BULLETIN OF THE CHEMICAL SOCIETY OF JAPAN VOL. 43 2167—2173 (1970)

Reactions of Some Olefins with *N*-Chlorourea in the Presence of Acetonitrile

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(Received November 24, 1969)

A new three-component reaction of *N*-chlorourea, olefins and acetonitrile is reported. Styrene gives *N*-(1-ureidoethylidene)-2-choro-1-phenylethylamine, *N*-(2-chloro-1-phenylethyl)acetamide and 4-phenyl-2-oxazolidone. Addition proceeds in a Markovnikov manner as shown by structural evidence. Cyclohexene gives *N*-(1-ureiodoethylidene)-2-chlorocyclohexylamine and *N*-(2-chlorocyclohexyl)acetamide. The stereochemistry of the reaction has been shown to be *trans* as demonstrated by chemical and physical evidence. Mechanisms for the reaction are proposed.

The chemistry of *N*-chlorourea given in literature is restricted predominantly to aqueous or alcoholic systems. In these cases *N*-chlorourea acts simply as a mild chlorinating or oxidizing agent. The present paper describes a new type of three-component reactions of *N*-chlorourea for the synthesis of *N*-(1-ureidoalkylidene)-2-chloroalkylamines and *N*-(2-chloroalkyl)amides. The synthesis involves interaction of *N*-chlorourea and olefin in the presence of a nitrile to give *N*-(1-ureidoalkylidene)-2-chloroalkylamine and imidochloride that can be hydrolyzed to an *N*-(2-chloroalkyl)amide.

In 1948, Ritter and co-workers discovered the reaction of nitriles with olefins in strongly acidic media to form *N*-substituted amides.[1,2]

The reaction can be explained to proceed *via* carbonium ion which is formed by addition of proton to olefins. Cairns and co-workers have discovered that halonium ion which is formed by addition of positive halogen to olefins can react with nitriles to form *N*-substituted amide.[3]

We have found the reaction of *N*-chlorourea with olefins in the presence of nitrile. The reaction has been shown to proceed in two steps.

The first step gives *N*-(1-ureidoalkylidene)-2-chloroalkylamine, chloroimide chloride and chlorinated hydrocarbon arising from the original olefin, and the second step gives an *N*-(2-chloroalkyl)-amide by the hydrolysis of chloroimide chloride.

The interaction of *N*-chlorourea and olefin in the presence of nitrile is postulated to proceed as follows:

$$NH_2CONHCl \longrightarrow Cl^+ + NH_2CONH^- \quad (1)$$

$$RCH=CH_2 + Cl^+ \longrightarrow RC^+HCH_2Cl \quad (2)$$

$$RC^+HCH_2Cl \xrightarrow{R'CN} RCHCH_2Cl \quad (3)$$

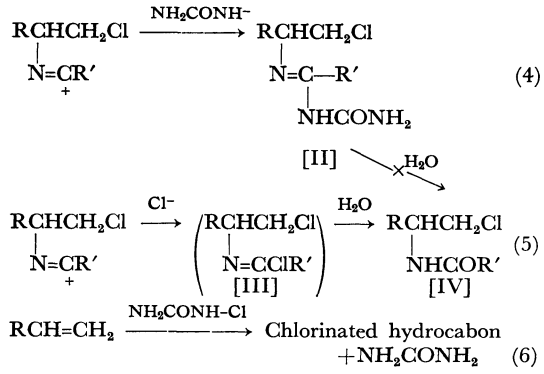
$$\qquad\qquad\qquad\qquad\qquad\quad \downarrow$$

$$\qquad\qquad\qquad\qquad\qquad\quad \overset{+}{N}{=}CR' \quad [I]$$

1) J. J. Ritter and P. P. Minieri, *J. Amer. Chem. Soc.*, **70**, 4045 (1948).

2) J. J. Ritter and J. Kalish, *ibid.*, **70**, 4048 (1948).

3) T. L. Cairns, P. J. Graham, P. L. Barrick and R. S. Schreiber, *J. Org. Chem.*, **17**, 751 (1952).



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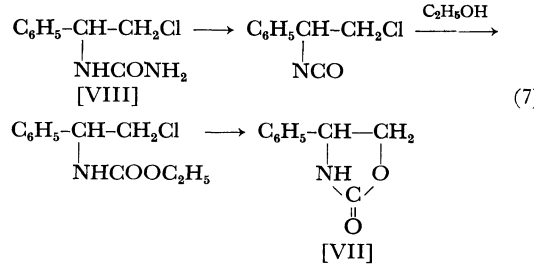
(5)

(6)

The chlorine attached to nitrogen has a positive halogen character and attacks olefin as an acidic substance Cl^+ to form a carbonium ion RC^+HCH_2Cl which may combine with nitrile. The carbonium ion [I] can be stabilized by reaction (4) with a negative ion NH_2CONH^- to produce *N*-(1-ureidoalkylidene)-2-chloroalkylamine [II]. [II] was isolated and analyzed but could not be hydrolyzed to *N*-(2-chloroalkyl)amide [IV]. Therefore, [IV] is not a hydrolyzed product of [II]. It is supposed that the carbonium ion [I] can also be stabilized by reaction (5) with a negative ion Cl^- derived from hydrogen chloride which is present in reaction medium as an impurity to produce chloroimide chloride [III]. [III] could not be isolated. But as reported by Cairns,[3] *N*-(2-chloroalkyl)amide is probably a hydrolyzed product of [III]. Reactions (4) and (5) are competing reactions and the products [II] and [IV] are expected. This interaction is a special case of the so-called Ritter reaction.[1,2]

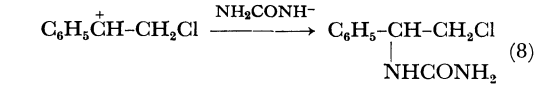
We have studied the interaction of *N*-chlorourea with styrene and cyclohexene in the presence of acetonitrile.

