pentyl and cyclohexyl *p*-toluenesulfonates. Winstein, *et al.*,[16] reported a difference of 21 for the acetolysis of cyclopentyl and cyclohexyl *p*-toluenesulfonates at 50°, a difference of 19 in the rates for the formolysis at 25° and a difference of 38 in the rates for ethanolysis with similar thermodynamic data as that reported by reference 12b. These differences in rate have been attributed to release of Pitzer or Hassel strain in going to the transition state in the cyclopentyl compounds, a factor not present in the chair configuration of the cyclohexyl compound and it is reasonable to assume that a similar reason is responsible for the difference in rates of the cyclopentyl and cyclohexyl azo compounds. A plot of the log of the rate constants for decomposition against ring size is shown in Fig. 3.

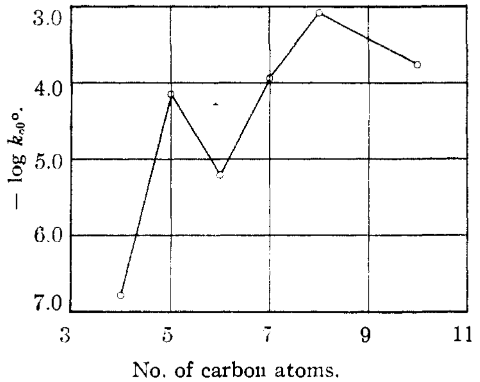

Fig. 3.—Variation of ring size with rate of decomposition.

The order of the activation energies is roughly approximated by the decomposition rates. The entropies of activation are all positive and some interesting differences are noted. The small entropy change for the cyclobutyl compound probably indicates considerable rigidity in its transition state and very little gain in degrees of freedom as the carbon–nitrogen bond is broken. The large change for the cyclopentyl compound indicates a large gain in degrees of freedom in the transition state over that in the ground state. Interestingly, Brown and Borkowski[12b] attribute most of the difference in rate of solvolysis of 1-chloro-1-methylcyclobutane and the cyclopentyl and cyclohexyl compounds to the heat term whereas as noted, a rather large portion of the difference in rates of decomposition of the cyclobutyl and cyclopentyl azo compounds is due to the entropy term. The lower positive values for the cycloheptyl, cyclooctyl and cyclodecyl compounds indicate more degrees of freedom in the ground state and thus less gain in going to the transition state. It seems logical to assume that much of this can be attributed to ring oscillation over and above simple rotational and vibrational degrees of freedom of single bonds.

Unpublished entropies of activation for linear compounds of the type described in reference 3a range from +8 to +15 e.u. so that no simple comparisons can be made at this time.

Brooklyn, New York

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[16] S. Winstein, B. K. Morse, E. Grunwald, H. W. Jones, J. Corse, D. Trifan and H. Marshall, This Journal, **74**, 1127 (1952).

[Contribution from the Department of Chemistry, Institute of Polymer Research, Polytechnic Institute of Brooklyn]

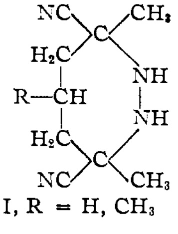
Reactions of Biradicals in Solution.[1] Decomposition Products Obtained from the Oxidation of 3,7-Dicyano-3,7-dimethylhomopiperidazine

By C. G. Overberger, Pao-tung Huang[2] and Thomas B. Gibb, Jr.[3]

Received December 22, 1952

On oxidation of 3,7-dicyano-3,7-dimethylhomopiperidazine, three products (V, VI, VII) resulting from the biradical $CH_3-\dot{C}(CN)-(CH_2)_3(CN)\dot{C}-CH_3$ have been isolated and their structures determined. Two of these products (V and VI) were shown to be *cis*- and *trans*-1,2-dicyano-1,2-dimethylcyclopentanes. The structure of a third product (VII), 2,6-dicyanoheptene-2 was demonstrated. A cyclic radical displacement mechanism to explain the formation of VII is proposed.

A previous paper in this series[4] has described the preparation of 3,7-dicyano-3,7-dimethylhomopiperidazine (I, R = H) and the corresponding 3,5,7-trimethyl compound (I, R = CH_3). Oxidation of I, R = H, gave a quantitative evolution of nitrogen, two solid products and one liquid product. This paper describes the isolation and proof of structure of these products. In particular, we were interested in determining the course of an internal radical displacement reaction (see Discussion).



