The Reactions of Carbonimidoyl Dichlorides with Metal Thioacetates, Acetates, Thiocyanates, and Selenocyanate

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The reactions of carbonimidoyl dichlorides with potassium thioacetate and thiocyanate in tetrahydrofuran afford the corresponding isothiocyanates. Similarly, the reaction with potassium selenocyanate gives isoselenocyanates. Thallium(I) acetate reacts with phenylcarbonimidoyl dichloride with greater facility than potassium acetate to give a mixture of phenyl isocyanate and acetanilide in which the latter is predominant. A displacement of one chlorine atom in the carbonimidoyl dichlorides by a SAc, OAc, SCN, or SeCN group, followed by elimination of AcCl or CNCl, has been proposed as a reasonable reaction path.

The carbonimidoyl dichlorides can be used as starting materials for the preparation of many types of organic substances.[1] As one of a series of studies on carbonimidoyl dichlorides[2] and isocyanides,[3] we now report the results of the reactions of phenyl- and cyclohexylcarbonimidoyl dichlorides (hereinafter abbreviated as PCD and CCD respectively) with various metal thioacetates, acetates, and thiocyanates, as well as with potassium selenocyanate. Although the substitution reactions of imidoyl chlorides and their derivatives with metal acetates,[4] thioacetates,[4] and thiocyanates[5] have been reported, information about similar reactions on carbonimidoyl dichlorides is rare.

Results and Discussion

Reactions with Metal Thioacetates and Acetates (Table 1). The heterogeneous reaction of PCD or CCD with two equivalents of KSAc in tetrahydrofuran (THF) proceeded smoothly at room temperature to give the corresponding isothiocyanate in a fair yield without affoding any other organic products except for acetic thioanhydride (runs 3 and 4). In the case of 1 : 1 molar ratio, nearly 50% of the dichloride (PCD) or more was recovered, though the yield based on the consumed dichloride was nearly quantitative (runs 1 and 2). Thus the reaction appeared to occur in accord with the stoichiometry shown in Scheme 1 (Z=S):

$$\begin{matrix} \text{R–N=CCl}_2 + 2\text{CH}_3\text{COZM} \longrightarrow \\ \text{PCD (R=Ph)} \\ \text{CCD (R=}\textit{cyclo}\text{-C}_6\text{H}_{11}\text{)} \end{matrix} \qquad \begin{matrix} \text{R–N=C=Z} + (\text{CH}_3\text{CO})_2\text{Z} + 2\text{MCl} \quad (1) \\ (\text{Z=S or O}) \end{matrix}$$

With TlSAc, probably less ionized than KSAc, the reaction was sluggish and was brought to completion by heating (run 5).

In a similar way, PCD reacted with two equivalents of metal acetates in boiling THF to give a mixture of phenyl isocyanate and acetanilide in which the latter was predominant; the combined yield was nearly quantitative (based on the consumed dichloride), but no acetic anhydride could be found in the reaction products. In order to examine whether acetanilide is formed by the reaction of phenyl isocyanate with acetic anhydride under the reaction conditions, some controlled

TABLE 1. REACTIONS OF RN=CCl$_2$ WITH METAL THIOACETATES AND ACETATES[a]

Run	Metal salt	(mmol)	Temp (°C)	Time (h)	Products and yield (%)[b] RN=CCl$_2$	RN=C=Z	PhNHCOCH$_3$
1	KSAc	5	20	3	61	39[c]	—
2	KSAc	5	20	22	48	52[c]	—
3	KSAc	10	20	3	0	92[c]	—
4[d]	KSAc	10	20	24	29[d]	65[c,d]	—
5	TlSAc	10	68	3	27	70[c]	—
6	KOAc	10	68	3	73	trace[e]	13[f]
7	KOAc	2[g]	68	3	0	9[e]	75[f]
8	TlOAc	5	68	3	49	4[e]	45
9	TlOAc	10	68	3	18	4[e]	75
10	TlOAc	2[g]	68	3	0	0	95
11	AgOAc	10	68	3	90	0	10
12	AgOAc	2[g]	68	3	49	trace[e]	51
13	HgOAc	10	68	3	76	trace[e]	19

