Pyrolysis of N-*t*-Butyl-N-alkylcarbamoyl Chlorides. A New Synthesis of Isocyanates

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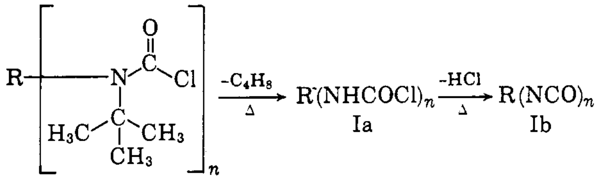
Received December 27, 1962

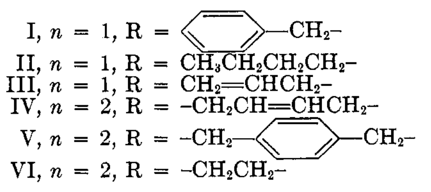
A number of N-*t*-butyl-N-alkyl carbamoyl chlorides have been synthesized by known methods. These compounds decompose readily at low temperature with or without catalysis to the corresponding alkyl isocyanates in high yield.

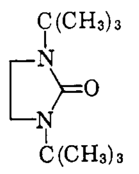
The pyrolysis of an N-*t*-Butyl-N-alkyl carbamoyl chloride (I) to the primary carbamoyl chloride (Ia) or even to the corresponding alkyl isocyanate (Ib) provides a synthetic approach to mono- and diisocyanates, some of which are not readily accessible by known synthetic methods.

Accordingly, a number of *t*-butylalkylamines were synthesized in high yield from *t*-butylamine and the corresponding alkyl chlorides using a modification of Bortnick's[1] method. The *t*-butylalkylamines were then phosgenated under a variety of conditions to the N-*t*-butyl alkyl carbamoyl chlorides which, in certain cases, were isolated, purified, and characterized; the yields depending both on the nature of the alkyl group and the method of phosgenation.



I





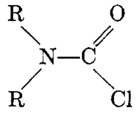
VII

Attempts to prepare VI from N,N′-bis-*t*-butylethylenediamine gave 1,3-bis-*t*-butyl-2-imidazolidinone (VII) instead.

The initial model selected, *t*-butylbenzylamine-N-carbonyl chloride (I), demonstrated the relative ease with which the decompositions to isocyanate may take place. Even during its formation in toluene (110°) traces of isocyanate were detectable. The pure material (I), a solid, in the melt at 130 to 160°, decomposed with vigorous gas evolution, to give hydrogen chloride, isobutylene, *t*-butyl chloride, and benzyl isocyanate in over 84% yield. The generality of the reaction has been established by similarly converting the *n*-butyl (II) and allyl (III) derivatives to the corresponding monoisocyanates, and the *p*-xylylene (IV) and 1,4-disubstituted butene-2 (V) derivatives to the corresponding diisocyanates in good yield.

Operational difficulties attendant with the more volatile II and III and with the more reactive IV and V when decomposed as the undiluted materials prompted a study, of the reaction in a variety of solvents. This study, using II as a model, revealed that the reaction proceeds with utmost ease in polar solvents[2] such as nitrobenzene at mild (100°) temperatures, while being slow in toluene. Moreover, the addition of catalytic amounts of ferric chloride, known to aid reaction of carbamoyl chlorides,[3] accelerated the reaction even to the extent that the reaction proceeded as well as with catalyst at 83° in ethylene dichloride as it had at 100° without catalyst in nitrobenzene. These results are shown in Fig. 1 and in Table I.

Synthesis of disubstituted carbamoyl chlorides (VIII) by phosgenation of secondary amines under various conditions is well known[4]; however, the formation of isocyanates from such carbamoyl chlorides or even during their synthesis has not been reported previously. Actually, compounds VIII appear to exhibit considerable thermal stability, especially the mono- and diaryl derivatives, but even straight-chain dialkyl derivatives are quite stable. This is demonstrated strikingly by the work of Slocombe[4i] who has obtained the dibutyl and diamyl derivatives in 80% yield by vapor phase phosgenation of the secondary amines at 200–275°. No isocyanate formation from these amines was mentioned.



