Reaction of Nitroparaffins with Alicyclic Ketones. III. The Solid By-Product from Nitromethane and Cyclohexanone

DOROTHY V. NIGHTINGALE, DONALD A. REICH,[1] AND FLOYD B. ERICKSON[1]

The solid by-product from the reaction of nitromethane with cyclohexanone in the presence of piperidine or sec-aliphatic amine catalysts may be a heterocyclic hydroxamic acid containing nitrogen and oxygen in the heterocyclic system. Other functional groups believed to be present are —C=C— and —C=N—, not conjugated. The chemical reactions and infrared absorption spectra of this solid and compounds derived from it are consistent for the most part with a structure containing these functional groups.
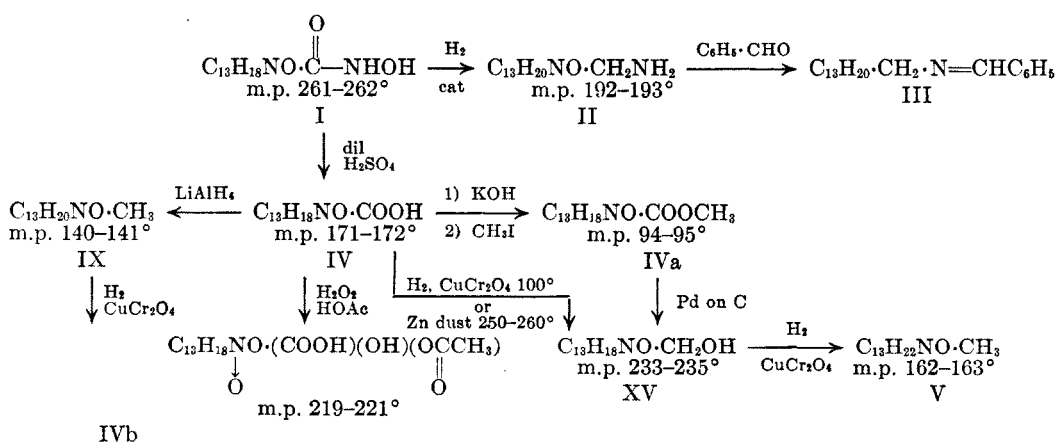
In this laboratory, the formation of a solid by-product, I, $C_{14}H_{20}N_2O_3$, m.p. 261–262° (dec.) in 8% yield from the reaction of nitromethane and cyclohexanone in the presence of piperidine or of di-n-propylamine had been noted in 1941.[2] Lambert and Lowe[3] reported this same solid when the condensation was catalyzed by diethylamine and stated that its constitution was unknown. In the present investigation, the yield of I was increased to 14% by the use of benzene as a solvent and removing the water as it was formed by azeotropic distillation. Analogous solids were obtained from 3- and 4-methylcyclohexanone[4] and cyclopentanone (XIX) but no solid was obtained from 2-methylcyclohexanone or cycloheptanone. No solid was obtained from nitroethane, nitropropane, or phenylnitromethane under the same experimental conditions. No solid was formed from nitromethane and cyclohexanone in the presence of sodium ethoxide.

I is slightly soluble in ether, benzene, and the petroleum ethers; slightly soluble in nitrobenzene, cold ethanol, and cold ethoxyethanol, but soluble enough in hot ethanol and hot ethoxyethanol to permit use of these solvents for cystallization. These solubilities, the high melting point, and the presence of one nitrogen and one oxygen which appear to be unaffected by most reagents, suggested that I may be heterocyclic and that it contained a polar group. I was insoluble in water and 10% hydrochloric acid but was soluble in sodium and potassium hydroxide and in concentrated sulfuric acid. Nitrogen containing groups which could confer solubility in base would be a nitro group with at least one alpha hydrogen, an oxime group, or an hydroxamic acid group. I was recovered unchanged either after boiling for twenty-four hours in 20% aqueous potassium hydroxide or after standing overnight in concentrated sulfuric acid. Upon treatment with nitrous acid I gave a reddish brown to orange solution.

The principal compounds obtained from I and compounds derived from them are shown in Charts I and II. Molecular weight determinations of II, the anil of II, Va and XV by the Rast method agree with the molecular formulas of these compounds.

CHART I

$$\underset{\substack{\text{m.p. 261–262°} \\ \text{I}}}{C_{13}H_{18}NO\cdot\overset{\displaystyle O}{\overset{\displaystyle \|}{C}}\text{—NHOH}} \xrightarrow[\text{cat}]{H_2} \underset{\substack{\text{m.p. 192–193°} \\ \text{II}}}{C_{13}H_{20}NO\cdot CH_2NH_2} \xrightarrow{C_6H_5\cdot CHO} \underset{\text{III}}{C_{13}H_{20}\cdot CH_2\cdot N{=}CHC_6H_5}$$

I $\xrightarrow{\substack{\text{dil} \\ H_2SO_4}}$

$$\underset{\substack{\text{m.p. 140–141°} \\ \text{IX}}}{C_{13}H_{20}NO\cdot CH_3} \xleftarrow{LiAlH_4} \underset{\substack{\text{m.p. 171–172°} \\ \text{IV}}}{C_{13}H_{18}NO\cdot COOH} \xrightarrow[\text{2) } CH_3I]{\text{1) KOH}} \underset{\substack{\text{m.p. 94–95°} \\ \text{IVa}}}{C_{13}H_{18}NO\cdot COOCH_3}$$

