5,8-Di-(ω-carboethoxymethoxy)-2-methylfuro-4′,5′,6,7-chromone (Ig).—Obtained from Ia and ethyl bromoacetate as described in Ib. End of reaction is known when a small portion of the filtered acetone solution gives no color with aqueous ferric chloride (about 48 hours reflux). Ig separated from dilute alcohol as colorless crystals m. p. 125° and gave with sulfuric acid an orange yellow color. It was very difficultly soluble in water and petroleum ether (60/90°) and soluble in alcohol. *Anal.* Calcd. for $C_{20}H_{20}O_9$: C, 59.4; H, 4.9. Found: C, 59.0; H, 4.8.

5,8-Di-(ω-carboxymethoxy)-2-methylfuro-4′,5′,6,7-chromone (If).—0.8 gram of Ig was dissolved in 20 cc. of glacial acetic acid and to the solution 20 cc. of water and 1 cc. of sulfuric acid (sp. gr. 1.84) were added and the mixture refluxed for twenty minutes, cooled and the crystalline precipitate filtered off, washed with water and then with alcohol; finally it was crystallized from alcohol as colorless crystals of If m. p. 276° with decomposition giving a brown melt. With sulfuric acid it gave an orange yellow color. It was very difficultly soluble in water and petroleum ether (60/90°) and benzene, soluble in hot alcohol. It dissolved in an aqueous solution of sodium bicarbonate and was precipitated by acidification with hydrochloric acid. *Anal.* Calcd. for $C_{16}H_{12}O_9$: C, 55.2; H, 3.4. Found: C, 55.5; H, 3.6.

Color Reactions with Potassium Hydroxide.—These were carried out as in the case of khellin[1] with the following results:

Visnagin (Vb)	Red violet
5,8-Diethoxyfuro-2-methylchromone (Ic)	Red violet
5,8-Di-(ω-carboxymethoxy)-furo-2-methyl-chromone (If)	Red violet
Norvisnagin (Va)	No color reaction
6-Hydroxy-4-methoxy-5-acetoacetyl-coumarone (IVb)	No color reaction
6-Hydroxy-4-methoxy-5-propioacetyl-coumarone (IVc)	No color reaction
2-Ethylnorvisnagin (Vc)	Weak brownish-red

Summary

1. Demethylation of khellin (Ib) by the action of magnesium iodide led to the production of Ia from which the derivatives Ic–Ig were obtained.

2. Norvisnagin (Va) and 2-ethylnorvisnagin (Vc) were synthesized (compare scheme "A").

3. By a similar route, using *o*-hydroxyacetophenone and ethyl formate, chromone was synthesized in good yield.

4. Khellin and visnagin analogs were submitted to the potassium hydroxide test and the results obtained emphasized the previous findings,[1] pointing to the importance of the methyl group in position 2 in chromones and in γ-pyrones for this test.

5. The chalkones (VIa–d) obtained from khellinone and visnaginone were synthesized.

6. The physiological activities of analogs of khellin and visnagin are stated in percentage beside the formulas, taking the activity of khellin as 100.

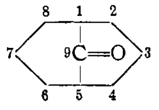
ABBASSIA-CAIRO, EGYPT RECEIVED NOVEMBER 21, 1949

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

Cyclic Polyolefins. IX. Synthesis from Carbonyl-bridged Intermediates. 2,4-Diphenylcycloöcta-1,4-diene

BY ARTHUR C. COPE, FRANK S. FAWCETT[1] AND GEORGE MUNN[2]

The synthesis of unsaturated eight-membered ring compounds by cleavage of the bridge of bicyclic structures is advantageous because only sterically favored cyclizations are required in some instances for preparation of the bicyclic intermediates. Moreover, cleavage of the bridge may provide groups which can be degraded with introduction of unsaturation into the ring. An example is the Willstätter synthesis[3] of cyclooctatetraene, in which cleavage of a methylamino bridge by successive Hofmann exhaustive methylations permits the introduction of two double bonds. Removal of the carbonyl bridge in compounds containing the bicyclo[3.3.1]nonan-9-one ring system (I) appeared to offer a promising method for the synthesis of substituted cyclooctapolyenes. This paper reports the synthesis of 2,4-diphenylcycloöcta-1,4-diene (XI) by a route involving cleavage of the carbonyl bridge of the easily synthesized bicyclic ketone, 2,4-diphenylbicyclo[3.3.1]non-2-en-9-one (III).



I

The bicyclic ketone III was prepared in 88% yield by cyclization of 2-(α-phenyl-β-benzoylethyl)-cyclohexanone (II),[4] which was obtained in 80% yield by the Michael addition of cyclohexanone to benzalacetophenone. Cyclization in the presence of acetic acid and hydrochloric acid gave an improved yield (88%) compared to concentrated sulfuric acid in absolute ethanol (55%).[4] The double bond in III was considered by Allen to be at the bridgehead (α,β) position, although this location would violate Bredt's rule,[5] on the basis of indirect evidence.[4,6] Direct evidence concerning the location of the double bond was obtained by comparing the ultraviolet absorption spectra of the 2,4-dinitrophenylhydrazones of III and the corresponding saturated ketone, IV, prepared from III by hydrogena-

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(1) du Pont Fellow, 1947–1948.

(2) du Pont Postdoctorate Fellow, 1948–1949.