VIII

From this work, it is evident that introduction of branching in the α-carbon reduces the thermal stability markedly. The highly stable examples cited are either aryl[5,6] or primary alkyl[4i] substituted. There are only a few secondary alkyl[4f,m,5] substituted carbamoyl chlorides reported. Isocyanate formation from these has not been observed, although Boon[4f] has de-

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(1) N. Bortnick, *et al.*, *J. Am. Chem. Soc.*, **78**, 4039 (1956).

(2) L. P. Hammett, "Physical Organic Chemistry," McGraw Hill Book Co., New York, N. Y., 1940, pp. 214, 215, 322, 323.

(3) F. Weygand and R. Mitgau, *Chem. Ber.*, **88**, 301 (1955); *Chem. Abstr.* **50**, 1663 (1956).

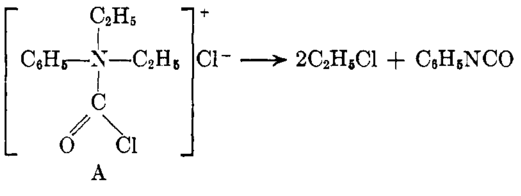
(4) (a) A. B. Boese, Jr., and R. T. Major, *J. Am. Chem. Soc.*, **57**, 175 (1935); *Chem. Abstr.*, **29**, 1412 (1935). (b) G. Lob, *Rec. trav. chim.*, **55**, 859–873 (1936); *Chem. Abstr.*, **31**, 1385 (1937). (c) M. M. Jamison and E. E. Turner, *J. Chem. Soc.*, 1954, (1937); *Chem. Abstr.*, **32**, 1666 (1938). (d) L. Raiford and K. Alexander, *J. Org. Chem.*, **5**, 300 (1940); *Chem. Abstr.*, **34**, 5065 (1940). (e) L. Orthner, U. S. Patent 2,251,892 (1941); *Chem. Abstr.*, **35**, 7586 (1941). (f) W. R. Boon, *J. Chem. Soc.*, 307–318 (1947); *Chem. Abstr.*, **41**, 5448–5451 (1947); British Patent 560,700 (1944); *Chem. Abstr.*, **40**, 3857 (1946); U. S. Patent 2,398,283 (1946); *Chem. Abstr.*, **40**, 4178 (1946). (g) O. Ya. Fedetova, *et al.*, *ibid.*, **53**, 1141 (1959). (h) P. E. Wilcox and W. A. Schroeder, *J. Org. Chem.*, **15**, 944 (1950); *Chem. Abstr.*, **45**, 2889 (1951). (i) R. J. Slocombe, *et al.*, *J. Am. Chem. Soc.*, **72**, 1888 (1950). (j) W. Siefken, *Ann.*, **562**, 75–136 (1949); *Chem. Abstr.*, **44**, 115 (1950). (k) S. Kushner and L. Brancone, U. S. Patent 2,467,895 (1949); *Chem. Abstr.*, **43**, 6245a (1949). (l) J. Weijlard and M. Tishler, U. S. Patent 2,642,450 (1953); British Patent 688,726 (1953); *Chem. Abstr.*, **48**, 2091 (1954). (m) A. Sekera, *et al.*, *Chem. Listy*, **46**, 762 (1952); *Chem. Abstr.*, **47**, 12302 (1953).

(5) T. W. Price, *J. Chem. Soc.*, 3230 (1926).

(6) R. Stolle, *J. prakt. Chem.*, **117**, 185–210 (1927); *Chem. Abstr.*, **22**, 422 (1928).

scribed some of them as undistillable liquids.[7] *t*-Alkyl substituted carbamoyl chlorides were not reported previously in the literature.

