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NEW SYNTHESES OF ALIPHATIC ISOCYANATES *VIA* CYANOGEN CHLORIDE

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Abstract—Alkylation of cyanogen chloride with alkyl chloride and ferric chloride gives an alkyl isocyanide dichloride-$FeCl_3$ complex 2. Such novel complexes react either with water to give alkylamines, or with alcohol or alcoholate to give the corresponding N-substituted carbamate, or are converted to alkyl isocyanates with various reagents. Cyanogen chloride, isopropyl chloride and ferric chloride give complex **2a** which, with zinc oxide, gives isopropylisocyanate. Salts of carboxylic acids also furnished the isocyanate in good yield. The *t*-butylisocyanide dichloride-$FeCl_3$ complex **2b** does not react with zinc oxide but was transformed into *t*-butylisocyanate with trifluoroacetic acid or dimethyl sulphoxide.

We wish to report the study of the alkylation of cyanogen chloride with an alkyl chloride in the presence of a Lewis acid catalyst.

It is already known that acyl chlorides add to cyanogen chloride to give acylimidoyl dichloride in 60–80% yield. However with an alkyl chloride such as chloromethyl-methyl ether only a 10% yield of alkylation compound **1** is obtained, this is the sole example of alkylation.[1,2]

$$ClCN + CH_3OCH_2Cl \longrightarrow \underset{\mathbf{1}}{CH_3OCH_2N{=}CCl_2}$$

We have carried out the alkylation of cyanogen chloride in the presence of $FeCl_3$ as Lewis acid. This alkylation which takes place *via* the known $ClCN.FeCl_3$ complex[3] gives, with isopropyl and *t*-butyl chlorides, high yields of the alkylimidoyl dichloride complexes (2) which are extremely hygroscopic and reproducible elemental analyses were only obtained working under dry N_2.

$$ClCN + RCl + FeCl_3 \longrightarrow (RN{=}CCl_2)_n(FeCl_3)_m$$

2a: R=*i*-Pr; $n = 3$; $m = 2$
b: R=t-Bu; $n = m = 1$

Analysis for Fe, Cl and C/N showed complex **2a** to be $2FeCl_3 . 2ClCN . 3i\text{-}PrCl$.

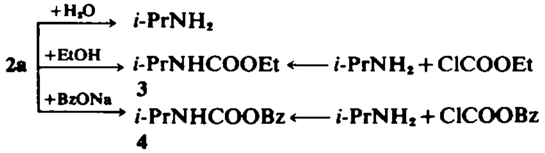
The calculated density for 8 molecules per cell is 1·89 g.cm³ which is reasonable for the expected molecular volume. Using the glove-box crystals of **2a** where transferred to pyrex capillary tubes which were immediately sealed. These crystals were stable for several weeks and gave good X-ray photographs. They are monoclinic space group c2/m, cm or c2 with $a = 10{\cdot}06$, $b = 10{\cdot}09$, $c = 51{\cdot}8$ Å, $\beta = 95°$†.

Since the complex with *t*-butyl chloride was obtained in 91% yield (experimental) starting from a 1:1:1-ratio of $FeCl_3$, *t*-BuCl and ClCN, it is assumed that $n = m = 1$ in **2b**.

The IR spectra of these very hygroscopic complexes have been examined as Nujol mulls and show a strong broad peak at 1600 cm⁻¹ (νC=N) and no absorption in the C≡N stretching frequency at 1300–1400 cm⁻¹ typical of a nitrilium species.[4] This rules out the possible alternative nitrilium structure 2′ in favour of the isocyanide dichloride 2.

$$\underset{\mathbf{2'}}{R{-}\overset{\oplus}{N}{\equiv}C{-}Cl.\,FeCl_4^{\ominus}}$$

Complex **2a** reacts violently with water to give isopropylamine, and with EtOH to give ethyl N-isopropylcarbamate **3**. An intermediate which could be a complex of **3**, with $FeCl_3$ was isolated by distillation, and on basic treatment gave pure carbamate **3** (experimental). Benzyl-N-isopropyl carbamate **4** was obtained from sodium benzylate with **2a**. Carbamates **3** and **4** were identified by an independant route from ethyl and benzyl chloroformate respectively with isopropylamine. These three reactions are typical of isocyanide dichloride derivatives.[5]



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†The X-ray analysis was carried out by Mr. G. King and the elemental analysis by Mr. F. J. Haftka.

