[Contribution No. 306 from the Chemical Department, Experimental Station, E. I. du Pont de Nemours & Company]

A NEW REACTION OF OLEFINS, NITRILES, AND HALOGENS[1]

T. L. CAIRNS, P. J. GRAHAM, P. L. BARRICK, and R. S. SCHREIBER

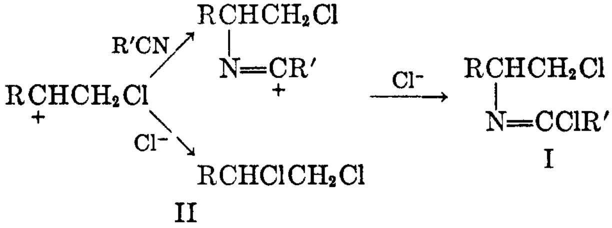
Received January 17, 1952

A new three-component reaction has been discovered for the synthesis of N-(2-chloroalkyl)amides. The synthesis involves interaction of chlorine and an olefin in the presence of a nitrile to give an imide chloride that can be hydrolyzed to an N-(2-chloroalkyl)amide. This interaction of chlorine, an olefin, and a nitrile has been found to be a general reaction applicable to aromatic and aliphatic nitriles and hydrogen cyanide in combination with such olefins as ethylene, cyclohexene, 1-octene, and styrene. In addition, this synthesis can be carried out with bromine to give N-(2-bromoalkyl)amides. The reaction has been shown to proceed in two steps. The first step gives a chloroimide chloride as well as a dichlorohydrocarbon arising from the original olefin, and the second step gives an N-(2-chloroalkyl)amide by hydrolysis of the chloroimide chloride. When hydrogen cyanide is used, the N-(2-chloroalkyl)formamide is very readily hydrolyzed to the corresponding 2-chloroalkylamine, which is isolated as the hydrochloride. Products produced in these various stages have been isolated and identified.

The interaction of chlorine and an olefin in the presence of a nitrile is postulated to proceed as follows:

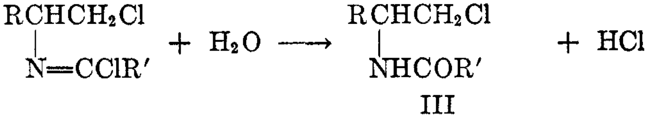
$$1. \quad RCH{=}CH_2 + Cl_2 \longrightarrow R\underset{+}{C}HCH_2Cl + Cl^-$$

2.



Whenever the imide chloride (I) is obtained from a nitrile having no *alpha* hydrogen atoms, it can be separated from the by-product (II) by rectification. When the imide chloride is formed from a nitrile containing *alpha* hydrogen atoms, it is susceptible to thermal bimolecular condensation (1) through loss of hydrogen chloride and should be hydrolyzed at once to the more stable N-(2-chloroalkyl)amide.

3.



$$3. \quad \begin{matrix} RCHCH_2Cl \\ | \\ N{=}CClR' \end{matrix} + H_2O \longrightarrow \begin{matrix} RCHCH_2Cl \\ | \\ NHCOR' \\ \text{III} \end{matrix} + HCl$$

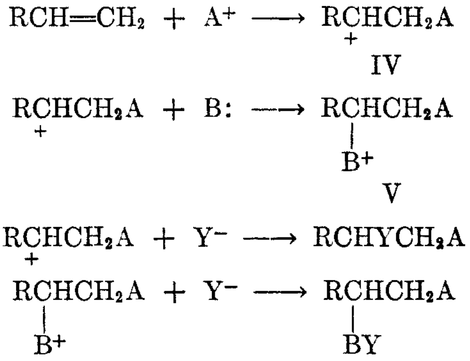
When the amide (III) does not crystallize readily, its separation from the by-

---

[1] Presented at the Delaware Chemical Symposium on January 12, 1952.

product (II) by rectification is difficult since N-(2-chloroalkyl)amides are also sensitive to heat.

