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A FACILE SYNTHESIS OF 1-CYCLOALKENYL ISOTHIOCYANATES WITH SILICON TETRAISOTHIOCYANATE

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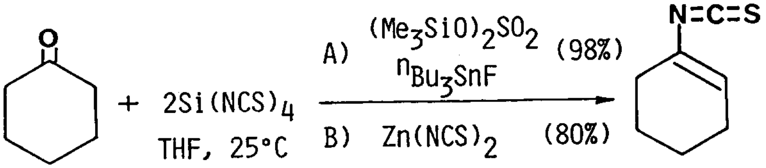
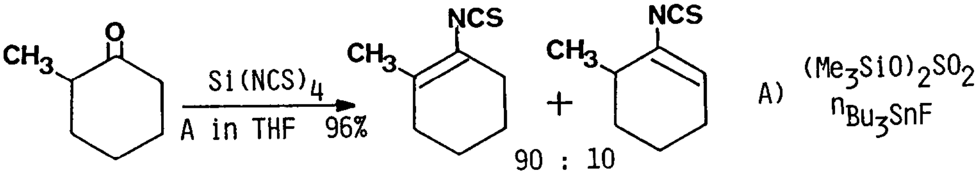
Abstract: The reaction of cycloalkanones with silicon tetraisothiocyanate in the presence of $(Me_3SiO)_2SO_2$-$^nBu_3SnF$ or $Zn(NCS)_2$ provides 1-cycloalkenyl isothiocyanates in good yields under mild conditions.

Isothiocyanates are reactive and important starting materials for the synthesis of a variety of organic compounds, especially heterocycles.[1] Here we wish to report that $Si(NCS)_4$[2] reacts with cycloalkanones in the presence of $(Me_3SiO)_2SO_2$[3]-$^nBu_3SnF$ or $Zn(NCS)_2$ to give 1-cycloalkenyl isothiocyanates in good yields, which are not easily accessible by known methods.[4]



Analogous reagents $MeSi(NCS)_3$, $Me_2Si(NCS)_2$, and Me_3SiNCS[2] proved to be less effective as compared to $Si(NCS)_4$. Heating a THF solution of cyclohexanone and $Si(NCS)_4$ without any catalysts gave no desired cyclohexenyl isothiocyanate and cyclohexanone was recovered unchanged. Among many catalysts examined, a combination of $(Me_3SiO)_2SO_2$-$^nBu_3SnF$ (method A) and $Zn(NCS)_2$ (method B) were found to be effective for the preparation of title compounds. KF, CsF, or $^nBu_4NF$ could be used instead of $^nBu_3SnF$ in the former case. Lewis acids such as $ZnBr_2$ and $EtAlCl_2$ were marginal[5] and $TiCl_4$ and $BF_3 \cdot OEt_2$ were ineffective. The choice of the solvent was also critical for the successful reactions. For instance, yields of 1-cycloheptenyl isothiocyanate[6] in the $(Me_3SiO)_2SO_2$-$^nBu_3SnF$ catalyzed reaction of cycloheptanone in various solvents were as follows: CH_2Cl_2, 25%[7]; $CHCl_3$, 12%[7]; THF, 49%; dioxane, 76%; dimethoxyethane (DME), 80%. Other cycloalkanones reacted similarly and 1-cyclopentenyl[8], cyclooctenyl[9], and cyclododecenyl isothiocyanate[10] were produced in 52%, 66%, and 77% yields, respectively under $Zn(NCS)_2$ catalyzed reaction in DME (method B).

Stereoselectivity was examined using 2-methylcyclohexanone as a substrate. 2-Methyl-1-cyclohexenyl isothiocyanate was obtained as a major product along with a regio isomer, 6-methyl-1-cyclohexenyl isocyanate.



A typical procedure: Synthesis of 1-cyclohexenyl isothiocyanate (Method A).

Cyclohexanone (0.10 ml, 1.0 mmol) was added to a THF solution of $Si(NCS)_4$ (0.52 g, 2.0 mmol), $(Me_3SiO)_2SO_2$ (24 mg, 0.10 mmol) and $^nBu_3SnF$ (31 mg, 0.10 mmol) at 25°C under argon atmosphere. After being stirred for 1 h, the mixture was successively treated with ether (20 ml), Na_2HPO_4 (1.0 g) and aqueous saturated Na_2SO_4 (1.0 ml). The resulting mixture was stirred for another 15 min and filtered. Combined filtrate and washings were dried (Na_2SO_4) and concentrated *in vacuo*. Purification by silica gel column chromatography (hexane) gave 1-cyclohexenyl isothiocyanate[4a] (0.15 g, 98% yield) as a colourless oil. In method B, $Zn(NCS)_2$ (18 mg, 0.1 mmol) was used instead of $(Me_3SiO)_2SO_2$-$^nBu_3SnF$.

References and Notes

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5. The yields of 1-cyclohexenyl isothiocyanate were 30% ($ZnBr_2$) and 40% ($EtAlCl_2$), respectively in THF.
6. Bp. 87-93°C (bath temperature)/12 Torr; ^1H-NMR (CCl_4) δ 1.3-1.9 (m, 6H), 1.9-2.3 (m, 4H), 2.3-2.6 (m, 4H), 5.78 (t, *J* = 7 Hz, 1H); IR (neat) 2890, 2040, 1635, 1440 cm^{-1}; MS (rel intensity) m/z 153 (M^+, 65), 135 (16), 95 (100), 67 (38), 53 (14). Found: C, 62.98; H, 7.29%. Calcd for $C_8H_{11}NS$: C, 62.70; H, 7.23%.
7. Cycloheptylidenediisothiocyanate was obtained in 43% (CH_2Cl_2) and 70% ($CHCl_3$) yields, respectively in addition to the isothiocyanate.
8. Bp. 52-58°C (bath temperature)/14 Torr; ^1H-NMR (CCl_4) δ 5.87 (m, 1H); IR (neat) 2030, 1620 cm^{-1}. Found: C, 57.55; H, 5.61; N, 11.09%. Calcd for C_6H_7NS: C, 57.57; H, 5.64; N, 11.19%.
9. Bp. 75-83°C (bath temperature)/3 Torr; ^1H-NMR (CCl_4) δ 5.60 (t, *J* = 8 Hz, 1H); IR (neat) 2050, 1635 cm^{-1}. Found: C, 64.69; H, 8.05; N, 8.36%. Calcd for $C_9H_{13}NS$: C, 64.63, H, 7.83, N, 8.37%.
10. Bp. 61-67°C (bath temperature)/0.2 Torr; ^1H-NMR (CCl_4) δ 5.23 (t, *J* = 8 Hz, 1H)); IR (neat) 2040, 1640 cm^{-1}. Found: C, 70.18; H, 9.73; N, 6.33%. Calcd for $C_{13}H_{21}NS$: C, 69.90; H, 9.48; N, 6.27%.

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