Anal. Calcd. for $C_{11}H_{12}BrCl_2NO_3$: N, 3.92. Found: N, 3.90.

Summary

A method for the synthesis of the antibiotic, chloramphenicol, has been extended to the preparation of compounds containing a halogen atom rather than a nitro group in the para position of the phenyl ring.

DETROIT, MICHIGAN RECEIVED MARCH 9, 1950

[CONTRIBUTION FROM THE SQUIBB INSTITUTE FOR MEDICAL RESEARCH]

Geometrical Isomerism of 2,4-Dibenzylidene-3-phenyl-5-oxazolidones. Their Rearrangement to 1,4-Diphenyl-2-benzylidene-3,5-pyrrolidiones

BY SVEND LARSEN[1] AND JACK BERNSTEIN

The preparation of 2,4-dibenzylidene-3-phenyl-5-oxazolidone by the condensation of benzaldehyde with N-phenacetyl-N-phenylglycine (I) in the presence of acetic anhydride was reported during the work on the synthesis of penicillin.[2] Additional investigation of this reaction has shown that the product was not homogeneous, but was apparently a mixture of geometrical isomers, II (red, m. p. 189.5–191°) and III (yellow, m. p. 171–173°). The presence of two isomers could be demonstrated by paper chromatography when hexane was used for the development, since III could be separated as a faster-moving yellow band from the slower-moving red band of II. These isomers could be separated by repeated fractional crystallization since II crystallized more rapidly from acetone than did III. A similar isomerism was observed in the oxazolidones obtained by the condensation of *p*-chlorobenzaldehyde with N-phenyl-N-phenacetylglycine in the presence of acetic anhydride. The two isomers were separated by fractional crystallization and existed as a red compound (IIa), corresponding to II, and a yellow compound (IIIa), corresponding to III.

III had the expected empirical formula, $C_{23}H_{17}NO_2$, and showed the usual reactions of a lactone. An amide was obtained when an acetone solution of III was treated with dry ammonia, and a methyl ester was isolated when III was treated with methanolic hydrogen chloride. Hydrolysis of the lactone occurred even upon refluxing in moist benzene or moist chloroform and the acid (V), $C_{23}H_{19}NO_3$, was isolated. This acid is apparently N-phenacetyl-N-phenyl-α-aminocinnamic acid since it readily absorbed one mole of hydrogen to give N-phenacetyl-β,N-diphenyl-α-alanine (VI). Treatment of V with hydriodic acid and red phosphorus gave reduction and hydrolysis to phenylacetic acid and the known β,N-diphenyl-α-alanine (VII). V upon treatment with acetic anhydride was reconverted to III.

Similarly II, isomeric with III, showed the reactions of a lactone and upon hydrolysis formed an acid (IV), isomeric with V. IV was also reduced to form VI, and by treatment with hydriodic acid and red phosphorus formed phenylacetic acid and VII. II was reformed by treatment of IV with acetic anhydride.

In practice, large amounts of the isomeric lactones were synthesized from the corresponding isomeric acids (IV and V). These were prepared by refluxing the original crude mixture of lactones in moist benzene, from which IV crystallized upon cooling, while V remained in solution. The lactones were then resynthesized by treatment of the acids with acetic anhydride.

It was interesting to note that either II or III could be isomerized to a mixture of the two by warming in acetic anhydride containing a trace of bromine, although only one of a pair of geometrical isomers is usually isomerized. Dufraisse[3] had observed a similar example with the isomers of α,β-dibromo-β-benzoylstyrene. The oxazolidones showed some differences in ultraviolet absorption[4] (Fig. 1), but attempts to analyze mixtures of II and III on the basis of the absorption were unsuccessful. Although either of the lactones could be isomerized to a mixture of the two isomers, the corresponding acids, IV and V, did not show this same property. IV was isomerized to V by heating in an inert atmosphere at 135° for eighteen hours. V, however, did not change under these conditions.

An interesting reaction was observed when II or III was treated with alcoholic potassium hydroxide instead of aqueous alkali. From II, IV was obtained as in other hydrolyses, but in addition another acidic compound (IX) was isolated. This acidic compound was obtained as the only reaction product when the lactone was treated with a solution of sodium in an alcohol. Analyses indicated an empirical formula $C_{23}H_{17}NO_2$, corresponding to a compound isomeric with the original lactone. III behaved similarly and gave the acidic compound (X), isomeric with IX.

IX and X were geometrical isomers since reduction of either of the compounds gave the same di-

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[1] American-Scandinavian Foundation Honorary Fellow; present address, Nörregade 72, Grindsted, Denmark.