I, R = H, CH_3

Discussion

Additional experimental confirmation that I is the structure indicated for the reaction product from δ-diketones, cyanide ion and hydrazine has

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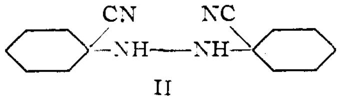
[1] This is the ninth in a series of papers concerned with the decomposition of azo compounds. For the eighth, see C. G. Overberger, Harry Biletch, A. B. Finestone, J. Lilker and J. Herbert, This Journal, **75**, 2078 (1953).

[2] A portion of a thesis submitted by Pao-tung Huang in partial fulfillment of the requirements for the degree of Doctor of Philosophy in the Graduate School of the Polytechnic Institute of Brooklyn.

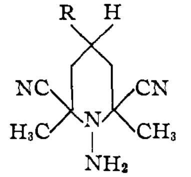
[3] A portion of a thesis submitted by Mr. T. B. Gibb, Jr., in partial fulfillment of the requirements for the degree of Master of Science in the Graduate School of the Polytechnic Institute of Brooklyn.

[4] C. G. Overberger, T. B. Gibb, Jr., Sheldon Chibnik, Pao-tung Huang and J. J. Monagle, This Journal, **74**, 3290 (1952).

been obtained. An infrared spectrum of I (R = H, CH_3) compared with the substituted hydrazine II thus serves to substantiate the absence of any primary amino groups ($-NH_2$), that would be found in an alternate structure III. Furthermore, it is unlikely that nitrogen would be evolved quantitatively from III on oxidation with bromine to give the corresponding biradical $CH_3\text{-}\dot{C}(CN)(CH_2)_3\text{-}(CN)\dot{C}\text{-}CH_3$ (IV). Usually this type of oxidation of a 1,1-disubstituted hydrazine results in the formation of a tetrazene.[5] Attempted reactions of I, R = H, with benzenesulfonyl chloride and benzaldehyde gave only starting material. A potentiometric titration revealed that the compound was not basic unlike most 1,1-substituted hydrazines.[5] It can therefore be concluded that structure III is untenable.

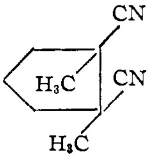


II

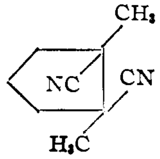


III

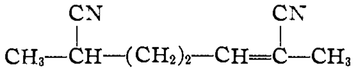
Oxidation of I, R = H, with bromine at 0–5° gave three products (V, VI and VII). An improved procedure for isolation of the isomers is described. VII was obtained in much higher yield than V or VI. This is rather surprising in view of the fact that the decomposition of 2,2′-azo-bis-isobutyronitrile at 80° in toluene gives over an 80% yield of the coupled product, *sym*-tetramethylsuccinonitrile, and is an indication that the internal radical displacement reaction either has a lower activation energy than the same reaction between two separate radicals in solution or, and more likely, there are steric requirements which reduce the yield of the five-membered ring coupled products.



V(Solid)



VI(Solid)



$$CH_3-\overset{CN}{\overset{|}{C}}H-(CH_2)_2-CH=\overset{CN}{\overset{|}{C}}-CH_3$$

VII (liquid)

The structure of V (16–26%) was determined in the following way. No reaction occurred with bromine and phosphorus tribromide[6] indicating the absence of any hydrogen on the carbon adjacent to the nitrile. Hydrolysis of V with alkaline hydroperoxide gave a monoamide in 89% yield. Hydrolysis with 60% sulfuric acid gave a 1,2-dicarboxy-1,2-dimethylcyclopentane anhydride, showing that probably the nitrile groups had the *cis* configuration. Hydrolysis of this anhydride with sodium hydroxide gave a new diacid. A determination of its dipole moment by measuring its dielectric constant[7] in benzene using the bridge method gave a value of 6.2 *D*. This large value is only possible for the *cis* configuration of the nitrile groups. The infrared spectrum unmistakably has shown the presence of only saturated nitrile groups (2250 cm.$^{-1}$). The spectra for some 70 saturated and α,β-unsaturated nitriles has recently been reported by Kiston and Griffith,[8] and furnished us with a very useful analytical tool. The infrared absorption band due to the nitrile stretching vibration occurs at 2250 ± 8 cm.$^{-1}$ in saturated or non-conjugated nitriles. In compounds where the nitrile group is in conjugation with the double bond, the band is shifted to 2225 ± 8 cm.$^{-1}$. Both bands are found for compounds which contain both groups.

