

nitrate was stirred at 50° for one and one-half hours and at room temperature for eighteen hours. The mixture was filtered, the filtrate was concentrated and the residual quaternary base was decomposed by distillation in a short-path still at 1 mm. and a heating block temperature of 100–160°. A solution of the distillate (2.4 g., 92%) in ether was washed with dilute hydrochloric acid, water, dried over sodium sulfate and concentrated. Redistillation through a short-path still at 0.5 mm. and a heating block temperature of 150–160°, yielded 2.0 g. of XVI, which was purified by another similar distillation and obtained as a colorless liquid with n_D^{20} 1.5913.

Anal. Calcd. for $C_{20}H_{22}$: C, 91.55; H, 8.45. Found: C, 91.35; H, 8.50.

Both XV and XVI were recovered unchanged after heating under reflux with a 10% solution of sodium methoxide in methanol in a nitrogen atmosphere for twenty-four hours.

1,3-Diphenylcyclooctane (XIIb).—Hydrogenation of 0.505 g. of XVI in 15 ml. of glacial acetic acid in the presence of 0.15 g. of 10% palladium-on-Norite was complete in one hour and 99% of one molar equivalent of hydrogen was absorbed. The catalyst was separated and a solution of the filtrate in ether was washed with dilute sodium hydroxide and water. After removal of the solvent under reduced pressure 0.49 g. (96%) of XIIb remained, m. p. 53–55°, which after recrystallization from methanol melted at 60.8–62°.

Anal. Calcd. for $C_{20}H_{24}$: C, 90.85; H, 9.15. Found: C, 90.93; H, 9.28.

A mixture of the isomers XIIa and XIIb melted at 58–73°, and the solidified melt remelted at the same temperature. Both isomers gave negative unsaturation tests with potassium permanganate in acetone or ethanol, and both were insoluble in cold concentrated sulfuric acid. Both were unchanged when they were heated under reflux with a 0.5 molar solution of potassium *t*-butoxide in *t*-butanol for twenty-four hours, and when they were dissolved in a solution of ethyllithium in ether and allowed to stand for four days at room temperature.

A 0.28-g. sample of XVI was reduced by heating under reflux with a solution of 3 ml. of 57% hydriodic acid in 15 ml. of glacial acetic acid for four hours. The product was isolated in the same manner as the product obtained from the diene XI by reduction with hydriodic acid, and was obtained as a crystalline solid (0.28 g., m. p. 55–57°). Repeated recrystallization from methanol yielded XIIa

with m. p. 84.2–85.2°, which did not depress the m. p. of a sample obtained from XI by catalytic hydrogenation.

3,5-Diphenylcyclohex-2-enone 2,4-Dinitrophenylhydrazone was prepared¹⁸ from 0.5 g. of 3,5-diphenylcyclohex-2-enone¹⁸ in a yield of 0.75 g., m. p. 194–203° (dec.). Recrystallization from nitromethane and from a mixture of chloroform and ethanol raised the m. p. to 224.6–225.2° (dec.).

Anal. Calcd. for $C_{24}H_{20}N_4O_4$: N, 13.08. Found: N, 13.06.

3,5-Diphenylcyclohexanone 2,4-Dinitrophenylhydrazone was prepared¹⁶ from 0.5 g. of 3,5-diphenylcyclohexanone¹⁹ in a yield of 0.85 g., m. p. 159–163° (dec.). When purified by recrystallization from a mixture of chloroform and ethanol, this compound melted at 169.8–170.8° (dec.).

Anal. Calcd. for $C_{24}H_{22}N_4O_4$: N, 13.02. Found: N, 13.32.

Summary

The possibility of synthesizing substituted unsaturated eight-membered ring compounds by removal of the carbonyl bridge in compounds containing the bicyclo[3.3.1]nonan-9-one ring system (I) has been investigated, using 2,4-diphenylbicyclo[3.3.1]non-2-en-9-one (III) as a model case. Application of the Beckmann rearrangement to the oxime (V) of III resulted in cleavage of the carbonyl bridge with the formation of a lactam (VI) which was converted by acid hydrolysis followed by the Hofmann exhaustive methylation procedure into 2,4-diphenylcycloocta-1,4-diene (XI).

Evidence concerning the location of the double bonds in a number of compounds in this series has been obtained by study of their ultraviolet absorption spectra.

(18) Knoevenagel and Schmidt, *Ann.*, **281**, 59 (1894).

(19) Petrow, *Ber.*, **62**, 642 (1929). The sample used was prepared by hydrogenation of 3,5-diphenylcyclohex-2-enone in acetic acid in the presence of 10% palladium-on-Norite and was recrystallized to constant m. p. and analytical purity from methanol; m. p. 143–144°.

