Tetrahedron Letters 50 (2009) 347–349

Contents lists available at ScienceDirect

Tetrahedron Letters

journal homepage: www.elsevier.com/locate/tetlet

$Mn(OAc)_3$-promoted regioselective free radical thiocyanation of indoles and anilines

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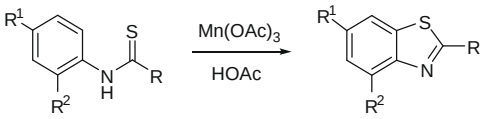
ARTICLE INFO

Article history:
Received 12 October 2008
Revised 1 November 2008
Accepted 4 November 2008
Available online 7 November 2008

ABSTRACT

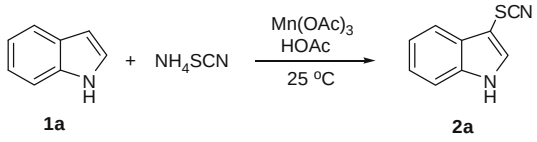
$Mn(OAc)_3$-promoted free radical thiocyanations of indoles and arylamines are introduced. Reactions performed under mild conditions give regioselective products in good to excellent yields.

Thiocyanate is a versatile synthon[1] which can be readily transferred to other functional groups such as sulfide,[2] aryl nitrile,[3] thiocarbamate,[4] and thionitrile.[5] The development of new synthetic methods for introducing thiocyanate functionality is always demanded. We recently reported $Mn(OAc)_3$-promoted free radical cyclization of thioformanilides to form benzothiozoles (Eq. 1).[6] We found that $Mn(OAc)_3$ could also mediate cyclization of heteroatom radicals to electron-rich aromatic rings to form O–C and P–C bonds.[7] Encouraged by the results obtained from the intramolecular reaction of sulfur radicals, we envisioned that this reaction may also be possible to achieve in an intermolecular fashion and used for synthesis of aryl thiocyanates.



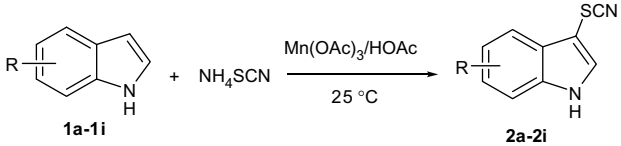
(1)

Ammonium thiocyanate was chosen for thiocyanation of indole **1a** under $Mn(OAc)_3$-promoted radical reaction conditions. Acetic acid was used as a solvent because it has a good solubility for $Mn(OAc)_3$. The reaction of **1a** at room temperature yielded the desired product 3-thiocyanato-1*H*-indole **2a** in 83% yield (Eq. 2 and Table 1, entry 1). The same reaction using *N*-methyl indole **1b** as the starting material gave **2b** in 85% yield (Table 1, entry 2). The reaction was further extended to include other substituted indoles. It was found that 2-methylindole **1c** gave 60% yield of **2c** (Table 1, entry 3). The lower yield is probably attributed to the steric hindrance of 2-substituted indole.

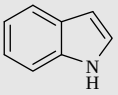
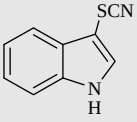
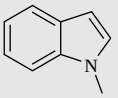
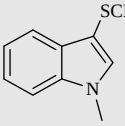
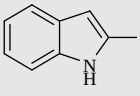
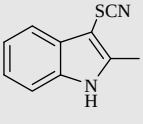
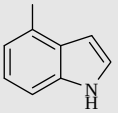
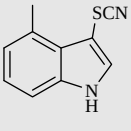


1a **2a** (2)

Table 1
Thiocyanation of indoles



1a-1i **2a-2i**

Entry	Substrate	Product[a]	Yield[b] (%)
1	 **1a**	 **2a**	83
2	 **1b**	 **2b**	85
3	 **1c**	 **2c**	60
4	 **1d**	 **2d**	85

(*continued on next page*)

