REACTION OF TERT-BUTYL ISOCYANIDE
WITH HYDROGEN CHLORIDE*

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tert-Butyl isocyanide reacts with hydrogen chloride with the formation of 2,3-di(tert-butylimino)-propiononitrile dihydrochloride. The latter yields by hydrolysis (tert-butylamino)cyanoacetic acid tert-butylamide, along with a small amount of 2,3-di(tert-butylamino)maleonitrile. Reaction with lithium ethoxide yields 2,3-bis(tert-butylamino)-3-ethoxyacrylonitrile.
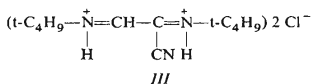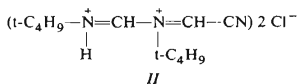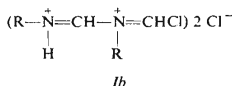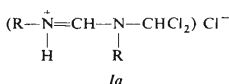
The primary and secondary alkyl isocyanides, as well as phenyl isocyanide[1] react with hydrogen chloride similarly to hydrogen cyanide[2], yielding compounds having the general formula 2 RNC . 3 HCl. The structure of these compounds (*I*) has been recently determined spectroscopically[3,4]; it has been established that they are also formed by a reaction of the corresponding formamides with phosgene[4]. The reaction of isocyanide with hydrogen chloride can therefore be represented as an electrophilic attack of the transition formimidoyl chloride at the nitrogen atom of another molecule of isocyanide, which is in agreement with the assumed higher electron density at the nitrogen atom than that at the neighbouring carbene carbon atom[5,6], confirmed by the calculations in a one-electron MO-approximation (HMO and EHT). Despite this fact, the reaction mechanisms of the reactions of isocyanides with acid agents are usually explained while considering the isocyanide carbon atom[7,8] as the nucleophilic centre. An exception is made by an attempted new explanation of the Passerini and Ugi reactions[9].

We considered it useful to check the course of the reaction of hydrogen chloride with tert-butyl isocyanide. The latter enters into specific reactions with acid agents; these reactions may be related to the easy splitting-off of the tert-butyl cation. It also dimerizes with a small amount of boron fluoride etherate to 2-(tert-butylimino)-

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3,3-dimethylbutyronitrile[10]. The reactions of tert-butyl isocyanide with cyclic unsaturated ketones in the presence of boron fluoride etherate lead to cyano derivatives of unsaturated ethers[11].

The reaction of tert-butyl isocyanide with hydrogen chloride yielded tert-butyl chloride and a colourless compound which similarly to the compounds of type *I* readily decomposes with water, has no definite melting point and cannot be recrystallized. The same product was also obtained by the reaction of N-tert-butylformamide with phosgene. However, the formula of this compound is not consistent with the compound of type *I*, but with a compound which would be obtained from *I* by substituting one chlorine atom with a nitrile group (possible structures *II* or *III*):

$$(\text{R}-\overset{+}{\underset{\underset{\text{H}}{|}}{\text{N}}}=\text{CH}-\underset{\underset{\text{R}}{|}}{\text{N}}-\text{CHCl}_2)\ \text{Cl}^-$$

Ia

$$(\text{R}-\overset{+}{\underset{\underset{\text{H}}{|}}{\text{N}}}=\text{CH}-\overset{+}{\underset{\underset{\text{R}}{|}}{\text{N}}}=\text{CHCl})\ 2\ \text{Cl}^-$$

Ib

$$(\text{t-C}_4\text{H}_9-\overset{+}{\underset{\underset{\text{H}}{|}}{\text{N}}}=\text{CH}-\overset{+}{\underset{\underset{\text{t-C}_4\text{H}_9}{|}}{\text{N}}}=\text{CH}-\text{CN})\ 2\ \text{Cl}^-$$