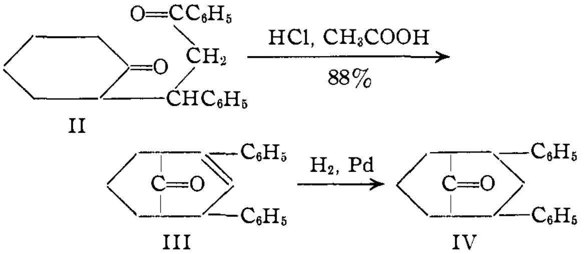
(3) Willstätter and Waser, *Ber.*, **44**, 3423 (1911); Willstätter and Heidelberger, *ibid.*, **46**, 517 (1913).

(4) Allen and Sallans, *Can. J. Research*, **9**, 574 (1933).

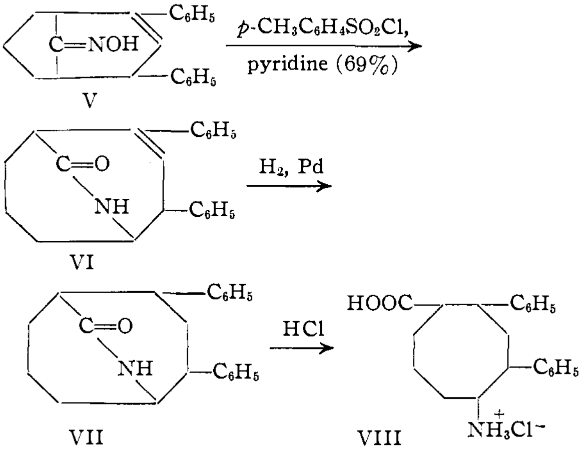
(5) Bredt, *Ann.*, **437**, 1 (1924).

(6) Allen, *Chem. Rev.*, **37**, 212, 215 (1945).

tion. It has been shown[7,8,9] that the position of the ultraviolet absorption maxima of 2,4-dinitrophenylhydrazones of α,β-unsaturated carbonyl compounds occurs at longer wave lengths than the maxima of corresponding derivatives of saturated carbonyl compounds. The absorption maxima for the 2,4-dinitrophenylhydrazone derivatives of several ketones in 95% ethanol were found to be as follows: III, 363 mμ; IV, 365 mμ; 3,5-diphenylcyclohexanone, 363 mμ (literature values[8] for comparison are cyclopentanone, 363 mμ; diisopropyl ketone, 363 mμ); 3,5-diphenylcyclohex-2-enone, 395 mμ. Since the absorption maximum of the 2,4-dinitrophenylhydrazone of III occurs at the same wave length as the dinitrophenylhydrazones of saturated ketones, the double bond can be assigned to the 2- rather than the bridgehead (α,β) position. This structure is supported by the ultraviolet absorption spectrum of the ketone III itself (Fig. 1 and Table I), which is similar to the spectrum of 1-phenylcyclohexene and 1-phenylcyclooöctene,[10] and unlike the spectrum of α,β-unsaturated ketones, indicating that the double bond is conjugated with a phenyl group but not with the carbonyl group.[11]



The oxime V was prepared from III in 60–70% yield and subjected to the Beckmann rearrangement by treatment with p-toluenesulfonyl chloride in pyridine solution. The rearrangement product, 5-amino-2,4-diphenylcyclooöct-2-enecarboxylic acid ϵ-lactam (VI), was isolated in 60–70% yield as a crystalline solid with a melting range (205–210.5°) which indicated that the product probably was a mixture of isomers. Acid hydrolysis of VI to IX (described below) provided tentative evidence in favor of formula VI rather than the isomer which would be formed if the Beckman rearrangement took the other possible course, 5-amino-2,4-diphenylcyclooöct-3-enecarboxylic acid ϵ-lactam. VI was hydrogenated quantitatively in the presence of a palladium catalyst to 5-amino-2,4-diphenylcyclooöctanecarboxylic acid ϵ-lactam (VII), which was hydrolyzed by long heating (six days) with constant boiling hydrochloric acid to the corresponding aminoacid hydrochloride (VIII). Treatment of VI with alcoholic potassium hydroxide or sodium methoxide produced an isomeric neutral product with a sharp melting point (194–195.2°), which had an ultraviolet absorption spectrum almost identical with the spectrum of VI (Fig. 2), and accordingly is believed to be a stereoisomer of VI or an isomer formed by migration of the double bond to the 3-position. Since all of these compounds derived from VI possessed sharp melting points, it is possible that the broad melting range of VI is caused by the presence of stereoisomeric forms. On hydrolysis with potassium hydroxide in diethylene glycol at 200° or fusion with a mixture of sodium hydroxide and potassium hydroxide, VI formed compounds of unknown structure which are being investigated further.