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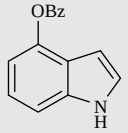
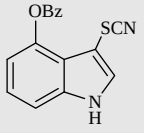
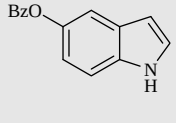
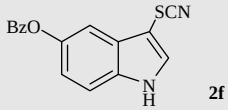
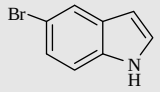
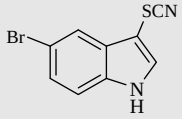
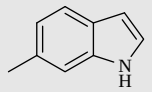
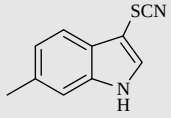
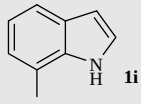
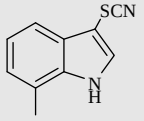
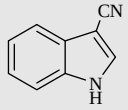
doi:10.1016/j.tetlet.2008.11.007

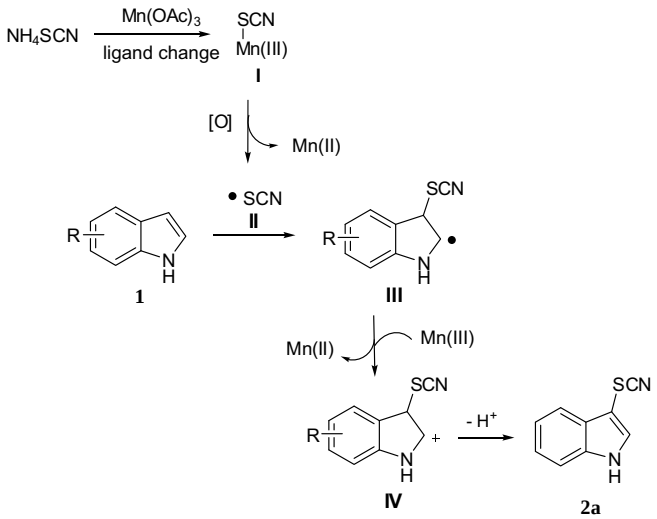
Table 1 (*continued*)

Entry	Substrate	Product[a]	Yield[b] (%)
5	 **1e**	 **2e**	91
6	 **1f**	 **2f**	87
7	 **1g**	 **2g**	92
8	 **1h**	 **2h**	50
9	 **1i**	 **2i**	93
10	 **1j**	n.r. [c]	—

[a] All products were characterized by NMR and MS spectra.
[b] Isolated yield.
[c] n.r. = no reaction observed.

Since 3-cyanoindole **1j** did not react with ammonium thiocyanate (Table 1, entry 10), it is a strong evidence that the addition is regioselective and only happens at the 3 position of indole.[8] Other indole derivatives **1d–i** also afforded good to excellent yields (50–93%) of the desired products **2d–i** (Table 1, entries 4–9).[9]

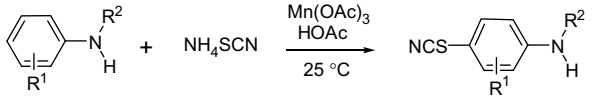
A plausible mechanism for this reaction is proposed in Scheme 1. Intermediate I formed by ligand-exchange is oxidized to NCS radical II. The radical then attacks the electron-rich site of indole to yield radical III. $Mn(OAc)_3$ oxidizes III to cation IV followed by the loss of a proton to afford product **2a**.

