region, which would indicate hydrogen attached to a double bond, excludes consideration of the double bond at the 4 or 8 positions.

The infrared spectrum of the residual product obtained after warming VIII with water and a drop of hydrochloric acid shows new bands indicating the presence of ketone (5.90 μ), primary amine, (3.02 and 11.1μ) and imine (6.02 μ). These data are in accord with the presence of an equilibrium mixture of the expected products, the isomeric cyclic imine and its hydrolytic cleavage product, the amino ketone.

EXPERIMENTAL[5]

2-(2-Cyanoethyl)-3,5,5-trimethyl-2-cyclohexeneone (I). The method of Bruson,[1] modified by the use of sodium methylate as catalyst, gave a 20% yield of I (b.p. 129–131°/2.4 mm., n_D^{30} 1.4908, d_{20}^{20} 0.9920).

Anal. Calcd. for $C_{12}H_{17}NO$: C, 75.40; H, 8.91; N, 7.34. Found: C, 75.42; H, 8.95; N, 7.38.

2-(2-Carboxyethyl)-3,5,5-trimethyl-2-cyclohexeneone (II). A mixture of 191 g. (1 mole) of I, 112 g. (2 moles) of potassium hydroxide and 1000 ml. of water was heated at reflux for 7 hr. The cooled mixture was then acidified with conc. hydrochloric acid to precipitate the product. Crystallization from heptane gave a 61% yield of refined II (m.p. 74.5–75.5°, reported[1] m.p. 76–77°).

2-(2-Carboallyloxyethyl)-3,5,5-trimethyl-2-cyclohexeneone (III). A mixture of 107 g. (0.51 mole) of II, 116 g. (2.0 moles) of allyl alcohol, 500 ml. of benzene, and 1.0 g. of *p*-toluenesulfonic acid was heated to reflux and the allyl alcohol-water-benzene azeotrope was taken off over a 5.5-hr. period. The reaction mixture was washed with 100 ml. of 20% aqueous sodium carbonate and then with 100 ml. of water. Distillation gave a 68% yield of III [b.p. 136°/1.7 mm., n_D^{30} 1.4861, d_{20}^{20} 1.0169. Infrared maxima at 3.24 μ ($CH_2{=}$), 5.8 μ (ester C=O), 6.03 μ (conj. ketone), 6.14 μ (conj. C=C), 7.24 and 7.32 μ [$(CH_3)_2C$], 8.7 μ (ester C—O—), 10.1 and 10.8 μ ($CH_2{=}C$)].

Anal. Calcd. for $C_{15}H_{22}O_3$: C, 72.00; H, 8.80. Found: C, 71.61; H, 8.49.

2-(2-Carbo-"Oxo"-decyloxyethyl)-3,5,5-trimethyl-2-cyclohexeneone (IV). A mixture of 110 g. (0.52 mole) of II, 316 g. (2.0 moles) of Enjay Company "Oxo" decanol, 500 ml. of benzene, and 1.1 g. of *p*-toluenesulfonic acid was heated to reflux and water was removed as the benzene azeotrope over a 7-hr. period. The reaction mixture was washed with 10% aqueous sodium carbonate and then with water. Benzene was removed by distillation and IV was taken as residual dark oil in 99% yield [n_D^{30} 1.4739, d_{20}^{20} 0.9499. Infrared maxima at 5.80 μ (ester C=O). 6.03 (conj. ketone C=O), 6.13 μ (conj. C=C), 8.6 μ (ester C—O—), 14.4 μ (*cis* RCH=CHR')].

Anal. Calcd. for $C_{22}H_{38}O_3$: C, 75.5; H, 10.85. Found: C, 75.58; H, 10.87.

2-(2-Carbovinyloxyethyl)-3,5,5-trimethyl-2-cyclohexeneone (V). A mixture of 664 g. (3.15 moles) of II, 1376 g. (16 moles) of vinyl acetate, 10 g. of mercuric acetate, and 3.1 g. of conc. sulfuric acid was allowed to stand at ambient temperature for 72 hr. The catalyst was neutralized with 6 g. of anhydrous sodium acetate and the precipitate was removed by filtration. Distillation gave a 30% yield of V (b.p. 130°C./1.3 mm., n_D^{30} 1.4889).