Styrene reacted with *N*-chlorourea and acetonitrile at 10°C within 2.5 hr to give *N*-(1-ureidoethylidene)-2-chloro-1-phenylethylamine [V] and *N*-(2-chloro-1-phenylethyl)acetamide [VI] after treating the reaction product with water. The reaction mixture was evaporated *in vacuo*, the residue was treated with water, and the aqueous solution was extracted with benzene. From the organic layer *N*-(2-chloro-1-phenylethyl)acetamide [VI] was obtained by vacuum distillation. Neutralization of the aqueous layer with sodium hydroxide resulted in immediate precipitation of *N*-(1-ureidoethylidene)-2-chloro-1-phenylethylamine [V]. It was separated by filtration, washed with water and analyzed correctly. On evaporation of the aqueous filtrate, extraction of the residue with ethyl alcohol and distillation of the extract *in vacuo*, 4-phenyl-2-oxazolidone [VII] was obtained in poor yield. It is well known that isocyanates are formed on heating urea derivatives. Hassner and coworkers[4] have shown that 4-phenyl-2-oxazolidone can be obtained by heating β-iodoalkane isocyanate with alcohol. Katchalsky and co-workers[5] have also shown that β-halocarbamate may be converted to 2-oxazolidone by pyrolysis at 120—200°C. A reaction scheme consistent with the obtained product is as follows:



(7)

This suggests that the carbonium ion $R\overset{+}{C}HCH_2Cl$ was stabilized by NH_2CONH^- to produce *N*-(2-chloro-1-phenylethyl)urea [VIII].



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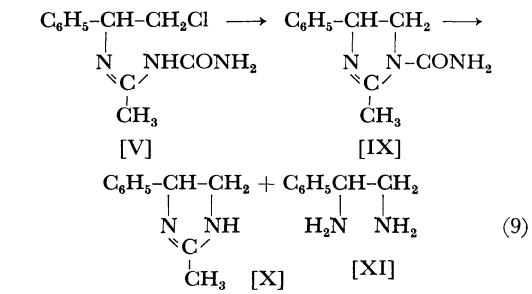
4-Phenyl-2-oxazolidone [VII] was characterized by identity of its melting point (137—137.5°C) and infrared spectrum with that of the known authentic compound prepared from styrene and iodine isocyanate followed by reaction with ethyl alcohol.[4] For 5-phenyl-2-oxazolidone the reported melting point is 88.8—90.2°C.[6]

The direction of addition is such that Cl^+ ion combines with the less substituted carbon. The composition and the structure of *N*-(1-ureidoethylidene)-2-chloro-1-phenylethylamine [V] were established by elemental analysis and infrared spectra. The spectrum shows essentially the patterns of urea, C–Cl, monosubstituted benzene and C=N bond. The structure of [V] was also established by its conversion, on treatment with aqueous sodium hydroxide solution, to 1-aminocarbonyl-2-methyl-4-phenyl-2-imidazoline [IX] and further to 2-methyl-4-phenylimidazoline [X] and 1,2-diaminoethylbenzene [XI].



(9)

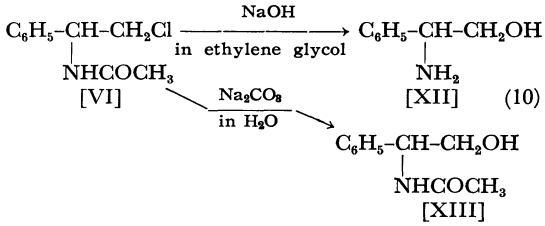
4) A. Hassner, M. E. Lobber and C. Heathcock, *J. Org. Chem.*, **32**, 540 (1967).

5) E. Katchalsky and D. B. Ishai, *ibid.*, **15**, 1067 (1950).

6) M. S. Newman and A. Kutner, *J. Amer. Chem. Soc.*, **73**, 4199 (1951).

[V] was found to be highly unstable to base hydrolysis or heat, and converted to [IX] at room temperature and more rapidly at elevated temperature. For example, when [V] was allowed to stand for one month at room temperature, complete isomerization to [IX] hydrochloride occurred. A more satisfactory procedure for the preparation of [IX] was to treat [V] with sodium hydroxide solution at elevated temperature for several minutes. A new compound [V], which was isolated and purified only by washing with cold water, had a melting point of 97—99°C and its elemental analysis corresponded to the empirical formula $C_{11}H_{14}N_3ClO$. When it was recrystallized from boiling water, however, a different substance having a melting point of 119—119.5°C was obtained. Elemental analysis of this compound corresponds to a value for [V] plus a mol of water, and infrared absorption bands at 3480 and 1130 cm^{-1} indicate the presence of C–OH.