Several methods for the transformation of isocyanide dichlorides into isocyanates are known.[5] In a recent example the isocyanide dichloride is treated with a strong acid such as chloro- or alkanesulphonic acid.[6] But this did not work with the complex **2a**. Use of silver oxide, one of the oldest methods[7] and other oxides such as those of calcium and mercury gave negative results. The reaction was usually too violent, very difficult to control and lead to decomposition of complex **2** into ClCN which trimerised into isocyanuryl chloride. We succeeded, however, in transforming the isopropylisocyanide dichloride complex **2a** into isopropylisocyanate by a smooth reaction with zinc oxide.

$$\underset{\mathbf{2a}}{[i\text{-PrN}{=}\text{CCl}_2]_3[\text{FeCl}_3]_2} + \text{ZnO} \longrightarrow \underset{\mathbf{5}}{3i\text{-PrN}{=}\text{C}{=}\text{O}} + 3\text{ZnCl}_2 + 2\text{FeCl}_3$$

In this method complex **2a** was not isolated and an 85% overall yield of isopropylisocyanate **5** was obtained (based on $FeCl_3$ used, as excess cyanogen chloride). The isopropylisocyanate isolated in ether solution has been estimated by the quantitative formation of N,N'-diisopropylurea **6** with isopropylamine.

$$\underset{\mathbf{5}}{i\text{-PrN}{=}\text{C}{=}\text{O}} + i\text{-PrNH}_2 \longrightarrow \underset{\mathbf{6}}{i\text{-PrNHCONH}i\text{-Pr}}$$

The yields of isocyanate are, however, much lower when the reaction is carried out starting from the isolated complex **2a** owing to its high sensitivity to moisture. However, it has been found easier to handle it from a stock bottle kept in a desiccator in order to try other reagents for the release of the isocyanate. With this procedure the use of zinc oxide gave only a 38% yield of **5** from the isolated complex **2a** (compared with the 85% overall yield). Successful results have also been obtained with various salts of carboxylic acids. These reagents have not previously been used for this purpose.[5] For example, complex **2a** with NaOAc in ether gave a 24% yield of isopropylisocyanate. When CH_2Cl_2 was used as solvent, only acetyl chloride was isolated and characterised (experimental). Probably ether, as a Lewis base prevents the subsequent formation of a complex between the isocyanate and $FeCl_3$; such complexes are described with other Lewis acids.[8]

$$\mathbf{2a} + 3\text{MeCOONa} \longrightarrow \underset{\mathbf{5}}{3i\text{-PrNCO}} + 3\text{MeCOCl} + 2\text{FeCl}_3 + 3\text{NaCl}$$

A similar smooth reaction also results with mercuric acetate and sodium oxalate giving isocyanate in 35 and 13% yields respectively.

$$\mathbf{2a} + \tfrac{3}{2}(\text{AcO})_2\text{Hg} \longrightarrow 3i\text{-PrNCO} + 3\text{AcCl} + \tfrac{3}{2}\,.\,\text{HgCl}_2 + 2\text{FeCl}_3$$

$$\mathbf{2a} + \tfrac{3}{2}(\text{COONa})_2 \longrightarrow 3i\text{-PrNCO} + 3(\text{COCl})_2 + 3\text{NaCl} + 2\text{FeCl}_3$$

Attempts have also been made to convert **2a** into isocyanate with Ac_2O but this method did not work with isocyanide dichlorides.[5a] We could however qualitatively identify the isopropylisocyanate formed together with the acetyl chloride when the reaction was conducted in ether as solvent. Without solvent only AcCl was characterized and isolated in 84% yield.

$$\mathbf{2a} + 3\text{Ac}_2\text{O} \longrightarrow 3i\text{-PrNCO} + 6\text{AcCl} + 2\text{FeCl}_3$$

The *t*-butylisocyanide dichloride $FeCl_3$ complex **2b** does not react with zinc oxide. Nor was any reaction observed with formic acid. This acid successfully converts dialkyloxyphosphoryl isocyanide dichloride into phosphorylated isocyanates.[9,10] However, when we used trifluoroacetic acid in the presence of tributylamine, *t*-butylisocyanate **7** was formed in 30% yield. It was estimated quantitatively by its conversion to N-isopropyl-N'-*t*-butylurea **8**.

