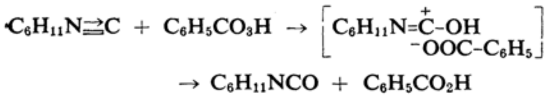
Studies of Isocyanide. II. The Reaction of Isocyanide with Some Radical Sources

By Tatsuya SHONO, Masatoshi KIMURA, Yoshihiko ITO,
Kiyoto NISHIDA and Ryohei ODA

(Received March 24, 1964)

The first paper¹⁾ of this series reported that the reactions of some electrophiles, such as *t*-butyl hypochlorite, *N*-bromosuccinimide and hydroxylamine, with isocyanide produce urethanes and ureas. On the other hand, the reactions of compounds with a lone pair on the nitrogen²⁾ or phosphorus³⁾ atom with some radical sources, for example, the reaction of dimethylaniline with benzoyl peroxide, are well known. Since the isocyanide also has a lone electron-pair on its terminal carbon atom, the reactions of isocyanide with radical sources seem interesting.

When cyclohexyl isocyanide was treated with perbenzoic acid, cyclohexyl isocyanate was obtained in a 61% yield, along with *N*-cyclohexyl benzamide. A reasonable path for this reaction would be the electrophilic attack of perbenzoic acid on the lone electron-pair of the isocyanide to form an adduct, which in turn decomposes to give cyclohexylisocyanate and benzoic acid :

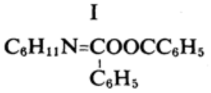


$$C_6H_{11}N\overset{\rightarrow}{\equiv}C + C_6H_5CO_3H \rightarrow \left[\begin{array}{l} C_6H_{11}N{=}\overset{+}{C}{-}OH \\ \qquad\quad {}^{-}OOC{-}C_6H_5 \end{array}\right] \rightarrow C_6H_{11}NCO + C_6H_5CO_2H$$

The reaction of the isocyanide with benzoyl peroxide gave three major products, I, II and III, and one minor product, IV :

$C_6H_{11}NHCOC_6H_5$ I

$C_6H_{11}N{=}CHOOCC_6H_5$ II

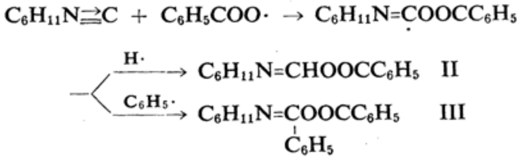


$$C_6H_{11}N{=}\underset{\substack{| \\ C_6H_5}}{C}OOCC_6H_5$$

III

$C_6H_{11}NHCONHC_6H_{11}$ IV

A preliminary test indicated that the isocyanide did not contribute kinetically to the decomposition of benzoyl peroxide. Thus, the decomposition of benzoyl peroxide must be spontaneous thermal decomposition according to the free radical mechanism. The formation of II and III is rationalized by the following reaction scheme :



$$C_6H_{11}N\overset{\rightarrow}{\equiv}C + C_6H_5COO\cdot \rightarrow C_6H_{11}N{=}\underset{\cdot}{C}OOCC_6H_5$$
$$\xrightarrow{H\cdot} C_6H_{11}N{=}CHOOCC_6H_5 \quad \text{II}$$
$$\xrightarrow{C_6H_5\cdot} C_6H_{11}N{=}\underset{\substack{| \\ C_6H_5}}{C}OOCC_6H_5 \quad \text{III}$$

An analogous reaction of isocyanide with *t*-butyl perbenzoate yielded similar products, such as I, II and IV, and also unexpected new minor products, V and VI :

$C_6H_{11}NH_3OOCC_6H_5$ V

$C_6H_{11}NHCHO$ VI

In the reaction of isocyanide with *N*-nitrosoacetanilide, two major products, VII and VIII, attributed to the reaction of isocyanide with acetoxy radical, were obtained as expected, along with two minor products, IV and VI :

$C_6H_{11}N{=}CHOOCCH_3$ VII

$C_6H_{11}NHCOCH_3$ VIII

The formation of VII is analogous to the formation of II, but the formation of VIII and other minor products still remains to be explained.

It seems that the isocyanide reacts predominantly with acyloxy radicals: therefore in the reactions with benzoyl peroxide, *t*-butyl perbenzoate or *N*-nitroso-acetanilide, no other products in which the acyloxy radicals are not involved can be obtained.

In order to obtain the product involved with the phenyl radical, the reaction of isocyanide with potassium phenylazoformate was tried, it was verified to yield one major product, IX, and one minor product, IV :

$C_6H_{11}N{=}CHC_6H_5$

IX

The formation of IX is rationalized by the following free radical reaction scheme :

$$C_6H_{11}N\overset{\rightarrow}{\equiv}C + C_6H_5\cdot \rightarrow C_6H_{11}N{=}\underset{\cdot}{C}{\cdot}C_6H_5 \rightarrow C_6H_{11}N{=}CHC_6H_5$$

Finally, the reaction of isocyanide with di-*t*-butyl peroxide was carried out in order to obtain the product involved with the methyl radical : however, only a resinous product and two minor products, X and IV, were obtained.