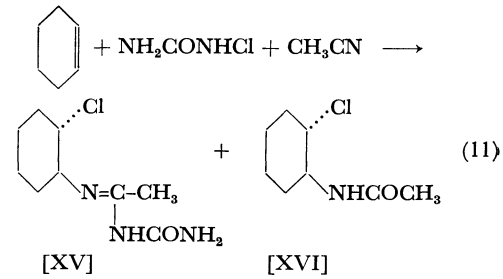
N-(2-chloro-1-phenylethyl)acetamide [VI] was confirmed by coincidence of its melting point with that of the known compound.[7] The NMR spectrum of [VI] indicates a doublet at τ 6.18 (2H, CH_2Cl), a multiplet at 5.5 (1H, CHN) owing to additional splitting by NH, a single peak at 2.68 (5H, aromatic protons), a typically broad peak at 4.7 (the proton on nitrogen) and a triplet at 7.95 (3H, CH_3). The structure of [VI] was also established by its conversion to the known 2-hydroxyl-1-phenylethylamine [XII], picrate of [XII] and hydrochloride of [XII]. An isomeric *N*-(2-chloro-2-phenylethyl)acetamide should yield 2-phenyl-2-hydroxyethylamine.



(10)

[VI] was also treated with sodium carbonate in water to give *N*-(2-hydroxy-1-phenylethyl)acetamide [XIII] having a melting point 123—124°C.[8] Lusskin and Ritter[7] reported the preparation of 2-methyl-4-phenyl-2-oxazoline having a melting point 120°C on treating chloroacetamide with potassium hydroxide at 60—65°C for 90 sec in ethyl alcohol. But the product obtained by the same reaction was a liquid having a boiling point of 96—96.5°C/5mmHg. Its infrared spectrum and elemental analysis correspond to those of 2-methyl-4-phenyl-2-oxazoline [XIV]. The hydrochloride of [XIV] had mp 145—146°C.

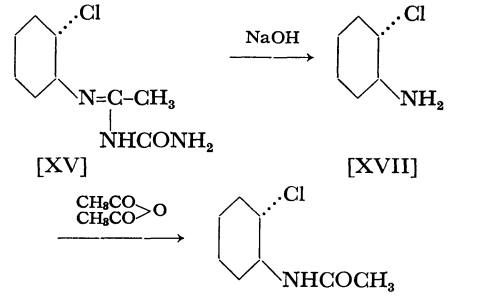
Cyclohexene reacted with *N*-chlorourea in the presence of acetonitrile to give *N*-(1-ureidoethylidene)-*trans*-2-chlorocyclohexylamine [XV] and *N*-(*trans*-2-chlorocyclohexyl)acetamide [XVI].



(11)

[XV] [XVI]

[XV] precipitated from the reaction mixture as a white solid. The filtrate was evaporated *in vacuo* to yield a very viscous semi-solid. This substance could not be recrystallized nor distilled. When it was treated with boiling water, [XVI] was obtained as white crystalline material. Reaction of cyclohexene with *N*-chlorourea and acetonitrile could yield *cis*- or *trans*-isomer. The stereochemistry of the reaction was shown to be *trans*, consistent with the ring opening of the intermediate halonium ion.[9] Thus, the product was identified as [XV] and [XVI]. The composition and structure of [XV] were established by elemental analysis and infrared spectra. The spectrum shows essentially the patterns of urea, C=N and *trans* C–Cl. The structure of [XV] was also established by its conversion to known *trans*-2-chlorocyclohexylamine [XVII] and further to *N*-(*trans*-2-chlorocyclohexyl)-acetamide [XVI].



[XV] [XVII]

(12)

2-Chlorocyclohexylamine may exist in two diastereoisomeric forms. The infrared spectrum of [XVII], with a stretching vibration of C–Cl at 728 cm^{-1}, was identical with that reported by Yoshida[10] for *trans*. On standing at room temperature for several days, it partly decomposed to form a solid material. This confirms the previous observation for this compound.[11] The acetylated

7) R. M. Lusskin with J. J. Ritter, *ibid.*, **72**, 5577 (1950).

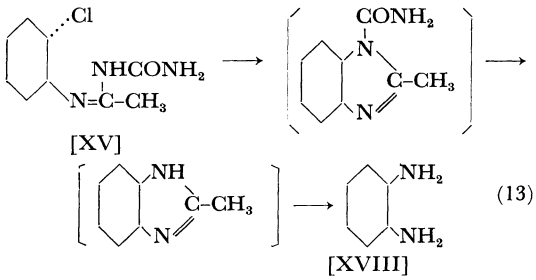
8) The melting point of [XIII] was reported as 114—116°C by R. M. Lusskin and J. J. Ritter.[7]

9) A. Hassner, L. A. Levy and R. Gault, *Tetrahedron Lett.*, **1966**, 3119 (1966).

10) Z. Yoshida and K. Nakagawa, *ibid.*, **1965**, 3753.

11) O. E. Paris and P. E. Fanta, *J. Amer. Chem. Soc.*, **74**, 3007 (1952).

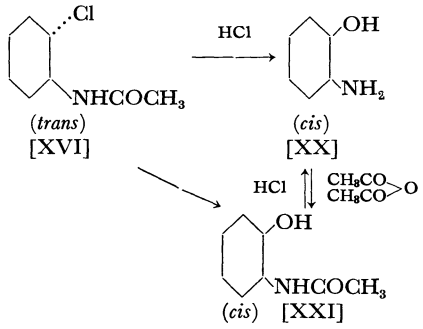
product of [XVII] was characterized by identity of its melting point with that of [XVI]. 1,2-Diaminocyclohexane [XVIII] was also obtained on treating [XV] with sodium hydroxide in poor yield. A reaction scheme consistent with the obtained product is as follows:



[XV] [XVIII] (13)

[XV] may react with sodium hydroxide to give [XVIII] *via* intermediates, imidazoline derivatives. [XVIII] reacted so readily with carbon dioxide that it was immediately converted to the picrate and subjected to analysis. [XV] was hydrogenated on treatment with sodium borohydride in ether to give *N*-(1-ureidoethyl)cyclohexylamine [XIX].

