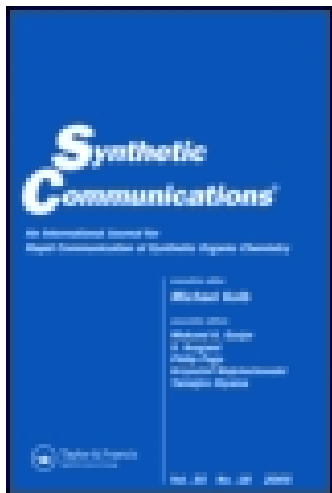


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A Convenient Synthesis of Isothiocyanates from Primary Nitroalkanes

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A CONVENIENT SYNTHESIS OF ISOTHIOCYANATES FROM PRIMARY NITROALKANES

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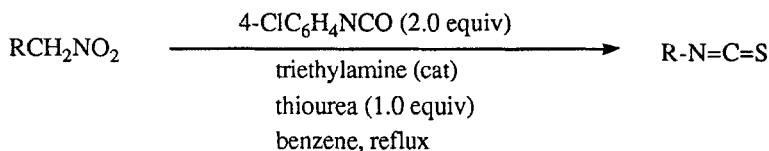
ABSTRACT: The reaction of primary nitroalkanes with thiourea in the presence of 4-chlorophenyl isocyanate and a catalytic amount of triethylamine in benzene afforded isothiocyanates in moderate yields.

Primary nitroalkanes are important synthetic intermediates in organic synthesis particularly in nitrile oxide chemistry.¹ These compounds can be converted to nitrile oxides *in situ* in the presence of dipolarophiles with phenyl isocyanates^{2a} (or more effectively with 4-chlorophenyl isocyanate^{2b}) and a catalytic amount of triethylamine. Recently we have reported on the efficient synthesis of isothiocyanates from the reaction of nitrile oxides and thiourea.³ Thus we examined the feasibility of converting primary nitroalkanes into isothiocyanates in a one-pot process.

The reaction of primary nitroalkanes with thiourea (1.0 equiv) in the presence of 4-chlorophenyl isocyanates (2.0 equiv) and a catalytic amount of

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triethylamine in benzene afforded the corresponding isothiocyanates in moderate yields as shown in **Scheme 1** and the results are summarized in **Table 1**.



Scheme 1

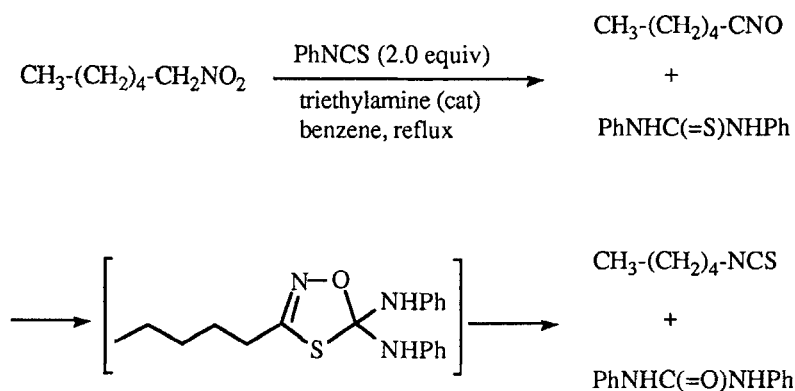
Table 1. Synthesis of Isothiocyanates from Primary Nitroalkanes.

Entry	R	Time (h)	Yield (%) ^a
1	<i>n</i> -butyl	5	75
2	<i>n</i> -amyl	5	90
3	C ₆ H ₅ -	5	65
4	2-ClC ₆ H ₄ -	5	60
5	4-MeC ₆ H ₄ -	5	63
6	C ₆ H ₅ CH ₂ -	5	73
7	<i>t</i> -BuPh ₂ SiOCH ₂ -	12	38
8	PhCH(O- <i>n</i> Pr)-	12	- ^b
9	PhCH(SBn)-	12	- ^b

a) Isolated yields of pure products. b) We could not isolate the corresponding isothiocyanates in appreciable amounts.

The reaction might proceed in a consecutive three-step process: 1) dehydration of primary nitroalkanes to nitrile oxides by 4-chlorophenyl isocyanate and catalytic triethylamine, 2) [3+2] cycloaddition reaction of nitrile oxides with thiourea to form the unstable 1,4,2-oxathiazoline derivatives,⁴ and 3) decomposition

of the intermediates to isothiocyanates and urea. As shown in **Table 1**, the reaction of normal carbon-linked primary nitroalkanes (entries 1-6) gave moderate yields of the corresponding isothiocyanates. However, in the case where there is a heteroatom in the β -position (entries 7-9), the reaction found to be not effective to produce isothiocyanates. The reason is not clear, however, it seemed like that the final rearrangement step of the generated 1,4,2-oxathiazoline derivative might be ineffective due to the inductive effect of the heteroatom to cause the migrating R group electron-deficient, which is unfavorable in such a 1,2-shift that involving nitrene-like intermediate.⁵



Scheme 2

We examined the possibility of converting 1-nitrohexane into *n*-amyl isothiocyanate by phenyl isothiocyanate (2.0 equiv) and a catalytic amount of triethylamine as shown in **Scheme 2**. However, the reaction is far less effective than the normal process discussed above, thus we could detect *n*-amyl isothiocyanate in 22 % yield on GC after refluxing in benzene during 24 h.

EXPERIMENTAL

¹H NMR spectra were recorded on a Varian Gemini-200 NMR spectrometer.

Mass spectra were recorded with a Shimadzu QP 1000 spectrometer.

A representative example is as follows. To a stirred solution of 1-nitrohexane (1.31 g, 10 mmol) and 4-chlorophenyl isocyanate (3.08 g, 20 mmol) in dry benzene (40 mL) was added thiourea (770 mg, 10 mmol) and triethylamine (5 drops). The reaction mixture was refluxed during 5 h, and cooled to room temperature. After diluting with hexane (100 mL) solid materials were filtered off. The filtrates were washed with water (100 mL), 1 N HCl solution (2 x 100 mL), and brine (100 mL), dried over MgSO₄. Removal of solvents gave the desired product which was purified by flash chromatography (hexane / ether, 4:1) to afford *n*-amyl isothiocyanate as a colorless oil, 1.16 g (90 %); ¹H NMR (CDCl₃) δ 0.92 (t, J = 6.9 Hz, 3H), 1.20-1.50 (m, 4H), 1.55-1.80 (m, 2H), 3.50 (t, J = 6.7 Hz, 2H); MS (20 eV) m/z (rel intensity) 43 (97), 55 (35), 96 (31), 101 (100), 114 (31), 129 (M⁺, 74).

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