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Preparation of Alkyl Thiocyanates by Electrochemical Oxidation of Thiocyanate Ion in the Presence of Alcohols and Triphenylphosphite

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Conversion of primary alcohols to the corresponding thiocyanates was effected by constant-current electrolysis of thiocyanate ion in dichloromethane containing an alcohol, triphenylphosphite, and 2,6-lutidinium perchlorate or tetrafluoroborate. The electrolysis was performed at ambient temperature in a one-compartment cell using a graphite plate and a platinum plate as the anode and the cathode, respectively. 2,6-Lutidinium cation effectively extracted thiocyanate ion into the organic phase from sodium thiocyanate suspended in the reaction mixture.

Keywords alkyl thiocyanate; primary alcohol; sodium thiocyanate; triphenylphosphite; electrochemical oxidation; cyclic voltammetry; anodic oxidation

The reaction of alkyl halides with metal thiocyanates may be the most practical way to obtain alkyl thiocyanates, which are useful synthetic intermediates.[1] Recently, however, an elegant transformation of alcohols to the corresponding thiocyanates by use of a combined reagent generated *in situ* from $\mathrm{Ph_3P}$ and $\mathrm{(SCN)_2}$ has been reported.[2] The reagent has also been shown to be useful for the preparation of indole and pyrrole carbonitriles and other synthetically interesting compounds.[2,3] As a continuation of our studies on anodic oxidation involving trivalent phosphorus compounds,[4] an electrochemical modification of the method was attempted. Electrochemical oxidation of $\mathrm{SCN^-}$ is known to give $\mathrm{(SCN)_2}$,[5] and the amount of the latter in a particular medium can be controlled easily by changing the current density. Thus, the conversion of alcohols to alkyl thiocyanates was expected to be feasible at ambient temperature rather than at the low temperature (−40 °C) employed in the reported method.[2] In the electrochemical method, use of $\mathrm{(PhO)_3P}$ in place of $\mathrm{Ph_3P}$ was found to be favorable for the conversion.

Results and Discussion

Benzyl alcohol was selected as a model compound, and its conversion to the thiocyanate was examined first. Table I summarizes the results of constant-current electrolysis (CCE) performed on a mixture of NaSCN, the alcohol, a phosphine or a phosphite, and 2,6-lutidinium perchlorate or tetrafluoroborate ($\mathrm{LutClO_4}$ or $\mathrm{LutBF_4}$) in MeCN or $\mathrm{CH_2Cl_2}$. As the solvent, $\mathrm{CH_2Cl_2}$ seems superior to MeCN (*cf.* runs 1 and 2), probably because the amout of water contaminating the medium is smaller in the former.[6] Although NaSCN alone is practically insoluble in $\mathrm{CH_2Cl_2}$, $\mathrm{SCN^-}$ is extracted into the solvent by the action of 2,6-lutidinium cation (see below). Among the phosphorus compounds employed, $\mathrm{(PhO)_3P}$ appeared to be the reagent of choice.

CCE of $\mathrm{SCN^-}$ in the presence of various alcohols was attempted under the conditions giving the best yield of benzyl thiocyanate (Table I, run 11). Primary alcohols were converted to the corresponding thiocyanates in fair to good yields (Table II). The result on PhCHMeOH suggests that the CCE method can also be applied to secondary alcohols, but no thiocyanate formation was detected from the tertiary alcohols, $\mathrm{PhCMe_2OH}$ and $\mathrm{Me_3COH}$. These results are comparable to those obtained with the $\mathrm{Ph_3P}$–$\mathrm{(SCN)_2}$ system,[2] where $\mathrm{(SCN)_2}$ is generated from $\mathrm{Pb(SCN)_2}$ and $\mathrm{Br_2}$ at −40 °C.