CAMBRIDGE, MASSACHUSETTS

RECEIVED JANUARY 13, 1950

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, MASSACHUSETTS INSTITUTE OF TECHNOLOGY]

Cyclic Polyolefins. X. Synthesis of Phenylcycloocta-1,3-diene¹

BY ARTHUR C. COPE AND EDWARD C. HERMANN

This paper reports the preparation of a phenylcycloocta-1,3-diene by application of a synthetic method involving cleavage of a carbonyl-bridged intermediate.²

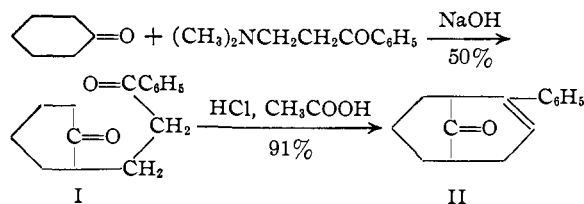
The first reaction in this seven-step synthesis was the preparation of 2-(β -benzoyl ethyl)-cyclohexanone (I) in 50% yield by the reaction of cyclohexanone with β -dimethylaminopropiophenone (a Mannich base obtained from acetophenone, formaldehyde and dimethylamine), in the presence of sodium hydroxide in aqueous ethanol. This reaction may proceed by a condensation of the Michael type between cyclohexanone and

phenyl vinyl ketone, produced by the decomposition of the Mannich base. Cyclization of I by an acid catalyzed internal aldol condensation formed 2-phenylbicyclo[3.3.1]non-2-en-9-one (II) in 91% yield. The position of the double bond in II is assigned on the basis of Bredt's rule,³ which excludes the bridgehead or α,β -position, and comparison of the ultraviolet absorption spectra of the 2,4-dinitrophenylhydrazones of II and the corresponding saturated ketone VIII (Fig. 1). The spectra of both derivatives contained maxima at 364 $m\mu$ with identical values of ϵ_{max} , indicating that II is not an α,β -unsaturated ketone.²

(1) Supported in part by the Office of Naval Research under Contract N5ori-07822, Project Designation NR-055-96.

(2) Cope, Fawcett and Munn, *THIS JOURNAL*, **72**, 3399 (1950).

(3) Bredt, *Ann.*, **437**, 1 (1924); Wittig, "Stereochemie," Akademisch Verlagsgesellschaft, Leipzig, 1930, p. 154.



The cyclic ketone II was converted into its oxime (III) in 76% yield by reaction with hydroxylamine hydrochloride in a mixture of ethanol and pyridine. The analytically pure oxime

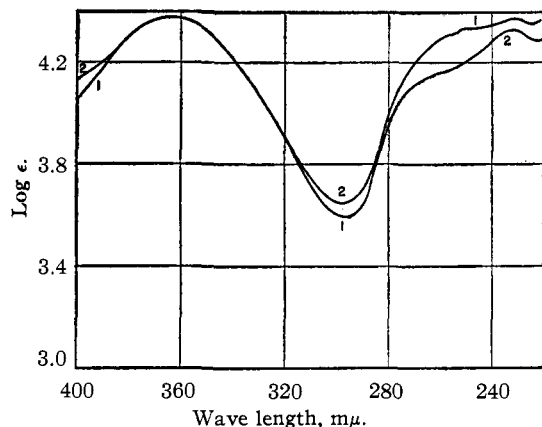
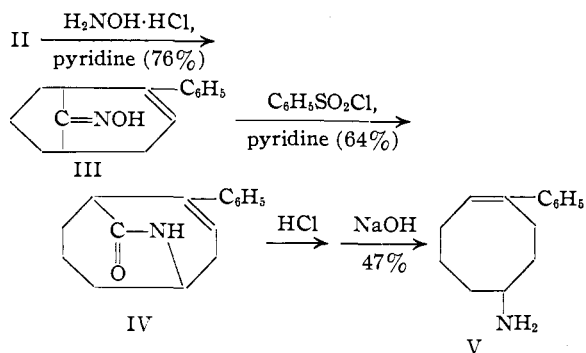
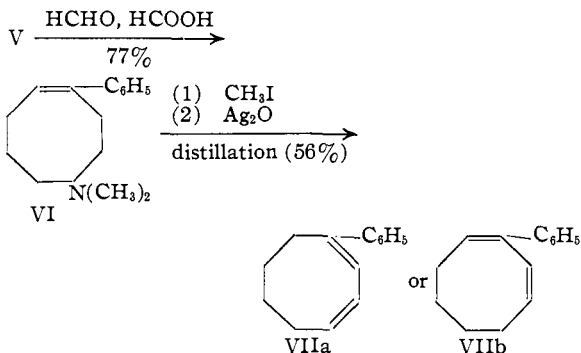


Fig. 1.—Curve 1, ultraviolet absorption spectrum of the 2,4-dinitrophenylhydrazone of 2-phenylbicyclo[3.3.1]non-2-en-9-one (II); curve 2, ultraviolet absorption spectrum of the 2,4-dinitrophenylhydrazone of 2-phenylbicyclo[3.3.1]nonan-9-one (VIII), both in 95% ethanol.

melted over a four degree range, which may indicate that it was a mixture of isomers, but no separation was attempted. The Beckmann rearrangement of the oxime formed the lactam IV in 64–79% yield, when conducted by slow addition of benzenesulfonyl chloride to a solution of III in pyridine at 35°. Lower yields were obtained using *p*-toluenesulfonyl chloride (34%) and thionyl chloride (38%), possibly because the reaction temperature was higher in these cases. Hydrolysis of the crude lactam IV by boiling with 6 *N* hydrochloric acid for periods of twenty-four hours or longer proceeded with simultaneous loss of carbon dioxide and formed 1-amino-4-phenylcyclooct-4-ene (V) in 47–54% yield. Occurrence of decarboxylation during hydrolysis provides a tentative basis for assignment of structure IV to the lactam, since a shift of the double bond in the intermediate acid from the β,γ - to the α,β -position would give a type of acid subject to acid catalyzed decarboxylation.² The structure assigned to the amine V is based on the assumption that such an isomerization occurred prior to decarboxylation, and isomeric structures (in particular 1-amino-4-phenylcyclooct-3-ene) are not excluded.