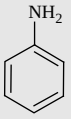
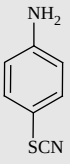
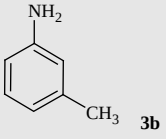
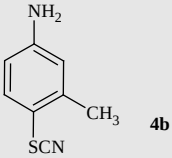
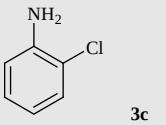
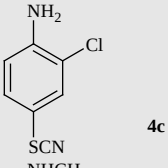
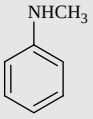
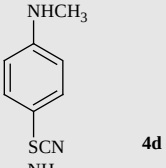
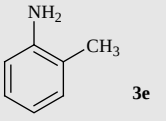
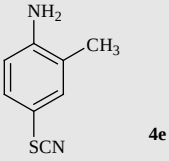
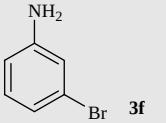
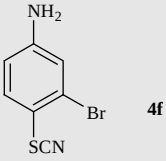
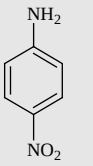
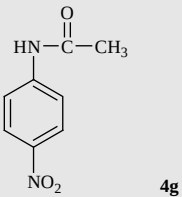


Scheme 1.

After successfully developed the free radical-promoted thiocyanation reactions of indoles, we then explored the reactions of aniline and its derivatives. Aniline is an electron-rich system bearing a free-amino group. The reaction of ammonium thiocyanate with aniline **3a** performed under the same condition described above afforded desired product **4a** in 83% yield (Eq. 3 and Table 2, entry 1). A comparison reaction on *N*-methylaniline **3d** afforded product **4d** in 84% yield (Table 2, entries 1 and 4). This result suggests that both free and methyl-substituted amino groups tolerated to

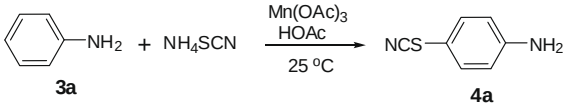
Table 2
Thiocyanation of anilines



Entry	Substrate	Product[a]	Yield[b] (%)
1	 **3a**	 **4a**	83
2	 **3b**	 **4b**	81
3	 **3c**	 **4c**	87
4	 **3d**	 **4d**	84
5	 **3e**	 **4e**	85
6	 **3f**	 **4f**	86
7	 **3g**	 **4g**	95[c]

[a] All products were characterized by NMR and MS spectra.
[b] Isolated yield.
[c] No thiocyanation, but only 4-nitro-*N*-acetylaniline **4g** was obtained.

$Mn(OAc)_3$ oxidation. Different mono-substituted anilines **3b**, **3c**, **3e**, and **3f** were also reacted with ammonium thiocyanate, and they all gave high yields (81–87%) of the corresponding products **4b**, **4c**, **4e**, and **4f** (Table 2, entries 2, 3, 5, and 6),[10] and the thiocyanato group is selectively added to the *para* position of the amino group. In the case of 4-nitroaniline **3g** which has the 4-position occupied, the thiocyanation could not take place, and gave only 4-nitro-*N*-acetylaniline **4g** as an N-acylated by-product (Table 2, entry 7).



(3)

In summary, $Mn(OAc)_3$ can effectively promote the reaction of ammonium thiocyanate with indoles or anilines to afford thiocyanated products. The reactions are conducted under mild conditions and afford regioselective thiocyanated products in good to excellent yields.

Acknowledgment

J.P.Z. thanks the National Natural Science Foundation of China for financial support (No. 20772088).

Supplementary data

Supplementary data (containing spectral data of **2a–i** and **4a**–**g**) associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2008.11.007.