The lactam VI was very resistant to acid hydrolysis, but on refluxing with constant boiling hydrochloric acid for nine days was hydrolyzed with simultaneous loss of carbon dioxide and formed 1-amino-2,4-diphenylcyclooöct-4-ene hydrochloride (IX). IX was characterized by conversion to the free amine and its benzoyl derivative, and by quantitative hydrogenation in the presence of a palladium catalyst, which required one molar equivalent of hydrogen (proving the presence of one double bond) and formed 1-amino-2,4-diphenylcyclooöctane hydrochloride. Occurrence of decarboxylation during acid hydrolysis affords a basis for choice of structure VI rather than an isomeric structure for the lactam, for shift of the double bond from the β,γ- to the α,β-position in the intermediate acid would give a cinnamic acid type of structure which would be expected to decarboxylate fairly easily.[12]

Methylation of 1-amino-2,4-diphenylcyclooöct-4-ene with dimethyl sulfate or better with formaldehyde and formic acid produced 1-dimethylamino-2,4-diphenylcyclooöct-4-ene (X), which by the Hofmann exhaustive methylation procedure through the methiodide and quaternary base yielded 2,4-diphenylcyclooöcta-1,4-diene (XI).

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(7) Braude and Jones, *J. Chem. Soc.*, 498 (1945).

(8) Roberts and Green, THIS JOURNAL, **68**, 214 (1946).

(9) Djerassi and Ryan, *ibid.*, **71**, 1000 (1949).

(10) Cope and D'Addieco, to be published.

(11) Prelog, Barman and Zimmermann, *Helv. Chim. Acta*, **32**, 1284 (1949), recently have used ultraviolet absorption spectra to assign the double bond in other derivatives of bicyclo[3.3.1]nonen-9-one to the 2-position.

(12) Johnson and Heinz, THIS JOURNAL, **71**, 2913 (1949).

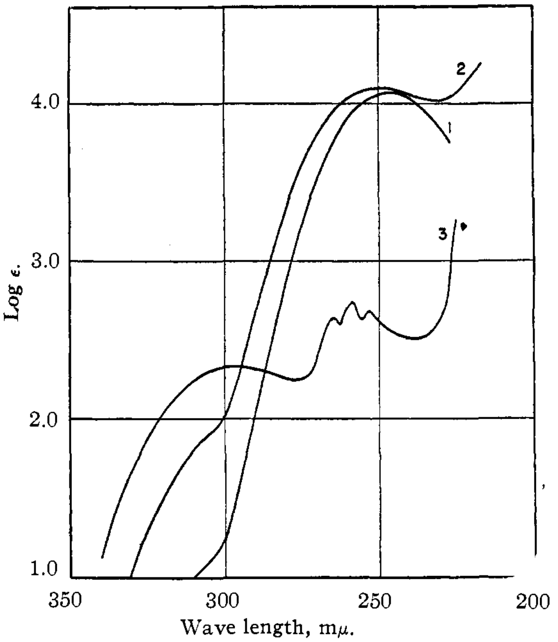


Fig. 1.—Ultraviolet absorption spectra: curve 1, 1-phenylcyclohexene; curve 2, 2,4-diphenylbicyclo[3.3.1]-non-2-en-9-one (III); curve 3, 2,4-diphenylbicyclo[3.3.1]-nonan-9-one (IV), all in cyclohexane solution.

Evidence for the structure of XI was obtained by quantitative hydrogenation, which required two molar equivalents of hydrogen, corresponding to the presence of two double bonds, and produced 1,3-diphenylcycloöctane (XIIa), m. p. 83.6–85.1°. Reduction of XI with hydriodic acid produced a mixture of compounds from which the same hydrocarbon (XIIa) was isolated by fractional crystallization. XI failed to react with maleic anhydride, and on ozonization followed by oxidation yielded glutaric acid and benzoic acid. Confirmatory evidence for this structure was obtained from the ultraviolet absorption spectrum (Fig. 3 and Table I), which contained a maximum at a wave length near the maximum observed for 1-phenylcyclohexene (and 1-phenylcycloöctene[10]), indicating the presence of a double bond conjugated with a phenyl group. The molecular extinction coefficient at the maximum was approximately twice that observed for 1-phenylcyclohexene, indicating the presence of two styrene-type structures in the molecule. XI is the only 1,3-diphenylcycloöctadiene containing two styrene-type groups in which the double bonds are not conjugated with each other.

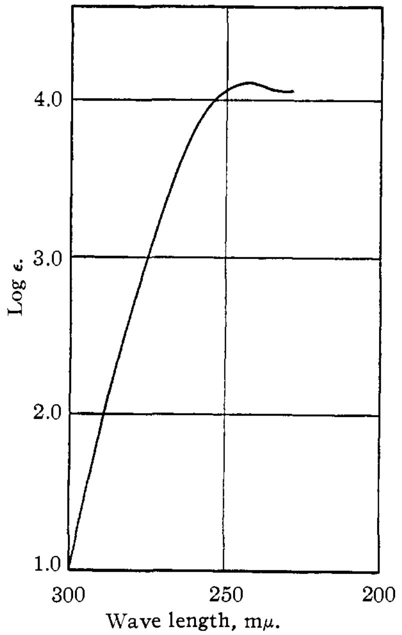
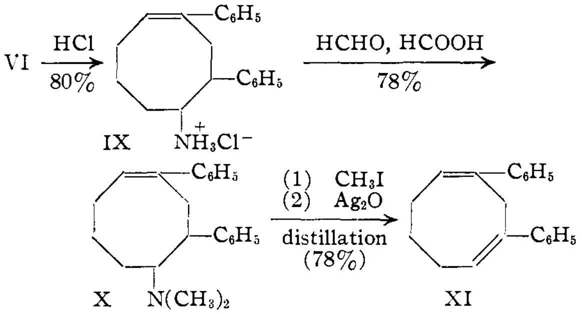


Fig. 2.—Ultraviolet absorption spectrum of 5-amino-2,4-diphenylcycloöct-2-enecarboxylic acid ε-lactam (VI) in 95% ethanol.