IX $\xrightarrow{\substack{H_2 \\ CuCr_2O_4}}$ IV $\xrightarrow{\substack{H_2O_2 \\ HOAc}}$ $\xrightarrow[\text{Zn dust 250–260°}]{\substack{H_2, CuCr_2O_4 100° \\ \text{or}}}$ IVa $\xrightarrow{\text{Pd on C}}$

$$\underset{\substack{\downarrow \\ O \\ \text{m.p. 219–221°} \\ \text{IVb}}}{C_{13}H_{18}NO\cdot(COOH)(OH)(OCCH_3)} \qquad \underset{\substack{\text{m.p. 233–235°} \\ \text{XV}}}{C_{13}H_{18}NO\cdot CH_2OH} \xrightarrow[CuCr_2O_4]{H_2} \underset{\substack{\text{m.p. 162–163°} \\ \text{V}}}{C_{13}H_{22}NO\cdot CH_3}$$
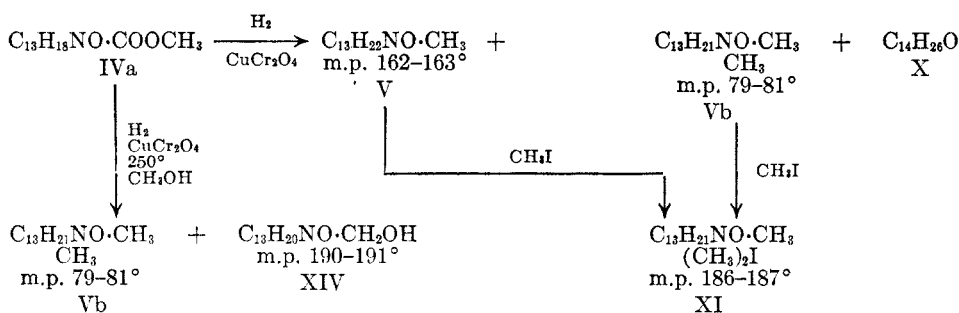
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(1) Abstracted from the Ph.D. dissertations of D. A. Reich, June 1956 and F. B. Erickson, August 1949. Presented in part at the American Chemical Society Meeting, Kansas City, Mo., March 1954.

(2) N. C. Knight, Master's dissertation, University of Missouri, 1943.

(3) A. Lambert and A. Lowe, J. Chem. Soc., 1517 (1947).

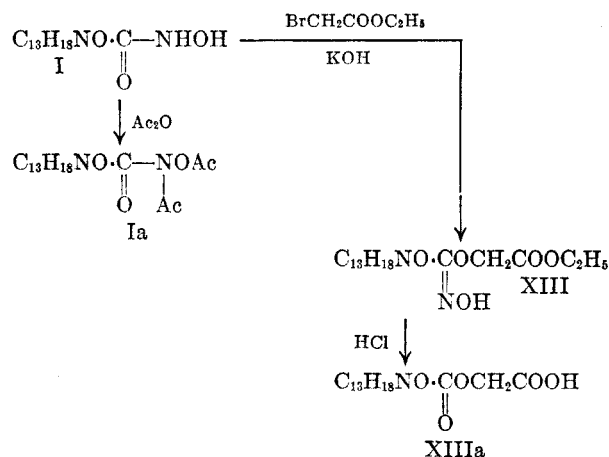(4) D. V. Nightingale, F. B. Erickson, and J. M. Shackelford, J. Org. Chem., 1005 (1952).

CHART II

$$C_{13}H_{18}NO\cdot COOCH_3 \xrightarrow[\text{CuCr}_2\text{O}_4]{\text{H}_2} C_{13}H_{22}NO\cdot CH_3 + \qquad C_{13}H_{21}NO\cdot CH_3 + C_{14}H_{26}O$$

IVa   m.p. 162–163°   CH₃   X
                         V   m.p. 79–81°
                                                      Vb

$C_{13}H_{21}NO\cdot CH_3 + C_{13}H_{20}NO\cdot CH_2OH$ ... (see chart)

H₂
CuCr₂O₄
250°
CH₃OH

CH₃I

CH₃I

$C_{13}H_{21}NO\cdot CH_3 + C_{13}H_{20}NO\cdot CH_2OH \qquad\qquad C_{13}H_{21}NO\cdot CH_3$
          CH₃   m.p. 190–191°   (CH₃)₂I
     m.p. 79–81°   XIV   m.p. 186–187°
          Vb   XI

When I was pyrolyzed at 280–290°, extensive decomposition occurred with the formation of cyclohexyl cyanide, ammonium carbonate and ammonia. I reacted vigorously when added rapidly to 85% sulfuric acid at 110° to yield some benzoic acid, accompanied by the evolution of sulfur dioxide and charring. This reaction and the formation of cyclohexyl cyanide by pyrolysis suggested that the unit $C_{13}H_{18}NO$ contained the group $C_6H_{11}C\!\!=\!\!N-$ or possibly $C_6H_9C\!\!=\!\!N-$.