The primary amine V was methylated by treatment with formaldehyde and formic acid. The

dimethylamino compound VI which was obtained in 77% yield appeared to be homogeneous, since all of the fractions obtained in distillation had approximately the same refractive index, and the amine formed a picrate with a narrow melting point range. An isomeric structure, particularly 1-dimethylamino-4-phenylcyclooct-3-ene, also is possible for VI. VI was converted to a methiodide in substantially quantitative yield by heating with an excess of methyl iodide in methanol, and the crude methiodide was treated with silver oxide without prior purification. Thermal decomposition of the quaternary base prepared in this manner formed a phenylcycloocta-1,3-diene (VIIa or VIIb) in 56% yield. The ultraviolet



absorption spectrum of VII (Fig. 2) contains a maximum at 265 $m\mu$ ($\log \epsilon = 4.09$), compared to a maximum at 248 $m\mu$ ($\log \epsilon = 4.068$) observed for 1-phenylcyclooctene (Cope and D'Addico, to

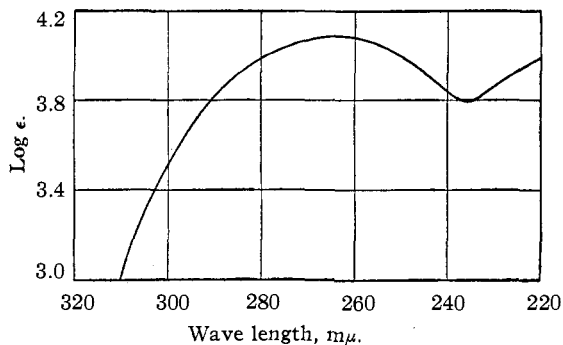
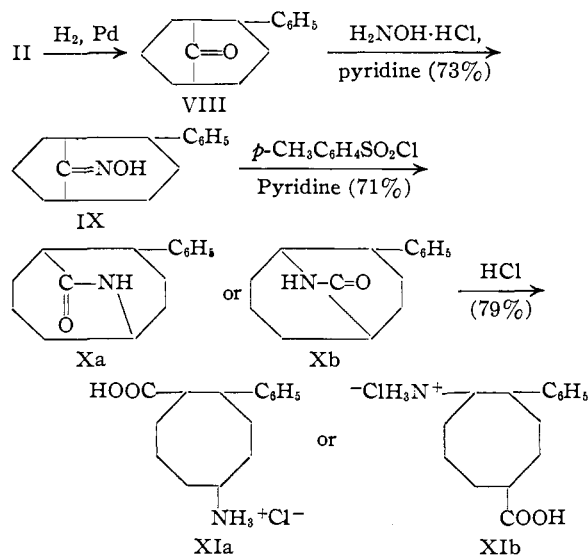


Fig. 2.—Ultraviolet absorption spectrum of phenylcycloocta-1,3-diene (VIIa or VIIb) in purified cyclohexane.

be published), and a maximum at 265–269 $m\mu$ ($\log \epsilon = 4.265$) reported for *cis*-1-phenyl-1,3-butadiene.⁴ Comparison of these absorption maxima affords evidence that the double bonds in VII are conjugated, and favors formula VIIa. Hydrogenation of the diene VII in the presence of a palladium catalyst in acetic acid required two molar equivalents of hydrogen and yielded phenylcyclooctane, m. p. 7–8°, which did not depress the m. p. of an authentic sample (prepared from cyclooctanone and phenylmagnesium bromide, by dehydration of the intermediate carbinol and subsequent hydrogenation of the 1-phenylcyclooctene obtained; Cope and D'Addico, to be published⁴).

2-Phenylbicyclo[3.3.1]nonan-9-one (VIII) was prepared by hydrogenation of the unsaturated ketone II in the presence of a palladium catalyst in glacial acetic acid, and was converted to the oxime (IX) in 73% yield. The analytically pure oxime had a melting range of 105–112°, possibly indicating that it was a mixture of isomers. The lactam obtained from the Beckmann rearrangement of IX by treatment with *p*-toluenesulfonyl chloride in pyridine in 71% yield was isolated in two dimorphous forms, m. p. 137.5–139.5° and 151.4–152.4°. The lactam may have either of the possible structures Xa or Xb. Hydrolysis of the lactam with boiling 6 *N* hydrochloric acid formed the corresponding amino acid hydrochloride, XIa or XIb, which was isolated in 79% yield.



Experimental⁵

2-(β -Benzoyl ethyl)-cyclohexanone (I).—Cyclohexanone (392.6 g., 4 moles) and 333 ml. (2 moles) of 6 *N* aqueous sodium hydroxide were added simultaneously to a solution of 197.5 g. (1.0 mole) of β -dimethylaminopropiophenone

hydrochloride⁶ in 2 l. of 95% ethanol heated to the boiling point. With continued heating the mixture regained the boiling point in a period of six minutes and was heated under reflux for an additional fifteen minutes. The deep yellow mixture was cooled in an ice-bath and neutralized to pH 7 (test paper) by careful addition of 167 ml. of concentrated hydrochloric acid. The mixture was concentrated under reduced pressure to remove ethanol (about 1.5 l.), and the residue was diluted with 2 l. of water and acidified with 167 ml. of concentrated hydrochloric acid. The mixture was extracted with three 250-ml. portions of benzene and the combined extracts were washed with 150 ml. of saturated sodium bicarbonate solution, 150 ml. of water and dried over sodium sulfate. The benzene and excess cyclohexanone were removed by distillation under reduced pressure, and the residue was distilled rapidly under reduced pressure in a nitrogen atmosphere through a Claisen still-head with a 15-cm. column. The diketone I was collected in a yield of 120 g. (52%) as a yellow oil, b. p. 160–185° (0.95–1.3 mm.), which crystallized slowly on cooling to a very light yellow solid, m. p. 47–49.2°. A large amount of a brown viscous distillation residue remained. An analytical sample of I was purified by crystallization to a constant melting point from a mixture of cyclohexane and pentane as fine white needles, m. p. 49–50.2°.

