatic ethers, anilines, and indoles promoted by $PDAIS^{a}$

(Continued on next page)

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Entry	Substrate	Product ^b	Time (h)	Yield (%) ^c	Mp (lit.) (°C)
m	MeO	MeO SCN	1.5	82	113–115 (113–115) ⁴⁴
n	F N H	F	1.5	84	110–112

Table 3 Thiocyanation of aromatic ethers, anilines, and indoles promoted by PDAIS^a (Continued)

^aReaction conditions: aromatic ethers, anilines or indoles (1 mmol); NH₄SCN (2 .5mmol); PDAIS (1.2 mmol); rt; CH₃CN.

 b All products except **2n** were identified by comparing their physical and spectral data with those of the authentic samples (see references 4f, 4g, 4n, 4o).

^cIsolated yield.

to form the intermediate. The overwhelming tendency of the intermediate to expel iodobenzene is expected to generate the rather unstable thiocyanogen required for the aromatic electrophilic thiocyanation reaction (Scheme 3).



To emphasize the effect of oxidant, the model reaction between anisole with NH_4SCN was described, and different hypervalent iodine oxidants were subjected to the reaction. All the reactions were run in the same conditions, and similar amounts of oxidant (1.2 equivalent) were used. As can be seen in Table 5, satisfactory results were obtained only with PDAIS (entry 7).

Table 4	The effect	of reusability	of PDAIS ^a
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Run	Cycle	Yield $(\%)^b$
1	0	90
2	1	90
3	2	88
4	3	88
5	4	86

^aReaction conditions: anisole (1 mmol); NH₄SCN (2.5 mmol); PDAIS (1.2 mmol); rt; CH₃CN. ^bIsolated yield.

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Entry	Hypervalent iodine oxidant	Time (min)	Solvent	Yield (%) ^b
1	Dess-Martin periodinane	60	CH ₃ CN	52
2	o-Iodoxylbenzoic acid	30	CH ₃ CN	70
3	HIO ₃	30	CHCl ₃	82
4	I ₂ O ₅	60	MeOH	62
5	HIO ₄	60	CHCl ₃	58
6	PhI(OAc) ₂	30	CH ₃ CN	81
7	PDAIS	60	CH ₃ CN	90

Table 5 Effect of hypervalent iodine oxidant on the reaction of anisole with NH₄SCN^a

^aReaction conditions: anisole (1 mmol); NH₄SCN (2.5 mmol); hypervalent iodine oxidant (1.2 mmol); rt. ^bIsolated yield.

CONCLUSION

In summary, PDAIS can effectively promote the reaction of ammonium thiocyanate with aromatic ethers, anilines, and indoles to afford thiocyanated products. The reactions are conducted under mild conditions and afford regioselective thiocyanated products in good to excellent yields.

EXPERIMENTAL

NMR spectra were determined on Bruker AV-400 spectrometer at room temperature using TMS as internal standard, and coupling constants (*J*) were measured in Hz. Elemental analyses were performed by a Vario-III elemental analyzer. Melting points were determined on a XT-4 binocular microscope and were uncorrected. PDAIS was synthesized according to the reported procedure.^{5b} Commercially available reagents were used throughout without further purification unless otherwise stated.

General Procedure for the Thiocyanation of Indoles and Anilines

To a solution of aromatic ethers, anilines, or indoles (1.0 mmol) and NH₄SCN (2.5 mmol) in CH₃CN (20 mL), PDAIS (1.2 mmol) was added at room temperature. The reaction mixture was stirred at room temperature for the appropriate time according to Table 3. After complete conversion as indicated by TLC, the reaction mixture was quenched with water (20 mL) and extracted with CHCl₃ (2 × 20 mL). The solvent was evaporated, and the crude product was purified by silica gel column chromatography using ethyl acetate/hexane (1:9) as an eluent to afford the pure product. The characterization data for the new product are given below.

5-Fluoro-3-thiocyanato-1H-indole (3n)

Solid, IR (KBr): *v* 3428, 2141, 1638, 1452 cm⁻¹.¹H NMR (400 MHz, CDCl₃): δ 8.72 (1H, brs), 7.29–7.00 (4H, m), 2.88 (3H, s); ¹³C NMR (100 MHz, CDCl₃): δ 137.2, 133.2, 131.8, 126.2, 125.0, 122.9, 115.6, 109.9, 90.5, 20.4. Anal. calcd for C₉H₅FN₂S_: C 56.24, H 2.62, N 14.57, S 16.68; found: C 56.18, H 2.71, N 14.50, S 16.50.

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