N-(*trans*-2-chlorocyclohexyl)acetamide [XVI] was confirmed by coincidence of its melting point (127.5°C) with that of the reported compound.[3] The infrared spectrum of [XVI] indicates a peak at 730 cm^{-1} based on stretching vibration of *trans* C–Cl.[10] The NMR spectrum of [XVI], in $CDCl_3$, had bands at τ 4.0 (the proton on nitrogen), 6.2 (doublet, 1H, CHCl), 7.07 (singlet, 1H, CHN), 8.0 (singlet, 3H, CH_3) and 7.7—8.87 (multiplet, cyclohexyl protons). [XVI] was hydrolyzed on treatment with aqueous hydrochloric acid solution to give *cis*-2-hydroxycyclohexylamine[3] [XX]. [XVI] was also hydrolyzed with sodium carbonate in aqueous solution or aqueous ammonium hydroxide solution to give *N*-(*cis*-2-hydroxycyclohexyl)-acetamide[12] [XXI], which was further hydrolyzed to give [XX]. [XX] was acetylated by acetic anhydride to give [XXI].[13]



(*trans*) [XVI] (*cis*) [XX] (*cis*) [XXI]

12) W. S. Johnson and E. N. Schubert, *J. Amer. Chem. Soc.*, **72**, 2187 (1950).

13) M. Mousseron and R. Jacquier, *Bull. Soc. Chim. Fr.*, **1950**, 238.

[XX], on standing at room temperature for several days, darkened and finally turned to a tarry matter. The structure of [XX] was confirmed by coincidence of the melting point of its hydrochloride (184—185°C) with that of the reported compound.[13] The infrared spectrum of [XX] had an absorption at 945 cm^{-1} based on *cis* C–O bond.[14] The NMR spectrum of [XX], in $CDCl_3$, had bands at τ 6.3 (singlet, 1H, CHO), 7.2 (singlet, 1H, CHN), 7.35 (the proton on nitrogen), 8.45 (1H, OH) and 8.55 (cyclohexyl protons). The spectrum was identical with that reported by Pavia and co-workers[15] for *cis*. Further proof of [XX] was demonstrated by its conversion to [XXI] having a melting point 145—146°C.[16] The melting point of *trans*-isomer was reported as 126—127°C.[16]

Experimental

All reagents were redistilled before use. Acetonitrile was predried over potassium hydroxide and distilled over calcium hydride. All the melting points are uncorrected. IR spectra were measured in KBr pellets or in liquid state using a Hitachi Model EPI-G3 IR spectrometer. NMR spectra were obtained using dilute solutions in CCl_4 or $CDCl_3$. Tetramethylsilane was used as an internal standard and chemical shifts are expressed in "tau" scale.

Reaction of *N*-Chlorourea with Styrene in the Presence of Acetonitrile. Simultaneous formation of *N*-(1-ureidoethylidene)-2-chloro-1-phenylethylamine[V], *N*-(2-chloro-1-phenylethyl)acetamide [VI] and 4-phenyl-2-oxazolidone [VII]. The compounds can be prepared from *N*-chlorourea or, more simply, from urea and chlorine forming *N*-chlorourea directly in the reaction solution.

A suspension of 0.6 mol (36 g) of pulverized urea in 450 m*l* of acetonitrile was cooled to 0°C and chlorinated while being stirred rapidly. Gas introduction was discontinued as soon as 0.3 mol (21.3 g) of chlorine had been absorbed. The resulting clear, colorless solution was stirred for an additional 30 min. The solution was purged with and kept under nitrogen atmosphere. A solution of 0.3 mol (31.2 g) of styrene in 100 m*l* of acetonitrile was then added dropwise over a period of 1 hr while maintaining the temperature at 10°C by external cooling. After the addition was complete, the reaction mixture was stirred for about 2 hr at 10°C until an HI test failed to produce iodine. The reaction mixture was allowed to separate into two phases. From the viscous lower phase was recovered urea after neutralizing with sodium hydroxide. The upper acetonitrile phase was then placed in a vacuum distillation flask to remove acetonitrile. The resulting viscous, pale yellow liquid was then poured into 300 m*l* of water, stirred vigorously for 20 min, and then shaken with benzene. The upper organic phase was separated and dried over

14) S. Winstein and N. J. Holness, *J. Amer. Chem. Soc.*, **77**, 5562 (1955).

15) A. Pavia, F. Winternitz and R. Wylde, *Bull. Soc. Chim. Fr.*, **1966** (8), 2506.

16) G. E. McCasland, R. K. Clark, Jr., and H. E. Carter, *J. Amer. Chem. Soc.*, **71**, 637 (1949).

anhydrous $MgSO_4$. After removing benzene and chlorinated styrene, the residue was distilled *in vacuo* to yield 14 g (23.6%) of *N*-(2-chloro-1-phenylethyl)acetamide, bp 121—127°C/1.2 mmHg, as a colorless liquid. The distillate solidified upon standing. Recrystallization from benzene gave colorless leaflets melting at 98—99.5°C (lit, mp 100°C,[7] 103—104°C[3]).

Found: C, 60.31; H, 6.28; Cl, 17.58; N, 6.94%. Calcd for $C_{10}H_{12}ClNO$: C, 60.76; H, 6.11; Cl, 17.93; N, 7.08%.