The structure of VI (3.9%) was determined in the following way. No reaction occurred with bromine and phosphorus tribromide indicating, as in isomer V, the absence of any hydrogen on the carbon adjacent to the nitrile. Hydrolysis of VI with alkaline hydrogen peroxide gave a diamide. Hydrolysis with 60% sulfuric acid gave only a diacid under identical conditions which produced the anhydride from V. This acid differed in its properties from that obtained from the *cis* anhydride. This strongly indicates that the nitrile groups are *trans*. A determination of its dipole moment by measuring its dielectric constant in benzene gave a value of 1.9 *D*. This small value of the dipole moment is conclusive evidence of the *trans* configuration. The infrared spectrum again shows the presence of only saturated nitrile groups (2250 cm.$^{-1}$).

The structure of VII (28–38%) was determined in the following way. Considerable difficulty was encountered in the purification of VII and only chromatography on alumina gave a pure product. The infrared spectrum (Fig. 1) revealed the presence of the α,β-unsaturated nitrile group (2225 cm.$^{-1}$) as well as the normal nitrile group (2250 cm.$^{-1}$).

Hydrogenation in ethanol over 10% palladium-on-charcoal quantitatively showed the presence of one double bond and gave the heretofore unknown α,α'-dimethylpimelonitrile. Hydrolysis of α,α'-dimethylpimelonitrile with 50% sulfuric acid gave the pure stereoisomeric mixture of α,α'-dimethylpimelic acid from which was isolated in crystalline form, one of the stereoisomers previously characterized by Perkin and Prentice.[9]

One of the most interesting questions concerns the position of the double bond. If an internal radical displacement reaction is occurring two transition states are possible, VIII and IX. If route VIII is taken, a seven-membered ring transition state is necessary and the double bond will be on the terminal carbon. On the other hand, if route IX is taken

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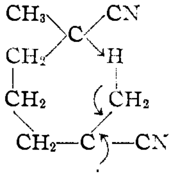
[5] N. V. Sidgwick, "The Organic Chemistry of Nitrogen," The Clarendon Press, second revised edition, 1942, p. 380.

[6] C. L. Stevens, THIS JOURNAL, **70**, 165 (1948); C. L. Stevens and T. H. Coffield, *ibid.*, **73**, 103 (1951). For a discussion of this reaction see C. G. Overberger and M. B. Berenbaum, *ibid.*, **73**, 4883 (1951).

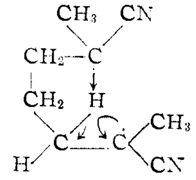
[7] Charles P. Smyth in Weissberger's "Physical Methods in Organic Chemistry," second edition, Interscience Publishers, Inc., New York, N. Y., 1949, p. 1617.

[8] R. E. Kiston and T. H. Griffith, *Anal. Chem.*, **24**, 334 (1952).

[9] W. H. Perkin, Jr., and B. Prentice, *J. Chem. Soc.*, **59**, 818 (1891).



VIII



IX

a five-membered ring transition state is involved with the double bond in the 2,3-position. Oxidation of VII with dilute neutral permanganate followed by hydrolysis of the crude γ-cyano-*n*-valeric acid gave a 31% yield of α-methylglutaric acid, identical with an authentic sample (mixed melting point). The direct oxidation product, γ-cyano-*n*-valeric acid, could be isolated in 45% yield. No oxidation products, either derivatives of adipic or pimelic acids, were isolated. Under the mild conditions of oxidation it is unlikely that the olefin derived from reaction path VIII would give γ-cyano-*n*-valeric acid or that any migration of the double bond could occur during oxidation. It is of course always possible that small amounts of other oxidation products were present which could not be isolated. *The evidence strongly indicates that a major portion of the displacement reaction proceeds by mechanism IX.*

In linear systems it is likely that two factors are governing radical displacement reactions when polar factors are essentially constant. Sterically, the primary terminal hydrogens are probably favored over internal secondary hydrogens in linear displacement reactions. This effect is partially overcome by the small difference in the ease of breaking the secondary carbon–hydrogen bond over that of the primary one. In the cyclic system described here, steric requirements for transition state VIII may be more severe than for IX.

Experimental[10]

Basicity Determination of I and II.—Samples I and II were titrated to the half neutralization point with standard hydrochloric acid and their *p*H determined with a standard Beckman model DU *p*H meter. An average value of 2.4 was obtained for I and 2.6 for II indicating the lack of any basic properties for either compound.

Attempted Preparation of Derivatives of I.—To 0.2 g. of the hydrazine compound were added 5 ml. of 10% sodium hydroxide and 0.4 g. of *p*-toluenesulfonyl chloride. On shaking, the compound was not dissolved and did not appear to react. Attempted reaction with benzaldehyde was also unsuccessful and starting material was recovered.