The interaction of chlorine, an olefin, and a nitrile is an example of a three-component ionic reaction involving carbonium ions and can be explained on the basis of established principles for ionic reactions (2, 3). It is a specific case of a more general three-component ionic reaction involving olefins; a mechanism for this general reaction is proposed as follows:



4.
$$\text{RCH{=}CH}_2 + \text{A}^+ \longrightarrow \underset{\text{IV}}{\text{R}\underset{+}{\text{C}}\text{HCH}_2\text{A}}$$

5.
$$\text{R}\underset{+}{\text{C}}\text{HCH}_2\text{A} + \text{B:} \longrightarrow \underset{\text{V}}{\text{R}\underset{\text{B}^+}{\underset{|}{\text{C}}}\text{HCH}_2\text{A}}$$

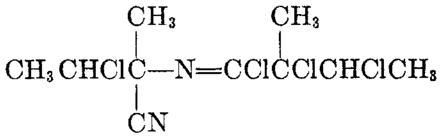
6.
$$\text{R}\underset{+}{\text{C}}\text{HCH}_2\text{A} + \text{Y}^- \longrightarrow \text{RCHYCH}_2\text{A}$$

7.
$$\text{R}\underset{\text{B}^+}{\underset{|}{\text{C}}}\text{HCH}_2\text{A} + \text{Y}^- \longrightarrow \text{R}\underset{\text{BY}}{\underset{|}{\text{C}}}\text{HCH}_2\text{A}$$

An acidic substance A^+ attacks the olefin to form a carbonium ion (IV) which may combine with a substance B: having an unshared electron pair (V). The carbonium ions from these two reactions can be stabilized either by reaction 6, 7 with a negative ion Y^- from the solution or by the expulsion of a proton. Reactions 5 and 6 are competing reactions and therefore the products $RCHYCH_2A$ and $RCH(BY)CH_2A$ are to be expected.

Numerous examples have been described in which olefins are involved in such three-component ionic reactions and these can be explained by the general mechanism. The most recent of these examples, some of which are summarized in Table I, is the N-substituted amide synthesis studied by Ritter (5, 12).

As suggested by recent workers (11), these data indicate that the compound obtained by the action of aluminum chloride on 2-(cyclohexenyl)cyclohexanone and acetonitrile and reported by Bruson (14) as an imino ether is probably the amide, 2-(1′-acetamido)cyclohexylcyclohexanone. Furthermore, the "dimer" reported by Lichty (15) in the chlorination of α-methylcrotononitrile may be a stable imide chloride (VIII).



$$\text{CH}_3\text{CHCl}\underset{\text{CN}}{\underset{|}{\overset{\text{CH}_3}{\overset{|}{\text{C}}}}}\text{—N=CCl}\overset{\text{CH}_3}{\overset{|}{\text{C}}}\text{ClCHClCH}_3$$

VIII

EXPERIMENTAL

Two general procedures used for the synthesis of N-(2-chloroalkyl)amides are described in the following examples. The imide chlorides and the N-(2-chloroalkyl)amides prepared by these procedures are listed in Table II and Table III, respectively.

N-(2-Chlorocyclohexyl)acetamide. A mixture of 82 g. (1.0 mole) of cyclohexene and 82 g. (2.0 moles) of acetonitrile was placed in a three-necked flask fitted with a mechanical stirrer, a gas inlet tube, a thermometer, and a gas exit tube. The mixture was treated with 65 g. (0.91 mole) of chlorine gas with rapid stirring at 15–20° during a one-hour period. If allowed to stand at room temperature, the colorless solution darkened rapidly with evolution of hydrogen chloride indicating bimolecular condensation (1). It was therefore poured immediately into 300 ml. of cold water, stirred vigorously for ten minutes, and then allowed to stand for 30 minutes to complete hydrolysis of the imide chloride. The mixture was then cooled in an ice-salt bath and filtered. The resulting white solid was air-dried to give 94 g. (0.535 mole, 59% yield based on chlorine) of crude N-(2-chlorocyclohexyl)acetamide. The pure amide, m.p. 129–130°, was obtained in 35% yield after several recrystallizations from methanol. This amide is apparently the *dl-trans*-N-(2-chlorocyclohexyl)-acetamide; the *cis* form is reported to melt at 88° (16).

Anal. Calc'd for $C_8H_{14}ClNO$: Cl, 20.19; N, 7.96.
Found: Cl, 20.02, 20.12; N, 7.90, 7.88.