$$\mathbf{2b} + \text{CF}_3\text{COOH} \xrightarrow{(\text{Bu})_3\text{N}} \underset{\mathbf{7}}{t\text{-BuNCO}} + \text{CF}_3\text{COCl} + \text{FeCl}_3$$

$$\mathbf{7} \xrightarrow{i\text{-PrNH}_2} \underset{\mathbf{8}}{t\text{-BuNHCONH}i\text{-Pr}}$$

t-Butylisocyanate has been also prepared from complex **2b** with dimethyl sulphoxide in 18% yield. This reaction principle has been mentioned in the literature[11] as a possible step in the bromine-catalysed conversion of isonitrile into isocyanate *via* isocyanide dibromide in dimethyl sulphoxide.

$$\mathbf{2b} + (\text{Me})_2\text{SO} \longrightarrow \underset{\mathbf{7}}{t\text{-BuNCO}} + (\text{Me})_2\text{S} + \text{Cl}_2 + \text{FeCl}_3$$

EXPERIMENTAL

Isopropyl isocyanide dichloride-$FeCl_3$ *complex* **2a**. 12 ml (0·234 M) of CNCl were added to a stirred suspension of 19 g (0·117 M) of $FeCl_3$ in 210 ml of *i*-PrCl cooled to 5°. The solution became red (due to the ClCN . $FeCl_3$ complex[3]). Stirring was continued for 20 hr at 0° and the colour changed from red to greenish-yellow while a precipitate of greenish-yellow crystals (**2a**) formed. These were filtered (absence of moisture) and washed with a little cold *i*-PrCl giving 19 g (44%) of **2a**. (True yield much higher as **2a** soluble in *i*-PrCl.) IR: (nujol) νC=N 1610 cm^{-1} sb. Atomic ratio found for $C_{12}H_{21}N_3Cl_{12}Fe_2$: C/N = 4·02 and Cl/Fe = 5·97.

t-*Butylisocyanide dichloride*-$FeCl_3$ *complex* **2b**. 12 ml (0·234 M) of CNCl were added to a stirred suspension of 38 g (0·234 M) $FeCl_3$ in a mixture of 100 ml CCl_4 and 100 ml of CH_2Cl_2 cooled with an ice bath. The temperature was kept at about 0° during 1 hr while the suspension turned from red to greenish-yellow then another 3 hr at room temp. The solid was filtered giving (67·5 g (91%) of **2b**. IR: (nujol) 1600 cm^{-1} sb band.

Hydrolysis of isopropyl isocyanide dichloride-$FeCl_3$ *complex* **2a**. Complex **2a** was dissolved in water and the solution saturated with K_2CO_3 and ether extracted. The organic layer was dried (K_2CO_3). Dry HCl was added to the filtered solution and the isopropyl amine hydrochloride precipitated, m.p. and m.m.p. with an authentic sample: 158°.

Ethyl N-*isopropylcarbamate* **3**. Complex **2a** (3 g) was added portionwise to 10 ml of absolute EtOH (exotherm). The mixture was refluxed for 2 hr, excess alcohol was evaporated and the residue distilled under high vacuum in a three-bulb-tube. At about 160° (air-bath temperature) a brownish liquid distilled (1·35 g) and was taken up in Na_2CO_3aq, $Fe(OH)_3$ precipitated and the mixture ether extracted. The ethereal solution was dried and evaporated leaving 0·65 g of pure ethyl N-isopropyl carbamate **3**; identified by IR and GLC comparison with those of an authentic sample.

Benzyl N-*isopropyl carbamate* **4**. To a suspension of sodium benzylate (prepared from 0·23 g Na in BzOH) in complex **2a** and the mixture kept 2 days at room temp. 2 g NaOH in 10 ml of water were added and the mixture ether extracted. The organic layer was dried (K_2CO_3) and concentrated to dryness. The residue distilled in a three-bulb-tube at 110°. 1 mm gave 1·25 g of the carbamate **4** (60% yield calculated on sodium benzylate). M.p. and m.m.p. with an authentic sample prepared from benzyl chloroformiate and isopropyl amine, 52°.