Oxidation of 3,7-Dicyano-3,7-dimethylhomopiperidazine and Isolation of the Oxidation Decomposition Products.—To 26.70 g. (0.15 mole) of the cyclic hydrazine suspended in 240 ml. of alcohol was added with stirring 24.0 g. (0.15 mole) of bromine, while the flask was cooled in an ice-bath to keep the temperature of the solution at 5°. After the addition was complete, most of the alcohol was removed from the clear solution by evaporation. To the remaining 50 ml. of the mixture was added 200 ml. of water, and the remaining alcohol was distilled azeotropically until the temperature of the distillate reached 100°.

The distillate contained white crystalline solid which was collected and washed with water. This crude *trans*-1,2-dicyano-1,2-dimethylcyclopentane weighed 0.35 g. and melted at 152–153°. After sublimation at 90°, the solid weighed 0.34 g. (1.53%), m.p. 156.6–157.2° (155.7–156.4°).[4]

The oil layer in the distilling flask was taken up with ether and the aqueous layer was extracted four times with ether. The combined ethereal solution, after drying with anhydrous magnesium sulfate, gave 20.7 g. of yellowish oil. The oil was repeatedly chilled in the Dry Ice box and the solid that separated was removed successively. After five filtrations, no more solid was obtainable in this manner and the total weight of the crude product after absorption of residual liquid on filter paper was 3.30 g. The crude liquid remaining weighed 15.2 g. The crude solid, 3.30 g., was recrystallized from 200 ml. of petroleum ether (b.p. 60–68°) to give 2.30 g. of pure *cis*-1,2-dicyano-1,2-dimethylcyclopentane, m.p. 161.8–162.8°; second crop 0.25 g., m.p. 161.8–162.8°; total yield of the pure *cis* cyclic isomer, 2.55 g. (11.5%) (161.5–162.1°, 10.3%).[4]

The remaining liquid was distilled under vacuum. Solid was first collected on the condenser cold-finger. The distillation was discontinued and the solid on the cold-finger was rinsed off with ether and the process repeated. After the ether had been removed, the combined residue was pressed dry and the solid was sublimed at a low temperature to give 1.06 g. of crude solid. Resublimation of the crude solid did not give a pure product; the m.p. of the sublimate was 139–152°. When this sublimate, 0.88 g., was recrystallized from 10 ml. of ether, 0.52 g. of solid was obtained, m.p. 154.0–154.6° (uncor.) (2.34%). When combined with the 0.34 g. obtained previously the yield of the lower-melting *trans* isomer was 0.86 g. (3.87%) (0.47%).[4]

The remaining liquid was redistilled and the fraction boiling at 88–91° (0.4–0.6 mm.) was collected, 12.0 g. (54.1%), $n^{25}{}_{\rm D}$ 1.4589, $d^{32}{}_4$ 0.9772.

Chromatographic Purification of 2,6-Dicyanoheptene-2.—Experimental evidence presented later indicated that the liquid as obtained in the manner described in the above section was contaminated with a small amount of *cis* cyclic dinitrile which was not completely removable by fractional crystallization, distillation or sublimation. In order to obtain a pure sample of 2,6-dicyanoheptene-2, the liquid was purified by chromatography. In the course of the experiment, besides the *cis* cyclic isomer, a small amount of *trans*-1,2-dicyano-1,2-dimethylcyclopentane was also isolated.

The liquid, 3.0 g., $n^{25}{}_{\rm D}$ 1.4587, was dissolved in a mixture of 20 ml. of petroleum ether (Skellysolve A) and 10 ml. of benzene and the solution was passed through a column of activated alumina, 1.5 cm. × 41 cm., previously washed with petroleum ether. The column was developed with a mixture of 80 ml. of petroleum ether and 20 ml. of benzene and was eluted with 500 ml. of 1:1 petroleum ether–ether mixture. Fractions of 30 to 50 ml. were collected and the solvent was evaporated. Nine initial fractions were removed.

From the first three fractions were obtained solid and liquid. The solid was purified by sublimation, 0.013 g., m.p. 153.0–154.0° (uncor.) (VI) (0.43% of the original weight). Fractions 4, 5, 6 and 8 were combined, dissolved in ether and refractionated. The chromatograph was developed and eluted with a 4:1 petroleum ether–ether solution and six additional portions obtained. From fractions 3, 4 and 5 were recovered small quantities of impure solids, which proved to be V on purification.