On cyclic voltammetry in MeCN, $\mathrm{SCN^-}$ (dissolved as NaSCN) showed an anodic peak at 0.70 V *vs.* S.C.E. (Fig. 1). Upon reversal of the sweep direction, a cathodic peak was observed at 0.35 V, which coincided with the reduction peak of $\mathrm{(SCN)_2}$ (not shown) prepared separately by the reported method.[2] The observed voltammetric behavior does not conflict with the results reported previously.[5] The cathodic peak disappeared in the presence of $\mathrm{Ph_3P}$ or $\mathrm{(PhO)_3P}$ (Fig. 1), indicating that $\mathrm{(SCN)_2}$ reacts rapidly with the phosphorus compounds. Figure 2 illustrates the extraction of $\mathrm{SCN^-}$ from suspended NaSCN into $\mathrm{CH_2Cl_2}$ by 2,6-

TABLE I. Results on CCE of a Mixture of $\mathrm{R_3P}$, NaSCN, $\mathrm{PhCH_2OH}$, and LutX

Run	$\mathrm{R_3P}$	Solvent	Electrolysis (current/mA)	X in LutX	Yield (%)[c] of $\mathrm{PhCH_2SCN}$
1[a]	$\mathrm{Ph_3P}$	MeCN	60	$\mathrm{ClO_4}$	32
2[a]	$\mathrm{Ph_3P}$	$\mathrm{CH_2Cl_2}$	60	$\mathrm{ClO_4}$	42
3[a]	$\mathrm{Ph_3P}$	$\mathrm{CH_2Cl_2}$	60	$\mathrm{BF_4}$	50
4[a]	$\mathrm{Ph_3P}$	$\mathrm{CH_2Cl_2}$	15	$\mathrm{BF_4}$	26
5[a]	$\mathrm{Ph_3P}$	$\mathrm{CH_2Cl_2}$	30	$\mathrm{BF_4}$	60
6[a]	$\mathrm{Ph_3P}$	$\mathrm{CH_2Cl_2}$	120	$\mathrm{BF_4}$	39
7[a]	$\mathrm{Bu_3P}$	$\mathrm{CH_2Cl_2}$	30	$\mathrm{BF_4}$	36
8[a]	$\mathrm{(EtO)_3P}$	$\mathrm{CH_2Cl_2}$	30	$\mathrm{BF_4}$	47
9[a]	$\mathrm{(PhO)_3P}$	$\mathrm{CH_2Cl_2}$	30	$\mathrm{BF_4}$	63
10[b]	$\mathrm{Ph_3P}$	$\mathrm{CH_2Cl_2}$	30	$\mathrm{BF_4}$	51
11[b]	$\mathrm{(PhO)_3P}$	$\mathrm{CH_2Cl_2}$	30	$\mathrm{BF_4}$	*ca.* 100[d]

a) $\mathrm{R_3P}$, 3.4 mmol; NaSCN, $\mathrm{PhCH_2OH}$, and LutX, 6.8 mmol each; solvent, 35 ml. *b)* $\mathrm{R_3P}$, 11 mmol; NaSCN, $\mathrm{PhCH_2OH}$, LutX, 22 mmol each; solvent 35 ml. *c)* Based on the amount of $\mathrm{R_3P}$: determined by GLC. *d)* Essentially the same result was obtained by the use of $\mathrm{LutClO_4}$.

TABLE II. Preparation of R′-SCN from R′-OH[a]

R′	Yield (%)[b] of R′-SCN	R′	Yield (%)[b] of R′-SCN
$\mathrm{PhCH_2}$–	99	$\mathrm{CH_3(CH_2)_5}$–	63[c]
p-F-$\mathrm{PhCH_2}$–	75	$\mathrm{PhCH{=}CHCH_2}$–	52[c,d]
p-MeO-$\mathrm{PhCH_2}$–	89	$\mathrm{PhCH(CH_3)}$–	60[e]
Furfuryl–	36	$\mathrm{PhC(CH_3)_2}$–	0[f]
$\mathrm{PhCH_2CH_2}$–	31[c]	$\mathrm{(CH_3)_3C}$–	0
$\mathrm{CH_3(CH_2)_{11}}$–	76[c]		

a) A mixture of $\mathrm{(PhO)_3P}$, R′–OH, $\mathrm{LutClO_4}$, and NaSCN in $\mathrm{CH_2Cl_2}$ was subjected to CCE (general procedure, see Experimental). *b)* Isolated yield based on $\mathrm{(PhO)_3P}$. *c)* $\mathrm{LutBF_4}$ was used in place of $\mathrm{LutClO_4}$. *d)* $\mathrm{PhCH{=}CHCH_2}$–NCS (23%) was also obtained. *e)* $\mathrm{PhCH(CH_3)}$–NCS (3%) was also obtained. *f)* $\mathrm{PhC(CH_3)_2}$–NCS (24%) was obtained.