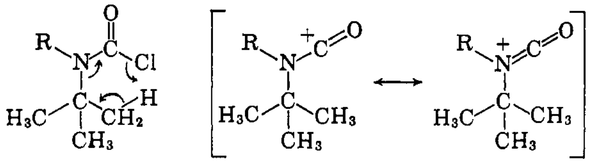
While the phosgene–tertiary amine reaction is a well known[8] reaction for synthesis of disubstituted carbamoyl chlorides, again, frequently under drastic (190°) conditions, there is only an isolated instance in which Wahl[8a] reports that the use of a large excess of phosgene at high temperature on di-*n*-alkylanilines afforded traces of phenyl isocyanate. This reaction could proceed *via* an intermediate such as A.



$$\left[C_6H_5-\overset{C_2H_5}{\underset{\underset{O\ \ \ Cl}{C}}{N}}-C_2H_5\right]^+Cl^- \longrightarrow 2C_2H_5Cl + C_6H_5NCO$$

A

The decomposition of the *t*-butylcarbamoyl chlorides occurs more readily in polar than in nonpolar solvents and is catalyzed by Lewis acids such as ferric chloride. These effects of solvent and catalysis are demonstrated in Fig. 1, whereby the rate of decomposition in the polar solvent nitrobenzene or with ferric chloride in ethylene dichloride solvent is considerably enhanced over that in the nonpolar solvent toluene. These facts are consistent with a cyclic concerted process similar to the Cope and Chugaev reactions,[9,10] and illustrated by B. An alternative mechanism involving the initial ionization of chloride ion to give the resonance stabilized carbonium ion (C), a step facilitated both by polar solvent and Lewis acid, is perhaps more attractive.



B C

Analogous to this reaction are the observations of Mukaiyama, *et al.*,[11] who have obtained isocyanates among other formed products from acetoacetamides and α-chloroacetanilides, albeit only at 350° and above in the vapor phase. Very significantly, the yields were greatly improved when the N–H was replaced by N–*t*-Bu in the latter types.

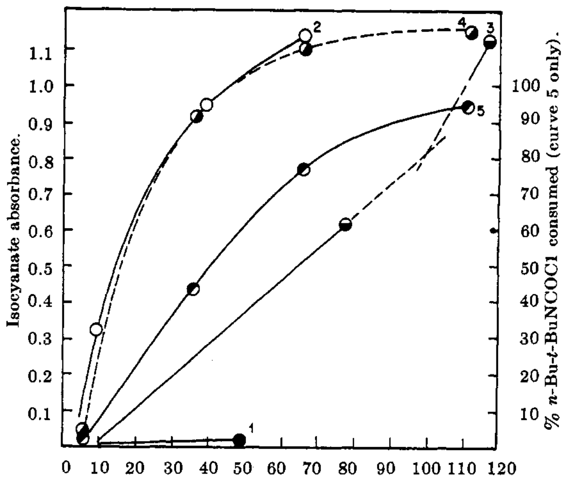
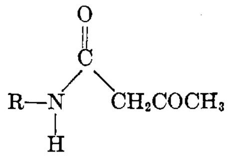
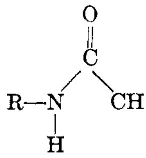


Fig. 1.—Formation of *n*-butyl isocyanate from *n*-butyl-*t*-butylcarbamoyl chloride. Curves 1 through 4 represent isocyanate absorbance (λ_{max} 4.45 μ, left ordinate) *vs.* time: (1) ●, in toluene at 100°; (2) ○, in nitrobenzene at 100°; (3) ⊖, in 1,1,2-trichloroethane at 100° with a trace of ferric chloride catalyst introduced at a reaction time of 97 minutes; (4) ◑, in 1,2-dichloroethane with ferric chloride catalyst at 83°. Curve 5, ◐ indicates the per cent *n*-butyl-*t*-butylcarbamoyl chloride consumed in 4 as determined by the carbonyl absorption at λ_{max} 5.75 μ (right ordinate).





Experimental

Analyses were by Schwarzkopf Microanalytical Laboratory, Woodside, N. Y.; infrared spectra were determined on a Perkin-Elmer Model 21 spectrophotometer.