Bromine titration of the vinyl group yielded a figure which was 102% of the calculated value. Infrared data was consistent with the assigned structure.

5,7,7-Trimethyl-3,4,6,7-tetrahydro-1,2-benzopyrone (VI). A mixture of 125 g. (0.596 mole) of II and 350 ml. of acetic anhydride was refluxed for 4 hr. during which time 105 ml. of distillate was removed. Distillation of the residual mixture gave 97 g., an 85% yield of VI [b.p. 125°/3.3 mm., n_D^{30} 1.5176, d_{20}^{20} 1.0571. Infrared maxima at 5.64 μ lactone C=O, strong), 6.1 μ (conj. C=C). Equivalent weight by saponification. Calcd.: 192. Found: 196].

Anal. Calcd. for $C_{12}H_{16}O_2$: C, 75.1; H, 8.34. Found: C, 74.64; H, 8.12.

5,7,7-Trimethyl-1,2,3,4,5,6,7,8-octahydroquinoline (VIII). A mixture of 382 g. (2 moles) of I, 300 ml. of dioxane, 10 g. of wet Raney nickel (rinsed twice with dioxane), and 145 g. (8.5 moles) of anhydrous ammonia was hydrogenated in a stainless steel rocking autoclave at 160° and 1000 p.s.i.g. over a 5-hr. period. The cooled reaction mixture was filtered and fractionated to give 213 g., a 59% yield, of III [b.p. 85°/1.8 mm., n_D^{30} 1.5164, d_{20}^{20} 0.9495. Equivalent weight by perchloric acid in acetic acid titration. Calcd.: 179. Found: 179.5. Infrared maxima at 3.14 and 6.21 μ (—NH—), 6.12 μ (C=C), and 10.4 μ (—NH— out of plane)].

Anal. Calcd. for $C_{12}H_{21}N$: C, 80.4; H, 11.7; N, 7.84. Found: C, 80.6; H, 11.5; N, 7.95.

The *N*-phenylurea was prepared by treatment of VIII with phenyl isocyanate in ether and crystallized from ethanol (m.p. 115–116°).

Anal. Calcd. for $C_{19}H_{26}N_2O$: C, 76.6; H, 7.73; N, 9.40. Found: C, 77.0; H, 7.84; N, 9.75.

Hydrolysis of VIII. A mixture of 3.6 g. of VIII, 80 ml. of water, and one drop of conc. hydrochloric acid was warmed on steam bath overnight, cooled, and extracted with ether. The extract was dried over sodium sulfate and evaporated *in vacuo*. The residual oil, which quickly blackened on exposure to air, exhibited infrared maxima at 3.02 and 11.1 μ ($—NH_2$), 5.90 μ (C=O), 6.02 μ (C=N).

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[5] All temperatures are uncorrected.

Decomposition of Quaternary Salts. V. Stereospecificity in the Methadon Series

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Previous papers[1] in this series have shown that ketones of the methadon type give ethylidenetetrahydrofurans on pyrolysis of their quaternary salts. It has also been shown[2] that this reaction does not proceed by an olefinic intermediate since the optical isomers of isomethadon give optically active products. We now wish to report that the optically active forms of the ethylidenetetrahydrofurans are obtained when the optically active forms of methadon methiodide are decomposed. This would indicate that a concerted reaction takes place and that at no time is a carbonium ion formed. The most