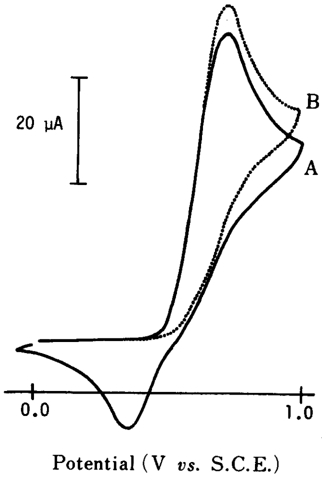

Fig. 1. Cyclic Voltammograms of SCN^-

(A) NaSCN (4.9 mM) in MeCN containing 0.1 M $LutClO_4$; (B) A+$(PhO)_3P$ (4.3 mM). At a glassy carbon electrode (geometric area, 0.07 cm^2); voltage sweep rate, 50 mV/s; at 27 °C.

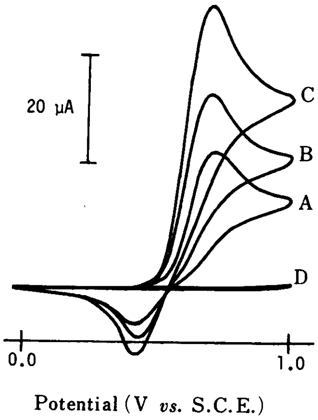

Fig. 2. Extraction of SCN^- into CH_2Cl_2

Suspensions of NaSCN (6.5 mmol) in CH_2Cl_2 (10 ml) containing 0.1 M $LutClO_4$ were stirred for (A) 5 min, (B) 15 min, (C) 60 min, and (D) in CH_2Cl_2 without $LutClO_4$ for 60 min. Each of the mixtures, after being filtered and diluted 200-fold with MeCN containing 0.1 M $LutClO_4$, was subjected to cyclic voltammetry: at a glassy carbon electrode; voltage sweep rate, 50 mV/s; at 27 °C.

lutidinium cation. Suspensions of NaSCN in CH_2Cl_2 containing 0.1 M $LutClO_4$ were stirred at ambient temperature for periods of up to 1 h. Each of the mixtures was filtered at appropriate time intervals, and the filtrate was diluted 200-fold with MeCN containing 0.1 M $LutClO_4$. A cyclic voltammogram of the resulting solution showed a peak due to the oxidation of SCN^-, which increased with the period of stirring (Fig. 2, A—C). No voltammetric peak was appeared when $LutClO_4$ was absent in the original suspension in CH_2Cl_2 (Fig. 2, D).

In the Ph_3P–$(SCN)_2$ system, a phosphonium salt of type $[Ph_3P^+\text{-}N=C=S]SCN^-$ has been suggested to exist as the thiocyanating agent, which then reacts with an alcohol (R′-OH) to afford R′-SCN and/or R′-NCS *via* the alkoxy phosphonium salt $[Ph_3P^+\text{–}OR']SCN^-$.[3a,7] Since the generation of $(SCN)_2$ occurs in the present electrochemical system, intermediacy of a similar phosphonium salt $[(PhO)_3P^+\text{-}N=C=S]SCN^-$ can be considered in the alkyl thiocyanate formation.

Although the Ph_3P–$(SCN)_2$ system has also been effective for the cyanation of indoles and pyrroles,[3a] the electrochemical $(PhO)_3P$–$(SCN)_2$ system was not effective. For example, a similar electrolysis in the presence of 2-methylindole gave 2-methyl-3-thiocyanoindole (36%) but no cyanated product. The thiocyanated indole (47%) was obtained simply by electrolysis without $(PhO)_3P$.[8] When Ph_3P was used in place of $(PhO)_3P$, 3-cyano-2-methylindole was actually formed, but in a low yield (21%). These results suggest that $(PhO)_3P$ is a weaker nucleophile toward $(SCN)_2$ than indoles and the application of the electrochemical $(PhO)_3P$–$(SCN)_2$ system is rather limited. However, the CCE method seems useful at least for the preparation of primary and secondary alkyl thiocyanates, because it can be conducted under a normal atmosphere and at ambient temperature.