Anal. Calcd. for $\text{C}_{15}\text{H}_{18}\text{O}_2$: C, 78.23; H, 7.88. Found: C, 78.21; H, 7.82.

In smaller-scale preparations the same yield of I was obtained by dilution, acidification and extraction of the reaction mixtures without prior concentration to remove ethanol. In preliminary work I was obtained in very small yield by alkylation of the sodium enolate of cyclohexanone, prepared from cyclohexanone and sodamide in ether, with β -dimethylaminopropiophenone methiodide.

2-(β -Benzoyl ethyl)-cyclohexanone bis-2,4-dinitrophenylhydrazone was prepared from I by the general procedure described by Shriner and Fuson.⁷ The crude derivative was purified by three crystallizations from boiling chloroform, to which carbon tetrachloride was added to the point of turbidity, as deep red crystals, m. p. 224–224.6° when introduced in a melting point bath at 200°, heated rapidly to 215° and then at 1° per minute.

Anal. Calcd. for $\text{C}_{27}\text{H}_{28}\text{N}_8\text{O}_8$: C, 54.91; H, 4.44; N, 18.98. Found: C, 54.92; H, 4.60; N, 19.05.

2-Phenylbicyclo[3.3.1]non-2-en-9-one (II).—A solution of 324 g. of I in 2.5 l. of glacial acetic acid and 500 ml. of concentrated hydrochloric acid was heated under reflux for forty-one hours. Most of the acetic acid was removed by distillation under reduced pressure, and the residue was diluted with 1.5 l. of water and extracted with three 500 ml. portions of benzene. The combined extracts were washed with three 250-ml. portions of saturated sodium bicarbonate solution, once with water, dried over sodium sulfate and concentrated by distillation under reduced pressure in a nitrogen atmosphere. The dark, viscous residue was distilled rapidly under reduced pressure in a nitrogen atmosphere through a Claisen still-head with a 15 cm. column. The yellow distillate of II (271 g., 91%), b. p. 143–155° (0.7–0.8 mm.) crystallized on cooling to a very light yellow solid, m. p. 46.8–50°. A mixture of II and I (m. p. 47.4–50.4°) liquefied at room temperature (28°). An analytical sample of II was obtained by crystallization from a 2:3 mixture of cyclohexane and pentane as a white crystalline solid with a constant m. p. of 51.8–52.8°.

Anal. Calcd. for $\text{C}_{15}\text{H}_{18}\text{O}$: C, 84.86; H, 7.60; mol. wt., 212. Found: C, 84.82; H, 7.72; mol. wt. (Rast method in borneol), 216.

II decolorized potassium permanganate in 95% ethanol⁸ but not in acetone. The fine white crystals of II obtained

(6) "Organic Syntheses," **23**, 30 (1943).

(7) Shriner and Fuson, "Identification of Organic Compounds," 3rd edition, John Wiley and Sons, Inc., New York, N. Y., 1948, p. 171.

(8) Ipatieff, Thompson and Pines, *THIS JOURNAL*, **70**, 1658 (1948).

(4) Grummitt and Christoph, *THIS JOURNAL*, **71**, 4157 (1949).

(5) Melting points are corrected and boiling points are uncorrected. We are indebted to Mr. S. M. Nagy and his associates for analyses.

by recrystallization proved to be unstable in contact with dry air, decomposing to a gummy solid after a few days, presumably by reaction with oxygen. II could be stored without decomposition for several weeks by allowing the liquid to solidify in a nitrogen atmosphere and excluding air.

2-Phenylbicyclo[3.3.1]non-2-en-9-one 2,4-dinitrophenylhydrazone was prepared⁷ from recrystallized II and crystallized to a constant m. p. of 195.4–196.4° as orange needles from boiling chloroform by adding 95% ethanol to the point of turbidity.

Anal. Calcd. for C₂₁H₂₀N₄O₄: C, 64.27; H, 5.14; N, 14.28. Found: C, 63.80; H, 5.22; N, 14.12.

The ultraviolet absorption spectrum of the dinitrophenylhydrazone of II (Fig. 1) contained maxima at 232 m μ (log ϵ = 4.378) and 364 m μ (log ϵ = 4.377).