Hydrolysis of I with dilute sulfuric acid yielded the base soluble compound IV, $C_{13}H_{18}NO\cdot COOH$ in 90–95% yields, and hydroxylamine. The neutral equivalent of IV agreed closely with the calculated value for the monocarboxylic acid, and the potassium salt of IV reacted with methyl iodide to form the methyl ester IVa, $C_{13}H_{18}NO\cdot COOCH_3$. Either a nitromethyl group or an hydroxamic acid group would form a carboxyl group and hydroxylamine, but both the chemical reactions and spectroscopic evidence favor the hydroxamic acid group. It may be written $C_{13}H_{18}NO\cdot CONHOH$.

Reactions of the hydroxamic group in I in addition to its hydrolysis include the formation of a diacetyl derivative Ia and the reaction with ethyl bromoacetate:

$$C_{13}H_{18}NO\cdot\underset{\underset{O}{\|}}{C}\!\!-\!\!NHOH \xrightarrow[\text{KOH}]{\text{BrCH}_2\text{COOC}_2\text{H}_5}$$
I

↓ Ac₂O

$$C_{13}H_{18}NO\cdot\underset{\underset{O}{\|}}{C}\!\!-\!\!NOAc$$
           Ac
Ia

$$C_{13}H_{18}NO\cdot\underset{\underset{\text{NOH}}{\|}}{C}OCH_2COOC_2H_5 \quad XIII$$

HCl ↓

$$C_{13}H_{18}NO\cdot\underset{\underset{O}{\|}}{C}OCH_2COOH$$
XIIIa

Lossen rearrangements attempted with I yielded intractable dark oils.

Bromination of I in refluxing carbon tetrachloride formed a monobromo compound Ib, $C_{13}H_{17}NOBr\cdot CONHOH$. This compound could be formed by di-

rect substitution or by addition to a double bond followed by the loss of hydrogen bromide. I did not react with aqueous bromine.

When I was hydrogenated over Raney nickel or copper chromium oxide, II, $C_{13}H_{20}NO\cdot CH_2NH_2$, was the principal product. With acetic anhydride, II formed a monoacetyl derivative IIa after heating for ten minutes and a diacetyl derivative IIb after three hours. The presence of a primary amino group was indicated by the reaction of II with benzaldehyde to form III, presumably a Schiff's base, which would not react with acetic anhydride. No further reaction took place when II was heated with hydrogen and fresh catalyst at 220° and 5490 p.s.i. for one hour. There was no odor of ammonia or of a volatile amine when the bomb was opened.

Treatment of the acid IV with 30% hydrogen peroxide in glacial acetic acid yielded IVb. The molecular formula $(C_{15}H_{22}NO_5\cdot COOH)$ of the latter suggested that a tertiary amine oxide and a monoacetyl derivative of a diol were formed during the oxidation.

Hydrogenation of IV at 100° over copper chromium oxide in ethanol yielded XV, $C_{13}H_{18}NO\cdot CH_2$-OH which on further hydrogenation formed V, C_{13}-$H_{22}NO\cdot CH_3$. When XV was analyzed in the Grignard machine, one mole of methane was liberated per mole of XV and one mole of reagent was added, presumably to a carbon to nitrogen double bond.

Reduction of IV with excess lithium aluminum hydride in refluxing ether yielded acid-soluble IX,[5] $C_{13}H_{20}NO\cdot CH_3$, and an intractable oil. This reagent should have reduced the carbon to nitrogen double bond but not the olefinic double bond.

Hydrogenation of IX over copper chromium oxide yielded V as the main product, along with a small amount of a nitrogen free oil, X, $C_{14}H_{26}O$.

Hydrogenation of the ester IVa in methylcyclohexane or in methanol led to a mixture of products which included those which would result from partial or complete reduction of the carbomethoxy group, the unsaturated groups, and cleavage products. The odor of ammonia or a volatile amine was usually noticeable when the bomb was opened.

(5) Under forcing conditions, reduction of the carboxyl group with lithium aluminum hydride may be carried beyond the primary alcohol stage to the hydrocarbon. W. G. Brown, *Org. Reactions*, **VI**, 477 (1951).

In methylcyclohexanone at a final temperature of 250°, the compounds isolated were V, $C_{13}H_{22}$-NO·CH$_3$, and Vb, $C_{13}H_{21}(CH_3)NO·CH_3$, both acid soluble. The formation of Vb may be accounted for by the methylation of V with the methanol formed during hydrogenolysis of IVa. With methyl iodide, V and Vb formed the same quaternary salt, XI, $C_{13}H_{21}(CH_3)_2INO·CH_3$. V readily formed a monoacetyl derivative, Va. Compound Vb did not react with acetic anhydride but it did form a hydrochloride.

When the final temperature for the hydrogenation of IVa was raised to 270–280° in an effort to cleave completely a hetero nucleus, the main products were V, Vb, and some X. Hydrogenation of IVa in methanol at a final temperature of 230° yielded Vb as the main product and some acid insoluble XIV, $C_{13}H_{20}NO·CH_2OH$, in which the olefinic double bond was presumably reduced but not the carbon to nitrogen double bond.

Compound X did not contain nitrogen. Carbon and hydrogen percentages found for X, m.p. 56–57°, and for its phenylurethane Xa, m.p. 155–156°, agreed well for $C_{14}H_{26}O$ and $C_{21}H_{31}NO_2$ for these respective compounds. The hydrogenation of IVa was repeated several times at 270–280° in an effort to accumulate enough of pure X for a series of structure determination reactions, but only variable smaller amounts were isolated.