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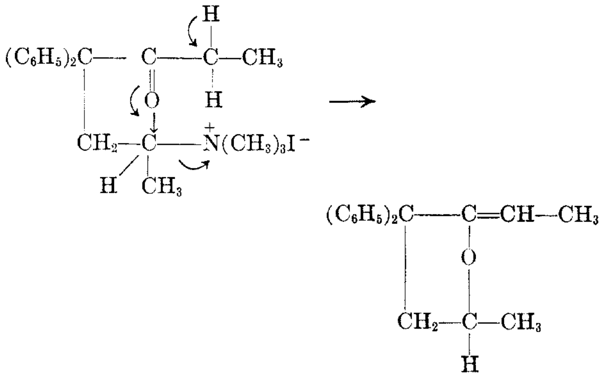
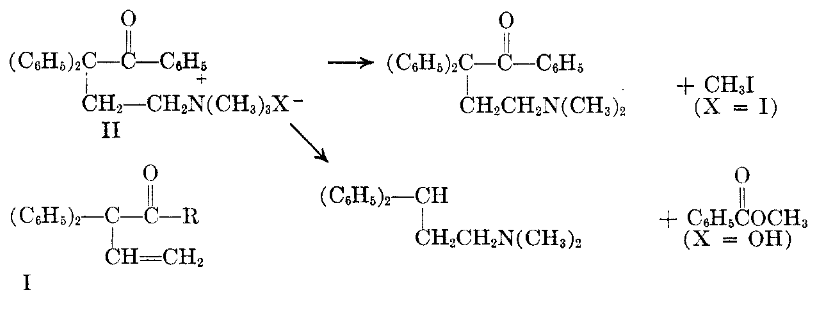
[1] Paper No. 4, S. J. Nelson, V. B. Fish, and N. R. Easton, *J. Am. Chem. Soc.*, **77**, 1908 (1955).

[2] N. R. Easton and V. B. Fish, *J. Am. Chem. Soc.*, **76**, 2836 (1954).

probable mechanism would be that of a rearward approach of the oxygen to the carbon attached to the nitrogen moiety, along with the cleavage of the nitrogen-carbon bond followed, or preceded, by the expulsion of the proton. Although it does not necessarily mean that inversion has taken place, the direction of the rotation is changed, the *d*- form of methadon methiodide gives the *l*- isomer of the cyclized compound. The optically active products were originally isolated as distillable oils which crystallized on long standing in the refrigerator. Although the *dl*- form is much higher melting and less soluble in methanol, none could be obtained in either reaction even by seeding alcoholic solutions of either oil with crystals of the *dl*- form. This indicates that very little, if any, racemization takes place during these pyrolyses.

In an attempt to prepare an unsaturated ketone of the type I several approaches were unsuccessful. The formation of this compound by the action of Grignard reagents on 4-bromo-2,2-diphenylbutanenitrile, 4-phenoxy-2,2-diphenylbutanenitrile or 2,2-diphenyl-3-butenenitrile was unsuccessful; in the second instance the phenoxy group was cleaved and in the third only the starting material and a nondistillable oil were obtained. It was hoped that by using a compound which contained no hydrogen atoms alpha to the carbonyl group, the cyclization could be prevented and the unsaturated ketone I would be obtained. When the methiodide of the phenyl ketone (II) was decomposed in the usual way, methyl iodide was split off and the original ketone was obtained. However, where the quaternary hydroxide was decomposed an unexpected cleavage resulted. Methyl benzoate and 1,1-diphenyl-3-dimethylaminopropane were formed.





The pyrolysis of the quaternary hydroxide of methadon has been reported[3] to give 1,1-diphenyl-3-dimethylaminobutane but the other products were not isolated. However, no cleavage of this type was found in the isomethadon series or where the dimethylaminoethyl side chain was involved.

EXPERIMENTAL

The methiodides of *d*- and *l*-methadon were prepared in the usual manner, m.p. 170–171°.

Decomposition of d- and l-methadon quaternary iodides. These were decomposed[3] by pyrolysis under reduced pressure. The distillate was taken up in ether, washed with dilute hydrochloric acid, dried, and distilled.

l-3,3-Diphenyl-2-ethylidene-5-methyltetrahydrofuran was obtained from *d*-methadon, b.p. 130–134°/2 mm., $\alpha_D^{25} = -246°$ ($c = 0.1026$, ethanol).