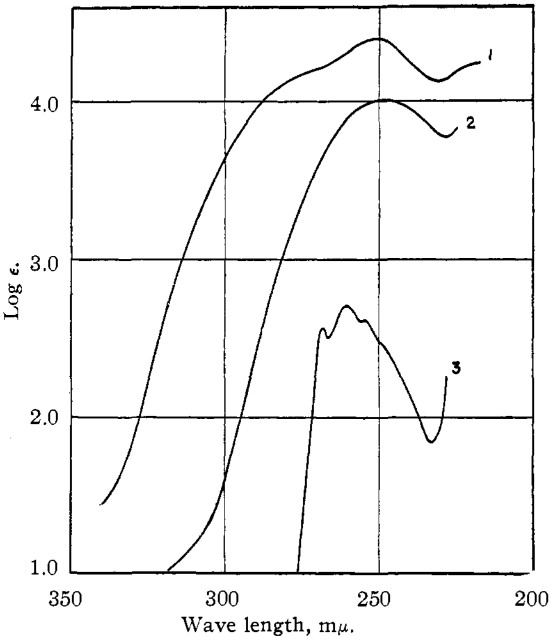


Fig. 3.—Ultraviolet absorption spectra: curve 1, 2,4-diphenylcycloöcta-1,4-diene (XI); curve 2, 2,4-diphenylcycloöctene (XVI); curve 3, 3,5-diphenylcycloöctene (XV), all in cyclohexane solution.

1-Dimethylamino-2,4-diphenylcycloöct-4-ene (X) was hydrogenated to form 1-dimethylamino-

2,4-diphenylcycloöctane (XIII). Pyrolysis of the methiodide (XIV) of this compound produced a solid olefin (XV), which absorbed one mole of hydrogen on catalytic reduction and yielded XIIa, the same hydrocarbon that was obtained by hydrogenation of the diene XI. The ultraviolet absorption spectrum of XV (Fig. 3 and Table I) was unlike the spectrum of compounds such as 1-phenylcyclohexene which contain styrene-type structures, and accordingly XV is believed to be 3,5-diphenylcycloöctene. When XIV was converted to the corresponding quaternary base and the base was distilled a liquid hydrocarbon (XVI) was obtained with an ultraviolet absorption spectrum (Fig. 3 and Table I) characteristic of compounds containing a styrene-type structure, indicating that it was 2,4-diphenylcycloöctene. In the presence of a palladium catalyst, XVI absorbed one molar equivalent of hydrogen and formed an isomer of 1,3-diphenylcycloöctane (XIIb), m. p. 60.6–61°, different from the isomer (XIIa) obtained by the catalytic reduction of XI and XV. However, reduction of XVI with hydriodic acid produced a mixture from which the higher melting form of 1,3-diphenylcyclooctane (XIIa) was isolated by fractional crystallization, showing that the ring systems in XI, XV and XVI are identical. It is concluded from this evidence that the two forms of XII are *cis* and *trans* isomers. These isomers were not interconverted by treatment with either potassium *t*-butoxide or ethyllithium. Neither of the two diphenylcycloöctenes (XV and XVI) isomerized on treatment with sodium methoxide in methanol.

Since the structures of the isomeric 1,3-diphenylcycloöctanes (XIIa and XIIb) have not as yet been established by comparison with authentic samples known to contain an eight-membered ring, nor have the olefins XI, XV and XVI been degraded into compounds in which all of the eight ring carbon atoms have been accounted for, evidence for the structure of this series of compounds depends in part upon analogy with a related series of compounds through which it was possible to synthesize phenylcyclo-octa-1,3-diene, which on hydrogenation yielded phenylcycloöctane.[13]

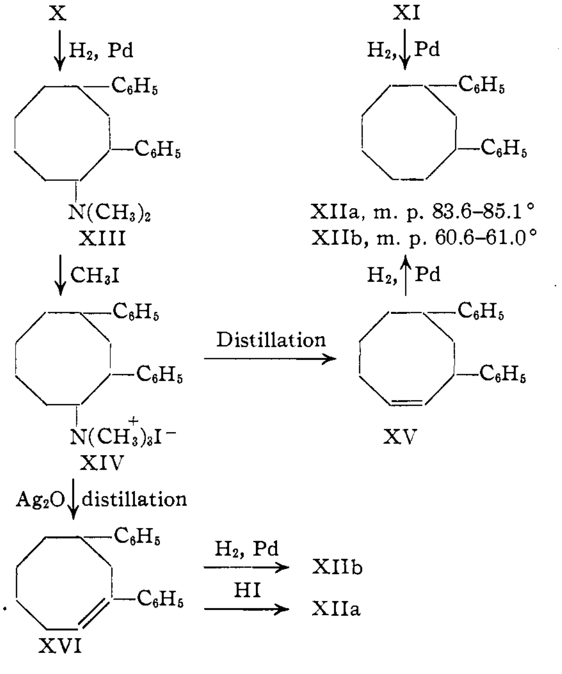


TABLE I

ULTRAVIOLET ABSORPTION MAXIMA[a]