A survey of all of the hydrogenation products isolated from IV and IVa in this study and their structural implications suggested that a 2-methyl-6-(cyclohexanemethyl)cyclohexanol, $C_{14}H_{26}O$, was a possible cleavage product. This cyclohexanol was synthesized by the hydrogenation of 2-hydroxy-3-methylbenzophenone over Raney nickel,[6] but this compound melted at 42–44° and its phenylurethane melted at 138–139°. The mixed melting point of this phenylurethane and the same derivative of X was 118–121°.

The infrared spectrum of X and of 2-methyl-6-(cyclohexanemethyl)-cyclohexanol both have the strong —OH band at 3.00 microns and are similar in many respects, but there are bands occurring at 9.35 microns and 10.15 microns in X which are not present in the spectrogram of the synthetic compound.

3 - Phenyl - 7 - methylbenzisoxazole was synthesized[6] and hydrogenated over Raney nickel at 220° to yield an oil which contained no nitrogen, the phenylurethane of which melted at 99–105° during several recrystallizations. The carbon and hydrogen percentages found for this derivative agreed with those calculated for $C_{21}H_{31}NO_2$. This product may be a mixture of stereoisomers of 2-methyl-6-(cyclohexanemethyl)cyclohexanol.

The fact that the carbomethoxy group of IVa was reduced to methyl without difficulty, suggested

that a second oxygen should be on the carbon beta to the carbomethoxy group or to the hydroxymethyl group of the possible intermediate XIV. Adkins[7] states that a hydroxyl group in the 3-position with respect to a second hydroxyl group facilitates the cleavage of the latter. For example, 1,3-cyclohexanediol is quantitatively converted to cyclohexanol at 200° while the 1,4-isomer is stable at 250°.

If IVa should have a heterocyclic nucleus containing oxygen, the oxygen in the hetero system could be in the 3-position with respect to the hydroxyl group of XIV, $C_{13}H_{20}NO·CH_2OH$, and could conceivably facilitate the conversion of the hydroxymethyl group to methyl.

The action of palladium on IVa, the distillation of IV with zinc dust, and the hydrogenation of IV over copper chromium oxide all yielded XV. Hydrogenation of XV from each of these reactions yielded V.

Reactions which gave results of little or no value included the oxidation of I, IV, and V with sodium dichromate and sulfuric acid or with postassium permanganate, the reaction of II with nitrous acid in 10% acetic acid, the reaction of V with 50% hydriodic acid, efforts to dehydrogenate IV with chloranil and to decarboxylate IV with copper and quinoline, ozonolysis of IV, and the reaction of the silver salt of IV with bromine. I, Ib, IV, and IVa were the only compounds in this study which gave a purple color with ferric chloride.

A study of the papers of Dunstan and Goulding,[8] Lippincott,[9] and Stork[10] which deal with reactions of nitromethane or cyclohexanone in the presence of amine catalysts and mechanisms for the formation of the principal products and some by-products leads to no simple explanation for the formation of I. The experimental conditions used in this study are similar to those used in a Michael reaction or a Stork alkaylation.[10] Increasing the amount of catalyst did not increase the yield of I.

Other compounds[3] which have been obtained from the reaction of cyclohexanone and nitromethane in the presence of sec-amine catalysts are 1-nitromethylcyclohexene, 1-nitromethylcyclohexanol, and 1,1-bis(nitromethyl)cyclohexane. Any of these compounds (or possibly cyclohexylidinecyclohexanone) could be considered as an intermediate in the formation of I. In this laboratory, I was obtained in smaller yields from both 1-nitromethylcyclohexene and 1-nitromethylcyclohexanol in the presence of the amine catalysts, and oc-

(6) D. A. Reich and D. V. Nightingale, J. Org. Chem., 21, 825 (1956).

(7) H. B. Adkins, Reactions of Hydrogen with Organic Compounds Over Copper Chromium Oxide and Nickel Catalysts, The University of Wisconsin Press, Madison, Wis., 1937, p. 104.

(8) W. R. Dunstan and E. Goulding, J. Chem. Soc., 77, 1262 (1900).

(9) S. B. Lippincott, J. Am. Chem. Soc., 62, 2604 (1940).

(10) G. Stork, R. Terrel, and J. Szumzkovicz, J. Am. Chem. Soc., 76, 2029 (1954).

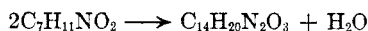casionally I separated slowly from 1-nitromethyl-cyclohexene which had been purified by distillation. Lambert and Lowe[3] also obtained some I from 1-nitromethylcyclohexanol and nitromethane in the presence of diethylamine.

The formation of I from the primary reactants may be written

$$2C_6H_{10}O + 2CH_3NO_2 \longrightarrow C_{14}H_{20}N_2O_3 + 3H_2O$$
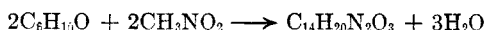
or from nitromethylcyclohexene

$$2C_7H_{11}NO_2 \longrightarrow C_{14}H_{20}N_2O_3 + H_2O$$

The presence of nitrite ion in the azeotroped water suggests that secondary reactions are involved. It is generally recognized that intramolecular oxidation-reduction reactions are not uncommon with aliphatic nitro compounds or with phenyl-nitromethane, and the allylic system —C=C—CH$_2$NO$_2$ in 1-nitromethylcyclohexene should be reactive.