IR: 3310 (NH), 1650 (C=O), 1530 (amide II), 770, 695 (mono subst. benzene) and 725 cm^{-1} (C–Cl); NMR: τ 2.68 (phenyl, singlet), 4.7 (NH, broad peak), 5.5 (CHN, multiplet), 6.18 (CH_2Cl, doublet) and 7.95 (CH_3, triplet).

The lower aqueous phase was made alkaline (pH≒8.5) with NaOH and the resulting white precipitate was separated by filtration, washed with a large amount of cold water and dried *in vacuo* to yield 22 g (30.6%) of *N*-(1-ureidoethylidene)-2-chloro-1-phenylethylamine having a melting point 97—99°C (dec.). Insoluble in cold water, ethyl alcohol and benzene, soluble in hot water and hot ethyl alcohol. If allowed to stand for one month at room temperature, it became liquid and then resolidified.

Found: C, 54.44; H, 5.88; Cl, 15.12; N, 17.19%. Calcd for $C_{11}H_{14}ClN_3O$: C, 55.11; H, 5.88; Cl, 14.79; N, 17.52%.

IR: 3400, 3240, 3120 (NH), 1730 (C=O), 1625 (C=N), 1520 (amide II), 765, 700 (mono subst. benzene) and 710 cm^{-1} (C–Cl).

The filtrate was concentrated *in vacuo*, the residue extracted with ethyl alcohol and the extract distilled *in vacuo* to yield 1.5 g of 4-phenyl-2-oxazolidone, bp 150—160°C/1.5 mmHg. An analytical sample, mp 137—137.5°C (lit,[4] mp 138—139.5°C), was obtained by recrystallization from water. The compound gave a mp 137—137.5°C in admixture with authentic sample (mp 137.5—138°C, prepared according to the method of Hassner, Lobber and Heathcock[4]).

Found: C, 66.17; H, 5.62; N, 8.70%. Calcd for $C_9H_9NO_2$: C, 66.24; H, 5.55; N, 8.58%.

IR: 3270 (NH), 1750, 1720 (C=O), 1230, 1040 (ester) and 760, 700 cm^{-1} (mono subst. benzene).

Reaction of *N*-Chlorourea with Cyclohexene in the Presence of Acetonitrile. Simultaneous formation of *N*-(1-ureidoethylidene)-*trans*-2-chlorocyclohexylamine [XV] and *N*-(*trans*-2-chlorocyclohexyl)acetamide [XVI]. A solution of 0.3 mol of *N*-chlorourea in acetonitrile was prepared as described above. Cyclohexene (0.3 mol, 24.6 g) in acetonitrile (70 m*l*) and the *N*-chlorourea solution were reacted in a similar manner. The resulting precipitate was separated by filtration, washed with cold water, ethyl alcohol and ethyl ether. Recrystallization from hot water produced 22.5 g of white precipitate melting at 174.5—175°C (dec.), soluble in hot water, insoluble in benzene and ethyl alcohol. This product was dissolved in 60 m*l* of hot water, and the solution was made alkaline with KOH (pH≒10). After cooling the solution, the resulting precipitate was separated by filtration, washed with water and dried *in vacuo* to yield 18.5 g (28.3%) of *N*-(1-ureidoethylidene)-*trans*-2-chlorocyclohexylamine. An analytical sample, mp 113.5—114.5°C, was obtained by recrystallization from ethyl alcohol, soluble in ethyl alcohol, benzene and hot water, insoluble in ethyl ether and cold water.

Found: C, 49.28; H, 7.27; Cl, 16.70; N, 19.18%. Calcd for $C_9H_{16}ClN_3O$: C, 49.65; H, 7.40; Cl, 16.28; N, 19.30%.

IR: 3430, 3250, 3100 (NH), 1700 (C=O), 1660 (C=N), 1560 (amide II) and 730 cm^{-1} (*trans* C–Cl).

The picrate of [XV] was prepared and had mp 193°C after recrystallization from ethyl alcohol.

Found: C, 40.30; H, 4.27; Cl, 8.17; N, 18.79%. Calcd for $C_{15}H_{19}ClN_6O_8$: C, 40.32; H, 4.28; Cl, 7.93; N, 18.80%.

The filtrate from the above product was allowed to separate into two phases. From the viscous lower phase was recovered urea after neutralizing with NaOH. The upper acetonitrile phase was placed in a vacuum distillation flask to remove acetonitrile, cyclohexene and chlorinated cyclohexene. The residue was poured into 500 m*l* of water, stirred vigorously for 30 min at 90°C. The solution was then cooled to room temperature, and the resulting white needles were separated by filtration, dried *in vacuo* to give 20 g (38%) of crude *N*-(*trans*-2-chlorocyclohexyl)acetamide [XVI]. After recrystallization from benzene twice, pure [XVI] having a melting point of 127.5°C (bp 110—116°C/0.8 mmHg) was obtained. The reported melting point for this compound is 129—130°C;[3] for *cis*-isomer the melting point is 98°C.[13]

Found: C, 54.81; H, 8.02; Cl, 20.11; N, 8.03%. Calcd for $C_8H_{14}ClNO$: C, 54.70; H, 8.03; Cl. 20.18; N, 7.97%.

IR: 3200 (NH), 1630 (C=O), 1560 (amide II), and 730 cm^{-1} (*trans* C–Cl); NMR: τ 4.0 (NH, broad peak), 6.2 (CHCl, doublet), 7.07 (CHN, singlet), 7.7—8.8 (cyclohexyl protons, multiplet) and 8.0 (CH_3, singlet).

