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Acyl Cyanide. IV. The Reduction of Phenyl-substituted Carbamoyl Cyanides with Metal Hydrides

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Synopsis. The reaction of phenylcarbamoyl cyanide with $LiAlH_4$ or $NaBH_4$ gave glycine anilide, *N*-phenylethylenediamine, and *N*-methylaniline. With the latter hydride, 4-amino-1,3-diphenyl-2-imidazolidinone was also formed. The reduction of diphenylcarbamoyl cyanide with $LiAlH_4$ gave *N*-methyldiphenylamine as the only reduction product.

The utilization of acyl cyanides (α-ketonitriles) as useful precursors in organic synthesis has been discussed in a number of literatures.[1] In contrast, carbamoyl cyanides, the nitrogen homologues of acyl cyanide, have not been extensively studied, and only a small quantity of information has accummulated about their chemical properties.[2]

Among the chemical reactions of acyl cyanides it has been known that the reduction by lithium aluminum hydride generally gives β-amino alcohols, β-(acylamino) alcohols, or aldehydes depending on the reaction conditions.[3] Can analogous products be obtained in the reduction of carbamoyl cyanides with metal hydrides? Is there any difference between the reactions of mono- and di-substituted carbamoyl cyanides? In answer to these questions, we would like to present the results obtained from the reduction of phenylcarbamoyl cyanide (**1**) and diphenylcarbamoyl cyanide (**8**) with metal hydrides.

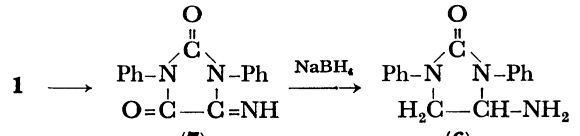
Results and Discussion

When phenylcarbamoyl cyanide (**1**) was treated with lithium aluminum hydride ($LiAlH_4$) in anhydrous ether, the following four products: aniline (**2**), *N*-methylaniline (**3**), glycine anilide (**4**), and *N*-phenylethylenediamine (**5**), were obtained. The time-depen-

$$\underset{(\mathbf{1})}{\text{Ph-NHCOCN}} \xrightarrow{LiAlH_4} \underset{(\mathbf{2})}{\text{Ph-NH}_2} + \underset{(\mathbf{3})}{\text{Ph-NHCH}_3} + \underset{(\mathbf{4})}{\text{Ph-NHCOCH}_2\text{NH}_2} + \underset{(\mathbf{5})}{\text{Ph-NHCH}_2\text{CH}_2\text{NH}_2}$$

dent increase of **5** with a decrease in **4**, as observed by a VPC analysis, indicated that the product, **4**, was the reduction intermediate to produce **5**. In addition, the yield of **3** increased from 6 to 21% as the $[LiAlH_4]/[\mathbf{1}]$ ratio increased from 1 to 5.

Analogously, when cyanide **1** was treated with sodium borohydride ($NaBH_4$) in tetrahydrofuran, the same products were produced. In addition, 4-amino-1,3-diphenyl-2-imidazolidinone (**6**) was isolated. The same product was also formed when 1,3-diphenyl-5-iminohydrantoin (**7**) was treated with the same hydride. Therefore, the base-induced condensation of cyanide **1** into **7** must occur under the present conditions[2a] competitively with the slow reduction. The yields of



(**7**) (**6**)

the other products depended significantly upon the reaction conditions, *i.e.*, the amounts of the reductant and additives such as $AlCl_3$,[4] and the time. For example, that the yield of aniline (**2**) decreased upon the lengthening in the reaction period indicates that **2** may be formed mainly by the hydrolysis of the unreacted **1**.[5] Indeed, the alkaline hydrolysis of **1** in aqueous NaOH proceeded very easily. However, the yield of **2** was only 30% at the maximum, and the main product was *N,N'*-diphenylurea. We found separately that a number of amines and alcohols induced **1** to undergo facile nucleophilic substitution.[6] Therefore, it seems reasonable that diphenylurea was formed by the reaction of **1** with aniline, which is the primary hydrolysis product of **1**.

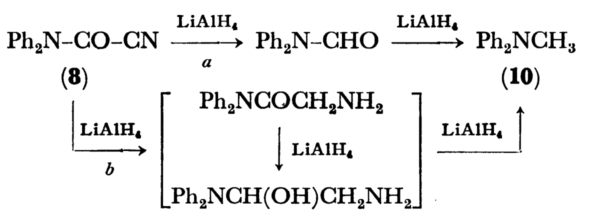
Diphenylcarbamoyl cyanide (**8**)[7] seems to be an appropriate compound to examine in order to ascertain the difference in reaction behavior between monosubstituted (*e.g.*, **1**) and disubstituted (*e.g.*, **8**) carbamoyl cyanides. The results obtained from the reduction of **8** with $LiAlH_4$ are listed in Table 1. The only products

Table 1. Reduction of diphenylcarbamoyl cyanide (**8**) with $LiAlH_4$[a)]

Run No.	Solvent	Product yield (%) Ph_2NH	Product yield (%) Ph_2NCH_3	**8**
1	Et_2O	38	58	0
2	THF	18	72	0
3	THF[b)]	22	0	78

a) $[\mathbf{8}]/[LiAlH_4]=1.0$, 1 h each at −50 and 35 °C.
b) $LiAlH_4$ was hydrolyzed prior to the addition of **8**.

detected by VPC were diphenylamine (**9**) and *N*-methyldiphenylamine (**10**). The former was apparently produced by the hydrolysis of **8** through the work-up process, as is evidently proved by Run 3. The latter, the only reduction product, must be formed by either Route *a* or Route *b*. Although conclusive evidence has not yet been obtained, it has been reported that



the cyanides, **1** and **8**, undergo a facile displacement of the cyano group by the appropriate nucleophiles.[3,6] Therefore, our tentative preference is Route *a*, where the displacement of the cyano group by the hydride anion takes place, as is evident in the case of acyl cyanides.[3]

Now, let us recall the reduction of **1** where *N*-methylaniline (**3**) was one of the major products. As has been reported recently,[6] cyanide **1** behaves as if it generates the phenyl isocyanate intermediate under various conditions (*i.e.*, it acts as a *carbamoylating reagent*). Also known is the reduction of phenyl isocyanate with $NaBH_4$, where **3** is the main product.[8] Nevertheless, the formation of **10** from **8** seems to present rational evidence in favor of the hypothesis that the derivation of **3** from **1** does not necessarily involve phenyl isocyanate as the intermediate.