a) RN=CCl$_2$ (5 mmol; R=Ph) and THF (10 ml) were used unless otherwise stated. b) Determined by GLC; Based on RN=CCl$_2$. c) Z=S. d) R=*cyclo*-C$_6$H$_{11}$. e) Z=O. f) Other products; two unidentified compounds (*ca.* 3% each). g) PhN=CCl$_2$ 1 mmol; dicyclohexyl-18-crown-6 (2 mmol) was added.

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experiments were carried out. When either phenyl isocyanate or acetic anhydride was heated in THF (at 68 °C for 3 h), no appreciable change (including their hydrolysis) occurred in either case. However, when an equimolar mixture of these two compounds (5 mmol each) was similarly treated in the same solvent (10 ml), 14% of acetoanilide was produced; this was probably formed by the participation of external moisture (originated from the solvent, the acetate, and/or the atmosphere) in the reaction between two components. In this case considerable amounts of phenyl isocyanate and acetic anhydride remained unreacted, as opposed to the case of the dichloride-acetate reaction in which only 4% of the isocyanate and no acetic anhydride were found (see run 9). Though the reason for this disagreement is not clear at present, it may be possible that some acidic impurities formed during the course of the reaction accelerate the above acetanilide formation.

Further, it was found unexpectedly that in the reaction with metal acetates TlOAc (less ionized[6]) reacts more easily than KOAc (more ionized) (runs 9 *vs.* 6). In the case of other monovalent heavy-metal acetates such as Ag(I) and Hg(I), however, no such striking results were observed (runs 11 and 13). Since crown ethers have been known to increase the concentrations of "naked" anions by complexing with counter-cations, we also examined the reaction with metal acetates in the coexistence of dicyclohexyl-18-crown-6.[7] Considerable improvements in the yields were achieved in all cases, but it was insufficient in the case of AgOAc (runs 7, 10, and 12).

Next, we will briefly consider a probable reaction path for the above two reactions. It is known that the 1 : 1 molar reactions of carbonimidoyl dichlorides with alkoxide ions and amines afford the corresponding monosubstituted products in good yields.[1] In the present reactions, however, no detectable amounts of such products (**1**) were found in the reaction mixtures. This may suggest their rapid disappearance owing to some subsequent reaction. In connection with the present reactions, it has been reported that PCD reacts with acetic acid to afford phenyl isocyanate and acetyl chloride with generation of HCl.[8] It has also been reported that the reaction of PCD with ethanol affords *N*-phenylethylurethane with the liberation of HCl and ethyl chloride, suggesting the intermediacy of ethyl *N*-phenylchloroformimidate.[9] Based on these facts and the stoichiometry of the reactions, the following pathway would be highly probable:

$$R\text{-}N{=}CCl_2 \xrightarrow[-Cl^-]{CH_3COZ^-} \underset{\mathbf{1}}{\left[R\text{-}N{=}C(Cl)(ZCOCH_3)\right]} \xrightarrow[-CH_3COCl]{} R\text{-}N{=}C{=}Z \quad (2)$$

$$CH_3COCl + CH_3COZ^- \longrightarrow (CH_3CO)_2Z + Cl^- \quad (Z{=}S \text{ or } O)$$

There may be another route for RNCZ which involes further displacement of the intermediate **1** by CH_3COZ^- to give $R\text{-}N{=}C(ZCOCH_3)_2$ (**2**), followed by elimination of $(CH_3CO)_2Z$, especially in the thioacetate reaction, since AcS^- is known to be a stronger nucleophile than AcO^-.