2-Phenylbicyclo[3.3.1]non-2-en-9-one Oxime (III).—A solution of 258 g. of II and 125 g. of hydroxylamine hydrochloride in a mixture of 400 ml. of pyridine and 400 ml. of absolute ethanol was heated under reflux for thirteen hours. The solvent was distilled under reduced pressure and 300 ml. of water and 200 ml. of concentrated hydrochloric acid were added to the residue. The mixture was extracted with three 400-ml. portions of benzene, and the combined extracts were washed with 250 ml. of 3 *N* hydrochloric acid, two 250 ml. portions of saturated sodium bicarbonate solution, 250 ml. of water and dried over sodium sulfate. The benzene was distilled under reduced pressure and the warm residue was diluted with 30 ml. of nitromethane, seeded with III from a previous preparation, and allowed to crystallize in a period of two days. The white crystalline product was separated by filtration, washed with nitromethane, ground in a mortar with nitromethane and again collected on a filter and washed with nitromethane (the total volume used for these operations was 260 ml.). The yield of III was 210 g. (76%), m. p. 95.2–100°. III was difficult to crystallize from nitromethane or mixtures of nitromethane and ethanol, and several crystallizations from these solvents failed to improve the melting point. A sample prepared by the procedure described with m. p. 96.6–100.4° was analyzed.

Anal. Calcd. for C₁₅H₁₇NO: C, 79.26; H, 7.53; N, 6.16. Found: C, 78.93; H, 7.66; N, 6.43.

5-Amino-2-phenylcyclooct-2-enecarboxylic Acid ϵ -Lactam (IV).—A solution of 210 g. of III in 500 ml. of pyridine was cooled with a water-bath and 168 g. of benzenesulfonyl chloride was added dropwise in a period of two hours with mechanical stirring at a rate which kept the temperature of the reaction mixture at 35°. Stirring was continued for one-half hour, at which time the temperature was 26°, after which the mixture was cooled in an ice-bath. Ice (250 g.), 250 ml. of chloroform and 1250 ml. of 6 *N* hydrochloric acid were added in that order, and the layers were separated. The aqueous layer was extracted with three 250 ml. portions of chloroform, and the combined chloroform extracts were washed with 250 ml. of 6 *N* hydrochloric acid, two 250-ml. portions of saturated sodium bicarbonate solution, 250 ml. of water and dried over sodium sulfate. The solution was concentrated under reduced pressure and 100 ml. of ether was added to the residue, which crystallized on scratching. The product was collected on a filter, washed with two 50-ml. portions of ether, triturated with 50 ml. of ether and re-washed with 50 ml. of ether. The cream-colored product (IV) weighed 135 g. (64%) and had a m. p. of 132–155°. Yields of 74–79% of IV were obtained in preparations on a 0.2 mole scale, in which the reaction temperature was maintained at 35° by slow addition of benzenesulfonyl chloride without external cooling. Analysis indicated that a sample of the crude lactam, m. p. 130–153°, contained impurities which were not isomeric (calcd. for C₁₅H₁₇NO: C, 79.26; H, 7.53; N, 6.16. Found: C, 77.86; H, 7.37; N, 6.05). A sample of IV purified by six crystallizations from 95% ethanol was obtained as beautiful white crystals, m. p. 168.8–169.8°.

Anal. Calcd. for C₁₅H₁₇NO: C, 79.26; H, 7.53; N, 6.16. Found: C, 79.24; H, 7.56; N, 6.18.

When IV was prepared by the Beckman rearrangement of III by treatment with *p*-toluenesulfonyl chloride, added in one portion to III in pyridine without cooling (procedure of ref. 2), the reaction mixture became very hot and darkened, and IV was isolated in 34% yield in a preparation on a 0.04 mole scale. Likewise rearrangement of 0.025 mole of III by treatment with thionyl chloride in a mixture of chloroform and pyridine was exothermic and gave a 38% yield of IV.

1-Amino-4-phenylcyclooct-4-ene (V).—The crude lactam IV (135 g., m. p. 132–155°) was added to 1 l. of 6 *N* hydrochloric acid, and the suspension was heated under reflux for twenty-four hours. The resulting clear amber solution was cooled in an ice-bath and made alkaline with 1.5 l. of 6 *N* sodium hydroxide. The mixture was extracted with three 500-ml. portions of ether, and the combined extracts were washed with three 250-ml. portions of water, dried over sodium sulfate, and concentrated under reduced pressure. The dark residue was distilled under reduced pressure through a 20 cm. Vigreux column, and yielded 56 g. (47%) of V as a colorless liquid, b. p. 133–135° (0.6 mm.), *n*_D²⁰ 1.5768. A very viscous residue remained. Redistillation did not change the refractive index of V.

Anal. Calcd. for C₁₄H₁₉N: C, 83.54; H, 9.50; N, 6.96. Found: C, 83.45; H, 9.66; N, 6.98.

In a similar preparation on a 0.12 mole scale, hydrolysis of IV with 270 ml. of 6 *N* hydrochloric acid by boiling under reflux for forty-eight hours yielded 54% of V.

1-Benzoylamino-4-phenylcyclooct-4-ene was prepared by stirring 1 g. of V, 2 ml. of benzoyl chloride and 25 ml. of 10% aqueous sodium hydroxide with cooling in an ice-bath. The mixture was allowed to stand overnight at room temperature and was warmed for several hours in a water-bath at about 50°. The crude product (1.36 g., m. p. 80–120°) was crystallized from 2 ml. of 95% ethanol as short, white needles (0.57 g., m. p. 138–141°). Two more crystallizations from 95% ethanol yielded an analytical sample with a constant m. p. of 140.4–141.4°. The melt was viscous and turbid and became clear at 149°.

Anal. Calcd. for C₂₁H₂₃NO: C, 82.58; H, 7.59; N, 4.59. Found: C, 82.37; H, 7.69; N, 4.61.