A variety of heterocyclic structures having the formula C$_{14}$H$_{20}$N$_2$O$_3$ can be devised from reactions of various components of the reaction mixture, including the self-condensation of 1-nitromethyl-cyclohexene either by a Michael reaction or a diene synthesis. Most of these structures, however, contain a secondary nitro group or an =N → O group, and they do not account for most of the observed reactions of I or of IV.

The infrared absorption spectra of these compounds were helpful to the extent that bands present in the spectra agreed qualitatively with functional groups thought to be present in the compounds. The significant bands are as follows:

I. The strong bands at 3.25 microns and 5.9 microns may be due to the —OH group and C=O group, respectively, of the hydroxamic group. The two bands at 6.05 and 6.10 microns may be due to the —C=N— and —C=C—. The ultraviolet spectrum of I indicates that these double bonds are not conjugated.

II. The two bands in the 3.0–3.25 region are characteristic of the —NH$_2$ groups and the strong band at 5.94 may be caused by the —C=N—.

V. Only one band is observed at 3.2 microns, characteristic of the —N—H, and there is no absorption characteristic of unsaturation.

XV. The band at 10.02 may be due to an —OH group and the two bands near 6 microns indicate unsaturation probably due to —C=C— and —C=N—.

IX. The bands at 3.20 and 3.29 microns may be due to a vinyl hydrogen and the —N—H, while the weak bands at about 6 microns could be caused by —C=C—.

There are two or three strong bands between 12 and 13 microns present in I, II, and XV but absent in V and IX which may be characteristic of a ring structure of these compounds.

The solids from nitromethane and 3-methyl-cyclohexanone, 4-methylcyclohexanone, and cyclo-pentanone gave the same purple color with ferric chloride as did I. On hydrolysis with dilute sulfuric acid they formed base soluble compounds analogous to IV.

The melting points were determined in a capillary tube in a copper block and are uncorrected.

Compound I. In a flask equipped with a Stark and Dean trap were placed 180 ml. (1.74 moles) of cyclohexanone, 102 ml. (1.90 moles) of nitromethane, 200 ml. of benzene, and 12 ml. of piperidine. The mixture was refluxed gently for 30 hr., then allowed to cool and the solid which separated was collected on a filter. Compound I was recrystallized from 2-ethoxyethanol, m.p. 262–263° (dec.), literature[3] value 270–271°, yield 33 g. (14.8%).

Anal. Calcd. for C$_{14}$H$_{20}$N$_2$O$_3$: C, 63.62; H, 7.63. Found: C, 63.61; H, 7.78.

The water in the trap had a pH of 8–9 (Hydrion universal indicator paper). When this water was acidified with hydrochloric acid and tested with starch iodide paper, the purple color characteristic of nitrous acid developed. Evaporation of the water left a white solid which gave a positive brown ring test with ferrous sulfate solution and sulfuric acid, and which liberated ammonia when treated with sodium hydroxide solution.

The diacetyl derivative of I was obtained by warming it with acetic anhydride for 10 min., m.p. 128–129°, the literature value.[3] Long boiling of I with acetic anhydride yielded a dark, viscous oil.

Reaction of I with ethyl bromoacetate. The procedure was that of Kitagawa and Takis[12] for benzhydroxamic acid. Compound I (10 g., 0.04 mole), 75 ml. of absolute ethanol, and 4.5 g. (0.08 mole) of potassium hydroxide were placed in a 100-ml. flask fitted with a condenser, stirrer, and dropping funnel. The ester (6.7 g., 0.04 mole) was added dropwise to the refluxing solution. After refluxing for 6 hr., the cooled solution was diluted with water, the solid product was collected on a filter and washed with dilute base. The solid, XIII, was recrystallized from aqueous ethanol, m.p. 163–165°, yield, 10 g. (71%).

Anal. Calcd. for C$_{18}$H$_{26}$N$_2$O$_5$: C, 61.70; H, 7.48. Found: C, 62.01; H, 7.52.

Hydrolysis of XIII with 5% hydrochloric acid yielded XIIIa, m.p. 137–138°.

Anal. Calcd. for C$_{16}$H$_{21}$NO$_5$: C, 62.52; H, 6.88. Found: C, 62.46; H, 6.95.

Bromination of I. When a solution of 2 g. of I in 50 ml. of carbon tetrachloride was refluxed on a steam bath with excess bromine, a monobromo compound Ib was obtained, m.p. 184–185°.

Anal. Calcd. for C$_{14}$H$_{19}$N$_2$O$_3$Br: C, 48.98; H, 5.83. Found: C, 48.66; H, 5.59.

Pyrolysis of I. Compound I (5 g.) was pyrolyzed in a small distilling flask in a metal bath at 280–290°. The receiver was connected to a barium hydroxide trap in which a white precipitate formed. A white solid and a brown liquid which collected in the receiver were extracted with ether and the white solid collected on a filter. The solid reacted with benzenesulfonyl chloride in basic solution to form benzene-sulfonamide, m.p. 150.5–152.5°, mixture melting point with an authentic sample, 151.5–153°. When an aqueous

(11) The carbon and hydrogen analyses were by Mr. R. A. Carpenter, Mr. P. D. Strickler, Mr. R. L. Elliott, Mr. R. E. Bolin, and Mr. A. Mendel. The Dumas nitrogen determinations were by Mr. D. A. Reich.