Compound	$\lambda_{max.}$, mμ	$\epsilon_{max.}$
1-Phenylcyclohexene[b]	247	12,000
1-Phenylcycloöctene[10]	248	11,700
Phenylcycloöcta-1,3-diene[13]	265	12,300
2,4-Diphenylcycloöctene (XVI)	248.5	10,000
3,5-Diphenylcycloöctene (XV)	(1) 255	(1) 413
	(2) 261	(2) 500
	(3) 268	(3) 374
2,4-Diphenylcycloöcta-1,4-diene (XI)	252	24,800
2,4-Diphenylbicyclo[3.3.1]non-2-en-9-one (III)	252	12,300
2,4-Diphenylbicyclo[3.3.1]nonan-9-one (IV)	(1) 253	(1) 477
	(2) 259	(2) 545
	(3) 265	(3) 433
5-Amino-2,4-diphenylcycloöct-2-enecarboxylic acid ε-lactam (VI)	243.5	12,900[a]

[a] Purified cyclohexane was the solvent except for compound VI, in which case 95% ethanol was employed because of the insolubility of the compound in cyclohexane. A Beckmann Model DU quartz ultraviolet spectrophotometer was used for the spectral measurements. [b] This compound was prepared by the method of Nametkin and Iwanoff, *Ber.*, **56**, 1805 (1923); b. p. 128° (16 mm.), n^{25}_{D} 1.5645.

Experimental[14]

2,4-Diphenylbicyclo[3.3.1]non-2-en-9-one (III).—2-(α-Phenyl-β-benzoylethyl)-cyclohexanone (II) was prepared from cyclohexanone and benzalacetophenone by the method of Allen and Sallens[4] in yields of 72–80%. The following cyclization procedure gave an improved yield of III. II (3.0 g., m. p. 145.5–149°), 100 ml. of glacial acetic acid and 20 ml. of concentrated hydrochloric acid were heated under reflux in a flask connected to a condenser by a ground glass joint. The suspension formed a colorless solution on heating, and refluxing was continued for forty-two hours. At that time 50 ml. of water was added to the hot, slightly yellow solution to produce incipient turbidity. Separation of the white crystals which deposited on cooling yielded 2.5 g. (88%) of III, m. p. 139–143.5°. When purified by recrystallization from 95% ethanol, III melted at 143.2–143.9°.

Anal. Calcd. for $C_{21}H_{20}O$: C, 87.46; H, 6.99. Found: C, 87.19; H, 7.08.

III reduced potassium permanganate in acetone at room temperature very slowly, but it reduced potassium permanganate in 95% ethanol readily.[15] In preparations of III on a larger (0.5 mole) scale from cyclohexanone and benzalacetophenone the intermediate II usually was not

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(13) Cope and Hermann, THIS JOURNAL, **72**, 3405 (1950).

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

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

recrystallized but was cyclized by the procedure described to give III in an over-all yield of about 80% for the two steps.

By the procedure described by Shriner and Fuson,[16] 2.3 g. of III yielded 4.5 g. of a crude 2,4-dinitrophenylhydrazone, m. p. 170–177°. Recrystallization from a mixture of chloroform and 95% ethanol yielded yellow crystals with m. p. 215.8–216.8° (dec.).

Anal. Calcd. for $C_{27}H_{24}N_4O_4$: C, 69.22; H, 5.16; N, 11.96. Found: C, 69.02; H, 5.14; N, 12.18.

2,4-Diphenylbicyclo[3.3.1]nonan-9-one (IV).—Hydrogenation of 2.0 g. of III in 50 ml. of glacial acetic acid in the presence of 0.4 g. of 10% palladium-on-Norite was complete in four hours and required 87% of one molar equivalent of hydrogen. The mixture was made basic with sodium hydroxide after separation of the catalyst and extracted with ether. The extracts were washed with water, dried over sodium sulfate and distilled; a white solid residue of IV (2.0 g.) remained, which was purified by two crystallizations from methanol; m. p. 143–143.8°. A mixed m. p. of IV with III was depressed to 120–124°. IV failed to reduce potassium permanganate either in acetone or in ethanol.

Anal. Calcd. for $C_{21}H_{22}O$: C, 86.85; H, 7.64. Found: C, 86.59; H, 7.86.

2,4-Diphenylbicyclo[3.3.1]nonan-9-one 2,4-Dinitrophenylhydrazone was prepared[16] from 0.5 g. of IV in a yield of 0.8 g. as yellow crystals, m. p. 240–244° (dec.). Several crystallizations from a mixture of chloroform and ethanol gave an analytical sample with a constant m. p. of 248.4–248.8° (dec.).

Anal. Calcd. for $C_{27}H_{26}N_4O_4$: N, 11.91. Found: N, 12.20.

2,4-Diphenylbicyclo[3.3.1]non-2-en-9-one Oxime (V).—Crude III (80 g., m. p. 126–139°), 40 g. of hydroxylamine hydrochloride and 1.2 l. of 95% ethanol were placed in a flask fitted with a dropping funnel, reflux condenser and an electric heating mantle. The mixture was heated and a solution of 66 g. of anhydrous sodium carbonate in 250 ml. of water was added to the boiling solution in a period of twenty minutes. After two hours the solid which remained undissolved was broken up with a rod and an additional 250 ml. of water was added. Heating was continued for two and one-half hours, and on cooling the product crystallized. The mixture was allowed to stand overnight and then was filtered. The cream-colored solid became white after washing with 1 l. of water on the filter. The crude product (m. p. 152.5–156°) was recrystallized from a mixture of 1.1 l. of 95% ethanol and 500 ml. of water. The yield of V was 55.5 g. (66%), m. p. 153.8–156.3°. Recrystallization from aqueous ethanol gave an analytical sample with m. p. 155–158° (lit. 156°[4]).