1-Dimethylamino-4-phenylcyclooct-4-ene (VI).—A mixture of 21.6 g. of V, 29.6 g. of 87% formic acid and 22 g. of 37% aqueous formaldehyde was heated under reflux in an atmosphere of nitrogen for eighteen hours. The mixture was cooled in an ice-bath, made alkaline by slow addition of 250 ml. of 10% aqueous sodium hydroxide, and extracted with three 100-ml. portions of ether. The combined extracts were re-extracted with two 100-ml. portions of 6 *N* hydrochloric acid, and the acid extracts were made alkaline by addition of 500 ml. of 10% sodium hydroxide solution, with cooling. The alkaline mixture was extracted with three 100-ml. portions of ether, and the combined ether extracts were washed with 100 ml. of water, dried over sodium sulfate and concentrated under reduced pressure. The residue was purified by a short-path distillation (after addition of a few crystals of hydroquinone) at 0.2 mm. and a heating bath temperature of 125–135°, which yielded 18.9 g. (77%) of nearly colorless VI, *n*_D²⁰ 1.5582, and separated 2.8 g. of a viscous red residue. An analytical sample redistilled under similar conditions was obtained as a colorless liquid, *n*_D²⁰ 1.5580. The compound turned yellow on standing and was stored under nitrogen in a refrigerator.

Anal. Calcd. for C₁₆H₂₃N: C, 83.78; H, 10.11; N, 6.11. Found: C, 83.69; H, 10.06; N, 6.40.

VI and picric acid were warmed in 95% ethanol and the bright yellow picrate was purified by three crystallizations from 95% ethanol to a constant m. p. of 148.8–149.8°.

Anal. Calcd. for C₂₂H₂₆N₄O₇: C, 57.63; H, 5.72; N, 12.22. Found: C, 57.83; H, 5.88; N, 12.20.

Phenylcycloocta-1,3-diene (VII).—A solution of 18.9 g. of VI and 30 ml. of methyl iodide in 100 ml. of dry methanol was heated under reflux in an atmosphere of nitrogen for one and one-half hours. Removal of the

solvent under reduced pressure left the slightly yellow crystalline methiodide of VI in substantially quantitative yield. The freshly precipitated, alkali-free silver oxide prepared from 14.4 g. of silver nitrate was added to a solution of the methiodide in 100 ml. of methanol, and the mixture was heated under reflux in an atmosphere of nitrogen for one hour. The silver salts were broken up with a stirring rod and the mixture was heated under reflux for an additional one-half hour, after which it was filtered and the filtrate was concentrated under reduced pressure. The quaternary base was decomposed by heating in a water-bath at 50–60° in a small flask attached to a 20-cm. Vigreux column at a pressure of 0.5 mm. The decomposition was vigorous, and occurred in a period of fifteen minutes. The temperature was raised gradually and VII was collected in a yield of 8.5 g. (56%), b. p. 93–115° (0.5–0.65 mm.), n_D^{25} 1.5873, followed by 1.9 g. of recovered VI as a higher boiling fraction. Redistillation of 10 g. of crude VII from two preparations through a 20-cm. Vigreux column after addition of a few crystals of hydroquinone yielded 7.7 g. of VII, collected as six fractions with a constant refractive index; b. p. 103–105.5° (0.5 mm.); n_D^{25} 1.5880; d_4^{25} 0.9970; M_D calcd. 60.12, found 62.20 (exaltation 2.08).

Anal. Calcd. for $C_{14}H_{16}$: C, 91.25; H, 8.75. Found: C, 91.22; H, 8.90.

The ultraviolet absorption spectrum of VII in purified cyclohexane (Fig. 2) contained a maximum at 265 $m\mu$ ($\log \epsilon = 4.09$).

Phenylcyclooctane was obtained by hydrogenation of 3.00 g. of VII in 60 ml. of glacial acetic acid in the presence of 0.5 g. of 10% palladium-on-Norite.⁹ Hydrogen absorption amounted to 102% of two molar equivalents in four and one-half hours. The catalyst was removed by filtration and the filtrate was concentrated by distillation under reduced pressure. A solution of the residue in 100 ml. of ether was washed with saturated sodium bicarbonate solution, water, dried over sodium sulfate and concentrated under reduced pressure. The residue of phenylcyclooctane (2.99 g.) was distilled through a 20-cm. Vigreux column and collected as four fractions with the same refractive index totaling 2.41 g., b. p. 100–102° (0.55–0.6 mm.); n_D^{25} 1.5300 (an authentic sample had n_D^{25} 1.5299); d_4^{25} 0.9535; m. p. 7–8°; mixed m. p. with an authentic sample with a m. p. of 7.3–8.5°, 7–8.3°.

Anal. Calcd. for $C_{14}H_{20}$: C, 89.29; H, 10.71. Found: C, 89.29; H, 10.49.

2-Phenylbicyclo[3.3.1]nonan-9-one (VIII).—A solution of 22.4 g. of II (m. p. 46.8–50°) in 100 ml. of glacial acetic acid was reduced in the presence of 2 g. of 10% palladium-on-Norite at an initial hydrogen pressure of 20 p. s. i. Hydrogen absorption amounted to 99% of one molar equivalent in three hours. The catalyst was separated by filtration and washed with acetic acid, and the filtrate was concentrated under reduced pressure. A solution of the residue in 100 ml. of ether was washed with sodium bicarbonate solution, water, dried over sodium sulfate and concentrated under reduced pressure, leaving a white crystalline residue of 21.4 g. (95%) of VIII, m. p. 67–71°. Recrystallization from 25 ml. of a 2:3 cyclohexane-pentane mixture yielded 12.23 g. of VIII in two crops, m. p. 76.3–77°. An analytical sample recrystallized three times from a 2:3 mixture of cyclohexane and pentane had the same m. p.