[2] O. S. R. D. Progress Reports on Synthesis of Penicillin, S, **20**, 7, June, 1944.

[3] Dufraisse, *Compt. rend.*, **158**, 1691 (1914).

[4] The coöperation of Dr. N. H. Coy of the Department of Applied Physics, Squibb Research and Development Laboratories, in providing the spectroscopic measurements cited in this paper is gratefully acknowledged.

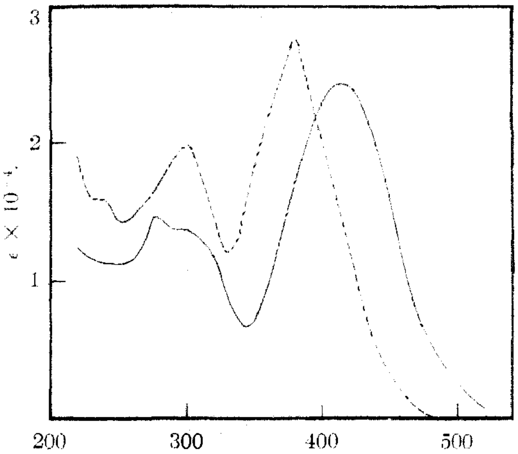
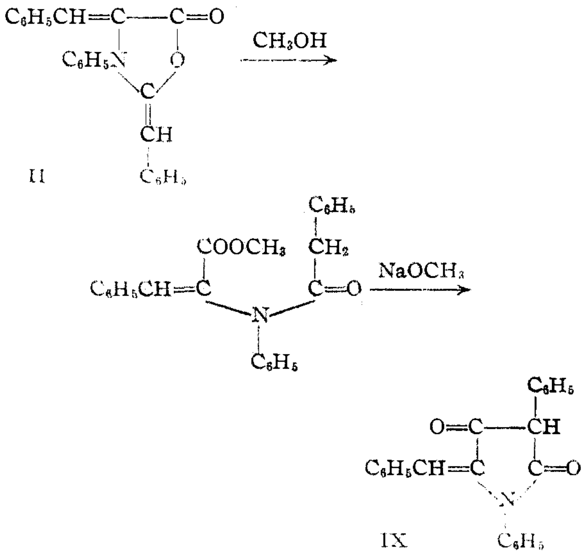


Fig. 1.—Ultraviolet absorption spectra of 2,4-dibenzylidene-3-phenyl-5-oxazolidones: II in anhydrous ether, ——; III in anhydrous ether, - - -.

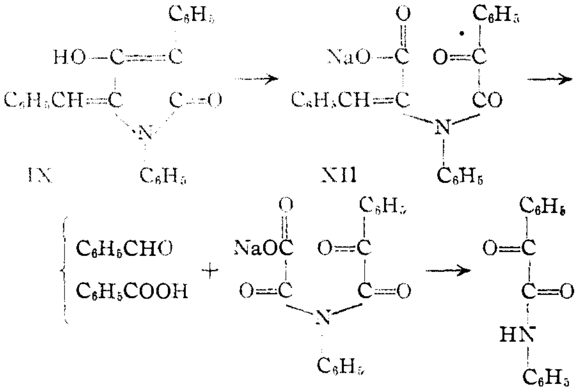
hydro derivative (XI). IX could be isomerized to X by heating at 150° for several hours. These compounds were not lactones since they were stable to boiling hydrochloric acid or aqueous sodium hydroxide. Their acidic properties were not due to a carboxylic acid group, possibly formed by opening of the lactone ring, since the compounds were weak acids, precipitated from alkaline solutions by carbon dioxide. Also, the usual methods of esterification failed. The evidence indicated that the acidic properties were due to the enol form of a carbonyl group, whose presence in the molecule was established by the formation of a phenylhydrazone. Derivatives of the enol form of the carbonyl group were prepared by acetylation and benzoylation. IX and X were, therefore, assumed to be the geometrical isomers of 2-benzylidene-1,4-diphenyl-3,5-pyrrolidione, formed by a Claisen condensation.



II

IX

This was confirmed by the synthesis of X from the methyl ester of V, using sodium ethylate as the condensing agent. No apparent reaction was observed if the free acid itself (V) was used. Further confirmation of the structure was obtained by oxidation of X with alkaline potassium permanganate. From this oxidation phenylglyoxylanilide was isolated, apparently formed by oxidative cleavage of the double bond in the 3-position of the pyrrolidione.