II

$$(\text{t-C}_4\text{H}_9-\overset{+}{\underset{\underset{\text{H}}{|}}{\text{N}}}=\text{CH}-\underset{\underset{\text{CN}}{|}}{\text{C}}=\overset{+}{\underset{\underset{\text{H}}{|}}{\text{N}}}-\text{t-C}_4\text{H}_9)\ 2\ \text{Cl}^-$$

III

In the mass spectrum of this compound (Fig. 1*a*) there are abundant ions *m/e* 193, due with all probability to the loss of two molecules of hydrogen chloride from the compound $C_{11}H_{21}Cl_2N_3$. If an all glass heated inlet system (AGHIS) at a temperature of 140°C is used, a quite different spectrum is obtained, not containing the *m/e* ions 193 (Fig. 1*b*). This spectrum is conspicuous by the presence of the signal of the 110 *m/e* ions, elementary composition $C_6H_{10}N_2$ (calculated: 110·0844; found: 110·0847), not represented in the original spectrum. Both spectra exhibited ions having the composition C_5H_9N (calculated: 83·0735; found: 83·0731). Their signal, if the above technique at 140°C is used, is more intensive by 2·5 times.

The thermal dissociation of the compound under investigation yields therefore a compound poorer by two molecules of hydrogen chloride. This elimination is in accordance with structure *III* and at variance with structure *II*. A further splitting, which occurs when AGHIS is used, will be discussed later. The infrared spectrum

of compound *III* contains an intensive nitrile band at 2 208 cm^{-1}. The band cor-
responding to the C=N bond, whose frequency in compounds of type *I* is about
1 700 cm^{-1} (Fig. 2a), is shifted to as far as 1 615 cm^{-1}, which indicates another
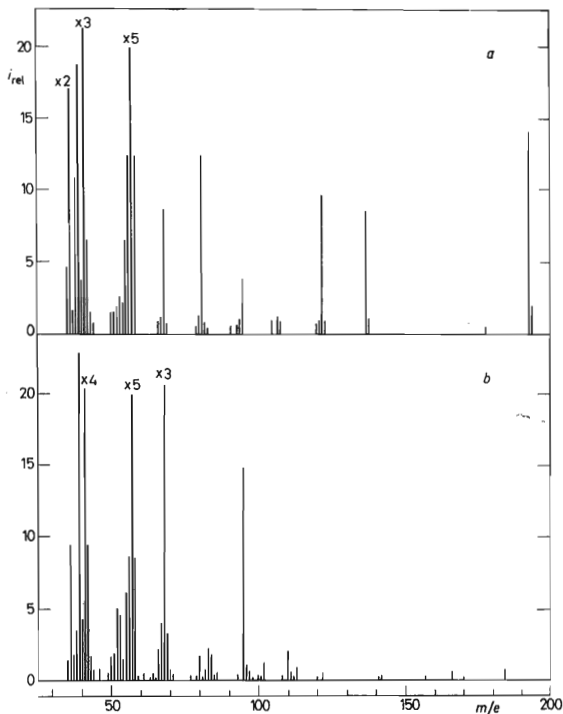system of the C=N bonds in this compound (Fig. 2b). The NMR spectrum contains,

Fig. 1

Mass Spectrum of Compound *III* Obtained by Direct Evaporation (a) or by Using AGHIS
at a Temperature of 140°C (b)

Intensities are related to the strongest signal (i_{rel}).

besides the proton lines of the tert-butyl groups (τ 8·47), another two lines, τ 2·25 and τ −0·68, in a ratio of approximately 1 : 2, which can be assigned to the proton of the methin group and the protons at the nitrogen atoms, respectively.