Anal. Calcd. for $C_{15}H_{18}O$: C, 84.07; H, 8.46. Found: C, 84.22; H, 8.40.

2-Phenylbicyclo[3.3.1]nonan-9-one 2,4-dinitrophenylhydrazone was prepared⁷ from 0.5 g. of VIII, and after one crystallization from a mixture of chloroform and carbon tetrachloride and two crystallizations from a mixture of chloroform and ethanol was orange-yellow in color and had a constant m. p. of 221.4–222.8°.

Anal. Calcd. for $C_{21}H_{22}N_4O_4$: C, 63.95; H, 5.62; N, 14.21. Found: C, 63.85; H, 5.58; N, 14.16.

The ultraviolet absorption spectrum of the 2,4-dinitrophenylhydrazone of VIII (Fig. 1) contained maxima at 234 $m\mu$ ($\log \epsilon = 4.332$) and 364 $m\mu$ ($\log \epsilon = 4.377$).

2-Phenylbicyclo[3.3.1]nonan-9-one Oxime (IX).—A solution of 5.43 g. of VIII (m. p. 76.3–77°) and 2.59 g. of hydroxylamine hydrochloride in a mixture of 25 ml. of pyridine and 25 ml. of absolute ethanol was heated under reflux for fifteen and one-half hours. The solution was concentrated under reduced pressure, and the residue was triturated with 25 ml. of ice water. The resulting white gum was extracted with two 50-ml. portions of ether, and the combined extracts were washed with 50 ml. of 0.5 *N* hydrochloric acid, 50 ml. of saturated sodium bicarbonate solution, 50 ml. of water and dried over sodium sulfate. Concentration under reduced pressure left a viscous, colorless residue, which was crystallized with difficulty from nitromethane containing a very small amount of ethyl acetate. The crystalline oxime IX was collected on a filter and washed with two portions of nitromethane; yield 4.24 g. (73%), m. p. 105–112°.

Anal. Calcd. for $C_{15}H_{19}NO$: C, 78.56; H, 8.34; N, 6.11. Found: C, 78.61; H, 8.42; N, 6.05.

5-Amino-x-phenylcyclooctanecarboxylic Acid ϵ -Lactam (X).—*p*-Toluenesulfonyl chloride (3.82 g.) was added in one portion to a solution of 4 g. of IX in 25 ml. of pyridine. The mixture became hot and darkened within a few minutes, and after standing overnight was of a dark yellow color. The mixture was poured onto 50 g. of ice and 35 ml. of concentrated hydrochloric acid, and the yellow viscous product was extracted with two 50-ml. portions of chloroform. The extracts were washed with 50 ml. of saturated sodium bicarbonate solution, 50 ml. of water, dried over sodium sulfate and concentrated under reduced pressure. The residue crystallized on dilution with 10 ml. of ether, and was collected on a filter and washed with ether; yield 2.84 g. (71%), m. p. 134.8–139°. Recrystallization from 3 ml. of hot 95% ethanol yielded 1.84 g. of nearly white crystals, m. p. 137.8–139.8°. A second crop of 0.095 g., m. p. 150.5–151.4°, was obtained by slow evaporation of the mother liquor. Recrystallization of the product with m. p. 137.8–139.8° from 95% ethanol raised the m. p. to 151.8–152.4°, but another similar crystallization lowered the m. p. to 137.5–139.5°. This product (X) proved to be a pure lower melting dimorphic form, for the resolidified melt had m. p. 151.2–152.4°, and a mixed m. p. with the high melting form was 151.4–152.4°.

Anal. (form with m. p. 137.5–139.5°). Calcd. for $C_{15}H_{19}NO$: C, 78.56; H, 8.34; N, 6.11. Found: C, 78.55; H, 8.28; N, 6.21.

5-Amino-x-phenylcyclooctanecarboxylic Acid Hydrochloride (XI).—A mixture of 1 g. of X and 30 ml. of 6 *N* hydrochloric acid was heated under reflux for four days. The lactam dissolved rapidly forming a colorless solution. Concentration of the solution followed by cooling yielded 0.97 g. (79%) of XI in two crops, both with m. p. 222–223.6° (dec.). Two crystallizations from 6 *N* hydrochloric acid yielded 0.66 g. of XI with virtually the same m. p., 222.4–223.4° (dec.). The compound appeared to be somewhat hygroscopic, and was dried for analysis at 80° and 0.25 mm. over phosphorus pentoxide. An aqueous solution of 0.1 g. of XI in 100 ml. of water had pH 3.28, and was titrated with sodium hydroxide using a Beckman pH meter to a sharp inflection point at pH 7.0. This behavior on titration is exactly similar to 5-amino-2,5-diphenylcyclooctanecarboxylic acid hydrochloride.³

Anal. Calcd. for $C_{15}H_{22}NO_2Cl$: C, 63.48; H, 7.82; N, 4.94; Cl, 12.49; mol. wt., 284. Found: C, 63.55; H, 7.99; N, 5.11; Cl, 12.52; neutral equivalent from the pH titration curve, 285.

Ultraviolet Absorption Spectra.—The absorption spectra shown in Figs. 1 and 2 were determined with a Beckman Model DU quartz spectrophotometer.