IX

XII

Oxidation of 2-*p*-chlorobenzylidene-1,4-diphenyl-3,5-pyrrolidione by the same reagent gave the same anilide, further indication of cleavage at the double bond in the 3-position. The 2-*p*-chlorobenzylidene-1,4-diphenyl-3,5-pyrrolidione had been prepared from 2-benzylidene-4-*p*-chlorobenzylidene-3-phenyl-5-oxazolidone by treatment with sodium methylate in methanol. Again, geometrical isomers were obtained, but in this case the melting points were similar and a mixed melting point showed no depression. However, the infrared analyses (Table II) of the pyrrolidiones indicated that the compounds were not identical.

Since II and III were hydrolyzed to isomeric cinnamic acids, the orientation of the 4-benzylidene group in relation to the ring was responsible for the isomerism. Also, the orientation of this benzylidene group was responsible for the isomerism in the pyrrolidiones.

Acknowledgment.—The authors are indebted to O. Wintersteiner and W. A. Lott for their interest and encouragement.

Experimental Part[5]

N-Phenacetyl-N-phenylglycine (I).—To a vigorously stirred solution of 100 g. (0.66 mole) of N-phenylglycine in 250 cc. of 4 *N* sodium hydroxide, cooled to 5° by the addition of ice, was added 175 cc. (1.33 mole) of phenacetyl chloride, in 25-cc. portions. The reaction mixture was kept below 5° by the addition of ice and kept alkaline by the addition of sodium hydroxide solution. The stirring was continued for thirty minutes after the addition was complete and the reaction mixture then extracted with chloroform. The aqueous alkaline solution was cooled by addition of ice and acidified with hydrochloric acid. The mixture was extracted with 500 cc. of chloroform, and the chloroform extract washed with water and dried. The addition of hexane to the chloroform solution precipitated

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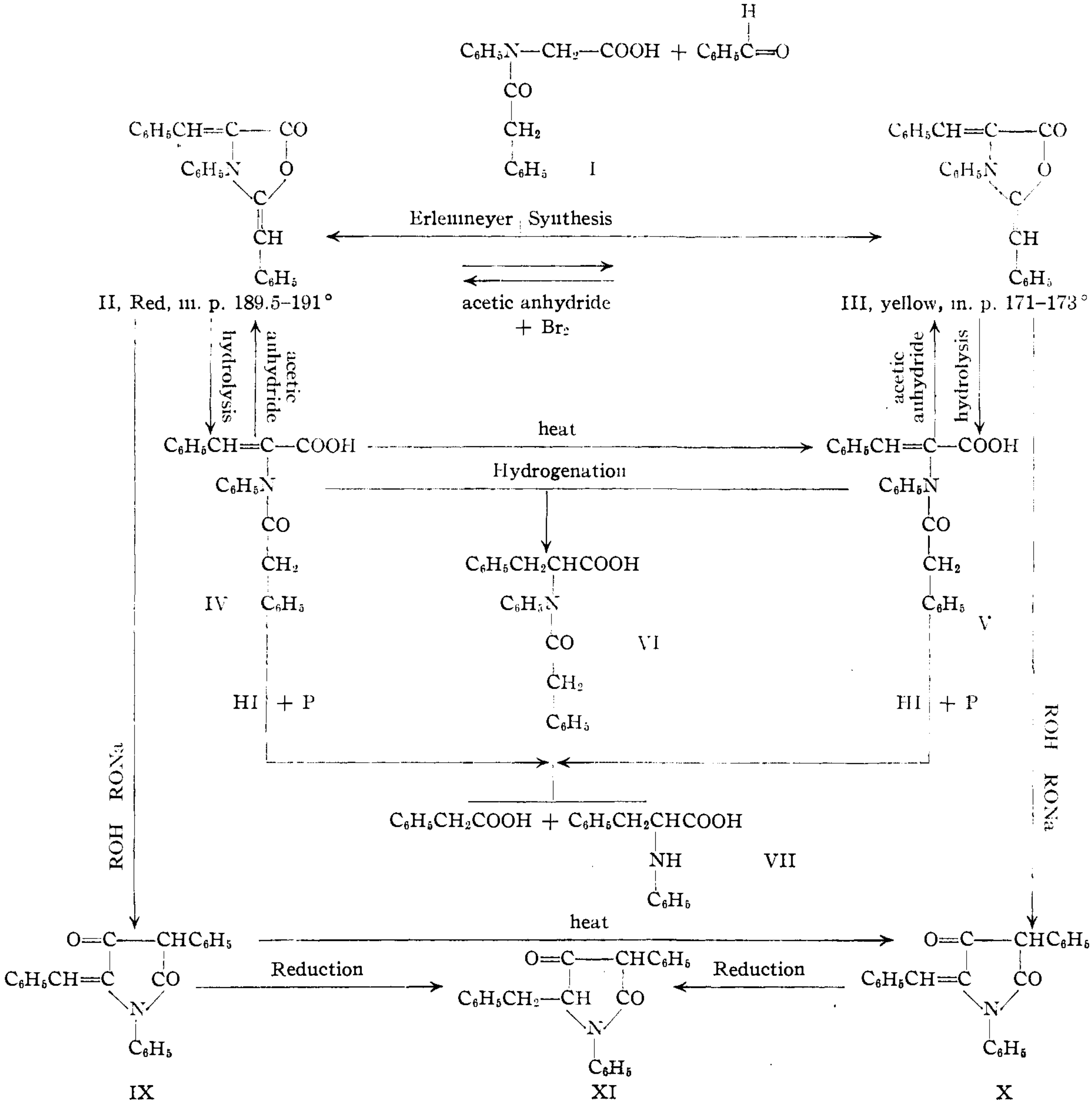
(5) All melting points are corrected. The microanalyses reported were carried out by Mr. J. F. Alicino.