We must add a short comment on the facile reaction with TlOAc in the absence of crown ether. We roughly compared the solubility of this salt in boiling THF with those of other acetates, but it appeared that no significant differences were present (*i.e.*, 0.012 mol/l for TlOAc, 0.016 mol/l for AgOAc, and 0.002 mol/l for KOAc). Besides, no variations in the yields were observed within the experimental error by changing the amount of the solvent by half or five times in the reactions with TlOAc or KOAc respectively. Thus it is clear that the rate of dissolution of metal acetates is not the dominant factor in affecting the reaction rate. Since the considerably covalent character of the Tl–O bonds of similar compounds has been recognized,[6] most of the dissolved TlOAc is expected to exist in un-ionized form. Thus, the contribution of a four-center-type reaction between un-ionized TlOAc and carbonimidoyl dichlorides affording **1** may be possible, though no direct evidence is available at present. Needless to say, when the crown ether is added to the reaction system, the attack of the "naked" OAc^- which is in equilibrium with the un-ionized species becomes predominant.

Reactions with Potassium Thiocyanate, Selenocyanate, and Cyanate (Table 2). When PCD was treated with two equivalents of KSCN in boiling THF, phenyl isothiocyanate was obtained (run 15). The yield was rather poor, and the reaction was accompanied with the formation of an unidentified yellow solid of which the

Table 2. Reactions of $RN{=}CCl_2$ with potassium thiocyanate and selenocyanate [KZCN(Z=S or Se)]

Run	$RN{=}CCl_2$ (mmol) R	KZCN (mmol) Z	Solvent (ml)	Temp (°C)	Time (h)	Products and Yield (%)[a] $RN{=}CCl_2$	Products and Yield (%)[a] $RN{=}C{=}Z$
14	Ph 5	S 5	THF 10	68	3	45	20[b]
15	Ph 5	S 10	THF 10	68	3	3	37[b]
16	Ph 10	S 10	EtOH 20	25	3	0	44[b]
17	Ph 5	S 10	EtOH 10	25	3	0	40[b]
18	Ph 5	Se 5	THF 10	68	3	45	32
19	Ph 5	Se 10	THF 10	68	3	8	58
20	*cyclo*-C_6H_{11} 5	Se 10	THF 10	68	3	34	37
21	*cyclo*-C_6H_{11} 5	Se 10	THF 10	68	9	10	44

a) Determined by GLC; based on $RN{=}CCl_2$. b) An unidentified yellow solid was also obtained.

IR spectrum did not show any absorptions due to –N=C=S or –S–C≡N groups.[10] Neither the improvement of the yield and the depression of the by-product formation could be achieved by changing molar ratios or solvents (*e.g.*, diglyme, acetone, ethanol, and *N,N*-dimethylformamide). In the case of ethanol solvent, phenyl isothiocyanate was obtained in a similar yield, but a larger amount of yellow solid was formed (runs 16 and 17, see also Experimental section). Since the displacement of one Cl atom in carbonimidoyl dichlorides by CN is known to be achieved by using CuCN, we examined the reaction between PCD and CuSCN in diglyme (at 162 °C for 1 h). The reaction with the Ag(I) or Hg(I) salts was also examined under similar conditions. However, the yield of phenyl isothiocyanate was quite poor (17—28%) in all cases.

The reaction of PCD or CCD with KSeCN, in which $SeCN^-$ is isoelectronic to SCN^-, gave the corresponding isoselenocyanate in a good yield, together with small amounts of an unidentified by-product (runs 19 and 21). The reaction with KOCN did not occur to any extent under similar conditions.