Anal. Calcd. for $C_{19}H_{20}O$: C, 86.32; H, 7.63. Found: C, 86.22; H, 7.60. From 15 g. of the methiodide 3.3 g. of the product was obtained.

d-3,3-Diphenyl-2-ethylidene-5-methyltetrahydrofuran was obtained from *l*-methadon, b.p. 129–133°/2 mm., $\alpha_D^{25} = 246°$ ($c = 0.1014$, ethanol).

Anal. Calcd. for $C_{19}H_{20}O$: C, 86.32; H, 7.63. Found: C, 86.26; H, 7.70. From 15 g. of the methiodide 4.6 g. of the product was obtained.

Equal quantities of the *d*- and *l*- isomers were mixed in ethanol. Crystals formed, m.p. 78–80°, identical with the *dl*- form previously reported.[3] On long standing in the refrigerator each crystallized. The product was recrystallized from methanol, m.p. 55–56°.

Methiodide of α-dimethylaminoethyl-α,α-diphenylacetophenone. The methiodide was prepared from α-dimethylaminoethyl-α,α-diphenylacetophenone[4] in the usual way. After recrystallization from water it melted at 270–271° dec.

Anal. Calcd. for $C_{25}H_{28}NOI$: I, 26.15. Found: I, 26.02.

Pyrolysis of α-Dimethylaminoethyl-α,α-diphenylacetophenone methiodide. The methiodide (10 g.) was decomposed by heating over a free flame under 3 mm. pressure. The oil which distilled was taken up in ether and extracted with dilute hydrochloric acid. (No appreciable quantity of neutral material was isolated.) The acid layer was neutralized and extracted with ether, the ether layer was concentrated and a hydrobromide of the product was identical with the hydrobromide of 4-dimethylaminoethyl-2,2-diphenylacetophenone.

Preparation and pyrolysis of the quaternary hydroxide of α-dimethylaminoethyl-α,α-diphenylacetophenone. A mixture of 4 g. of the methiodide and 3 g. of silver oxide in warm aqueous ethanol was stirred vigorously until no iodide ion could be detected. After being filtered the precipitate was washed with water and with ethanol and the filtrate was concentrated under reduced pressure. After being trans-

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[3] N. R. Easton, S. J. Nelson, V. B. Fish, and P. N. Craig, *J. Am. Chem. Soc.*, **75**, 3751 (1953).

[4] M. Bockmuhl and G. Ehrhart, *Ann.*, **561**, 52–85 (1948).

ferred to a Claisen flask it was subjected to a pyrolytic distillation under 20 mm. pressure. The oily product was dissolved in ether and washed with dilute hydrochloric acid. The ether solution was dried and concentrated and the residue distilled 50–55° at 3 mm. pressure. Its odor was similar to methyl benzoate. $n_D^{20} = 1.5190$. Lit. $n_D^{16} = 1.5181$. Hydrolysis gave benzoic acid, m.p. 121–121.5°; mixed with benzoic acid, m.p. 121–121.5°. The acid solution above was neutralized and extracted with ether. The ether layer was dried and alcoholic hydrogen chloride added; a precipitate formed (0.7 g.) which melted at 162–164°. After recrystallization from a mixture of ethanol, ethyl acetate, and isopropyl ether, it melted at 165–167°.

Anal. Calcd. for $C_{17}H_{22}NCl$: Cl, 12.85. Found: Cl, 12.73.

A mixed melting point with this compound and that prepared below showed no depression.

3-Dimethylamino-1,1-diphenylpropane. This was prepared by the treatment of 4-dimethylamino-2,2-diphenylbutanenitrile with sodium in isopropyl alcohol;[5] hydrochloride, m.p. 167–169°; methiodide, m.p. 190–192°.

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[5] N. R. Easton, L. R. Bartron, F. Meinhofer, and V. B. Fish, *J. Am. Chem. Soc.*, **75**, 2088 (1953).

Synthesis of Some Symmetrical Aliphatic Quaternary Ammonium Iodides

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As part of an investigation of the effect of ionic dimensions on electric conductance,[2] a series of aliphatic quaternary ammonium iodides has been prepared (Table I).