(12) M. Kitagawa and A. Takis, *J. Agr. Chem. Soc. Japan*, **11**, 1007 (1936); *Chem. Abstr.*, **30**, 3409 (1936).

solution of the solid was treated with hydrochloric acid, the evolved gas formed a precipitate with barium hydroxide. These reactions identified the solid as ammonium carbonate.

When the ether extract was dried and the solvent removed on a steam bath, the residue (7 g. collected from five runs) was fractionated to yield 2.2 g. of cyclohexyl cyanide, b.p. 65–66° (10 mm.), n_D^{30} 1.4575, which was hydrolyzed in concd. sulfuric acid to yield the amide of cyclohexanecarboxylic acid, m.p. 184.5–186°.[13] Carbon and hydrogen percentages found for both the cyanide and the amide agreed with the calculated values.

Hydrogenation of I. A. Over Raney nickel. Compound I (13.2 g., 0.05 mole) in 100 ml. of ethanol was hydrogenated in conventional high pressure hydrogenation equipment over 3 g. of Raney nickel at an initial pressure of 2900 p.s.i. After heating began, there was a large pressure drop at 105–130° and heating was continued until the temperature reached 160° and 4240 p.s.i. The catalyst was removed from the solution by filtration and the solvent evaporated to yield ·10.9 g. (92%) of II, m.p. 192–193°, after recrystallization from petroleum ether (86–100°).

Anal. Calcd. for $C_{14}H_{24}N_2O$: C, 71.14; H, 10.24; N, 11.85; mol. wt. 236. Found: C, 71.49; H, 10.29; N, 11.74; mol. wt. 213, 238, 223 (Rast).

B. Over copper chromium oxide. Hydrogenation of 16 g. of I in 170 ml. of ethanol over 20 g. of copper chromium oxide at 90–110° and 3400 p.s.i. yielded 12 g. (85%) of II.

The monoacetyl derivative IIa of II was prepared by refluxing it with acetic anhydride for 10 min.; m.p. 271–272°.

Anal. Calcd. for $C_{16}H_{26}N_2O_2$: C, 69.03; H, 9.41. Found: C, 68.79; H, 9.60.

The diacetyl derivative of II was prepared by refluxing it with acetic anhydride for 3 hr.; m.p. 224.5–226°.

Anal. Calcd. for $C_{18}H_{28}N_2O_3$: C, 67.46; H, 8.88. Found: C, 67.72; H, 8.62.

Compound II formed an anil III when heated with benzaldehyde at 150–160° for 30 min.; m.p. 239–240° (from ethanol).

Anal. Calcd. for $C_{21}H_{28}N_2O$: C, 77.70; H, 8.96; mol. wt. 324. Found C, 77.04; H, 8.78; mol. wt. 300, 298 (Rast).

Reaction of I with hot sulfuric acid. When 19 g. of I was added all at once to 50 ml. of 85% sulfuric acid at 100°, there was a violet reaction accompanied by charring and the evolution of sulfur dioxide, and the temperature rose rapidly to 170°. The cooled reaction mixture was extracted continuously with ether, and the ether extract was washed and dried. Removal of the solvent yielded 3 g. of benzoic acid, m.p. 119–120°, mixture melting point with an authentic sample 121–122°.

Hydrolysis of I with dilute sulfuric acid. Compound I 5 g.) was refluxed for 53 hr. with 400 ml. of dilute sulfuric acid (1:4). After the solution had cooled over night, the separated acid IV was collected on a filter and recrystallized from aqueous ethanol. Yield, 4.3 g. (91%), m.p. 170–172°.

Anal. Calcd. for $C_{14}H_{19}NO_3$: C, 67.44; H, 7.69; Neut. equiv. 249. Found: C, 67.55; H, 7.81; Neut. equiv., 246, 249, 242.

The methyl ester of IV. In a 250-ml. flask fitted with a reflux condenser were placed 20 g. (0.08 mole) of IV, 4.55 g. (0.08 mole) of potassium hydroxide and 150 ml. of methanol. Methyl iodide (11.4 g., 0.08 mole) was added through the condenser and the mixture was refluxed for 3 hr. When the contents of the flask were cooled and diluted with water, the solid which separated was collected on a filter and washed with water. After recrystallization from aqueous methanol, the ester IVa melted at 94–95°, yield 17 g. (80%).

Anal. Calcd. for $C_{15}H_{21}NO_3$: C, 68.41; H, 8.04. Found: C, 68.75; H, 8.20.

Reaction of IV with hydrogen peroxide in acetic acid.[14] In a 50-ml. flask were placed 5 g. (0.02 mole) of IV, 8 ml. (0.06 mole) of 30% hydrogen peroxide and 50 ml. of glacial acetic acid. The mixture was heated on a steam bath for 5 hr., then diluted with 50 ml. of water and the water and acid removed under reduced pressure. The oily residue was dissolved in methanol and on cooling, crystals of IVb separated and were recrystallized from methanol. Yield, 2.1 g. (30%), m.p. 219–221°.

Anal. Calcd. for $C_{16}H_{23}NO_7$: C, 56.29; H, 6.79. Found: C, 56.04; H, 6.67.