In view of the facts that the stoichiometry of the reaction with KSCN (runs 14 and 15) or KSeCN (runs 18 and 19) was the same as that of the reaction with KSAc or KOAc, a reaction path quite similar to Scheme 2 may be postulated in this case:

$$R\text{–}N{=}CCl_2 \xrightarrow[-Cl^-]{ZCN^-} \left[R\text{–}N{=}C\begin{matrix}Cl\\ \diagdown\\ \diagup\\ ZCN\end{matrix}\right] \xrightarrow{-ClCN} R\text{–}N{=}C{=}Z \qquad (3)$$

3

$$ClCN + ZCN^- \longrightarrow (CN)_2Z + Cl^- \quad (Z=S \text{ or } Se)$$

In connection with this, the following result is worth noting. In an attempt to prepare the compound **3** (Z=S) by the reaction of phenyl isocyanide with ClSCN (formed *in situ* from a mixture of $Pb(SCN)_2$ and $SbCl_5$[11]), phenyl isothiocyanate rather than **3** was obtained in 8.5% yield, in addition to a slight amount of PCD (1.4%) and considerable amounts of a tarry compound (mostly a polymer of the isocyanide). Here, it was confirmed that the isothiocyanate was not formed by the reaction of PCD or the isocyanide with $Pb(SCN)_2$.

Experimental

The IR and NMR spectra were recorded with a Hitachi EPI-S2 and a Varian EM-360 apparatus respectively. GLC analyses were carried out on a Shimadzu 5APTF apparatus, using Apiezon-L (30%)–Celite (1m) and EGSS-X (30%)–Chromosorb-W (1m) columns (N_2 as the carrier gas, iodobenzene as an internal standard).

Materials. Two carbonimidoyl dichlorides ($R\text{–}N{=}CCl_2$) were prepared by the method of Kühle *et al.*:[12] R=*cyclo*-C_6H_{11} (CCD), bp 88—91 °C/23 Torr (lit,[12] bp 79—82 °C/13 Torr); R=Ph (PCD), bp 79—80 °C/8 Torr (lit,[12] bp 83—85 °C/11 Torr). KSAc was prepared by the method of Barnish *et al.*[13] TlSAc was prepared from thioacetic S-acid and $Tl(OAc)_3$.[14] Other organic materials and solvents were purified before use by distillation. Commercial inorganic materials, except KSCN, were used without further purification. KSCN was used after drying at *ca.* 70 °C under reduced pressure.

Reaction of PCD with KSAc. To a stirred suspension of KSAc (1.14 g, 10 mmol) in THF (10 ml) was slowly added PCD (0.87 g, 5 mmol) at room temperature. The mixture was stirred for 3 h at 20 °C and then the precipitated inorganic salt was filtered off. GLC analysis of the filtrate showed the presence of 4.58 mmol (92% yield based on PCD) of phenyl isothiocyanate as a product. The distillation gave 0.52 g of phenyl isothiocyanate: the IR spectrum [2120 cm^{-1} ($\nu_{N=C=S}$)] and the retention time in GLC were identical with those of an authentic sample. The formation of acetic thioanhydride was also confirmed by the IR spectrum of the distillate.

Reaction of PCD with TlSAc. To a stirred suspension of TlSAc (2.79 g, 10 mmol) in THF (10 ml) was slowly added PCD (0.87 g, 5 mmol) at room temperature. The mixture was stirred for 3 h under reflux. After being cooled down to room temperature the precipitated inorganic salt was filtered off. GLC analysis of the filtrate showed the presence of 3.50 mmol (70% yield based on PCD) of phenyl isothiocyanate and unreacted PCD (1.36 mmol, 27%).

Reaction of CCD with KSAc. A mixture of CCD (0.90 g, 5 mmol) and KSAc (1.14 g, 10 mmol) was stirred in THF (10 ml) at 20°C for 24 h. GLC analysis of the filtrate showed the presence of cyclohexyl isothiocyanate (3.23 mmol, 65%) and unreacted CCD (1.47 mmol, 29%).

Reaction of PCD with KOAc. A mixture of PCD (0.87 g, 5 mmol) and KOAc (0.98 g, 10 mmol) was stirred in THF (10 ml) under reflux for 3 h. GLC analysis of the filtrate showed the presence of acetanilide(0.64 mmol, 13%), unreacted PCD (3.63 mmol, 73%), and small amounts of two unidentified compounds (*ca.* 3% each, as calculated from peak area in GLC).