2-Hydroxy-1-phenylethylamine [XII]. Twenty grams of *N*-(2-chloro-1-phenylethyl)acetamide was refluxed with a solution consisting of 19 g of aqueous 45% NaOH solution and 48 m*l* of ethyleneglycol on an oil bath for 5 hr. After cooling the solution, the precipitate was filtered, the filtrate was acidified with HCl and then evaporated to dryness. Cold aqueous 50% NaOH solution was added to the residue and the resulting oil was extracted with ether. The ethereal extracts were dried over anhydrous $MgSO_4$, ether was removed *in vacuo* and the residue distilled *in vacuo*. 2-Hydroxy-1-phenylethylamine (9 g, 65%), bp 102—108°C/1.5 mmHg (lit,[17] bp 104—106°C/1 mmHg) was obtained, which solidified to a white solid, mp 51—52°C (lit,[17] mp 48—49.5°C).

Found: C, 69.78; H, 8.11; N, 10.20%. Calcd for $C_8H_{11}NO$: C, 70.04; H, 8.08; N, 10.21%.

IR: 3400 (OH), 3300, 1610 (NH), 1055 (C–O) and 765, 705 cm^{-1} (mono subst. benzene).

The picrate of [XII] had mp 204—204.5°C after recrystallization from ethyl alcohol. The reported melting point for this compound is 205—206°C;[18] for 2-hydroxy-2-phenylethylamine-picrate the melting point is 158°C.[19]

Found: C, 46.17; H, 4.03; N, 15.12%. Calcd for $C_{14}H_{14}N_4O_8$: C, 45.90; H, 3.85; N, 15.29%.

The hydrochloride, prepared by addition of dry HCl

17) M. S. Newman and W. M. Edwards, *ibid.*, **76**, 1840 (1954).

18) Wm. E. McEwen, W. E. Conrad and C. A. Vanderwerf, *ibid.*, **74**, 1168 (1952).

19) M. S. Kharasch and H. M. Priestley, *ibid.*, **61**, 3425 (1939).

gas to an alcoholic solution of the free base and recrystallization from ethyl alcohol, melted at 131—132°C, resolidified and subsequently remelted at 145°C. The results confirm those reported for this compound[3] (melts at 132—135°C, resolidifies and remelts at 147—149°C). The reported melting point for 2-hydroxy-2-phenylethylamine hydrochloride is 213°C.[20]

N-(2-Hydroxy-1-phenylethyl)acetamide [XIII]. Five grams of *N*-(2-chloro-1-phenylethyl)acetamide and a solution of 3.5 g of Na_2CO_3 in 75 m*l* of water were allowed to stand for 12 hr at room temperature and then refluxed for 1 hr. The solution was extracted with ethyl acetate. After removal of ethylacetate, the residue was recrystallized from benzene-ethyl alcohol to yield 3 g (66%) of white crystals, having a new mp 123—124°C (lit,[7] mp 114—116°C).

Found: C, 66.81; H, 7.38; N, 7.79%. Calcd for $C_{10}H_{13}NO_2$: C, 67.01; H, 7.31; N, 7.81%.

IR: 3350 (OH), 3140 (NH), 1650 (C=O), 1560 (amide II), 1055 (C–O) and 760, 700 cm^{-1} (mono subst. benzene).

2-Methyl-4-phenyl-2-oxazoline [XIV]. *N*-(2-chloro-1-phenylethyl)-acetamide (0.1 mol, 19.7 g) was mixed 90 sec at 60—65°C with 0.1 mol (5.6 g) of KOH in 200 m*l* of ethyl alcohol. One gram of $NaHCO_3$ was added and the solution was filtered. After removal of ethyl alcohol, the residue was distilled *in vacuo* to yield 7 g (44%) of the product, bp 96—96.5°C/5 mmHg (lit,[7] mp 120°C).

Found: C, 73.94; H, 6.85; N, 8.62%. Calcd for $C_{10}H_{11}NO$: C, 74.50; H, 6.87; N, 8.68%.

IR: 1670 (C=N), 1230, 990 (C–O) and 760, 700 cm^{-1} (mono subst. benzene).

The hydrochloride, prepared by addition of dry HCl gas to an alcoholic solution of [XIV], had mp 145—146°C (lit,[3] 160.5—161°C).

IR: 2720—2400, 1980 (C=N⁺H), 1745 (C=N⁺), 1240, 1060, 1050 (C–O) and 765, 700 cm^{-1} (mono subst. benzene).

N-(1-Ureido-1-hydroxyethyl)-2-chloro-1-phenylethylamine. *N*-(1-Ureidoethylidene)-2-chloro-1-phenyl ethylamine was recrystallized from water. A white precipitate melting at 119—119.5°C was obtained.

Found: C, 51.28; H, 6.43; Cl, 13.80; N, 16.40%. Calcd for $C_{11}H_{16}ClN_3O_2$: C, 51.26; H, 6.25; Cl, 13.75; N, 16.30%.

IR: 3480 (OH), 3400, 3230, 3130 (NH), 1725 (C=O), 1520 (amide II), 1130 (C–O), 770, 700 (mono subst. benzene) and 720 cm^{-1} (C–Cl).