1. General Procedure for *t*-Butylamines

The procedure is a modification of Bortnick's method,[1] and is illustrated for *t*-butylbenzylamine. A solution of 75.9 g. (0.6 mole) of benzylchloride and 87.6 g. (1.2 moles) of *t*-butylamine in 150 ml. of dimethylformamide was heated at a gentle boil for 3 hr. during which the temperature rose from 80° to 140° with some crystals forming and redissolving. Thereafter, excess (78% recovery) *t*-butylamine was slowly (3 hr.) distilled. From the cooled mixture 112 g. (93% theory) of crude amine hydrochloride was obtained dry, m.p. 249–253°. Treatment with 15% caustic (no exotherm) afforded 76.1 g. of an oil which was dried over potassium hydroxide pellets and distilled *in vacuo*; b.p. 100° (17 mm.), b.p. 107° (20 mm.), b.p. 99° (14 mm.); $n^{22.7}D$ 1.4951 [reported b.p. 91° (12 mm.), $n^{25}D$ 1.4941].

Because the reaction of the allylic halides with *t*-butylamine was very exothermic, these halides were added dropwise to the preheated amine solution at 65–75° without additional heating until the addition was complete; by contrast, complete reaction with *n*-butyl chloride or ethylene dichloride required nearly 2 days.

2. Phosgenation of *t*-Butylamines

Method A. (a) *t*-Butylbenzylamine-N-carbonyl Chloride (I).—A solution of 48.6 g. (0.3 mole) of *t*-butylbenzylamine in 100 m. of toluene was added (25 min.) to a stirred, ice-cooled solution of 30 g. (0.3 mole) of phosgene in 500 ml. of toluene while passing excess phosgene at a rate of 0.1–0.2 mole/hr. The resulting thick suspension was refluxed until clear (100°, 16 hr.) while continuing to add phosgene. Evaporation *in vacuo* afforded a crystalline residue, pale brown to yellow, with a sweet and pungent odor, 66 g. (96%), m.p. 85–89°.

Spectrum: $\lambda_{max}^{CHCl_3}$ 3.42, 5.75, 6.85, 7.14, 7.34–7.45, 8.50, 8.95, 10.40 μ.

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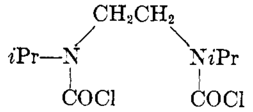
(7) Among these were, however, compounds of the ethylenediamine type which have a structure predisposed to the elimination of phosgene with concomittant cyclization to ethyleneureas,[4b,4f] which we have rather similarly observed on attempted synthesis of VI (*cf.* Experimental section 6)



(8) (a) A. Wahl, *Bull. soc. chim.*, [5] **1**, 244–246 (1934); *Chem. Abstr.*, **28**, 5430 (1934). (b) C. Scholtissek, *Chem. Ber.*, **89**, 2562 (1956); *Chem. Abstr.*, **51**, 14712 (1957). (c) V. A. Rudenko, *et al.*, *J. Gen. Chem., USSR*, **17**, 2256–2258 (1947); *Chem. Abstr.*, **42**, 4918 (1948). (d) E. Stein and O. Bayer, U. S. Patent 2,698,343 (1954).

(9) D. J. Cram, "Steric Effects in Organic Chemistry," M. S. Newman, Ed., John Wiley and Sons, Inc., New York, N. Y., 1956, p. 310.

(10) C. H. DePuy and R. W. King, *Chem. Rev.*, **60**, 431 (1960).

(11) T. Mukaiyama, *et al*, *J. Org. Chem.*, **26**, 4381 (1961); **27**, 803 (1962).

(b) ***n*-Butyl-*t*-butylamine-N-carbonyl Chloride** (II).—This procedure on *n*-butyl-*t*-butylamine in benzene gave a solution containing much unchanged suspended amine hydrochloride even after 24 hr. at 80°, but this filtered hydrochloride was completely phosgenated in 5.5 hr. in toluene at 110°. The carbonyl chloride was not isolated, but rather pyrolyzed on concentration.

(c) **Bis-*t*-butylamino-*p*-xylylene-N,N′-dicarbonyl Chloride** (V).—The procedure of method A using chlorobenzene solvent at reflux (130°) during 3 days still had 22% unchanged dihydrochloride present, which was insoluble and identical with original hydrochloride. The filtrate, on concentration, afforded a bright yellow solid which became colorless on standing in the air, crude V.