In addition, it became evident in our study that amide carbonyl groups can undergo $NaBH_4$ reduction, at least when the vicinal substituent to the carbonyl is an unsaturated group such as CN or C=NH, though it has been our general understanding that amide carbonyls are resistant against that reagent.[9] Also proved is the transformability of the cyanocarbonyl group of carbamoyl cyanides into a methyl group by treatment with such metal hydrides as $LiAlH_4$ or $NaBH_4$.

Experimental

General. The NMR, mass, and IR spectra were taken on JEOL 4H-100, Hitachi RMU-6L, and JASCO IRA-1 spectrometers respectively. Some typical experimental procedures are shown below.

Reduction of Phenylcarbamoyl Cyanide (1) with $LiAlH_4$. To a solution of **1** (4.4 g, 30 mmol) in dry THF (100 ml) was added a suspension of $LiAlH_4$ (2.3 g, 60 mmol) in dry THF (30 ml) over a 40-min period at 5 °C. After stirring for 30 min, a mixture of THF (20 ml) and water (6 ml) was added and the decomposed mixture was filtered. The filtrate was dried over anhyd $MgSO_4$ and distilled under a vacuum. The first fraction (55 °C/3 Torr, 0.8 g) was found by VPC (Apiezon L, 10%, 1 m) to consist of aniline (**2**, 15%) and *N*-methylaniline (**3**, 10%). The third fraction (95—97 °C/1.5 Torr, 1.5 g, 37%) formed a picrate (mp 175—177 °C) which did not show any mp depression when mixed with an authentic picrate of *N*-phenylethyleneadimine. The fifth fraction (145—148 °C/1 Torr, 12 g, 27%) was a solid (mp 98—100 °C) containing a small amount of impurity with a higher mp. Therefore, the fraction was heated with Ac_2O in AcOH to give an acetylated product (98%); mp 195.5—196.5 °C (from ethanol). Found: C, 62.59; H, 6.29; N, 14.61%. Calcd for $C_{10}H_{12}N_2O_2$: C, 62.48; H, 6.29; N, 14.58%.

Reduction of 1 with $NaBH_4$. A mixture of **1** (4.4 g, 30 mmol) and dry $NaBH_4$ (1.2 g, 30 mmol) in dry THF (50 ml) was stirred for 4 h at 40 °C. The reaction mixture was poured into cold 5% NaOH, the solution was extracted with ether, and the extract was dried. After removing the solvent, the residue was analyzed by VPC to find that it consisted of **2**+**3** (22%), **4** (6.2%), and **5** (1%). After these were distilled off, the residue was chromatographed (silica gel, $CHCl_3$) to give a colorless solid of **6** (45%); mp 178 °C; P^+ (*m/e*) 253; IR (cm^{-1}) 1690 (C=O), 3400, and 3330 (NH); NMR (δ, $CDCl_3$) 1.90 (2H, bs), 3.57 (H, q, J_1=10, J_2=5.0 Hz), 4.14 (H, q, J_1=10, J_2=8.5 Hz), 5.23 (H, q, J_1=8.5, J_2=5.0 Hz), 7.0—7.65 (10H, m). Found: C, 71.35; H, 6.01; N, 16.40%. Calcd for $C_{15}H_{15}N_3O$: C, 71.12; H, 5.97; N, 16.60%.

Hydrolysis of 1 by Aq NaOH. A dioxane solution of **1** was hydrolyzed in 5% aq NaOH at 20 °C for 2 h. After a similar work-up, VPC and column chromatographic analysis of the product mixture showed it to consist of **4** (30%) and *N,N′*-diphenylurea (45%).

Reduction of Diphenylcarbamoyl Cyanide (8) with $LiAlH_4$. To a solution of **8** (2.22 g, 10 mmol) in dry ether (20 ml) was added a suspension of $LiAlH_4$ (0.4 g, 10 mmol) in dry ether (10 ml) over 10 min at −50 °C. After stirring the mixture for 1 h each at −50 and 35 °C, the mixture was decomposed under ice cooling by the addition of a cold mixture of THF (20 ml) and water (0.8 g), followed by the addition of a saturated NH_4Cl solution (30 ml). After work-up, the ethereal extract weighed 1.69 g and was analyzed by VPC (Apiezon L, 10%, 1 m, 200—250 °C). Diphenylamine (**9**, 38%, identified with an authentic sample) and *N*-methyldiphenylamine (**10**, 58%, NMR Me at δ 3.28, and by MS P^+ 183) were detectable products. See Table 1.

Treatment of 8 with Water-treated $LiAlH_4$. The same treatment of **8** as described above, but with the $LiAlH_4$ preliminarily decomposed by an equivalent mole of water, was carried out in order to examine the hydrolysis product. After work-up, the VPC of the reaction mixture proved that diphenylamine (**9**) was its only product (22%), together with the recovered **8** (78%).

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