Hydrolysis of *III* yields (tert-butylamino)cyanoacetic acid tert-butylamide (*IV*), along with a small amount of 2,3-bis(tert-butylamino)maleonitrile (*V*). The constitution of *IV* was demonstrated by its hydrolysis and decarboxylation to N-tert-butyl-glycine (*VI*); the constitution of *V* was determined spectroscopically (infrared and NMR spectra). The NMR spectrum contains — apart from the proton bands of the tert-butyl group (τ 8·69) — a single band at τ 6·24, which can be assigned to the protons of the NH functions; the infrared spectrum contains an intensive nitrile band (2 210 cm^{-1}), a band of the NH bond (3370 cm^{-1}), and a band at 1590 cm^{-1}, corresponding to the C=C bond. The band of the C=C bond was also found in the Raman spectrum. From the fact that the known 2,3-dimorpholinomaleonitrile has an analogous band in its infrared spectrum[12] (missing in the fumaronitrile derivative) it can be concluded that *V*, too, has the *cis*-configuration. If *III* is hydrolyzed in the presence of *p*-nitrophenylhydrazinium chloride, glyoxylonitrile *p*-nitrophenylhydrazone (*VII*) is obtained. The reaction of *III* with lithium ethoxide yielded 2,3-bis(tert-butylamino)-3-ethoxyacrylonitrile (*VIII*) in a yield 86%. The structure of this compound was demonstrated by a gradual hydrolysis to tert-butylaminomalonic acid N-tert-butylamide (*IX*) and *VI* (*cf.* Scheme 1). The infrared and Raman spectra of *VIII* are in accordance with the structure; the NMR spectrum exhibits an unusually
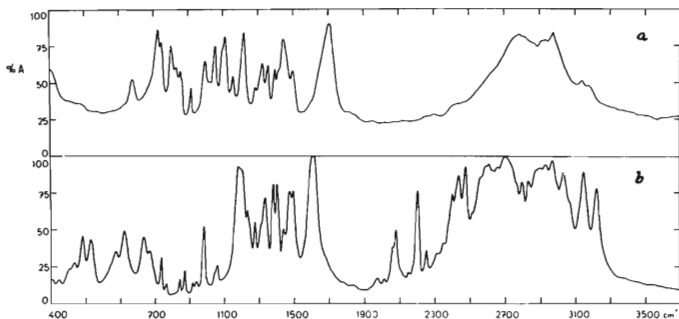

Fig. 2

Infrared Spectra of N,N′-Diethyl-N′-(dichloromethyl)formamidinium Chloride (*a*) and Compound *III* (*b*)

large displacement of the lines of both protons at the nitrogen atoms (τ 8·10 and 4·27).

A comprehensive interpretation of the mechanism of reactions of tert-butyl isocyanide (and also some other tertiary alkyl isocyanides) with the Lewis acids is given in a paper by Saegusa and coworkers[13], which appeared at the final stage of the experiments presented here. The first stage is assumed to be the splitting of isocyanide
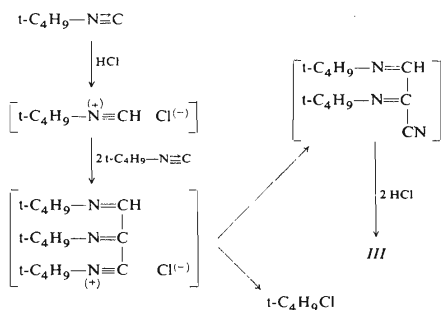
Scheme 1