Fraction 2, an all liquid portion, was combined with fraction 7 from the first chromatogram and chromatographed for a third time. The solvent used was a 1:1 petroleum ether–benzene mixture. The column was developed with a mixture of 80 ml. of petroleum ether and 20 ml. of benzene and was eluted with 400 ml. of 1:1 petroleum ether–ether mixture. Nine fractions contained the recovered material after evaporation of the solvent. Traces of solid were found in the first two fractions (0.01 g.) and no solid was found in the end fractions. The middle fractions (4,5), totaled 0.97 g., were pure 2,6-dicyanoheptene-2, b.p. 93–94° (0.6 mm.), $n^{25}{}_{\rm D}$ 1.4557, $d^{30}{}_4$ 0.9522.

Anal.[11] Calcd. for $C_9H_{12}N_2$: C, 72.97; H, 8.11; N, 18.92. Found: C, 72.57; H, 8.36; N, 18.73.

Hydrogenation of Liquid Products.—Quantitative hydrogenations were carried out in a semimicro hydrogenator with a 10% palladium-on-activated charcoal as catalyst. The purified 2,6-dicyanoheptene-2 (0.0617 g.) in 10 ml. of absolute alcohol with 0.09 g. of catalyst absorbed quantitatively one molar equivalent of hydrogen.

With the liquid as obtained directly from the oxidation procedure, a theoretical amount of hydrogen was not absorbed, thus 0.5533 g. in 10 ml. of absolute ethanol with 0.19

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[10] All melting points are corrected unless otherwise noted.

[11] Analysis by Drs. Weiler and Straus, Oxford, England, and Dr. F. Schwarzkopf, New York, N. Y.

g. of catalyst absorbed 88.7% of the theoretical amount; 0.3185 g. obtained from another preparation, absorbed 87.6% of the theoretical amount. These results indicated that the liquid samples were not completely free from the solid cyclic isomers before chromatography.

Characterization of the Hydrogenation Products.—In order to characterize the hydrogenation product, the chromatographic-purified 2,6-dicyanoheptene-2 was hydrogenated on a larger scale to 2,6-dicyanoheptane (α,α'-dimethylpimelonitrile). The liquid, 0.8 g., was hydrogenated in 30 ml. of alcohol at atmospheric pressure at room temperature with 0.5 g. of 10% palladium-on-charcoal as catalyst. After removing the catalyst and solvent, the liquid residue was distilled under vacuum, b.p. 90° (0.3 mm.), 0.41 g. (50%), $n^{25}_{\rm D}$ 1.4421, d^{26}_4 0.9308.

Anal. Calcd. for $C_9H_{14}N_2$: C, 72.00; H, 9.33; N, 18.67. Found: C, 72.20; H, 9.20; N, 18.46.

A large sample of the unpurified liquid was hydrogenated and the product was isolated. From 5.92 g. of the liquid, there was obtained a yield of 5.7 g., b.p. 111.0–115.0° (0.6 mm.), $n^{25}_{\rm D}$ 1.4432. Although the analysis checked with the formula of α,α'-dimethylpimelonitrile, it is certain that some cyclic dinitrile is present. As high as 25% of the cyclic dinitrile $C_9H_{12}N_2$ in the straight-chain saturated dinitrile does not affect materially the analysis of the latter.

Hydrolysis of the Crude Hydrogenation Product and Separation of 1,2-Dicarboxy-1,2-dimethylcyclopentane Anhydride from α,α'-Dimethylpimelic Acid.—To 40 ml. of 50% sulfuric acid was added 2.1 g. (0.142 mole) of the crude liquid hydrogenation product as obtained in the last part of the previous section. The solution was refluxed at 150° for 3.5 hours. After cooling, the solution was poured on chopped ice. From the acidic solution, 0.407 g. of crude α,α'-dimethylpimelic acid was collected (20.4% based on the liquid mixture minus the cyclic dinitrile recovered, see below), m.p. 63–70°. Recrystallization of this crude from petroleum ether (b.p. 90–100°) gave 0.1 g., m.p. 70–74.5°. A second recrystallization gave the pure *anti* form of α,α'-dimethylpimelic acid, m.p. 76.8–78.0° (cor.) (76–76.5°, prepared by reaction of ethyl methylmalonate and trimethylene bromide).[9] Crops from the filtrate possessed a wide range of melting point.

From the aqueous solution was recovered by ether extraction 0.424 g. of the anhydride of the *cis*-1,2-dicarboxy-1,2-dimethylcyclopentane, corresponding to 17.5% of the *cis*-dinitrile in the original liquid. A portion of the solid was sublimed three times in vacuum to give the pure anhydride, m.p. 116.0–116.6° (cor.). A mixed m.p. with a sample of the anhydride obtained from the hydrolysis of the *cis*-1,2-dicyano-1,2-dimethylcyclopentane, m.p. 115.5–116.1°, did not depress, m.p. 117.0–118.0°.