TABLE I

THREE-COMPONENT IONIC REACTIONS

SYNTHESIS (REF.)	COMPONENTS		
	A^+	B:	Y^-
N-Alkylformamides (4)	H^+	HCN	$AlCl_4^-$
N-Alkylamides (5)	H^+	RCN	HSO_4^-
1,3-Dioxanes (6)	CH_2OH^+	CH_2O	Expulsion H^+
N-Alkylformamides (7)	H^+	HCN	HSO_4^-
β-Bromoalkylpyridinium bromide (8)	Br^+	C_5H_5N	Br^-
β-Bromoethers (9)	Br^+	ROH	Expulsion H^+
β-Chloroalkylacetates (10)	Cl^+	CH_3CO_2H	Expulsion H^+
Polyamides from azelanitrile (11)	CH_2OH^+	RCN	HSO_4^-
N-(2-Halo-1-ethyl)amides (12)	H^+	RCN	HSO_4^-
Ethyl α-ethyl-α-methylbutyrate (13)	H^+	CO	C_2H_5OH Expulsion H^+

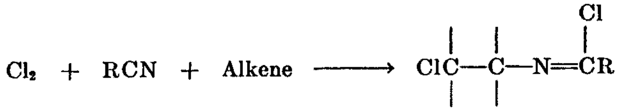
The filtrate from the amide separation contained a water-insoluble oil, which was separated, washed with water, and dried with "Drierite." Rectification gave 11.3 g. (0.14 mole) of cyclohexene, 31 g. (0.202 mole) of 1,2-dichlorocyclohexane, b.p. 62–63° (10 mm.), n_D^{25} 1.4877, and a few grams of tarry residue. These properties correspond to the physical constants given by previous investigators (17) for 1,2-dichlorocyclohexane.

N-(2-Bromocyclohexyl)acetamide. In a similar experiment a solution of 82 g. (1.0 mole) of cyclohexene in 164 g. (4.0 moles) of acetonitrile was treated with 115 g. (0.72 mole) of bromine for 75 minutes at −5°. Hydrolysis of the imide bromide was performed during a 60-hour period at room temperature and 41.5 g. (26% yield based on bromine) of a tan solid was isolated. After recrystallization from ethyl acetate containing a small amount of methanol, 25 g. (16% yield) of pure N-(2-bromocyclohexyl)acetamide was obtained, m.p. 109–110°.

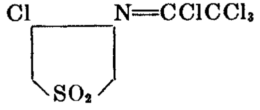
Anal. Calc'd for $C_8H_{14}BrNO$: Br, 36.34; N, 6.36.
Found: Br, 36.54, 36.71; N, 6.28, 6.10.

N-(2-Chloroethyl)trichloroacetimidyl chloride. Ethylene and chlorine gas were passed simultaneously into 82 g. (2.0 moles) of acetonitrile cooled to 15° with an ice-bath. The mixture was stirred rapidly while 1.08 moles of ethylene gas was measured by a flowmeter and introduced during a $2\frac{1}{2}$ hour period. Chlorine was added by gradual warming of a cold trap containing a weighed quantity of liquid chlorine. When all the ethylene gas had been

TABLE II
SYNTHESIS OF IMIDE CHLORIDES



$$Cl_2 + RCN + Alkene \longrightarrow ClC{-}C{-}N{=}\overset{Cl}{C}R$$

R	ALKENE	β-CHLORO IMIDE CHLORIDE	YIELD, %	B.P., °C.	PRESSURE, MM.	n_D^{25}	ANALYSES Calc'd N	ANALYSES Calc'd Cl	ANALYSES Found N	ANALYSES Found Cl
CH_3	Ethene	$ClCH_2CH_2N{=}CClCCl_3$	50	71–73	3.0	1.5150	5.76	72.80	5.92	72.03
$H_2C{=}CH$	Ethene	$ClCH_2CH_2N{=}CClCCl_2CH_2Cl$	34	94–95	4.0	1.5200	5.44	68.88	5.68	67.57
$(CH_3)_3C$	Ethene	$ClCH_2CH_2N{=}CClC(CH_3)_3$	40	57–58	6.0	—	7.69	39.01	7.89	38.62
CH_3			30	m.p. 136–140	—	—	4.20	53.20	4.30	52.40

added, the chlorine addition was continued for 4½ hours thereafter. The reaction temperature was allowed to rise to 30–35° during this period and the reaction was stopped when 360 g. (5.07 moles) of chlorine had been introduced. The mixture was purged with nitrogen to remove hydrogen chloride and then rectified. After removing a small amount of low-boiling material, consisting chiefly of acetonitrile and 1,2-dichloroethane, 122 g. of N-(2-chloroethyl)trichloroacetimidyl chloride was obtained, b.p. 71–73° (3 mm.), n_D^{25} 1.5150. This represents a 50% yield based on the ethylene used.

Anal. Calc'd for $C_4H_4Cl_5N$: Cl, 72.87; N, 5.78.
Found: Cl, 72.11, 71.95; N, 5.83, 6.01.