Method B. (a) **1,4-Bis-*t*-Butylaminobutene-2-N,N′-dicarbonyl Chloride** (IV).—A solution of 19.8 g. (0.1 mole) of 1,4-bis-*t*-butylaminobutene-2 and 20.2 g. (0.2 mole) of triethylamine in 100 ml. of benzene was added to an ice-cooled (3–8°) solution of *ca.* 19.8 g. (0.2 mole) of phosgene in 150 ml. of benzene (40 min., 3–8°). After 1-hr. stirring at 20–30°, the mixture was purged and heated to 65°. The solid triethylamine hydrochloride was filtered off and triturated once with hot benzene (100 ml., 60°). The combined filtrates afforded 25.8 g. of fine crystals, m.p. 132–134°; and another 3.6 g., m.p. 132–133°, from the mother liquor (total 91%).

Anal. Calcd. for $C_{14}H_{24}N_2O_2Cl_2$: C, 52.01; H, 7.48; N, 8.67. Found: C, 52.14; H, 7.35; N, 8.72.

Spectrum: $\lambda_{max}^{CHCl_3}$ 3.40, 5.75, 6.80, 7.16, 7.3–7.5, 8.50, 8.90, 9.33, 10.45 μ.

(b) ***n*-Butyl-*t*-butylamine-N-carbonyl Chloride** (II).—This was also prepared by method B; however, filtering and triturating the triethylamine hydrochloride was done in the cold (20–30°). The filtrate, on concentration, afforded an oil which, on centrifuging free of trace impurities, weighed 16.6 g. (86% from 12.9 g., 0.1 mole, amine), m.p. −23 to −25°.

Spectrum: λ_{max}^{neat} 3.42, 5.75, 6.80, 7.3, 7.45, 7.75, 8.43, 9.25, 10.65, 11.83, 13.3, 13.65, 14.0, 14.8 μ.

Method C. Combined Phosgenation and Pyrolysis to Isocyanate. (a) **Allyl Isocyanate.**—Into an ice-cold, stirred solution of 100 ml. of *o*-dichlorobenzene and 27.8 g. (0.15 mole) of tributylamine was condensed *ca.* 15 g. (0.15 mole) of phosgene and then was added 17.0 g. (0.15 mole) of *t*-butylallylamine during 10 min. III was not isolated; rather 1.15 hr. later, the mixture was heated to 115–125° while adding another 0.15 mole of tributylamine. With a short distilling column attached, a receiver at room temperature, and a Dry Ice-cooled trap in series, the reaction mixture was heated to 175° (1 hr.) and then to 200° (1 hr.). During the latter period 9.3 g. (75%) of slightly impure allyl isocyanate distilled, b.p. 80–85° (760 mm.) [reported[12] b.p. 82° (760 mm.)]. Isocyanate equivalent, 83.9; theory, 83.1.

Infrared spectrum: λ_{max}^{neat} 2.75, 3.27, 4.42, 6.05, 6.92, 7.05, 7.4, 7.5, 10.07, 10.75–10.9 μ. The Dry Ice trap contained 7.6 g. of volatile material, b.p. mostly −10 to +1° (760 mm.) (reported for isobutylene −6°) with a strong olefinic odor; $\lambda_{max}^{CHCl_3}$ (5–15%) 4.42 μ for traces of isocyanate; traces *t*-butyl chloride, λ_{max} 6.84, 7.29, 8.07, 8.65 μ; and much isobutylene, λ_{max} 3.28, 3.45, 6.04, 11.30 μ. On overnight standing at room temperature the trap contents evaporated to a few drops of residue; λ_{max}^{neat} 4.45, 7.29, 8.65 μ were strong, while 6.04 μ was much decreased, and 11.30 μ entirely absent, consistent with a residue of *t*-butyl chloride and allyl isocyanate.

