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A clay-mediated eco-friendly thiocyanation of indoles and carbazoles

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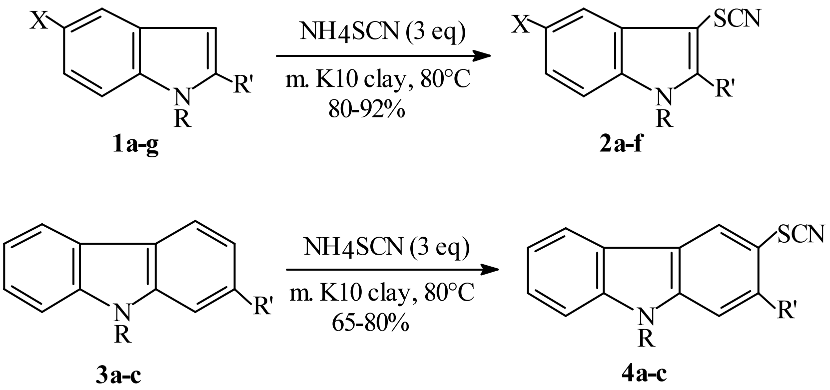
Abstract—Indoles **1a**–**f** and carbazoles **3a**–**c** on treatment with ammonium thiocyanate on montmorillonite K10 clay at 80°C furnished the corresponding 3-thiocyanato derivatives **2a**–**f** and **4a**–**c** in good to high yields. Skatole **5** furnished the dimeric oxindole **6**, which resulted from autoxidation.

Thiocyanation of arenes and heteroarenes is a very useful reaction in organic synthesis since it constitutes a direct method for the introduction of sulphur into aryl rings and the thiocyanate group can be converted into other sulphur-bearing functionalities.[1] Thiocyanations have earlier been achieved utilising varied reagents and conditions,[2,3] most of which are cumbersome and utilise toxic metal thiocyanates and reagents. Thiocyanation of indoles has been achieved only three times using bromine and potassium thiocyanate (only for indole),[3a] *N*-thiocyanatosuccinimide[3b] (only for 5-methoxy-2-methylindole, forming two bisthiocyanates) and ammonium thiocyanate in the presence of ceric ammonium nitrate in methanol.[3c] In continuation of our interests in exploring the potential of montmorillonite K10 clay and in the solvent-free reactions and synthesis of heteroaromatics,[4] we have now developed a solvent-free method for the thiocyanation of indoles and carbazoles using ammonium thiocyanate and montmorillonite K10 clay.

Initially, a solution of indole **1a** and 3 equiv. of ammonium thiocyanate in the required minimum volume of methanol was adsorbed on montmorillonite K10 clay and the solvent was allowed to evaporate off at room temperature. The reaction mixture was kept at 80°C in an oven until completion of the reaction. Leaching of the clay with dichloromethane furnished 3-thiocyanatoindole **2a**[3a,c] in a very good yield. This method was applied to a number of other 3-unsubstituted indoles **1b**–**f** and the reaction succeeded in all cases.[5] The indole



Scheme 1.

Keywords: thiocyanation; indoles; carbazoles; montmorillonite clay; ammonium thiocyanate.

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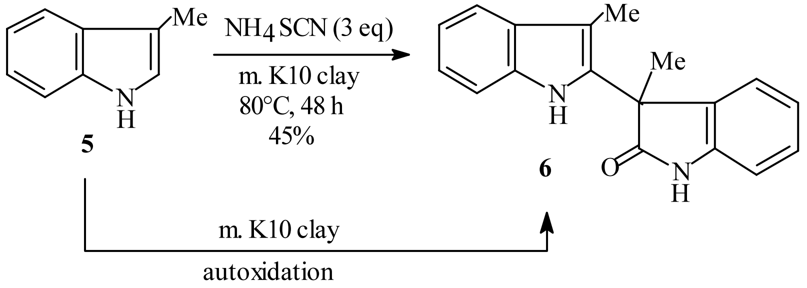
Table 1. Thiocyanation of indoles (**1a**–**f**) and carbazoles (**3a**–**c**) with NH_4SCN (3 equiv.) on montmorillonite K10 clay at 80°C

Entry	Substrate[a]	X	R	R′	Product	Time (h)	Yield (%)[b]
1	**1a**	H	H	H	**2a**[3a,c] (Lit.[3a] mp 76.5–78°C)	2	85
2	**1b**	H	H	Me	**2b**[3c]	3	92
3	**1c**	H	Me	H	**2c**[3c]	2.5	89
4	**1d**	Br	H	H	**2d**	2	80
5	**1e**	OMe	H	H	**2e**	2	90
6	**1f**	NO_2	H	H	**2f**[6]	4	89
7	**1g**[c]	H	Ac	H	–	24	–
8	**3a**	–	H	H	**4a**[7]	8	72
9	**3b**	–	Me	H	**4b**	10	65
10	**3c**	–	H	Me	**4c**	8	80
11	**5**	–	–	–	**6**[8] (Lit. mp 222–224°C)	48	45

[a] 1 mmol of substrates was used.