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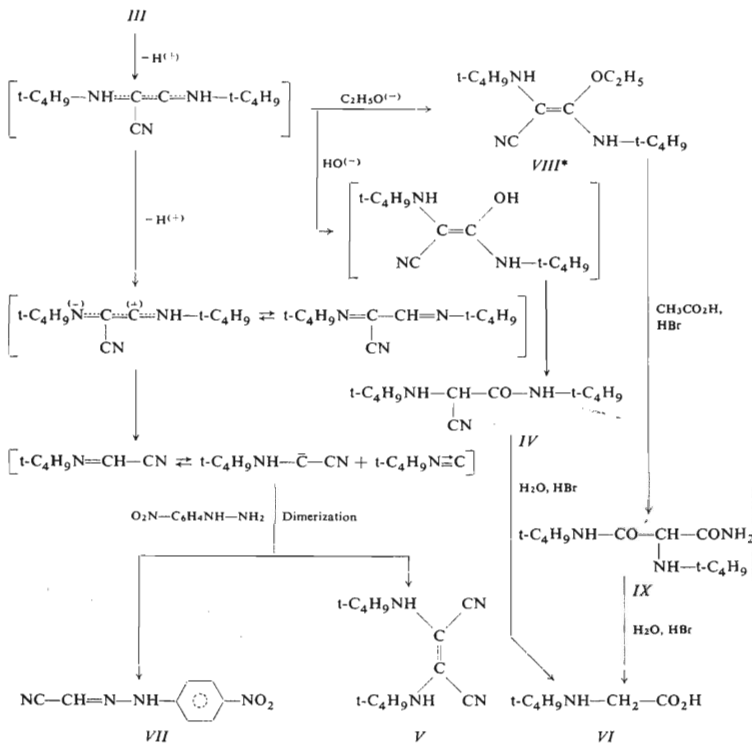
*   Configuration on the double bond is not known.

with a Lewis acid, which generates tert-butyl cation. The tert-butyl cation reacts with isocyanide to yield a positively charged intermediate product, which in its turn can either decompose to pivalonitrile with regeneration of tert-butyl cation, or react with one or more molecules of isocyanide while yielding oligomers. Moreover, it can also react with the nitrile formed, which was checked on model experiments.

In the present case, an acid rearrangement of isocyanide to nitrile is not likely, owing to the different character of the protic acid. To explain the reaction, the formation of formimidoyl chloride and its gradual reaction with another two molecules of isocyanide should be assumed, followed by the splitting of the tert-butyl cation and protonation of the Schiff base (Scheme 2).

SCHEME 2

Compound *III* is also formed in the reaction of N-tert-butylformamide with phosgene. In contrast with the reactions of N-alkylformamides of the $HCONHCH_2R^1$ and $HCONHCHR^1R^2$ type, which were interpreted as direct condensations of formimidoyl chloride with N-alkylformamide, we assume in this case that isocyanide is the intermediate product.

The reaction of *III* with water or lithium ethoxide occurs probably in such a way that the deprotonized compound carrying one positive charge reacts with the hydroxyl or ethoxyl ion. The formation of compound *V* may be explained by dimerization* of the transitionally formed (tert-butylimino)acetonitrile. Formerly, dimerization

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* (tert-Butylimino)acetonitrile, the synthesis of which was published (J. H. Boyer and H. Dabek: Chem. Commun. *1970*, 1204) after this paper had been submitted for publication, does not dimerize spontaneously at room temperature, according to the authors; its behaviour under conditions similar to the hydrolysis of compound *III* (in dilute hydrochloric acid) is not described in the paper by Boyer and Dabek.

of iminoacetonitrile to 2,3-diaminomaleonitrile was assumed while interpreting the formation of this compound during oligomerization of hydrogen cyanide. This assumption has recently been checked by preparing aminocyanocarbene, which can be considered a tautomer of iminoacetonitrile[14]. This compound yields 2,3-diaminomaleonitrile already at very low temperatures. The formation of (tert-butylimino)acetonitrile by deprotonation of compound *III* and thermal decomposition of the deprotonized base may be assumed from the results of mass spectrometry, when according to the conditions chosen either a molecular ion of the deprotonized *III* or a molecular ion of (tert-butylimino)acetonitrile can be obtained, along with a more intensive peak of tert-butyl isocyanide. (tert-Butylimino)acetonitrile also seems to be most likely intermediate product while explaining the formation of glyoxylonitrile *p*-nitrophenylhydrazone during hydrolysis of *III* in the presence of *p*-nitrophenylhydrazinium chloride. (tert-Butylimino)acetonitrile could also react with isocyanide and water according to the Ugi reaction[9,15], yielding *IV*.