---

1) M. Okano, Y. Ito, T. Shono and R. Oda, This Bulletin, **36**, 1314 (1963).

2) L. Horner and K. Scherf, *Ann.*, **573**, 35 (1951).

3) M. A. Greenbaum, D. E. Denney and A. K. Hoffmann, *J. Am. Chem. Soc.*, **78**, 2563 (1956).

This resinous product may result from the polymerization of the azomethine compound which is formed by the reaction of the isocyanide with the methyl radical:

$C_6H_{11}NHCOCONHC_6H_{11}$

X

Experimental

The Reaction of Cyclohexyl Isocyanide with Perbenzoic Acid. — Into a solution of 12.75 g. (0.117 mol.) of cyclohexyl isocyanide in dry chlorofrom, a solution of 16.21 g. (0.117 mol.) of freshly-prepared perbenzoic acid in 300 ml. of dry chloroform was added drop by drop with stirring at such a rate that the reaction temperature was below 0°C.

After the reaction mixture had been allowed to stand overnight at 0°C, the solvent was removed and the residue was distilled in vacuo to yield 8.9 g. (61%) of cyclohexyl isocyanate (b.p. 39°C/2 mmHg). The distillation residue consisted of 4.6 g. of *N*-cyclohexylbenzamide and 16 g. of benzoic acid.

The Reaction of Cyclohexyl Isocyanide with Benzoyl Peroxide.—Under a nitrogen atmosphere, a solution of 8 g. (0.033 mol.) of benzoyl peroxide in 73 g. of cyclohexyl isocyanide was heated while being stirred at 80~90°C for 5 hr. The reaction mixture was washed with aqueous sodium carbonate and then dried and distilled in vacuo to yield 5.5 g. of an oily product (b. p. 120~135°C/3 mmHg) and 2 g. of a resinous product. The oily product was crystallized on standing and separated into four parts. The part which was easily soluble in ligroin was II (2 g., m. p. 65~67°C), and the hardly soluble part was IV (0.1 g., m. p. 217~220°C). The moderately ligroin-soluble part consisted of two parts; one was III (1 g. recrystallized from acetone, m. p. 129~130.5°C), while the other was I (1 g., recrystallized from ligroin, m. p. 148~150°C). The resinous product afforded 0.6 g. of I after recrystallization from ligroin. The products I and IV were identified by a mixed melting point determinations with the respective authentic samples. The structures of the products II and III were inferred on the basis of their infrared spectra and results of analysis and of hydrolysis. When the II or III was hydrolyzed, benzoic acid and cyclohexylamine were obtained.

The two spectra resembled closely each other. They showed the existence of an ester group (1715 cm^{-1}, 1270 cm^{-1}, 1120 cm^{-1} in III; 1750 cm^{-1}, 1270 cm^{-1}, 1120 cm^{-1} in II), a double bond between nitrogen and carbon (1675 cm^{-1} in II; 1660 cm^{-1} in III), and a monosubstituted phenyl group (735 cm^{-1}, 700 cm^{-1} in II; 725 cm^{-1}, 700 cm^{-1} in III), but exhibited neither a secondary amide group nor a hydroxy group. The results of the analysis of these products were as follows:

Found (for I): C, 76.86; H, 8.41; N, 6.79.
Calcd. for $C_{13}H_{17}NO$: C, 76.81; H, 8.43; N, 6.89%.
Found (for II): C, 73.00; H, 7.49; N, 6.07.
Calcd. for $C_{14}H_{17}NO_2$: C, 72.72; H, 7.36; N, 6.06%.
Found (for III): C, 78.55; H, 7.10; N, 4.60.
Calcd. for $C_{20}H_{21}NO_2$: C, 78.14; H, 6.88; N, 4.55%.
Found (for IV): C, 69.92; H, 10.73; N, 12.23.
Calcd. for $C_{13}H_{24}N_2O$: C, 69.59; H, 10.78; N, 12.48%.

The Reaction of Cyclohexyl Isocyanide with *t*-Butyl Perbenzoate. — The procedure and conditions employed were similar to that used for the above reaction, except that the radical source was divided into ten parts and added at intervals of one hour. 54.5 g. (0.5 mol.) of the isocyanide and 9.7 g. (0.05 mol.) of the perbenzoate were allowed to react. Working-up of the reaction mixture, as described above, gave I (2.1 g.), II (1.6 g.) and IV (0.1 g.) and two new minor products, V (0.2 g.) (recrystallized from acetone, m. p. 179~181°C) and oil (1.4 g.) presumed to be VI on the basis of its infrared spectrum (b. p. 107°C/2 mmHg).