TABLE I



the product, which was filtered, washed with benzene–hexane (1:4) and finally with hexane. The product weighed 125 g. (70% yield) and melted at 138.5–141.5°. It was sufficiently pure for the following reactions.

Anal. Calcd. for $C_{16}H_{15}NO_3$: C, 71.37; H, 5.58; N, 5.20. Found: C, 71.60; H, 5.29; N, 5.08.

2,4-Dibenzylidene-3-phenyl-5-oxazolidone (II and III).—A mixture of 100 g. (0.37 mole) of N-phenacetyl-N-phenylglycine, 39.5 g. (0.37 mole) of benzaldehyde, 31 g. (0.38 mole) of freshly fused and powdered sodium acetate and 120 g. (1.17 moles) of acetic anhydride was warmed on a steam-bath for two hours and then allowed to cool overnight. The mixture was filtered and the solid washed successively with a small amount of acetic anhydride, water, 5% sodium bicarbonate solution, water, 5% sodium bisulfite solution and finally with water. The dried product weighed 27.5–30 g. (22–24% yield), and melted at 145–162°. A second crop of 7–10 g. could be obtained by allowing the mother liquor to stand an additional day. From the mixture pure II, m. p. 189.5–191°, was obtained after repeated fractional crystallization from acetone.

Anal. Calcd. for $C_{23}H_{17}NO_2$: C, 81.40; H, 5.02; N, 4.13. Found: C, 81.58; H, 5.29; N, 4.44.

Isolation of II from the Mixture.—Six grams of the mixture in 15 cc. of benzene, containing 2 cc. of water, was refluxed until the bright red color disappeared (about thirty minutes). If the hydrolysis was occurring too slowly, it could be accelerated by the addition of a drop of acetic acid. The water layer was removed and the solution cooled overnight. The white precipitate (IV) was filtered off and weighed 2.2 g., m. p. 160–163°. A mixture of 2 g. of IV and 7 cc. of acetic anhydride was warmed on a steam-bath for ten minutes to give 1.75 g. of the oxazolidone (II), m. p. 189–191°, after crystallization from acetone.

Isolation of III from the Mixture.—The benzene filtrate from IV was concentrated to dryness under reduced pressure to give an oily residue (V). By heating 2 g. of this oil with 4 cc. of acetic anhydride as described above, there was obtained 1.15 g. of yellow crystals (III), m. p. 171–173°, after crystallization from acetone.

Anal. Calcd. for $C_{23}H_{17}NO_2$: C, 81.40; H, 5.02; N, 4.13. Found: C, 81.70; H, 5.16; N, 4.36.

Isomerization of II and III.—A mixture of 0.3 g. of II, m. p. 189–191°, and 0.6 cc. of acetic anhydride, to which a trace of bromine had been added, was warmed on a steam-bath for forty minutes and then cooled to give 0.21 g. of orange crystals, m. p. 149–170°. Hydrolysis of this material as described above and subsequent conversion to the oxazolidones showed the presence of both II and III in the mixture. From a similar treatment of 0.39 g. of III, m. p. 171–173°, there was obtained 0.22 g. of orange crystals, m. p. 147–170°, also shown to be a mixture of II and III.