(b) ***n*-Butyl Isocyanate.**—Method C was used on *t*-butyl-*n*-butylamine with the variation that the reaction mixture was heated at 120–145° for 1 hr. and then cooled to 90° before adding the second 0.15 mole of tributylamine. During the initial period 9 g. of volatiles consisting of isobutylene and *t*-butyl chloride was collected. The distillation that followed provided a mid-cut, b.p. 114–117° (760 mm.) (reported 115°), 12.9 g. of butyl isocyanate (87%). The spectrum (neat) was identical with that of authentic material prepared from *n*-butylamine and phosgene. Since no λ_{max}^{neat} 7.77, 13.75, 15.32 μ, characteristic of *n*-butyl chloride were present, this material had not been formed.

3. Decomposition of Pure (Isolated) N-Carbonyl Chloride

(a) **Benzyl Isocyanate.**—The crude *t*-butylbenzyl-N-carbonyl (I) (66 g., 0.292 mole previously described) was melted and heated further, darkening from yellow to brown to greenish black at 120–160° while sweeping out volatile products with nitrogen into a Dry Ice-cooled flask. This distillate, 21 g. (77%), proved to be virtually pure *t*-butyl chloride by spectral comparison with purchased (Eastman) material. On cessation of gas evolution the residue was distilled; b.p. 104–110° (31–36 mm.); $n^{22}D$ 1.5242; 33.5 g. (86%) of benzyl isocyanate. The spectrum was identical with that of authentic material prepared from benzylamine and phosgene, having $n^{21.5}D$ 1.5242; $\lambda_{max}^{CHCl_3}$ 2.75, 4.45, 6.65, 6.85, 7.47, 11.5, 14.4 μ. The absence of any 7.89 μ absorption indicated that no benzyl chloride was produced.

(b) ***p*-Xylylene Diisocyanate.**—Eight grams (0.0215 mole) of crude V was pyrolyzed similarly and distilled; b.p. 138–147° (4–6 mm.); 2.5 g. (62%), m.p. 37–39°. Calcd. for isocyanate equivalent: 94.09. Found: 98.2. Spectrum (10% in chloroform) identical with authentic material having m.p. 37°, prepared by phosgenation of *p*-xylylenediamine.

4. Decomposition of (Pure) N-Carbonyl Chloride in Solution. Semiquantitative Kinetic Study

(a).—The oily II obtained [*cf.* method B (b)] was used. Solvent, 38 g., and 2.0 g. of II were heated quickly by insertion of the containing flask into a preheated oil bath. The well stirred solution was sampled at intervals by pipetting through a short reflux condeneer. The cooled samples were examined in the infrared usually from 4 to 6 μ *vs.* pure solvent in sodium chloride cells (0.095 mm.). Catalyst (5 to 30 mg.), when used, was added just prior to heating. In several cases hydrogen chloride evolution was detectable. Solvents nitrobenzene, toluene, ethylene dichloride, and trichloroethane were used (see Fig. 1, Table I).[13]

(b).—Because the method (undiluted) used for decomposing I and V caused much tar formation with IV, the solvent study

TABLE I

FERRIC CHLORIDE[a]-CATALYZED DECOMPOSITION OF II AND IV IN ETHYLENE DICHLORIDE

Compound, initial concn.	Sample point	Time, min.	Temp., °C.	% CC[b,c]	% NCO[d]	A_{NCO}[e]
II, 5% by weight[a]	1	0	25	100	0	0.00
	2	5	83	98	2	0.055
	3	35	83	56	44	0.910
	4	65	83	23	(77)	1.1[b]
	5	115	83	6	(94)	1.1[b]
IV, 2.5% by weight	1	0	25	100	0	0.0
	2	5	83	98	2	0.01
	3	35	83	73	∼30	0.245
	4	65	83	63	∼40	0.357
	5	330	83	28	∼70	0.63