Anal. Calcd. for $C_{21}H_{21}NO$: C, 83.13; H, 6.98; N, 4.62. Found: C, 83.22; H, 7.22; N, 4.49.

5-Amino-2,4-diphenylcycloöct-2-enecarboxylic Acid ε-Lactam (VI).—*p*-Toluenesulfonyl chloride (21 g.) was added in one portion to a solution of 30.3 g. of the oxime V in 175 ml. of pyridine at room temperature. The mixture was swirled for a few minutes until the solid dissolved (a slight heat of reaction was apparent), and then was allowed to stand overnight at room temperature. The dark red solution was poured into a stirred mixture of ice water containing 200 ml. of concentrated hydrochloric acid and 250 ml. of ether. The viscous mass which separated solidified after a few minutes and was collected on a filter and washed with water and with ether. The solid after air-drying weighed 20.9 g. (69%) and melted at 177–203°; recrystallization from aqueous ethanol yielded 15.2 g. (50%) of VI, m. p. 189–205° as a white crystalline solid, and a second crop of 1.7 g. A similar sample of VI was purified for analysis by extraction with ether in a Soxhlet apparatus and recrystallization of the insoluble portion from 95% ethanol; m. p. 205–210.5°.

Anal. Calcd. for $C_{21}H_{21}NO$: C, 83.13; H, 6.98; N, 4.62. Found: C, 83.30; H, 6.97; N, 4.68.

An isomeric lactam was obtained by heating 1.0 g. of VI under reflux for seventy-six hours with a solution of 5 g. of potassium hydroxide in 3.5 ml. of water and 12 ml. of methanol. A solid phase was present in the mixture during the entire period. The mixture was cooled, acidified, filtered, and the solid was crystallized twice from 95% ethanol; m. p. 194–195.2°.

Anal. Calcd. for $C_{21}H_{21}NO$: C, 83.13; H, 6.98; N, 4.62. Found: C, 82.84; H, 7.13; N, 4.45.

The isomer of VI gave a depression in a mixed m. p. with VI to 166–175°. The same product was obtained by heating a sample of VI under reflux with sodium methoxide in methanol for forty hours.

5-Amino-2,4-diphenylcycloöctanecarboxylic Acid ε-Lactam (VII).—Hydrogenation of 10 g. of VI (m. p. 197–204°) in 250 ml. of dioxane in the presence of 3 g. of 10% palladium-on-Norite (added in three portions) stopped after fifty hours and the absorption of 112% of one molar equivalent of hydrogen. The catalyst was removed by filtration and the filtrate was concentrated under reduced pressure, leaving a crystalline residue, m. p. 183–186°. Recrystallization from 95% ethanol yielded 9.02 g. (90%) of VII, m. p. 187–189°. A sample purified by crystallization to constant m. p. melted at 188.6–189.7° and depressed the m. p. of VI to 157–167°.

Anal. Calcd. for $C_{21}H_{23}NO$: C, 82.58; H, 7.59; N, 4.59. Found: C, 82.36; H, 7.61; N, 4.64.

5-Amino-2,4-diphenylcycloöctanecarboxylic Acid Hydrochloride (VIII).—A mixture of 3.0 g. of the lactam VII, 150 ml. of concentrated hydrochloric acid and 150 ml. of water was heated under reflux for six days. The solid appeared to dissolve gradually, while another solid separated as short needles. The mixture was cooled, filtered, and the crystals were air-dried; m. p. 215.5–215.8° (dec.). The product (VIII) was soluble in dilute sodium hydroxide and in warm water, and was precipitated by addition of an excess of hydrochloric acid. An aqueous solution of VIII had a *p*H of approximately 3.2, and the compound could be titrated with standard sodium hydroxide using a *p*H meter with a glass electrode to a sharp inflection point at *p*H 7.0. VIII was purified by recrystallization from aqueous hydrochloric acid; m. p. 216.5–217.2° (dec.).

Anal. Calcd. for $C_{21}H_{26}O_2NCl$: C, 70.08; H, 7.28; N, 3.89; Cl, 9.85; mol. wt., 359.9. Found: C, 69.31; H, 7.33; N, 3.89; Cl, 9.31; neutral equivalent from *p*H titration curve, 363.

1-Amino-2,4-diphenylcycloöct-4-ene Hydrochloride (IX).—A suspension of 40 g. of VI in 1.5 l. of water and 1.5 l. of concentrated hydrochloric acid was heated under reflux with stirring for nine days. The mixture was cooled and the solid was collected on a filter. The product was dissolved in 2.5 l. of hot water by adding dilute sodium hydroxide until the *p*H was approximately 6.0 (test paper), and the solution was filtered to remove a small amount of insoluble material. Concentrated hydrochloric acid (100 ml.) was added to the hot filtrate, and IX began to separate at once. The mixture was cooled and filtered, yielding IX (33.5 g., 80%) as a fluffy white solid which decomposed gradually without melting above 250°. IX was purified by recrystallization from aqueous hydrochloric acid as fine white needles. An aqueous solution of IX had a *p*H of approximately 6.0, and on titration with sodium hydroxide using a *p*H meter inflections in the titration curve occurred near *p*H 6.0 and 9.5.