Isopropylisocyanate **5** *without isolation of* **2a**. The isopropylisocyanide dichloride-$FeCl_3$ complex **2a** was made as described above from 4·8 g (0·03 M) of $FeCl_3$ in 200 ml of *i*-PrCl and 6 ml (0·117 M) of CNCl. After 20 hr between −5° and 0° excess CNCl and *i*-PrCl were distilled under water-pump vacuum and at room temp. To the crude crystalline residue 50 ml of absolute ether were added. The mixture was cooled to 0° then 12 g of ZnO (0·15 M) were added. The suspension was stirred, the cooling bath removed when the ether slowly began to distill. When the temperature decreased the remaining ether and isopropyl-isocyanate were taken off from the mixture under water-pump vacuum and condensed into an acetone/dry ice-cooled trap. To the overall mixture of ether and isopropylisocyanate an excess of isopropylamine (0·15 M) was added dropwise and the precipitated urea (**6**) was collected 5·51 g, yield: 85% (based on 0·03 M of $FeCl_3$, thus 0·045 M of ClCN consumed in theory), m.p. 193°. A pure sample of isopropylisocyanate was separated from ether by distillation in a spinning band column, b.p. 67° and identified by NMR.

Isopropylisocyanate from the complex **2a** *and* ZnO. To a suspension of 3 g (0·00403 M) of **2a** in 6 ml of ether at 0° was added 1·2 g (0·015 M) of zinc oxide and the mixture stirred for 1 hr at 0°. The cooling bath was removed, producing a temperature increase to ether reflux. After 30 min the ether and the isopropylisocyanate **5** were distilled giving 0·66 g of urea derivative (38% yield).

Isopropylisocyanate from the complex **2a** *and sodium acetate*. To a suspension of 3 g (0·00403 M) of **2a** in 10 ml of ether at 0° was added 0·82 g (0·01 M) of NaOAc. The mixture was stirred 24 hr at room temp. Solvent and isopropylisocyanate were removed from the mixture under water-pump vacuum, condensing the distillate into a dry ice-acetone cooled trap. To this distallate was added excess *i*-$PrNH_2$ the precipitated urea **6** was collected; 0·400 g (27%); m.p. 193°. Under similar conditions with CH_2Cl_2 as solvent no isocyanate **5** was formed but instead AcCl identified by the addition of isopropylamine to the distillate and the isolation of 0·42 g (35%) of isopropylamine hydrochloride, m.p. 158°, and N-isopropylacetamide. 0·40 g (35%).

Isopropylisocyanate from the complex **2a** *and mercuric acetate*. Using conditions similar to those for NaOAc, 35% yield of isopropylisocyanate was obtained with mercuric acetate and was collected by distillation at normal pressure ten min after acetate addition.

Isopropyl isocyanate from the complex **2a** *and sodium oxalate*. Using conditions similar to those above, sodium oxalate after 20 hr at room temp. gave the isopropylisocyanate (13%) which was collected at normal pressure.

Isopropylisocyanate **5** *from* **2a** *and acetic anhydride*. To 3 g (0·00403 M) of **2a** was added dropwise 5 g Ac_2O. The mixture was kept 20 min at room temp. then heated to 125°. AcCl slowly distilled, 1·5 g (84%). Under similar conditions with ether as solvent a little isopropylisocyanate was also formed and characterized as N,N′-diisopropylurea **6**.

t-*Butylisocyanate* **7** *from* **2b** *and TFA*. To a stirred and ice-cooled suspension of 3·16 g (0·01 M) of *t*-butylisocyanide dichloride-$FeCl_3$ complex **2b** in 10 ml of CH_2Cl_2 was added 1·14 g (0·01 M) of trifluoroacetic acid. The mixture was stirred for 10 min, 18·5 g (0·01 M) of tributylamine were added dropwise, the mixture stirred for 3 hr at room temp., then heated to 150° and to the collected volatile material was added excess isopropylamine. The CH_2Cl_2 was distilled and water added to the oily residue. The undissolved solid was pure N-isopropyl-N′-*t*-butylurea **8**; m.p. 197°, 0·5 g (30%).

t-*Butyl-isocyanate from* **2b** *and DMSO*. To a stirred and ice-cooled suspension of 3·16 g of **2b** in 10 ml CH_2Cl_2 was added dropwise 1·4 g (0·02 M) of dimethylsulphoxide in 5 ml of CH_2Cl_2. The solid dissolved and the mixture was then heated to 150°. To the collected volatile material was added excess of isopropylamine. The urea **8** was isolated as described above: 0·3 g (18% yield).

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