[a] About 10–30 mg. of catalyst in a total 40 g. of reactant–solvent solution. [b] Per cent of unchanged carbonyl chloride, estimated from λ_{max} 5.75, this being the only carbonyl (and very sharp) absorption found in the ethylene dichloride systems. [c] A plot of % CC *vs.* time for II fits first-order kinetics quite well [log (% CC) *vs.* *t* is fairly linear]. With IV, however the plot is better described by % CC = 2 (A) + (B) for a system[14] $A \xrightarrow{k_1} B \xrightarrow{k_2} C$ in which $k_1/k_2 \approx 7$, and A is biscarbonyl chloride, B is monocarbonyl chloride monoisocyanate, and C is diisocyanate. [d] With II the yield of isocyanate formed is by difference only; with IV the values are rough averages of values obtained both by difference and by A_{NCO}, the values agreeing to within 4% of theoretical (*e.g.*, let % NCO = $A_{NCO}/0.63 \times 72$) in point 5 for IV. [e] Isocyanate absorbance in the reaction solution at λ_{max} 4.45. [f] The discrepancy here probably is due to volatility of butyl isocyanate.

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(12) Beilstein, Vol. 4, p. 214.

(13) Only in ethylene dichloride and toluene was there unambiguously a single carbonyl absorption at 5.75 μ assignable to pure II or IV throughout the entire reaction, whereas in the other solvent systems, shoulders at 5.8–5.9 and 5.67 μ eventually appeared, attributable to R–NHCOCl and perhaps urea formation.

(14) F. Daniels and R. Alberty, "Physical Chemistry," John Wiley and Sons, Inc., New York, N. Y., 1957, p. 337–338.

was initiated on II. Thereafter, the butene-2 derivative IV was decomposed in ethylene dichloride and trichloroethane, 1 g. of IV in 39 g. of solvent with added ferric chloride catalyst (see Table I).

5. (*trans*[15]?)-1,4-Diisocyanatobutene-2

A solution of 10.0 g. (0.031 mole) of IV, 30 mg. of ferric chloride (hexahydrate), and 90 g. of ethylene dichloride was refluxed (83°), while passing a gentle stream of nitrogen to entrain volatiles, for 25 hr., then cooled, filtered, and concentrated to a brownish oil. The oil was distilled *in vacuo*, b.p. 106–111° (13–19 mm.), affording 2.8 g. (65%) of a clear oil, n^{23}_D 1.4728, m.p. −2 to 0°; $\lambda_{max}^{CHCl_3}$ 2.75, 3.24, 4.45, 6.92, 7.10, 7.45, 10.3, 11.6 μ. The bismethylurethane (glistening flakes from methanol) had m.p. 143–144° (reported[8] m.p. 137°). The isocyanate turned brown on standing several days.

6. 1,3-Bis-*t*-butyl-2-imidazolidinone (VII)

When 17.2 g. (0.1 mole) of N,N′-bis-*t*-butylethylenediamine was added to 0.2 mole of a phosgene (20 g.)–triethylamine (20.2 g.) complex in cold benzene, followed by stirring and gentle warming, the reddish brown mixture gave a 67% yield of triethylamine hydrochloride and a filtrate which, on evaporation, gave a semicrystalline oil, 22.2 g. Crystallization (hexane) or distillation afforded solid, soft needles, m.p. 73–74°, b.p. 127° (16.5 mm.), b.p. 245° (760 mm.); $\lambda_{max}^{CHCl_3}$ 5.98, also 6.75, 6.85, 7.13, 7.35, and 7.8–8.3 μ.

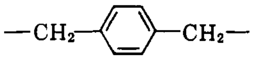
Anal. Calcd. for $C_{11}H_{22}N_2O$: C, 66.60; H, 11.18; N, 14.13. Found: C, 66.73; H, 11.14; N, 14.27.

The distillation yielded a considerable forecut, b.p. 80° (16 mm.), b.p. 180–185° (760 mm.), identified additionally as diethylcarbamoyl chloride [reported[4i] b.p. 81–85° (20 mm.)] by isolation of diethylamine (spectrum identical with authentic material) by mild alkaline hydrolysis.