Reaction of PCD with KOAc in the Presence of Crown Ether. A mixture of PCD (0.174 g, 1 mmol), KOAc (0.196 g, 2 mmol) and dicyclohexyl-18-crown-6 (0.745 g, 2 mmol) was stirred in THF (10 ml) under reflux for 3 h. GLC analysis of the filtrate showed the presence of phenyl isocyanate (0.09 mmol, 9%) and acetanilide (0.75 mmol, 75%).

Reaction of PCD with TlOAc. A mixture of PCD (0.87g, 5 mmol) and TlOAc (2.63 g, 10 mmol) in THF (10 ml) was stirred under reflux for 3 h. GLC analysis of the filtrate showed the presence of phenyl isocyanate (0.21 mmol, 4.2%), acetanilide (3.74 mmol, 75%), and unreacted PCD (0.9 mmol, 18%). The presence of phenyl isocyanate was also confirmed by the IR spectrum ($\nu_{N=C=O}$, 2250 cm^{-1}) of the residue after evaporation of the solvent from the filtrate. The distillation of the residue gave 0.32 g of crude acetanilide, which was recrystallized from aqueous ethanol: the IR and NMR spectra were identical with those of an authentic sample.

Reaction of PCD with KSCN. A mixture of PCD (0.87 g, 5 mmol) and KSCN (0.97 g, 10 mmol) in THF (10 ml) was stirred under reflux for 3 h. GLC analysis of the filtrate showed the presence of phenyl isothiocyanate (1.85 mmol, 37%) and unreacted PCD (0.15 mmol, 3%). Similar treatment of PCD (10 mmol) with KSCN (10 mmol) in EtOH (20 ml) at 0—5 °C for 5 h, followed by extraction with $CHCl_3$, evaporation of the solvent, and addition of hexane to the residue, gave 0.84 g of yellow solid besides 17% yield of phenyl isothiocyanate. The solid was purified by repeated reprecipitation from DMF (DMF dissolves this solid) and water: mp 215—243 °C; IR, broad absorptions, with distinct ones due to phenyl group, and no absorptions due to –S–C≡N or –N=C=S groups; Found: C, 47.98; H, 3.36; N, 18.54; S, 18.08; Cl, 1.81%.

Reaction of PCD with KSeCN. A mixture of PCD (0.87 g, 5 mmol) and KSeCN (1.44 g, 10 mmol) in THF (10 ml) was stirred under reflux for 3 h. GLC analysis of the filtrate showed the presence of phenyl isoselenocyanate (2.91 mmol, 58%) and unreacted PCD (0.38 mmol, 8%). The distillation gave 0.38 g of phenyl isoselenocyanate: bp 81—83 °C/5 Torr (lit,[15] bp 82 °C/7 Torr); IR, 2130 and 2060 cm^{-1} ($\nu_{N=C=Se}$).

The IR and NMR spectra and the retention time in GLC were identical with those of an authentic sample.[15]

Reaction of Phenyl Isocyanide with ClSCN. A mixture of $SbCl_5$ (2.99 g, 10 mmol) and $Pb(SCN)_2$ (3.23 g, 10 mmol) in CCl_4 (10 ml) was heated to 60 °C under stirring. To this mixture was slowly added a CCl_4 (10 ml) solution of phenyl isocyanide (1.03 g, 10 mmol), keeping the temperature at 60—70 °C. The resulting mixture was then stirred for 1 h. After being cooled down to room temperature the precipitated inorganic salt and tarry compounds were filtered off. The organic layer was washed with water and dried over Na_2SO_4. GLC analysis of the organic layer showed the presence of phenyl isothiocyanate (0.85 mmol, 8.5%), PCD (0.14 mmol, 1.4%), unreacted phenyl isocyanide (*ca.* 20%), and two unidentified compounds (*ca.* 8—10% each, as calculated from peak area in GLC) which did not show any absorptions due to -S-C≡N in the IR spectrum.

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