EXPERIMENTAL

Crystallizations from pentane and dichloromethane were carried out by gradual cooling of solutions saturated at room temperature to −75°C. The melting points were determined on Kofler's block and have not been corrected. Mass spectra were obtained with a MS 902 apparatus; IR spectra were recorded with a UR 10 spectrometer in the KBr pellets; the Raman spectra in the solid state and the NMR spectra in CDCl$_3$ (compound *III*) and CCl$_4$ (the other compounds) were recorded with a JEOL-JNM-3-60 (60 Mcps) spectrometer.

2,3-Di(tert-butylimino)propiononitrile Dihydrochloride (*III*)

a) *Reaction of tert-butyl isocyanide with hydrogen chloride.* To a solution of 7·2 g of freshly distilled tert-butyl isocyanide in 40 ml of dry ether, 70 ml of dry ether saturated with dry hydrogen chloride was added while stirring. A white precipitate immediately appeared, which was filtered off and dried *in vacuo*; the yield was 7·7 g (100%). In the ether mother liquor, tert-butyl chloride was detected by GLC. IR spectrum *cf.* Fig. 2*b*. NMR spectrum: τ 8·47 (tert-C$_4$H$_9$), τ 2·25 (CH) and τ −0·68 (NH); peaks τ 2·25 and τ −0·68 are in a ratio 1 : 2. For C$_{11}$H$_{21}$Cl$_2$N$_3$ (266·2) calculated: 49·62% C, 7·95% H, 26·64% Cl, 15·79% N; found: 50·25% C, 7·93% H, 26·10% Cl, 16·22% N.

b) *Reaction of N-tert-butylformamide with phosgene.* To a solution of 20·4 g N-tert-butylformamide in 50 ml of dry tetrahydrofuran, cooled in a glacial bath, a solution of 26·1 g phosgene in 50 ml tetrahydrofuran cooled to −20°C was added dropwise while continuously stirred. A fine precipitate was formed, which was stirred overnight, sucked off and dried *in vacuo;* the yield was 14·3 g (80%). According to its IR spectrum, the product is identical with the compound described sub *a*). Found: 49·84% C, 8·24% H, 25·50% Cl, 15·64% N.

Hydrolysis of *III*

Compound *III* (4·54 g) was stirred with water (30 ml) for two min. The insoluble fraction (0·34 g) yields on filtration, drying, and crystallization from pentane 2,3-bis(tert-butylamino)maleonitri-

le(V), m.p. 77°C. IR spectrum: 1590 (C=C), 2210 (C≡N), 3370 (NH) cm^{-1}. The Raman spectrum 1588 (C=C) cm^{-1}. NMR spectrum: τ 8·69 (tert-C$_4$H$_9$), τ 6·24 (NH). For C$_{12}$H$_{20}$N$_4$ (220·2), calculated: 65·42% C, 9·15% H, 25·43% N; found: 65·66% C, 9·15% H, 25·36% N. The filtrate on alkalization with a saturated solution of sodium carbonate, yielded a precipitate of (tert-butylamino)cyanoacetic acid tert-butylamide (IV), m.p. after crystallization from pentane 67·5°C, yield 2·12 g (59% theor.). IR spectrum: 1705 (C=O), 2235 (C≡N), 3310 (NH) cm^{-1}. NMR spectrum: τ 8·83 (9 H) and τ 8·66 (9 H of tert-butyl), τ 7·57 and τ 5·92 (two doublets each containing 1 H with splitting 7c, CH—NH), τ 2·73 (a sharp singlet, 1 H of NH). For C$_{11}$H$_{21}$.N$_3$O (211·3) calculated: 62·53% C, 10·02% H, 19·89% N; found: 62·77% C, 10·16% H, 19·59% N.