Anal. Calcd. for $C_{20}H_{24}NCl$: C, 76.53; H, 7.71; N, 4.46; Cl, 11.30; mol. wt., 313.9. Found: C, 76.76; H, 7.73; N, 4.59; Cl, 11.00; neutral equivalent from the *p*H titration curve, 317.

1-Amino-2,4-diphenylcycloöctane hydrochloride was prepared by reducing 0.322 g. of IX in 12.5 ml. of ethanol and 6 ml. of water in the presence of 0.2 g. of 10% palladium-on-Norite. Hydrogen absorption amounted to 99% of one molar equivalent in seventy minutes. The

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[16] Shriner and Fuson, "The Systematic Identification of Organic Compounds," 3rd Edition, John Wiley and Sons, New York, N. Y., p. 171.

catalyst was separated, the filtrate concentrated under reduced pressure to remove ethanol, diluted with water, and the hydrochloride was precipitated by addition of a few drops of concentrated hydrochloric acid. The hydrochloride was recrystallized from dilute hydrochloric acid, and like IX decomposed gradually above 250° without melting.

Anal. Calcd. for $C_{20}H_{26}NCl$: C, 76.04; H, 8.30; N, 4.43; Cl, 11.23. Found: C, 76.04; H, 8.40; N, 4.60; Cl, 11.03.

1-Amino-2,4-diphenylcycloöct-4-ene was prepared by adding 25 ml. of 10% sodium hydroxide solution to a suspension of 2 g. of IX in ether, and extracting the base with ether. The base was purified by a short-path distillation at 1 mm. with a heating block temperature of 150°. The distillate crystallized and yielded 1.64 g. (93%) of a white solid, m. p. 61–64.5°, which on recrystallization from aqueous ethanol formed long needles, m. p. 63.5–66.5°.

Anal. Calcd. for $C_{20}H_{23}N$: C, 86.59; H, 8.36; N, 5.05. Found: C, 86.46; H, 8.42; N, 5.18.

1-Benzoylamino-2,4-diphenylcycloöct-4-ene was prepared by stirring 2 ml. of benzoyl chloride, 1 g. of IX and 25 ml. of 10% sodium hydroxide for ten hours, initially with cooling in an ice-bath and then at room temperature. The mixture was heated with a warm water-bath for one and one-half hours and filtered to separate the solid product, which was washed with water; yield 1.13 g., m. p. 200–218°. Recrystallization from 95% ethanol gave an analytical sample with m. p. 226.9–227.2°.

Anal. Calcd. for $C_{27}H_{27}NO$: C, 85.00; H, 7.14; N, 3.67. Found: C, 85.00; H, 7.20; N, 3.62.

1-Dimethylamino-2,4-diphenylcycloöct-4-ene (X).—1-Amino-2,4-diphenylcycloöct-4-ene was prepared from 25 g. of the hydrochloride IX and separated by ether extraction as described above. The residue remaining after distillation of the ether was heated on a steam-bath with 24 g. of 85% formic acid and 16.2 g. of 37% aqueous formaldehyde solution for eleven hours.[17] Water (150 ml.) containing 20 ml. of concentrated hydrochloric acid was added, and the solution was concentrated under reduced pressure to one-third of its original volume. Ether and an excess of dilute sodium hydroxide were added, and the combined ether layer and an ether extract of the aqueous layer were extracted with dilute hydrochloric acid. The acid extracts were made alkaline and the amine X was again extracted with ether. The extracts were dried over sodium sulfate and concentrated under reduced pressure. The residue crystallized, yielding 22.8 g. (93.5%) of X, m. p. 100–106°. Recrystallization from 95% ethanol yielded 21.1 g. (87%), m. p. 106–107.3°, and an analytical sample recrystallized from the same solvent melted at 107.5–108.3°.

Anal. Calcd. for $C_{22}H_{27}N$: C, 86.50; H, 8.91; N, 4.59. Found: C, 86.31; H, 8.80; N, 4.55.

Methylation with dimethyl sulfate and sodium hydroxide gave the same product in poorer (61%) yield.

2,4-Diphenylcycloöcta-1,4-diene (XI).—A solution of 9.05 g. of X and 15 ml. of methyl iodide in 100 ml. of dry methanol was heated under reflux in an atmosphere of nitrogen for two hours in a water-bath at 80°. The solvent was removed under reduced pressure and the solid residue was washed with pentane, yielding 13.3 g. of the crude methiodide of X. A solution of the methiodide in 175 ml. of methanol was stirred with the freshly precipitated, alkali-free silver oxide prepared from 6 g. of silver nitrate for one and one-quarter hours at 45–50° and for seven hours at room temperature. The mixture was filtered, the silver salts were washed with warm methanol, and the filtrate containing the quaternary ammonium base was concentrated and decomposed by a short-path distillation at approximately 1 mm. A solution of the distillate in ether was washed with dilute hydrochloric acid, dilute sodium hydroxide, water, and dried over sodium sulfate. Concentration left a residue which crystallized; 6.0 g. (78%), m. p. 39.5–46°. Redistillation through a molecular-type still and crystallization from absolute ethanol raised the m. p. to 47.8–48.6°.