Anal. Calcd. for $C_9H_{12}O_3$: C, 64.29; H, 7.14. Found: C, 64.59; H, 7.27.

In another hydrolysis experiment using 60% sulfuric acid, the α,α'-dimethylpimelic acid was recovered together with the cyclic anhydride from the ether extract of the acidic reaction solution. After the cyclic anhydride was sublimed off from the mixture, the unsublimable viscous liquid was distilled through a small Claisen flask; b.p. 160–161° (3.4 mm.), $n^{25}_{\rm D}$ 1.4539.

Anal. Calcd. for $C_9H_{16}O_4$: C, 57.45; H, 8.51; neut. equiv., 94.0. Found: C, 57.51; H, 8.62; neut. equiv., 96.0.

This liquid solidified into a white solid, the α,α'-dimethylpimelic acid, mixture on standing in the Dry Ice box.

Acid Hydrolysis of the Lower-melting Solid Isomer (VI).—A sample of 0.4 g. of the solid low-melting isomer was added to a mixture of 10 ml. of 60% sulfuric acid and 0.4 g. of sodium chloride. The mixture was heated in an air-bath at 165° for 0.5 hour and then at 205° for 45 minutes. Charring was observed at the higher temperature. After cooling to room temperature, the acid mixture was poured into 80 ml. of ice-water. An insoluble material was filtered off and the yellowish solution was extracted eight times with ether. After drying over anhydrous magnesium sulfate, the ether extract gave 0.28 g. of solid, soluble in methanol. The crude solid was heated with 10 ml. of 10% sodium hydroxide solution whereby all the solid was dissolved, and the solution treated with carbon. The colorless filtrate was acidified with 20% sulfuric acid and was then extracted ten times with ether. From the ether extract was obtained 0.21 g. of crude solid (42% yield), m.p. 240–248° (uncor.). Successive sublimation at 130° at 0.2 mm. gave 0.16 g. of pure *trans*-1,2-dicarboxy-1,2-dimethylcyclopentane (32% yield), m.p. 259–262° with sublimation.

Anal. Calcd. for $C_9H_{14}O_4$: C, 58.06; H, 7.53. Found: C, 58.27; H, 7.59.

Acid Hydrolysis of the Higher-melting Solid Isomer (V).—Two grams (0.135 mole) of the cyclic dinitrile was added to 100 ml. of 60% sulfuric acid at 110° and the solution was heated at refluxing temperature (162–164°) for 2.5 hours. During the course of heating, another 100 ml. of 60% sulfuric acid was added to wash down the sublimed material in the condenser. The mixture was allowed to stand for four hours and was then poured onto chopped ice. The undissolved solid was collected by filtration and recrystallized from hexane, to give 0.50 g. of product melting at 116.8–117.2°. From the ether extract of the acid solution was recovered 1.20 g. of solid, m.p. 116–117°. The total yield of the anhydride was 1.70 g. (75%). An analytical sample was prepared by recrystallization of the product from water, m.p. 116.6–117°.

Anal. Calcd. for $C_9H_{12}O_3$: C, 64.29; H, 7.14. Found: C, 64.57; H, 7.33.

Saponification of the Anhydride of the *cis*-Diacid.—The anhydride, 0.7 g. (0.00417 mole), was refluxed in 50 ml. of 40% sodium hydroxide and no solution of the solid was effected. To the aqueous solution was added 25 ml. of alcohol and the refluxing was continued for another three hours. Any resulting solid was collected by filtration, then heated with 20 ml. of water and any insoluble portion removed by filtration. The combined filtrates were acidified with sulfuric acid to give a white precipitate with foaming. The reaction mixture was allowed to stand overnight and the solid collected and washed with water, 0.45 g., m.p. 131.0–131.2° (58.1%).

Anal. Calcd. for $C_9H_{14}O_4$: C, 58.06; H, 7.53. Found: C, 58.08; H, 7.50.

Alkaline Hydrogen Peroxide Hydrolysis of the Lower-melting Solid Isomer (VI).—The nitrile was hydrolyzed to the amide by the method of Mooradian and Cloke.[12] From 0.25 g. (0.0017 mole) of the solid nitrile in a mixture of 5 ml. of 10% hydrogen peroxide, 1.5 ml. of 10% sodium hydroxide and 6 ml. of acetone, there was obtained after the solution had stood in an ice-chest for one and a half days and after removal of the acetone, a white solid, 0.09 g. (29%), m.p. 260–265° (melts with the development of a red color and decomposition). The crude diamide was sublimed at 140–150° at 0.7–0.8 mm. to give 0.06 g. of pure diamide, m.p. in a sealed tube, 258–263°.