TABLE III

N-(2-CHLOROALKYL)AMIDES, R′NHCOR

R	ALKENE	R′	YIELD, %	M.P.,[a] °C.	ANALYSES			
					Calc'd		Found	
					N	Cl	N	Cl
CH_3	Styrene	2-Chloro-1-phenyl-ethyl	28	103–104[b]	7.09	17.94	6.43	18.16
$(CH_3)_3C$	Ethene	2-Chloroethyl	40	162[c]	8.56	21.66	7.71	21.10
CH_3	Cyclohexene	2-Chlorocyclohexyl	58	129–130[d]	7.97	20.18	7.89	20.10
$(CH_3)_2COH$	Cyclohexene	2-Chlorocyclohexyl	11	147–147.5[e]	6.38	16.14	6.42	16.80
$(CH_3)_3C$	Cyclohexene	2-Chlorocyclohexyl	47	151[f]	6.43	16.28	6.34	16.12
C_6H_5	Ethene	2-Chloroethyl	24	104–105.5[g]	7.63	19.31	7.38	19.27
CCl_3[i]	Isobutene	2-Chloro-1,1-dimethyl	30	53–54[g]	5.54	56.1	5.46	55.6
C_6H_5	Cyclohexene	2-Chlorocyclohexyl	21	165[h]	5.89	14.91	5.82	15.08

[a] All melting points taken on a Fisher-Johns melting point block.

[b] Crystallized from ethyl acetate. After 2 years this compound apparently rearranged to the oxazoline hydrochloride having the new m.p. 160.5–161°. The amide was reported by Lusskin and Ritter (12).

[c] From chloroform-petroleum ether.

[d] From methanol; m.p. of *dl-cis* form reported as 88° by Osterberg and Kendall (16).

[e] From ethanol.

[f] From benzene-methanol mixture.

[g] From benzene.

[h] From benzene; *dl-cis* form melts at 153–154° (18).

[i] Starting material, acetonitrile, was completely chlorinated during the reaction.

N-(2-Chloroethyl)trichloroacetamide. N-(2-Chloroethyl)trichloroacetimidyl chloride (42 g., 0.17 mole) was refluxed with 100 ml. of water, 100 ml. of methanol, and 15 ml. of conc'd hydrochloric acid for two hours. The mixture was cooled to ice temperature, crystallized, and filtered. The 30 g. of white solid obtained represented an 82% yield of N-(2-chloroethyl)-trichloroacetamide. The pure compound, m.p. 76–76.5°, was obtained in 48% yield (18 g.) after recrystallization from benzene and showed no melting point depression when mixed with an authentic sample of N-(2-chloroethyl)trichloroacetamide synthesized from 2-chloroethylamine and trichloroacetyl chloride.

Anal. Calc'd for $C_4H_5Cl_4NO$: Cl, 63.08; N, 6.22.
Found: Cl, 62.89, 62.78; N, 6.26, 6.10.

2-Chlorocyclohexylamine hydrochloride. A mixture of 82 g. (1.0 mole) of cyclohexene and 84 g. (3.1 moles) of hydrogen cyanide was cooled to 10° and treated with 85 g. of chlorine gas during a two-hour period while maintaining rapid stirring. The resulting mixture was poured onto ice and the organic layer separated and washed several times with water. The remaining organic liquid was refluxed with 200 ml. of 3 *N* hydrochloric acid on a steam-bath for 12 hours. The mixture was then treated with 30 ml. of methanol, refluxed two hours longer, and steam-distilled. The distillate consisted of 2.0 g. of cyclohexene and 18.0 g. of 1,2-dichlorocyclohexane. The residue was filtered from about 2.5 g. of tar and evaporated to dryness. The tan-colored hydrochloride weighed 59 g., representing a 35% yield of 2-chlorocyclohexylamine hydrochloride. The pure hydrochloride, m.p. 213–214° (sub. 175–213°), was obtained in 26% yield by recrystallization from ethanol. This is apparently the *dl-trans*-form; the *dl-cis*-2-chlorocyclohexylamine hydrochloride is reported to melt at 185–186° dec. (18).

Anal. Calc'd for $C_6H_{13}Cl_2N$: Cl, 41.76; N, 8.24.
Found: Cl, 41.42, 41.40; N, 8.03, 7.88.