1-Aminocarbonyl-2-methyl-4-phenyl-2-imidazoline [IX]. Twenty grams of *N*-(1-ureidoethylidene)-2-chloro-1-phenylethylamine were mixed for 30 min at 50°C with 200 m*l* of aqueous 40% NaOH solution. The precipitate was separated by filtration, washed with cold water and dried *in vacuo* to yield 9 g (53%) of [IX] melting at 76—76.3°C.

IR: 3200 (NH), 1680 (C=O), 1640 (C=N), 1620 (amide II) and 755, 695 cm^{-1} (mono subst. benzene).

The picrate of [IX] had mp 139—140°C after recrystallization from ethyl alcohol.

Found: C, 47.17; H, 3.68; N, 19.39%. Calcd for $C_{17}H_{16}N_6O_8$: C, 47.22; H, 3.73; N, 19.43%.

2-Methyl-4-phenyl-2-imidazoline [X] and 1,2-Diaminoethylbenzene [XI]. Twenty-five grams of 1-aminocarbonyl-2-methyl-4-phenyl-2-imidazoline were refluxed with 90 m*l* of aqueous 40% NaOH solution for 2.5 hr and the resulting mixture was extracted with chloroform. The extracts were dried over anhydrous $MgSO_4$, concentrated *in vacuo* and the residue was distilled *in vacuo* to yield the following two fractions:

Cut-1, bp 95—117°C/1.5mmHg, 7 g

Cut-2, bp 135—136°C/1.5mmHg, 3 g (lit,[21] bp 121—122°C/0.2mmHg)

Cut-1 was redistilled *in vacuo* to yield pure 1,2-diaminoethylbenzene, bp 85—88°C/1.0 mmHg (lit,[22] bp 243—246°C/760 mmHg).

Found: C, 70.17; H, 8.95; N, 20.39%. Calcd for $C_8H_{12}N_2$: C, 70.55; H, 8.88; N, 20.56%.

IR: 3300, 3100, 1605, 880 (NH) and 750, 700 cm^{-1} (mono subst. benzene).

The picrate of [XI] had mp 165.5—166.5°C after recrystallization from ethyl alcohol (lit,[22] mp 160°C).

Found: C, 45.94; H, 4.09; N, 18.93%. Calcd for $C_{14}H_{15}N_5O_7$: C, 46.03; H, 4.13; N, 19.17%.

Cut-2. solidified upon standing and had mp 78.5—79°C.

Found: C, 75.08; H, 7.68; N, 17.16%. Calcd for $C_{10}H_{12}N_2$ [X]: C, 74.96; H, 7.54; N, 17.48%.

IR: 3200, 3120 (NH), 1620 (C=N, NH) and 755, 700 cm^{-1} (mono subst. benzene).

The picrate of [X] had mp 131.5—132.5°C after recrystallization from ethyl alcohol.

Found: C, 49.13; H, 3.78; N, 17.65%. Calcd for $C_{16}H_{15}N_5O_7$: C, 49.36; H, 3.88; N, 17.98%.

***cis*-2-Hydroxycyclohexylamine [XX].** Ten grams of *N*-(*trans*-2-chlorocyclohexyl)acetamide were refluxed with 100 m*l* of aqueous 20% HCl solution for 2 hr. The mixture was made alkaline with NaOH and subjected to steam distillation. The distillate was acidified with HCl and evaporated to dryness. Cold aqueous 50% NaOH solution was added to the residue. The resulting oil was extracted with ether. The etheral extracts were dried over anhydrous $MgSO_4$, concentrated *in vacuo* and the residue was distilled *in vacuo* to yield 4 g (61%) of *cis*-2-hydroxycyclohexylamine, bp 98—99°C/12 mmHg, which solidified upon standing. An analytical sample, mp 76.5—78°C, was obtained by recrystallization from ether. The product darkened on prolonged standing in air. The reported melting point for this compound is 107—108°C,[13] 72—73°C,[16] 71—72°C[12]; for *trans*-isomer the melting point is 66—67°C.[13]

Found: C, 62.25; H, 11.74; N, 12.10%. Calcd for $C_6H_{13}NO$: C, 62.57; H, 11.37; N, 12.16%.

IR: 3400 (OH), 3300, 3100, 1615 (NH), 990, 965 and 945 cm^{-1} (*cis* C–O); NMR: τ 6.3 (CHO, singlet), 7.2 CHN, singlet), 7.35 (NH_2, singlet), 8.45 (OH, singlet) and 8.55 (cyclohexyl protons).

The hydrochloride, prepared by addition of dry HCl gas to an alcoholic solution of the free base, melted at 183—184°C after recrystallization from ethyl alcohol. The reported melting point for this compound is 184—185°C[13]; for *trans* isomer the melting point is 175°C.[13]

N-(*cis*-2-Hydroxycyclohexyl)acetamide [XXI] from N-(*trans*-2-Chlorocyclohexyl)acetamide [XVI]. Five grams of *N*-(*trans*-2-chlorocyclohexyl)-acetamide and a solution of 3.5 g of Na_2CO_3 in 75 m*l* of water were allowed to stand for 12 hr at room tempera-

20) J. Read and I. G. M. Campbell, *J. Chem. Soc.*, **1930**, 2682.

21) H. Isler, U.S. 2505247, Apr. 25, 1950.

22) Beilsteins Handbuch der Organischen Chemie **13**, 177.

ture and then refluxed for 1 hr. The solution was extracted with ethyl acetate. After removal of the solvent the residue was recrystallized from benzene-ethyl alcohol to yield 2.5 g (55%) of *N*-(*cis*-2-hydroxycyclohexyl)-acetamide as a colorless plate, mp 145—146°C. The reported melting point for this compound is 146—147°C;[13,16] for *trans* isomer the melting point is 126—127°C.[16] The same result was obtained by treating [XVI] with aqueous 20% NH_4OH solution.