Experimental

The CCE was performed using a Hokuto Denko HA-301 potentiostat/galvanostat, but the use of a conventional DC power supply (50 V—2A) also seems to be effective. A 50 ml sample tube (diameter, 3.5 cm; height, 7.5 cm) was employed as the electrolysis cell, which was equipped with a graphite plate anode (2 × 10 cm) and a platinum plate cathode (1 × 10 cm) through a silicon stopper. Cyclic voltammetry was carried out as described previously.[9]

Melting points and boiling points are uncorrected. Infrared (IR) and proton nuclear magnetic resonance (^{1}H-NMR) spectra were recorded on JASCO A-202 and Hitachi R-22 spectrometers, respectively.

Materials Phosphines and phosphites were purified either by distillation or recrystallization, and alcohols were obtained from commercial sources and were purified, if necessary, by conventional methods. $LutClO_4$ and $LutBF_4$ were prepared as described previously.[10] MeCN was purified by the method of Kiesele,[11] and CH_2Cl_2 was distilled from P_2O_5. NaSCN was of reagent grade, and was used without further purification.

General Procedure for the Runs in Table II A solution of $(PhO)_3P$ (11 mmol), an alcohol (22 mmol), and $LutClO_4$ or $LutBF_4$ (22 mmol) in CH_2Cl_2 (35 ml) with suspended NaSCN (22 mmol) was subjected to CCE (30 mA; current density, *ca.* 1 mA/cm^2) in the electrolysis cell at ambient temperature until 2 F per mol of the phosphite had been consumed (590 min). The solvent in the electrolyzed mixture was removed under reduced pressure. Water (50 ml) was added to the residue and the mixture was extracted with $CHCl_3$ (3 × 50 ml). The organic layer, after being dried over anhydrous $MgSO_4$, was evaporated under reduced pressure. The residue was subjected to column chromatography on silica gel with hexane–AcOEt (20 : 1) as an eluant to give the products.

The physical data for R′-SCN are given in the following order: R′-, bp (°C/mmHg) [lit.] or mp (°C) (solvent) [lit.]; IR $\nu_{max}^{CHCl_3}$ cm^{-1} ; ^{1}H-NMR ($CDCl_3$) δ. $PhCH_2$-, 39.5—40 (hexane) [41—42.5][2]; 2165; 4.17 (2H, s), 7.34 (5H, s). *p*-F-$PhCH_2$-, 129.5/8; 2175; 4.11 (2H, s), 6.96—7.45 (4H, m). *p*-MeO-$PhCH_2$-, 132—134/2 [135—139/0.7][2]; 2175; 3.78 (3H, s), 4.11 (2H, s), 6.80—6.96 (2H, m), 7.26—7.34 (2H, m). Furfuryl-, 100—103/15 [105—108/14][2]; 2165; 4.18 (2H, s), 6.28—6.48 (2H, m), 7.36—7.50 (1H, m). $PhCH_2CH_2$-, 149/12 [161—165/20][2]; 2175; 3.06 (4H, s), 7.05—7.44 (5H, m). $CH_3(CH_2)_{11}$-, 163—166/10 [170—175/10][2]; 2175; 0.75—2.08 (23H, m), 2.94 (2H, t, J=7 Hz). $CH_3(CH_2)_5$-, 106/17; 2160; 0.68—2.15 (11H, m), 2.94 (2H, t, J=7 Hz). $PhCH=CHCH_2$-, 72—72.5 (ether) [71.5—72.5][2]; 2175; 3.71 (2H, d, J=7 Hz), 6.20 (1H, dt, J=16, 7 Hz), 6.66 (1H, d, J=16 Hz), 7.18—7.82 (5H, m). $PhCH(CH_3)$-, 103—105/5; 2175; 1.88 (3H, d, J=7 Hz), 4.60 (1H, q, J=7 Hz), 7.34 (5H, s).

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