7. Properties of the Intermediate Amines (See Table II)

TABLE II

t-BUTYLAMINES $R—NH—C(CH_3)_3$

Compound (R–)	M.p., °C.	B.p., °C (mm.)	Ref. index
$CH_2=CH—CH_2—$	...	112 (760 mm.)	$n^{22.5}_D$ 1.4160
$CH_3CH_2CH_2CH_2—$	...	83 (140 mm.)	$n^{22.7}_D$ 1.4086
		91 (177 mm.)	
	68–70	...	...
$—CH_2CH_2—$[b]	(42)[a]	99 (32 mm.)[c]	...
$—CH_2CH=CH—CH_2—$	(40–50)[a]	95–100 (6 mm.)	n^{22}_D 1.4494

[a] Hydrates. [b] Base equivalent, 85.8 (theory 86.15). [c] Lit. b.p. 198° (760 mm.).[4f]

Acknowledgment.—The authors wish to express their gratitude to Mr. F. Geremia and Mr. E. Foster for valuable assistance in infrared and analytical determinations.

[15] The starting 1,4-dichlorobutene-2 (Eastman) was labeled *trans*.

Direct Syntheses of Some Cyano and Nitro Derivatives of Carbohydrates by Nucleophilic Displacement[1]

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Received January 28, 1963

Methyl 2,3,4-tri-*O*-acetyl-6-deoxy-6-iodo-α-D-glucopyranoside (I) and 2,3,4,5-di-*O*-benzylidene-1,6-dideoxy-1,6-diiodo-D-mannitol (II) reacted with sodium cyanide and with sodium nitrite in *N*,*N*-dimethylformamide to give the cyano and nitro derivatives expected following nucleophilic displacement of iodide. 6-Deoxy-6-iodo-1,2:3,4-di-*O*-isopropylidene-D-galactopyranose (III) was appreciably less reactive toward sodium cyanide. *O*-Benzylidenepentaerythritol dibenzenesulfonate (IX) reacted with sodium nitrite in *N*,*N*-dimethylformamide at the reflux temperature to form *O*-benzylidenepentaerythritol benzenesulfonate (XII).

In previous investigations,[3] 1,2-*O*-isopropylidene-D-glucofuranose 6-*p*-toluenesulfonate and 1,3-*O*-benzylidene-L-arabinitol 5-*p*-toluenesulfonate reacted with potassium cyanide to afford the corresponding cyano derivatives. In these reactions, the carbon undergoing displacement is removed from the rings by an intervening carbon bearing a hydroxyl group, which was proposed[3] to form an intermediate epoxide that then added hydrogen cyanide to give product. Success realized in effecting nucleophilic displacement reactions of neopentyl-type sulfonate esters with cyanide ion[4] prompted an investigation in which carbohydrate derivatives with functional groups without hydroxyls on the adjacent carbon were subjected to similar reaction conditions with the objective of achieving direct displacement, which was previously reported[3] to have failed. Iodides were selected over sulfonate esters since the former tend to be more reactive[5] than the latter in reactions with SN2-type character and moreover are readily preparable from the latter.[6] Methyl 2,3,4-tri-*O*-acetyl-6-deoxy-6-iodo-α-D-glucopyranoside (I),[7] 2,3,4,5-di-*O*-benzylidene-1,6-dideoxy-1,6-diiodo-D-mannitol (II),[8] and 6-deoxy-6-iodo-1,2:3,4-di-*O*-isopropylidene-D-galactopyranose (III)[9] were selected as substrates for displacement reactions with sodium cyanide in *N*,*N*-dimethylformamide (DMF). Both I and II reacted readily to give the expected products of displacement, methyl 2,3,4-tri-*O*-acetyl-6-deoxy-α-D-*gluco*-heptopyranurononitrile (IV) and 3,4,5,6-di-*O*-benzylidene-2,7-dideoxy-D-*manno*-octaronitrile (V), respectively, in yields of 54 and 51%.

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[1] Abstracted from portions of the Ph.D. theses of W. J. T. and S. M. D.

[2] Members of the "Research Participation for Teacher Training" Program at the University of Utah, 1962, sponsored by the National Science Foundation.

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