Summary

A phenylcycloocta-1,3-diene (VII) has been

(9) "Organic Syntheses," **26**, 32 (1946).

prepared by a seven-step synthesis from cyclohexanone and β -dimethylaminopropiophenone through the carbonyl-bridged intermediate, 2-phenylbicyclo[3.3.1]non-2-en-9-one (II). The

phenylcyclooctadiene has been proved to contain an unbridged eight-membered ring by quantitative hydrogenation to phenylcyclooctane.

CAMBRIDGE, MASS.

RECEIVED JANUARY 13, 1950

[CONTRIBUTION FROM THE WELLCOME RESEARCH LABORATORIES]

Catalytic Debenzylation. II. The Evaluation of the Relative Effect of Ring Substituents on the Stability of the N-Benzyl Linkage¹

BY RICHARD BALTZLY AND PETER B. RUSSELL

In a previous study of catalytic debenzylation² it was shown that a variety of substituents in a benzyl group of a dibenzylamine hydrochloride tended to stabilize the carrier benzyl group against hydrogenolytic cleavage. For the most part these earlier competitive debenzylations involved comparison only of the substituted with an unsubstituted benzyl group and consequently the effect of the various groups relative to each other was largely undetermined. Insofar as comparisons could be made they were to the following effect (in order of decreasing stability): $(\text{MeO})_2 \approx \text{O}-\text{CH}_2-\text{O} > \text{MeO} \approx \text{OH} > \text{H}$; $p\text{-MeO} \approx m\text{-MeO} \approx o\text{-MeO}$; $\text{NH}_3^+ > \text{NH}_2 > \text{H}$; $\text{Me} > \text{H}$; $\text{Cl} > \text{H}$. The essential equivalence of the methoxyl group in the three different positions is taken to mean that the position of a substituent is not of much importance.

By means of the competitive debenzylations presented in Table I these previously disjointed relationships have been completed. The substituents that lend themselves to such a study fall into three classes: I, $p\text{-MeO}$, CH_3CONH , COOMe , and Cl ; II, NH_3^+ and Me ; III, NH_2 . On the basis of earlier work,² class I may be extended by the addition of OH . The members of a given class stabilize the benzyl group to about the same extent. Thus, competitive debenzylations involving comparisons between the members of class I afforded a mixture of products varying from an equimolecular ratio to one of perhaps 4:1. A precise determination of the proportions in such a mixture would, in most cases, be a matter of great experimental difficulty and of doubtful value.

The order of stabilization of the three classes to each other and to the unsubstituted benzyl group (H) is: I > II > III > H. When members of class I are compared to the member (NH_2) in class III or to the unsubstituted benzyl group (H), the reaction is essentially unilateral; only the p -aminobenzyl group, or unsubstituted benzyl group, is removed by hydrogenolysis. With members of adjacent groups, some cleavage with removal of the more stabilized group occurs also. Thus, hydrogenolysis of the hydrochloride of 4-

carbomethoxybenzyl-4-methylbenzylmethylamine (Reaction 7) takes place chiefly with removal of the 4-methylbenzyl group (as p -xylene) and formation of the hydrochloride of 4-carbomethoxybenzyl-methylamine (isolated in 70% yield), but some removal of the 4-carbomethoxybenzyl group occurs also, for p -toluic acid was isolated in 10% yield after hydrolysis of the products. In most other reductions that appeared to be unilateral, products present in such small amount would not be isolable and their complete absence cannot be assumed.

The results presented in Table I require some further explanation and discussion. The compounds listed as "Products Isolated" are not necessarily those produced in cleavage, but are sometimes modifications used for convenience in isolation. The instance of p -toluic acid has already been mentioned. Similarly, p -toluidine (Reductions 4, 5 and 10) was at times isolated as the hydrochloride, at others as p -acetotoluidide. In Reduction 3, p -acetotoluidide was an initial cleavage product. The vertical dotted lines crossing the formulas in Table I indicate the cleavages observed. In Reductions 4, 5, 6 and 8 cleavage was essentially unilateral. In Reductions 1, 1a, 2, 3 and 9, evidence was obtained that both possible cleavages occur to comparable extents. With reductions 7 and 10, both possible cleavages occurred and are indicated, with the letter P denoting the principal line of fission.

As arranged, Reductions 1-5 involve comparison of the methoxyl group with $-\text{Cl}$, $-\text{COOMe}$, $-\text{NHCOCH}_3$, $-\text{NH}_2$ and $-\text{NH}_3^+$, respectively. Reductions 6-9 show the results of comparison of the methyl group with $-\text{Cl}$, $-\text{COOMe}$, $-\text{NH}_2$ and $-\text{NH}_3^+$. Obviously, other combinations could have been added but the present group sufficed, in our opinion, for the purpose.

Reduction 1 was inconclusive. No hydrogen was absorbed at 25° and at 65° too much was taken. The p -methoxybenzylmethylamine hydrochloride isolated constituted a poor yield and we suspected that hydrogenolysis of chlorine had preceded debenzylation to a considerable extent. Since benzyl tertiary amines are more readily cleaved than their secondary analogs, it seemed likely that quaternization would afford a still more labile substance. This proved to be the

(1) Presented before the Organic Division of the American Chemical Society, Atlantic City meeting, September 1949.

(2) Baltzly and Buck, *THIS JOURNAL*, **65**, 1984 (1943).