[b] Isolated yields. No attempt was made to optimise the yields.

[c] No reaction took place.



Scheme 2.

1f required a somewhat longer period to furnish **2f**,[6] which is clearly due to the electron-withdrawing effect of the nitro group. This effect was confirmed when *N*-acetylindole **1g** failed to undergo thiocyanation even after a prolonged period. The reaction was then extended to carbazoles **3a**–**c** when the 3-thiocyanatocarbazoles **4a**–**c**[7] were obtained in good yields. The reactions are shown in Scheme 1 and the results in Table 1. The isolation of the products involved an easy work-up, as in case of indole itself.

Skatole (**5**) behaved differently. Similar treatment required the unusually long period of 48 h for completion and furnished the dimer **6**, instead of the expected 2-thiocyanato derivative (Scheme 2). This dimer may be considered to have been formed by the autoxidation of **5**, since skatole alone, when similarly adsorbed on montmorillonite K10 clay and heated at 80°C, furnished **6** as the only product. This dimer has been reported earlier having been formed from skatole and *N*-chlorosuccinimide.[8]

To conclude, we have developed the first solvent-free protocol for a simple but effective thiocyanation of indoles and carbazoles, which is mild, clean, does not employ any toxic reagent and furnishes the thiocyanates in good to high yields following a simple isolation procedure. Indoles and carbazoles constitute core units of numerous biologically active compounds. Since the thiocyanates can be converted into mercaptans, sulphonic acids, sulfides, disulfides, thiocarbonic acid amides, etc., this eco-friendly thiocyanation procedure can be employed for synthesising sulphur-bearing condensed indoles and carbazoles.

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5. *General procedure for thiocyanation*: A solution of indoles/carbazoles (1 mmol) and NH_4SCN (3 mmol) in MeOH (2 ml) was adsorbed on montmorillonite K10 clay (2 g) and the methanol was allowed to evaporate off at room temperature when the clay turned reddish brown in colour. The clay with substrates adsorbed was kept at 80°C until completion of the reaction (TLC). The clay was then leached with CH_2Cl_2 (3×10 ml) and the products were purified by crystallisation. Of the products, only **2a**–**c** and **6** are known. All products were identified by IR, LR EI-MS, elemental analysis, ^1H (500 MHz), ^{13}C (125 MHz) and DEPT 135 NMR spectra.
6. **2f**: Yellow fluffy flakes, mp 210–212°C (CH_2Cl_2); IR (Nujol): 3370, 2163 (SCN), 1527 and 1328 (NO_2), 1083, 738 cm^{-1}; ^1H NMR (DMSO-d_6): δ 12.61 (1H, br s), 8.52 (1H, d, $J=2$ Hz), 8.26 (1H, s), 8.12 (1H, dd, $J=9$, 2 Hz), 7.70 (1H, d, $J=9$ Hz); ^{13}C NMR: δ 143.0, 140.3, 127.7, 112.7, 94.0 (all C), 137.9, 119.0, 115.2, 114.5 (all CH); MS: m/z 219 (M^+; 100%), 173 (65), 146 (54), 119 (26).
7. **4a**: Pale yellow needles, mp 98–100°C (CH_2Cl_2–petroleum ether); IR (Nujol): 3416, 2150 (SCN), 1600, 758 cm^{-1}; ^1H NMR (DMSO-d_6): δ 8.34 (1H, br s), 8.24 (1H, s), 8.02 (1H, d, $J=8$ Hz), 7.54 (1H, dd, $J=8.5$, 1.5 Hz), 7.48 (1H, d, $J=8$ Hz), 7.45 (1H, t, $J=8$ Hz), 7.39 (1H, d, $J=8.5$ Hz), 7.29 (1H, t, $J=7.5$ Hz); ^{13}C NMR: δ 140.5, 140.3, 125.2, 122.5, 113.0, 112.5 (all C), 130.0, 127.5, 125.6, 121.0, 120.8, 112.7, 111.4 (all CH); MS: m/z 224 (M^+; 100%), 197 (16), 191 (47).

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