References and notes

1. Guy, R. G. In *The Chemistry of Cyanates and their Thio Derivatives*; Patai, S., Ed.; John Wiley and Sons: New York, 1977.
2. (a) Billard, T.; Langlois, B. R.; Medebielle, M. *Tetrahedron Lett.* **2001**, *42*, 3463; (b) Nguyen, T.; Rubinstein, M.; Wakselman, C. *J. Org. Chem.* **1981**, *46*, 1938; (c) Billard, T.; Large, S.; Langlois, B. R. *Tetrahedron Lett.* **1997**, *38*, 65; (d) Grieco, P. A.; Yokoyama, Y.; Williams, E. *J. Org. Chem.* **1978**, *43*, 1283.
3. Zhang, Z. H.; Liebeskind, L. S. *Org. Lett.* **2006**, *8*, 4331.
4. (a) Riemschneider, R.; Wojahn, F.; Orlick, G. *J. Am. Chem. Soc.* **1951**, *73*, 5905; (b) Riemschneider, R. *J. Am. Chem. Soc.* **1956**, *78*, 844.
5. Lee, Y. T.; Choi, S. Y.; Chung, Y. K. *Tetrahedron Lett.* **2007**, *48*, 5673 and references cited therein.
6. Mu, X. J.; Zou, J. P.; Zeng, R. S.; Wu, J. C. *Tetrahedron Lett.* **2005**, *46*, 4345.
7. (a) Mu, X. J.; Zou, J. P.; Qian, Q. F.; Zhang, W. *Tetrahedron Lett.* **2006**, *47*, 2323; (b) Mu, X. J.; Zou, J. P.; Qian, Q. F.; Zhang, W. *Org. Lett.* **2006**, *8*, 5291.
8. (a) Nair, V.; George, T. G.; Nair, L. G.; Panicker, S. B. *Tetrahedron Lett.* **1999**, *40*, 1195; (b) Chakrabarty, M.; Sarkar, S. *Tetrahedron Lett.* **2003**, *44*, 8131; (c) Yadav, J. S.; Reddy, B. V. S.; Shubashree, S.; Sadashiv, K. *Tetrahedron Lett.* **2004**, *45*, 2951; (d) Wu, G. L.; Liu, Q.; Shen, Y. L.; Wu, W. T.; Wu, L. M. *Tetrahedron Lett.* **2005**, *46*, 5831.
9. *Typical experimental procedure for preparation of 3-thiocyanato-1H-indole* **2a**: The indole **1a** (1 mmol) and ammonium thiocyanate (1.2 mmol) were dissolved in 10 mL acetic acid and treated with manganese(III) acetate (3.0 mmol) at room temperature. The reaction mixture was stirred for 2 h. It was then diluted with water (20 mL) and then extracted with dichloromethane (15 mL × 3), the combined organic layer was dried over anhydrous Na_2SO_4. After removal of the solvent under reduced pressure, the crude product was purified by column chromatography on silica gel (eluted with acetone–petroleum ether = 1:4) to give **2a** in 83% yield, mp 73–76 °C. ^1H NMR (400 MHz, $CDCl_3$): δ 8.79 (1H, br s, NH), 7.78–7.22 (5H, m, C_8H_5N); ^{13}C NMR (100 MHz, $CDCl_3$): δ 136.4, 131.6, 128.0, 124.2, 122.2, 119.0, 112.8, 112.6, 92.0; HRMS: *m/z* (%), calcd for $C_9H_6N_2S$ (M^+) 174.0252, found 174.0256 (M^+, 100.00).
10. *Typical experimental procedure for preparation of 4-thiocyanatoaniline* (**4a**): The aniline **3a** (1 mmol) and ammonium thiocyanate (1.2 mmol) were dissolved in 10 mL acetic acid and treated with manganese(III) acetate (3.0 mmol) at room temperature. The reaction mixture was stirred for 2 h. It was then diluted with water (20 mL) and then extracted with dichloromethane (15 mL × 3), the combined organic layer was dried over anhydrous Na_2SO_4. After removal of the solvent under reduced pressure, the crude product was purified by column chromatography on silica gel (eluted with acetone–petroleum ether = 1:4) to give **4a** in 83% yield, mp 52–53 °C. ^1H NMR (400 MHz, $CDCl_3$): δ 7.33–6.63 (4H, m, C_6H_4), 4.04 (2H, br s, NH_2); ^{13}C NMR (100 MHz, $CDCl_3$): δ 149.3, 134.8, 116.4, 112.9, 109.5; HRMS: *m/z* (%), calcd for $C_7H_6N_2S$ (M^+) 150.0252, found 150.0251 (M^+, 100.00).