***cis*-2-Hydroxycyclohexylamine Hydrochloride from *N*-(*cis*-2-Hydroxycyclohexyl)acetamide.** Ten grams of *N*-(2-hydroxycyclohexyl)acetamide were refluxed with 60 m*l* of aqueous 20% HCl solution for 2 hr, and distilled *in vacuo* to dryness. The residue was recrystallized from ethyl alcohol to yield 6 g (62%) of colorless crystals, mp 183—185°C.

***N*-(*cis*-2-Hydroxycyclohexyl)acetamide [XXI] from *cis*-2-Hydroxycyclohexylamine [XX].** A solution of five grams of *cis*-2-hydroxycyclohexylamine in 20 m*l* of ethyl alcohol was added dropwise to 50 m*l* of acetic anhydride. The white precipitate was separated by filtration, recrystallized from ethyl acetate to yield 5.5 g (80%) of colorless plates, mp 145.5—146°C. The compound gave a mp 145—146°C in admixture with the sample in the preceding example prepared from *N*-(*trans*-2-chlorocyclohexyl)acetamide [XVI].

Found: C, 60.97; H, 9.78; N, 8.91%. Calcd for $C_8H_{15}NO_2$: C, 61.11; H, 9.61; N, 8.90%.

IR: 3350 (OH), 3100 (NH), 1650 (C=O), 1545 (amide II) and 985 cm^{-1} (*cis* C–O).

***N*-(1-Ureidoethyl)cyclohexylamine [XIX].** Five grams of $NaBH_4$ were added to 6.5 g of *N*-(1-ureidoethylidene)-*trans*-2-chlorocyclohexylamine [XV] solution in 150 m*l* of methyl alcohol over a period of 1 hr at 15°C. After the addition was complete, the reaction mixture was stirred for 1 hr at 15°C, then 1 hr at 40—50°C. The solution was treated with 5 m*l* of acetone, concentrated *in vacuo* to dryness and the residue extracted with ether. After drying with anhydrous $MgSO_4$, the ether was removed *in vacuo* and the resulting precipitate was separated by filtration. Recrystallization from ether gave white precipitate melting at 162—162.5°C.

Found: C, 58.31; H, 9.81; N, 22.56%. Calcd for $C_9H_{19}N_3O$: C, 58.34; H, 10.33; N, 22.68%.

IR: 3350, 3200 (NH), 1660 (C=O), 1605 (NH) and 1540 cm^{-1} (amide II).

***trans*-2-Chlorocyclohexylamine [XVII] and 1,2-Diaminocyclohexane [XVIII].** Twenty-eight grams of *N*-(1-ureidoethylidene)-2-chlorocyclohexylamine was refluxed with a solution consisting of 21 g of NaOH in 26 m*l* of water and 70 m*l* of ethylene glycol on a oil bath for 3 hr. The solution was acidified with HCl, filtered and the filtrate was evaporated to dryness *in vacuo*. Cold aqueous 50% NaOH solution was added to the residue and the resulting oil was extracted with ether. The ethereal extracts were dried over anhydrous $MgSO_4$, concentrated *in vacuo* and the residue was distilled *in vacuo* to yield the following two fractions:

Cut-1 [XVII] bp 62/9—63.5°C/8 mmHg, 4.5 g (26%) (lit,[11] bp 69°C/12 mmHg)

Cut-2 [XVIII] bp 115—121°C/3.5 mmHg, 1.0 g (7%) (lit,[23] 36—38°C/0.05 mmHg)

Cut-1 was a colorless oil when it was freshly distilled. But on standing at room temperature for several days, it decomposed to give a deposit of crystals. The result is in line with that reported for this compound.[11] IR: 3370, 3270, 1605 (NH) and 728 cm^{-1} (C–Cl).

The hydrochloride, prepared by addition of dry HCl gas to an alcoholic solution of the freshly distilled free base, melted at 208—210°C after recrystallization from ethyl alcohol. The reported melting point is 205—207°C,[24] 213—214°C;[3] the *cis*-isomer is reported to melt at 185—186°C.[16]

On being treated with acetic anhydride, the freshly distilled free base [XVII] was converted to the *N*-(*trans*-2-chlorocyclohexyl)acetamide. Recrystallization from ethyl acetate gave white needles melting at 128.5—129°C. There was no depression of melting point on admixture with the sample in the preceding example prepared from cyclohexene, *N*-chlorourea and acetonitrile.

Cut-2, obtained as a colorless oil, absorbed carbon dioxide rapidly on exposure to atmosphere as indicated by the immediate formation of solid on the surface. It was dissolved in ethyl alcohol and the solution was added to a picric acid solution in ethyl alcohol. A yellow solid precipitated immediately, the precipitate was washed with ethyl alcohol and analyzed. It became dark by heating at 220—260°C.

Found: C, 37.60; H, 3.70; N, 19.62%. Calcd for $C_6H_{14}N_2 \cdot 2C_6H_3N_3O_7$: C, 37.77; H, 3.52; N, 19.57%.

23) G. Swift and D. Swern, *J. Org. Chem.*, **32**, 511 (1967).

24) F. Winternitz, M. Mousseron and R. Dennilauler, *Bull. Soc. Chim. Fr.*, **1956**, 382. *Chem. Abstr.*, **50**, 14573 (1956).