Anal. Calcd. for $C_{20}H_{20}$: C, 92.26; H, 7.74. Found: C, 92.29; H, 7.83.

A solution of 1 g. of XI in 10 ml. of carbon tetrachloride was ozonized at −20° for two hours. The ozonide was decomposed by heating with hydrogen peroxide in glacial acetic acid, and yielded small amounts of benzoic acid, identified by m. p. and mixed m. p., and glutaric acid, identified as the di-*p*-bromophenacyl ester. A sample of XI and maleic anhydride failed to react in benzene solution at the boiling point.

1,3-Diphenylcycloöctane (XIIa).—Reduction of 0.312 g. of XI in 12 ml. of benzene in the presence of 0.08 g. of 10% palladium-on-Norite was complete in two hours and 98% of two molar equivalents of hydrogen was absorbed. The catalyst was separated and the filtrate concentrated, leaving 0.303 g. of XIIa, m. p. 78–81.5°. Recrystallization from absolute ethanol raised the m. p. to 83.6–85.1°.

Anal. Calcd. for $C_{20}H_{24}$: C, 90.85; H, 9.15. Found: C, 90.86; H, 9.30.

A solution of 0.5 g. of XI in 15 ml. of glacial acetic acid and 5 ml. of 57% aqueous hydriodic acid was heated under reflux for four hours. The mixture was poured into water, made basic with sodium hydroxide, and extracted with ether. The ether solution was dried over sodium sulfate and concentrated under reduced pressure, leaving 0.5 g. of a white crystalline residue, m. p. 54–56°. Fractional crystallization from methanol yielded a small amount of XIIa, identified by m. p. and mixed m. p. with the sample obtained by catalytic hydrogenation of XI.

1-Dimethylamino-2,4-diphenylcycloöctane (XIII).—Reduction of 3.3 g. of X in 50 ml. of glacial acetic acid in the presence of 1 g. of 10% palladium-on-Norite was complete in three hours and 104% of one molar equivalent of hydrogen was absorbed. The catalyst was separated, the filtrate was made basic with sodium hydroxide and extracted with three portions of ether. The extracts were washed with water, dried over sodium sulfate, and distilled under reduced pressure, leaving a residue of 3.3 g. of XIII, m. p. 94.4–96°. XIII was recrystallized from methanol as white needles, m. p. 96.4–97.4°.

Anal. Calcd. for $C_{22}H_{29}N$: C, 85.93; H, 9.51; N, 4.56. Found: C, 85.70; H, 9.56; N, 4.44.

3,5-Diphenylcycloöctene (XV).—A solution of 1 g. of XIII and 4 ml. of methyl iodide in 35 ml. of methanol was heated under reflux in a nitrogen atmosphere for two hours. Concentration under reduced pressure yielded essentially the theoretical amount (1.46 g.) of the crude methiodide XIV, which melted at 90–115° and decomposed at 150°. XIV was pyrolyzed without purification by heating at 170–195° and 0.5 mm. in a short-path still. A solution of the viscous distillate (0.5 g.) in ether was washed with dilute hydrochloric acid, dried over sodium sulfate, and concentrated. Redistillation of the residue through a short-path still at 0.5 mm. and a heating block temperature of 150–160° yielded 0.3 g. of a distillate which crystallized. Recrystallization from methanol raised the m. p. to 94.6–95.2°.

Anal. Calcd. for $C_{20}H_{22}$: C, 91.55; H, 8.45. Found: C, 91.54; H, 8.44.

Hydrogenation of 0.20 g. of XV in 15 ml. of glacial acetic acid in the presence of 0.1 g. of 10% palladium-on-Norite resulted in the absorption of 103% of one molar equivalent of hydrogen. The product amounted to 0.18 g. (90%) of XIIa, m. p. 83–85.2°, which did not depress the m. p. of XIIa obtained by hydrogenation of XI.

2,4-Diphenylcycloöctene (XVI).—A solution of 3.07 g. of XIII and 5 ml. of methyl iodide in 35 ml. of dry methanol was heated under reflux for two hours and allowed to stand overnight. Concentration under reduced pressure left 4.55 g. of the crude methiodide XIV. A solution of the methiodide in 50 ml. of methanol and the moist, freshly prepared silver oxide obtained from 2 g. of silver

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(17) Essentially the procedure of Clarke, Gillespie and Weisshaus, THIS JOURNAL, **55**, 4571 (1933).

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 $n^{25}\text{D}$ 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-Diphenylcycloöctane (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 prepared[16] from 0.5 g. of 3,5-diphenylcyclohex-2-enone[18] 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 prepared[16] from 0.5 g. of 3,5-diphenylcyclohexanone[19] 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-diphenylcycloöcta-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.

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[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°.

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

Cyclic Polyolefins. X. Synthesis of Phenylcycloöcta-1,3-diene[1]

BY ARTHUR C. COPE AND EDWARD C. HERMANN

This paper reports the preparation of a phenylcycloöcta-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-benzoylethyl)-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 mμ with identical values of $\epsilon_{\max}$, indicating that II is not an α,β-unsaturated ketone.[2]

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

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