Hydrolysis of N-(2-chloroalkyl)amides. Acid hydrolysis of an N-(2-chloroalkyl)amide gives a salt of the corresponding hydroxyamine. N-(2-Chloro-1-phenylethyl)acetamide synthesized from chlorine, styrene, and acetonitrile was hydrolyzed by heating with conc'd hydrochloric acid on a steam-bath for 24 hours and then evaporating to dryness. Recrystallization of the crude product from a mixture of ethyl acetate and methanol (90–10 by vol.) gave a 90% yield of β-hydroxy-α-phenylethylamine hydrochloride, m.p. 132–135°. This compound appears to decompose at this initial melting point, resolidify, and subsequently remelt at 147–149°. These observations confirm those previously reported for this compound (19).

Similar hydroxyamine hydrochlorides were prepared starting from 1-octene and from cyclohexene using acetonitrile as the nitrile component. 1-Octene gave N-2-(1-chloroöctyl)acetamide which was hydrolyzed with conc'd hydrochloric acid to give a 15.4% yield (based on 1-octene) of 1-hydroxymethylheptylamine hydrochloride, m.p. 106° from benzene-ethanol mixture.

Anal. Calc'd for $C_8H_{20}ClNO$: Cl, 19.54; N, 7.72.
Found: Cl, 20.28; N, 7.66.

Cyclohexene gave N-(2-chlorocyclohexyl)acetamide, which was hydrolyzed to 2-hydroxycyclohexylamine hydrochloride, m.p. 188–189°, recrystallized from ethanol.

Anal. Calc'd for $C_6H_{14}ClNO$: Cl, 23.43; N, 9.29.
Found: Cl, 23.42; N, 9.24.

This product appears to be the *dl-cis*-2-hydroxycyclohexylamine hydrochloride which has been reported to melt at 189–190°; the *dl-trans*-2-hydroxycyclohexylamine hydrochloride melts at 176–177° (18).

SUMMARY

A new three-component reaction has been discovered in which chlorine or bromine interacts with an olefin and a nitrile to form an imide halide. The imide halide can be isolated if the nitrile has no *alpha* hydrogen atoms; it can also be hydrolyzed to the corresponding N-(2-haloalkyl)amide. The reaction has been applied to the preparation of a number of new N-(2-haloalkyl)amides from such olefins as ethylene, cyclohexene, 1-octene, and styrene in combination with hydrogen cyanide, acetonitrile, acrylonitrile, pivalonitrile, and benzonitrile. When hydrogen cyanide was used, the formamide derivative was readily hydrolyzed to a 2-haloalkylamine.

WILMINGTON, DELAWARE

REFERENCES

(1) VON BRAUN, *Angew. Chem.*, **47**, 611 (1934).
(2) REMICK, *Electronic Interpretation of Organic Chemistry*, 2nd Edition, J. Wiley & Sons, Inc., New York, 1949, p. 45.

(3) Price, *Mechanisms of Reactions at Carbon-Carbon Double Bonds*, Interscience Publishers, New York, 1946, p. 45.
(4) Wieland and Dorrer, *Ber.*, **63**, 404 (1930).
(5) Ritter and Minieri, *J. Am. Chem. Soc.*, **70**, 4045 (1949).
(6) Baker, *J. Chem. Soc.*, 296 (1944).
(7) Casanova, to I. G. Farbenindustrie, French Patent 902,342 (Dec. 4, 1944).
(8) Barnett, Cook, and Peck, *J. Chem. Soc.*, **125**, I, 1035 (1924).
(9) Bartlett and Tarbell, *J. Am. Chem. Soc.*, **58**, 466 (1936).
(10) Weber, Hennion, and Vogt, *J. Am. Chem. Soc.*, **61**, 1457 (1936).
(11) Mowry and Ringwald, *J. Am. Chem. Soc.*, **72**, 4439 (1950).
(12) Lusskin and Ritter, *J. Am. Chem. Soc.*, **72**, 5577 (1950).
(13) Roland, Wilson, and Hanford, *J. Am. Chem. Soc.*, **72**, 2122 (1950).
(14) Bruson, Riener, and Riener, *J. Am. Chem. Soc.*, **70**, 483 (1948).
(15) Lichty, to Wingfoot Corp., U. S. Patent 2,425,432 (Aug. 12, 1947).
(16) Osterberg and Kendall, *J. Am. Chem. Soc.*, **42**, 2616 (1920).
(17) Fortey, *J. Chem. Soc.*, **73**, 944 (1898).
(18) McCasland, Clark, Jr. and Carter, *J. Am. Chem. Soc.*, **71**, 640 (1949).
(19) Gabriel and Colman, *Ber.*, **47**, 1866 (1914).