Anal. Calcd. for $C_9H_{16}O_2N_2$: C, 58.70; H, 8.70; N, 15.2. Found: C, 58.98; H, 8.78; N, 15.3.

Alkaline Hydrogen Peroxide Hydrolysis of the Higher-melting Solid Isomer (V).—By the same procedure as employed for the lower-melting isomer, this *cis* isomer was transformed into a monoamide. One gram of the solid was suspended in a mixture of 10 ml. of 10% hydrogen peroxide and 2 ml. of 10% sodium hydroxide. The solid was dissolved by adding 8 ml. of acetone. The reaction was instantaneous and white solid precipitated immediately. After standing overnight in an ice-chest, the solid was collected, washed with water and dried; 1.0 g. (89% yield), m.p. 321–325°. A portion of the crude, 0.4 g., was recrystallized from 30 ml. of methanol from which 0.174 g. of pure monoamide was obtained, m.p. 343.6–345.0° [336° (dec.)].[4]

Anal. Calcd. for $C_9H_{14}N_2O$: N, 16.9. Found: N, 17.1.

Permanganate Oxidation of the Unsaturated Isomer.—To a suspension of 2.96 g. (0.02 mole) of the liquid, which contained the contaminating cyclic isomers, in 100 ml. of water (suspended by means of vigorous stirring) was added a solution of 6.32 g. (0.04 mole) of potassium permanganate in 200 ml. of water. After standing overnight, the solution was filtered by suction with a filtering aid to remove the manganese dioxide. The filtrate was saturated with 200 g. of ammonium sulfate and the precipitated solid was collected; 0.87 g. This on sublimation gave 0.46 g., m.p. 145–156°, and 0.29 g., m.p. 130–150°, a total of 0.75 g. Recrystallization from ether gave 0.45 g. of *cis*-1,2-dicyano-1,2-dimethylcyclopentane, m.p. 159–160°. A mixed m.p. with an authentic sample, m.p. 160.0–160.5°, obtained from

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(12) A. Mooradian and J. B. Cloke, THIS JOURNAL, 68, 785 (1946).

the direct freezing of the bromine oxidation products, melted at 159.5–160.5°.

The filtrate was made more alkaline by adding 2 ml. of 10% sodium hydroxide and extracted ten times with ether. The ether solution, after drying, gave 0.37 g. of a mixture of yellowish thick liquid and a small amount of solid. Attempts to make an amide by the method of Mooradian and Cloke failed. Extraction of the filtrate with ether gave a negligible amount of viscous liquid which was not identified.

The alkaline aqueous solution was acidified with 20% sulfuric acid and extracted ten times with ether. From the ethereal solution was obtained 1.64 g. of a clear, mobile, yellowish liquid (81% based on the original liquid minus the recovered cyclic isomers). Distillation of the liquid gave, after a small forerun, γ-cyano-*n*-valeric acid, b.p. 119° (0.4 mm.), 0.85 g. (45%). The liquid solidified on cooling, m.p. 91–96°. The solid was allowed to dry on filter paper for two weeks, m.p. 96.5–97.5° (95–96°, prepared from γ-valerolactone and potassium cyanide).[13]

Anal. Calcd. for $C_6H_9O_2N$: C, 56.69; H, 7.09; N, 11.02. Found: C, 56.90; H, 7.34; N, 10.79.

In another experiment, 0.70 g. of the crude cyano-acid obtained from the oxidation of 1.38 g. of the liquid unsaturated dinitrile was hydrolyzed with 20 ml. of 50% sulfuric acid by refluxing at 180° for 1.5 hours. At the end of this time, the tea-colored acid solution was cooled and poured onto chopped ice. The resulting solution was extracted ten times with ether. The ether extract on being processed in the usual manner and decolorized with carbon gave 0.70 g. of yellowish liquid which solidified. The solid was purified by allowing a liquid contaminant to distil at 0.4 mm. at 80°. The liquid distillate, $n^{25}D$ 1.4422, was dried in ether solution. An attempt to prepare an anilide derivative from the residue was not successful. The residual solid, 0.25 g. (31%), m.p. 65–72°, was pressed dry on filter paper. The α-methylglutaric acid was dissolved in an ether–petroleum ether mixture and the solution was allowed to stand overnight in a Dry Ice box, to give a solid m.p. 77.0–78.0° (77.5°, prepared by oxidation of 1-methyl-3-isopropylidenecyclopentanone-2)[14] (77–78°)[15] (79°, prepared by oxidation of γ-methyl-δ-acetylvaleric acid).[16]

Anal. Calcd. for $C_6H_{10}O_4$: C, 49.32; H, 6.85; neut. equiv., 73.0. Found: C, 49.48; H, 6.60; neut. equiv., 74.2.