Glyoxylonitrile p-Nitrophenylhydrazone (VII)

Compound III (1·50 g) was dissolved in a saturated solution of 1·80 g of p-nitrophenylhydrazine in 2N-HCl, and the solution was left to stand twelve hours at 0—5°C. From the solution, 0·38 g (35%) of orange-coloured glyoxylonitrile p-nitrophenylhydrazone (VII) precipitated, m.p. 211—213°C; after crystallization from dichloromethane, m.p. was 214·5°C (compound melts partly between 180—188°C, then solidifies again). IR spectrum: 850 (deformation CH of 1,4-disubstituted benzene ring), 1565 and 1610 (C=N or benzene ring), 2218 (C≡N), 3235, 3215 (NH) cm^{-1}. For C$_8$H$_6$N$_4$O$_2$ (190·2) calculated: 50·53% C, 3·18% H, 29·46% N; found: 50·33% C, 3·34% H, 29·15% N. The same compound was prepared by Brecknell and coworkers[16] by decarboxylation of (N-p-nitrophenylhydrazono)cyanoacetic acid. No melting point of the product has been given; the data on the bands of the IR spectrum in the region above 2200 cm^{-1} are not sufficient for identification.

2,3-Bis(tert-butylamino)-3-ethoxyacrylonitrile ($VIII$)

5·7 g of III was gradually added to a suspension of 2·56 g lithium ethoxide in 50 ml of dry tetrahydrofuran while stirring. The solution was evaporated to dryness, the dry residue was extracted with dry ether, and the extract was evaporated again. The distillation in vacuo of semiliquid dry residue (oil pump, bath temperature 90°C) yielded 4·4 g (86%) of chromatographically uniform yellowish distillate; on crystallization from pentane, the distillate formed white crystals, m.p. 48·5°C. IR spectrum: 1600 (C=C), 2165 (C≡N), 3295 and 3355 (NH) cm^{-1}. The Raman spectrum 1600 (C=C) cm^{-1}. NMR spectrum: τ 8·10 and τ 4·27 (NH), τ 8·88 and τ 8·75 (tert-C$_4$.H$_9$), τ 8·57 and τ 5·55 (C$_2$H$_5$). For C$_{13}$H$_{25}$N$_3$O (239·3) calculated: 65·23% C, 10·53% H, 17·56% N; found: 65·36% C, 10·65% H, 17·94% N.

tert-Butylaminomalonic Acid N-tert-Butylamide (IX)

In 5 ml of acetic acid, saturated with hydrogen bromide at 0°C, 0·8 g of 2,3-bis(tert-butylamino)-3-ethoxyacrylonitrile was dissolved; the solution was left to stand twelve hours and evaporated to dryness in vacuo. The dry residue was dissolved in a saturated solution of sodium carbonate and extracted with ether. The latter was distilled off; crystallization from toluene yielded 0·6 g (78%) of compound having m.p. 124·5—125°C. IR spectrum: 1655 and 1795 (C=O), 3190, 3290, 3370 and 3415 (NH or NH$_2$) cm^{-1}. For C$_{11}$H$_{23}$N$_3$O$_2$ (229·3) calculated: 57·61% C, 10·11% H, 18·33% N; found: 57·39% C, 10·02% H, 18·28% N. The same compound was formed by hydrolysis of (tert-butylamino)cyanoacetic acid tert-butylamide carried out under identical conditions (identified by IR spectroscopy).

Total Hydrolysis of *VIII*

2,3-Bis(tert-butylamino)-3-ethoxyacrylonitrile (1·28 g) was refluxed three hours with azeotropic hydrogen bromide. On evaporation to dryness, dissolving in water and re-evaporation, the aqueous solution of the dry residue was deionized on a strongly basic ion-exchange resin (Dowex 2). The resin was washed with 4M-CH$_3$COOH, the washing solution was evaporated to dryness, and the dry residue (0·56 g — 76%) was recrystallized from N,N-dimethylformamide. When heated, the sample decomposes at 180—190°C. According to the IR spectrum, this compound is identical with the authentic sample of N-tert-butylglycine, prepared by the authors by deionization of hydrochloride[17] with an ion-exchange resin. The identity was also proved by transforming the compound into hydrochloride and comparison of the IR spectra. N-tert-butylglycine was obtained by the same procedure also when compounds *IV* and *IX* were hydrolyzed.

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