Reduction of IV with lithium aluminum hydride. In the conventional apparatus were placed 3 g. (0.07 mole) of lithium aluminum hydride and 150 ml. of dry ether. A solution of 15 g. (0.06 mole) of IV in 1 l. of dry ether was added as rapidly as possible. After addition was complete, the mixture was refluxed for 5 hr. The complex was decomposed in the usual manner. The oily residue from the ether solution slowly crystallized, and after recrystallization from benzene and petroleum ether (60–70°), 2.3 g. of acid soluble IX was obtained, m.p. 140–141°.

Anal. Calcd. for $C_{14}H_{23}NO$: C, 75.97; H, 10.47. Found: C, 76.28; H, 10.42.

Reaction of IV with zinc dust. In a 125-ml. distilling flask were placed 25 g. of IV and 20 g. of zinc dust. The flask was placed in a metal bath preheated to 140° and the temperature of the bath was slowly raised. At 250–260°, there was vigorous bubbling in the melted mixture and at 275° some sublimation began. A water aspirator was attached to the receiver and the pressure reduced to 24 mm., but the refluxing material would not distill at a bath temperature of 340°.

The charred, tarry mixture was extracted with acetone. The acetone was then evaporated leaving a solid residue (14 g.) which was washed with dilute base and recrystallized, first from aqueous ethanol, then from petroleum ether (86–100°) and finally from 95% ethanol to yield XV, m.p. 232–234°.

Anal. Calcd. for $C_{14}H_{21}NO_2$: C, 71.45; H, 9.00; mol. wt. 235. Found: C, 71.48; H, 9.09; mol. wt. 248, 246, 247 (Rast).

Hydrogenation of 6 g. of XV in 100 ml. of methylcyclohexane over 20 g. of copper chromium oxide catalyst at 220–235° yielded 4 g. of V, m.p. and mixture m.p. with V from the hydrogenation of IVa, 162–163°. The acetate Va of this sample of V did not depress the melting point of Va from the hydrogenation of IVa.

Hydrogenation of IV over copper chromium oxide. Compound IV (15 g.) in 150 ml. of ethanol was hydrogenated over 20 g. of catalyst. The initial pressure was 2500 p.s.i. and the temperature was raised to 100° and held there until no more hydrogen was absorbed. The slightly soluble reduction product and catalyst were extracted in a Soxhlet extractor with acetone to yield 10.5 g. (75%) of XV, m.p. and mixture m.p. with XV from the zinc dust reaction, 233–234°.

Hydrogenation of IVa over copper chromium oxide in methylcyclohexane. Compound IVa (5.2 g., 0.02 mole) in 100 ml. of methylcyclohexane was hydrogenated over 23 g. of catalyst, at an initial pressure of 2500 p.s.i. There was a small drop in pressure at 65° and a large drop at 125–130°. The final temperature was 250° at 4200 p.s.i. The catalyst and liner were washed with ether and the washings added to the methylcyclohexane solution. The ether was removed from the mixture of solvents by distillation. As the remaining methylcyclohexane cooled, compound V separated and after recrystallization from aqueous ethanol it melted at 162–163°.

Anal. Calcd. for $C_{14}H_{23}NO$: C, 75.28; H, 11.28. Found: C, 75.50; H, 11.28.

The acetate Va of V melted at 142–143°.

(13) E. H. Huntress and S. P. Mulliken, *Identification of Pure Organic Compounds,* New York, John Wiley and Sons, 1946.

(14) E. C. Taylor and A. J. Crovetti, *J. Org. Chem., 19,* 1633 (1954).

Anal. Calcd. for $C_{16}H_{27}NO_2$: C, 72.41; H, 10.26; mol. wt. 265. Found: C, 72.41; H, 10.34; mol. wt. 287, 289 (Rast).

The methylcyclohexane filtrate from V was concentrated to less than 5 ml. and petroleum ether (60–70°) was added. Compound Vb separated and was collected on a filter. After recrystallization from petroleum ether (28–38°) it melted at 79–80°.

Anal. Calcd. for $C_{15}H_{27}NO$: C, 75.87; H, 11.47. Found: C, 75.74; H, 11.39.

The hydrochloride of Vb melted at 212–214°.

Anal. Calcd. for $C_{15}H_{28}NOCl$: C, 65.45; H, 10.23; N, 5.15. Found: C, 65.70; H, 10.31; N, 5.14.

Another hydrogenation of 12 g. of IVa in methylcyclohexane at a final temperature of 270–280° and 4000 p.s.i. yielded 3.4 g. of V, 1.5 g. of Vb, 2 g. of an acid soluble oil which was not identified, and 2 g. of a nitrogen-free oil X which became semi solid on standing. Compound X was purified by distillation through a short column at 122–123° (2 mm.) and melted at 56–57°.

Anal. Calcd. for $C_{14}H_{26}O$: C. 79.93; H, 12.46. Found: C, 79.79; H, 12.32.

The phenylurethane Xa of X melted at 155–156°.

Anal. Calcd. for $C_{21}H_{31}NO_2$: C, 76.55; H, 9.48. Found: C, 76.29; H, 9.44.

A mixture of Xa and the phenylurethane of authentic 2-methyl-6-(cyclohexanemethyl)cyclohexanol (m.p. 138–139°) melted at 118–121°.