To further prove that the above hydrolysis product was α-methylglutaric acid, an authentic sample was prepared. The ethyl β-iodopropionate required in the synthesis was prepared according to Perkin.[17] From 20 g. (0.1 mole) of β-iodopropionic acid (Eastman Kodak, recrystallized from water, white solid, m.p. 84–85°), there was obtained 20.0 g. of the ester (87.7% yield), b.p. 53–56° (1.1–1.2 mm.), $n^{25}D$ 1.4961, d^{30}_4 1.6226 [136° (100 mm.), 94% yield].[17] Esterification at temperatures higher than room temperature was found to be unsuccessful. The condensation of the ethyl β-iodopropionate with ethyl methyl malonate was carried out according to the direction of Auwers.[15] From 17.57 g. (1.101 moles) of ethyl β-iodopropionate there was obtained 18.03 g. of the triester (64.9% yield), b.p. 120–124° (1.5 mm.), $n^{25}D$ 1.4328 [65%, 164.5° (15 mm.)].[15] An attempted condensation with free β-iodopropionic acid with twice the amount of sodium used for the ester was unsuccessful. To saponify and decarboxylate the triester to α-methylglutaric acid, 5.56 g. (0.02 mole) of the above triester was refluxed with 5 ml. of concentrated hydrochloric acid and 5 ml. of water (*ca.* 1 hour). The residue was distilled under vacuum to give, after a forerun, a product distilling at 116–118° (1.6–1.7 mm.), 2.24 g., 76.7% (81%, b.p. 220–227°, m.p. 77–78°).[15] After the product was chilled in the Dry Ice box, a white precipitate separated and was removed by filtration. The solid, after removal of traces of liquid in vacuum, had a melting point of 77.5–78.0°. A mixed m.p. with the α-methylglutaric acid (77.0–78.0°) obtained from the permanganate oxidation melted at 77.5–78.0°.

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[13] W. Wislicenus, *Ann.*, **233**, 101 (1886).

[14] W. Koenigs and A. Eppens, *Ber.*, **25**, 260 (1892).

[15] K. Auwers, *Ann.*, **292**, 209 (1896).

[16] H. Rupe, H. Schobel and E. Abegg, *Ber.*, **45**, 1528 (1912).

[17] W. H. Perkin, Jr., *J. Chem. Soc.*, **84**, 416 (1904).

BROOKLYN, NEW YORK

[CONTRIBUTION FROM THE W. H. CHANDLER CHEMISTRY LABORATORY, LEHIGH UNIVERSITY]

Synthesis of Some Substituted 3-Piperidones[1]

BY NELSON R. EASTON, LESTER R. BARTRON,[2] FRANCIS L. MEINHOFER AND VELMER B. FISH

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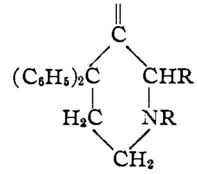
The synthesis of a series of substituted piperidones which possess the general structure I was accomplished in the following manner: Diphenylacetonitrile was converted into γ-bromo-α,α-diphenylbutyronitrile and this substance was allowed to react with the appropriate secondary amine. The amino nitriles were then converted into the desired ketones by use of the proper Grignard reagent. Bromination of the hydrobromides of the ketones yielded the monobrominated products. Neutralization of these compounds with sodium bicarbonate was followed by a rapid cyclization to the quaternary salt of the desired piperidone. Pyrolyses of these salts gave the expected piperidones in varying yields.

In light of the interest in methadon as an analgesic, we were interested in preparing a series of 3-piperidones (I) which would correspond structurally to a cyclized methadon (II). Since experimental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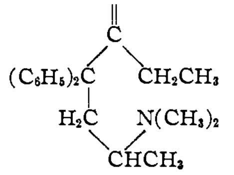
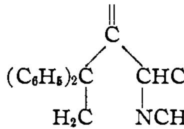

methadon


cyclized methadon

II

Ia, R = CH_3, R′ = H; Ib, R = CH_3, R′ = CH_3; Ic, R = CH_3CH_2, R′ = H; Id, R = CH_3CH_2, R′ = CH_3

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[1] The synthesis of some of these compounds was reported by F. F. Blicke and John Krapcho at the Spring Meeting of the American Chemical Society, April, 1948. Recently they have been described by these authors in THIS JOURNAL, **74**, 4001 (1952).

[2] Abstracted in part from the Thesis submitted in partial fulfillment of the requirements for the degree of Doctor of Philosophy.