The principal quaternization procedure consisted in refluxing alcoholic solutions of primary or tertiary amines with the required alkyl iodides. In some instances, the reaction mixtures were maintained at a *p*H of approximately 9 by the periodic addition of ethanolic potassium hydroxide.

As the quaternary salts were to be used for conductivity studies, their purity was of critical importance. Anion impurities were detected by titration with aqueous silver nitrate using calomel and silver-silver chloride electrodes. The titration procedure was initially applied to the successive recrystallization liquors rather than to solutions of the recrystallized salts. This time-saving step was applicable as it was found that after repeated recrystallizations, no appreciable change in effect on ionic conductance of subsequent recrystallization liquors was noted. At this point the ultimate criterion of purity was established by titration of the quaternary salts in methanol after they had been subjected to further successive recrystallizations. If the conductance of samples from recrystallization to recrystallization differed by less than 5%, the salts were deemed sufficiently pure for the conductance work.

Repeated recrystallization of tetraoctylammonium iodide failed to provide a product having satisfactory ionic conductance properties or analytical characteristics. Subjecting tetrahexadecylammonium iodide to repeated recrystallizations finally gave a product, however, which showed no alteration in its ionic conductance from recrystallization to recrystallization, but which gave unsatisfactory analytical results.

Confirmation of the presence of a quaternary nitrogen atom in the latter compound was established by measurement of the change in its ionic conductance effected by silver hydroxide, as compared with similar measurements of authentic samples of a representative quaternary ammonium iodide, and representative secondary and tertiary amine hydroiodides.

EXPERIMENTAL

Melting points are uncorrected. Microanalyses are by the Microanalytical Laboratory, Department of Chemistry, University of California.

Materials. The alkyl iodides which were not commercially available were prepared by the methods of Hartman, Byers, and Dickey[3a] and Finkelstein.[3b] The tertiary amines were obtained commercially or prepared by known methods.[4a,b]

General Procedures. The molecular amounts of reactants and other reaction data appear in Table I.

A. A mixture of the amine and the corresponding alkyl iodide was refluxed in a suitable solvent. Refluxing was discontinued intermittently, followed by cooling the reaction mixture and removing the reaction product.

B. Procedure A was modified in the following manner. After refluxing the reaction mixture was cooled, adjusted to *p*H 9 with 5% ethanolic potassium hydroxide, followed by the addition of an equal volume of water. The product was filtered and washed with water and ether. The yield of tetraheptylammonium iodide was increased to 31.4 g. (73%) by the addition of 50 ml. of commercial absolute ethanol and 12.5 g. (0.055 mole) of heptyl iodide to the diluted alkaline reaction filtrate and refluxing for 72 hr.

C. Procedure B was modified by maintaining the reaction mixture at a *p*H of approximately 9 by the periodic addition of 5% ethanolic potassium hydroxide. After refluxing, an equal volume of water was added and the mixture cooled.

D. A mixture of the tertiary amine and the alkyl iodide was heated in an open flask at 80°, following the procedure of Vernon and Masterson.[5]

E. Following the procedure described by Girard and Forneau,[6] ammonia gas was bubbled through the liquefied

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[1] Taken from a dissertation submitted by Stuart P. Eriksen in partial fulfillment of the requirements for the Ph.D. degree in Pharmaceutical Chemistry, 1956.

[2] In preparation.

[3] (a) W. W. Hartman, J. R. Byers, and J. B. Dickey, in A. H. Blatt, *Org. Syntheses*, **Coll. Vol. II**, John Wiley and Sons, New York, N. Y., 1943, p. 322; (b) H. Finkelstein, *Ber.*, **43**, 1528 (1910).

[4] (a) M. R. McCorkle, *Iowa State Coll. Jour. Sci.*, **14**, 64 (1939); (b) A. W. Ralston, C. M. Hoerr, and P. L. DuBrow, *J. Org. Chem.*, **9**, 259 (1944).

[5] A. A. Vernon and J. P. Masterson, *J. Am. Chem. Soc.*, **64**, 2822 (1942).

[6] A. Girard and E. Forneau, *Bull. Soc. Chim.*, **37**, 1670 (1925).