Preparation of the quaternary salts of V and Vb. Compound V (6.7 g., 0.03 mole), 9 g. (0.06 mole) of methyl iodide, and 1.5 g. of potassium hydroxide were added to 200 ml. of absolute ethanol and the mixture allowed to stand for two days at room temperature. The separated potassium iodide was removed and the filtrate concentrated to precipitate the quaternary salt XI, m.p. 186–187° after recrystallization from absolute ethanol and ether.

Anal. Calcd. for $C_{16}H_{30}NOI$: C, 50.66; H, 7.91. Found: C, 50.97; H, 8.13.

The quaternary salt XI of Vb was obtained in the same way, m.p. and mixture m.p. with XI from V, 186–187°.

Hydrogenation of IVa over copper chromium oxide in methanol. Compound IVa (17 g., 0.06 mole) in 150 ml. of methanol was hydrogenated over 60 g. of catalyst and an initial pressure of 2600 p.s.i. There was a large drop in pressure at 110°, and the final temperature was 230°. The alcohol solution was diluted to 4 l. with ether and the solution extracted with dilute hydrochloric acid. When the acid extract was made basic with dilute sodium hydroxide solution, 9.3 g. of Vb was obtained. When the ether layer was evaporated, 1.5 g. of acid insoluble XIV was obtained, m.p. 190–191° (from ethanol).

Anal. Calcd. for $C_{14}H_{23}NO_2$: C, 70.85; H, 9.77. Found: C, 70.80; H, 10.09.

Reaction of IVa with palladium on carbon. Compound IVa (9 g.) and 0.4 g. of 5% palladium on carbon were introduced into a nitrogen filled 50-ml. Claisen distilling flask equipped with a nitrogen inlet tube, thermometer, and receiver. The flask was heated in a metal bath to 200° while nitrogen was passed in. Then the nitrogen tube was replaced with a stopper, the receiver was placed in a dry ice bath and attached to a barium hydroxide trap. At 275° the evolution of gas was vigorous and some barium carbonate separated in the

trap. When gas was no longer evolved, the temperature was raised to 210° and held there for 6 hr.

The dark, solid residue in the reaction flask was extracted with ethanol and the solution decolorized with Norite. Compound XV, insoluble in acid and base, was obtained by removal of the solvent and melted at 233–234°, after recrystallization from ethanol.

Anal. Calcd. for $C_{14}H_{21}NO_2$: C, 71.45; H, 9.00. Found: C, 71.28; H, 9.01.

The melting point of a mixture of this sample of XV with a sample of XV from the reaction of IV and zinc dust was 233–234°.

Reaction of cyclopentanone with nitromethane. In a 500-ml. flask equipped with a Stark and Dean trap were placed 89 ml. (1 mole) of cyclopentanone, 55 ml. (1 mole) of nitromethane, 6 ml. of piperidine, and 200 ml. of dry benzene. The mixture was refluxed for 24 hr., and after cooling some solid separated. The solution was diluted with an additional 300 ml. of benzene and allowed to stand several days. The solid (6.5 g., yield 8%) which separated was collected on a filter and after recrystallization from ethanol, XIX melted at 242–245° (dec.).

Anal. Calcd. for $C_{12}H_{16}N_2O_3$: C, 61.00; H, 6.83. Found: C, 61.13; H, 7.90.

This compound gave a purple color with ferric chloride solution, and its solubilities were the same as those of I.

Hydrolysis of XIX. In a 250-ml. flask were placed 100 ml. of 1:4 sulfuric acid and 2.5 g. of XIX. After refluxing the mixture for one hour all of XIX had dissolved and the solution was allowed to cool. The needles which separated were collected on a filter and recrystallized from absolute ethanol and petroleum ether (60–70°). The yield of XX was 1.7 g. (72%), m.p. 157–158°.

Anal. Calcd. for $C_{12}H_{15}NO_3$: C, 65.14; H, 6.83. Found: C, 64.99; H, 7.00.

Reaction of 4-methylcyclohexanone with nitromethane. A benzene solution of 61 g. (1 mole) of nitromethane, 112 g. (1 mole) of 4-methylcyclohexanone, and 6 ml. of piperidine was refluxed for 30 hr. Compound XXI which separated was recrystallized from 2-ethoxyethanol. The yield of XXI, m.p. 257–258° (dec.) was 10.5 g. (9%) as compared with a 4.5% yield obtained by Erickson[4] without solvent.

Hydrolysis of XXI. Compound XXI (2 g.) was refluxed 50 hr. with 160 ml. of 1:4 sulfuric acid. The acid XXII was isolated as described for the hydrolysis of I. Compound XXII sintered at 153° and melted at 160–162°, yield, 1.5 g. (81%).

Anal. Calcd. for $C_{16}H_{23}NO_3$: C, 69.28; H, 8.55. Found: C, 69.90; H, 8.48.

Absorption spectra. The absorption spectra were determined and interpreted by Prof. E. E. Pickett of the spectrographic laboratory of the University of Missouri. The ultraviolet spectra were determined on alcoholic solutions of the samples by means of a Cary Recording Spectrophotometer, Model 11, Serial 36. The infrared spectra were determined on a Beckman Infrared Spectrophotometer, Model IR-2A, with automatic slit adjustment. Nujol mulls of the solids were used for the infrared measurements.

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