The product V showed no depression in melting point when mixed with an authentic material.

Found (for V): C, 70.72; H, 8.61; N, 6.14.
Calcd. for $C_{13}H_{19}NO_2$: C, 70.55; H, 8.65; N, 6.32%.

The Reaction of Cyclohexyl Isocyanide with *N*-Nitroso Acetanilide.—By the method and conditions described above, the reaction of 136 g. (1.245 mol.) of cyclohexyl isocyanide with 22.8 g. (0.143 mol.) of *N*-nitrosoacetanilide was carried out. The reaction mixture was distilled in vacuo to yield 11.5 g. of an oily product (b. p. 98~125°C/3 mmHg). This was dissolved in ether and washed successively with 5% cold aqueous hydrochloric acid, aqueous sodium carbonate, and finally water. After the oil had been dried, the ether was evaporated off and the residual oil was distilled in vacuo to give 4 g. of VII (b. p. 98~99°C/3 mmHg). The 5% aqueous hydrochloric acid layer was alkalified with sodium carbonate, and the oil which separated was extracted with ether. The ethereal solution was evaporated and distilled in vacuo to yield 2.8 g. of an oily product (b. p. 103~105°C/3 mmHg), which consisted of two parts; one was VIII (1 g., melting at 100~101°C after recrystallization from ligroin), and other was an oil (1.7 g.), presumed on the basis of its infrared spectrum to be VI. The structure of product VII was also presumed on the basis of its infrared spectrum and analytical data.

The spectrum had the absorption resulting from the ester group (1740 cm^{-1}, 1220 cm^{-1}) and double bond between carbon and nitrogen (1675 cm^{-1}) but showed no absorption originating in hydroxy group and secondary amide group. The melting point of the product VIII was undepressed on admixture with an authentic sample.

Found (for VII): C, 64.61; H, 9.23; N, 7.98.
Calcd. for $C_9H_{15}NO_2$: C, 63.88; H, 8.94; N, 8.28%.

The Reaction of Cyclohexyl Isocyanide with Potassium Phenylazoformate.4)—In a similar way 43.7 g. (0.4 mol.) of cyclohexyl isocyanide and 7.5 g. (0.04 mol.) of potassium phenylazoformate were allowed to react. After the removal of the unreacted isocyanide, the residue was distilled under reduced pressure to afford an oily product (1.4 g., b. p. 92°C/2 mmHg) and IV (0.1 g.).

The oily product had the same infrared spectrum as the authentic sample of IX, and it reacted

---

4) A Nagasaka and R. Oda, *J. Chem. Soc. Japan, Ind. Chem. Sec.* (*Kogyo Kagaku Zassi*), **58**, 48 (1955).

with 2, 4-dinitrophenylhydrazine to give benzaldehyde 2, 4-dinitrophenylhydrazone in the theoretical yield. These facts clearly indicate that the oily product is IX.

The Reaction of Cyclohexyl Isocyanide with Di-*t*-butyl Peroxide. — The reaction of 35.5 g. (0.325 mol.) of cyclohexyl isocyanide with 14.6 g. (0.1 mol.) of di-*t*-butyl peroxide was performed in a similar manner described above.

The reaction mixture was distilled to remove the unchanged isocyanide and peroxide. The resulting resinous product (4.8 g.) was dissolved in ethanol, and IV (0.1 g.) and X (0.15 g., m. p. 270∼271.5°C, recrystallized from dioxane) were separated from the ethanol solution. The product X showed no depression in melting point when mixed with an authentic sample prepared from cyclohexylamine and oxalyl chloride.

Found (for X) : C, 66.05 ; H, 9.46 ; N, 11.29. Calcd. for $C_{14}H_{24}N_2O_2$: C, 66.63 ; H, 9.59 ; N, 11.10%.

Summary

The reactions of cyclohexyl isocyanide with some radical sources, such as perbenzoic acid, benzoyl peroxide, *t*-butyl perbenzoate, *N*-nitrosoacetanilide, potassium phenylazoformate and di-*t*-butyl peroxide, have been studied. The isocyanide does not contribute kinetically to the mechanism of the decomposition of benzoyl peroxide, but the lone pair electrons existing on the carbon atom of isocyanide react very easily with free radicals, especially with acyloxy radicals.

In the reaction with benzoyl peroxide, *t*-butyl perbenzoate or the *N*-nitrosoacetanilide acyloxy radical chiefly contributes to the reaction. With potassium phenylazoformate, the phenyl radical is the main reacting species. However, in the case of perbenzoic acid, the reaction is heterolytic, and the main product is cyclohexyl isocyanate.

Department of Synthetic Chemistry
Faculty of Engineering
Kyoto University
Sakyo-ku, Kyoto