N-Phenacetyl-N-phenyl-α-aminocinnamic Acid IV.—From the hydrolysis, as described above, of a mixture of the oxazolidones (II and III) or of pure II, the crude acid could be isolated. The same acid could be isolated when II was hydrolyzed in moist acetone, moist chloroform, dilute acid or dilute alkali. After crystallization from benzene, IV melted at 163–165°.

Anal. Calcd. for $C_{23}H_{19}NO_3$: C, 77.26; H, 5.37; N, 3.92. Found: C, 77.03; H, 5.60; N, 4.13.

The **amide of IV** was prepared by passing dry ammonia into a solution of 0.1 g. of II in 0.5 cc. of acetone. The color disappeared and the amide crystallized. After crystallization from alcohol, the product melted at 175.5–176.5°.

Anal. Calcd. for $C_{23}H_{20}N_2O_2$: N, 7.86. Found: N, 7.68.

N-Phenacetyl-N-phenyl-α-aminocinnamic Acid (V).—The crude acid was isolated as indicated above by hydrolysis of the mixture of oxazolidones (II and III), or by hydrolysis of III. The benzene solution was extracted with 0.1 *N* sodium hydroxide and the alkaline solution acidified. The oil that precipitated was extracted with ether, the ether extract washed with water and concentrated under reduced pressure to give an oil that could not be induced to crystallize.

Anal. Calcd. for $C_{23}H_{19}NO_3$: C, 77.26; H, 5.37; N, 3.92. Found: C, 76.67; H, 5.65; N, 3.79.

The **barium salt of V** was prepared by refluxing a solution of V in 50% ethyl alcohol with the calculated quantity of barium oxide. The barium salt, that precipitated out upon cooling, was crystallized from ethyl alcohol. The acid liberated from the barium salt was still an oil.

Anal. Calcd. for $(C_{23}H_{18}NO_3)_2Ba$: Ba, 16.1. Found: Ba, 16.3.

The **amide of V** was prepared, similarly to its isomer, by treatment of III with ammonia, and after crystallization from alcohol melted at 177.5–180.5°. A mixed melting-point of this compound with its isomer, m. p. 175.5–176.5°, was 153–158°.

Anal. Calcd. for $C_{23}H_{20}N_2O_2$: N, 7.86. Found: N, 7.77.

The **methyl ester of V** was prepared by treatment of 0.1 g. of III with 1 cc. of 0.5 *N* methanolic hydrogen chloride at room temperature. After a few minutes the color disappeared and the methyl ester began to crystallize. The solid, after crystallization from methyl alcohol, weighed 0.0789 g., m. p. 113–115°. The same compound was obtained if a mixture of II and III was used instead of pure III.

Anal. Calcd. for $C_{24}H_{21}NO_3$: C, 77.63; H, 5.67; N, 3.78. Found: C, 77.44; H, 6.28; N, 4.00.

Isomerization of IV.—One hundred milligrams of IV was heated at 135° for eighteen hours in a sealed tube, filled with carbon dioxide. The contents of the tube were then converted to the oxazolidone by treatment with acetic anhydride and gave pure III, indicating that IV had been completely converted to V. Treatment of V in a similar manner also gave pure III, indicating that V had not been changed.

N-Phenacetyl-N,β-diphenyl-α-alanine (VI).—Five hundred milligrams of IV was dissolved in 5 cc. of dioxane, 0.05 g. of palladium black added, and the mixture shaken with hydrogen at atmospheric pressure. After two hours the absorption of hydrogen stopped, the calculated quantity having been absorbed. The mixture was filtered, and concentrated to dryness. Crystallization of the residue from benzene–hexane and then from aqueous alcohol gave 0.32–0.35 g. of product, m. p. 128.5–130.5°.

Anal. Calcd. for $C_{23}H_{21}NO_3$: C, 76.86; H, 5.89; N, 3.89. Found: C, 76.78; H, 5.92; N, 4.15.

A similar reduction of V gave the identical compound as indicated by the melting point and mixed melting point.

N-Phenacetyl-N-phenyl-α-aminocinnamic Acid (IV or V). Reduction and Hydrolysis with Phosphorus and Hydriodic Acid.—A mixture of 0.1 g. of IV, 0.1 g. of red phosphorus, 0.5 cc. of 56% hydriodic acid and 0.5 cc. of acetic anhydride was refluxed for ninety minutes and then 20 cc. of water added. The mixture was filtered and the filtrate extracted twice with hexane. The hexane solution, after washing with 2 *N* hydrochloric acid and water, was concentrated to dryness and the residue crystallized from water to give a solid, m. p. 75.5–76°. A mixed melting point with an authentic sample of phenylacetic acid showed no depression.

The hexane-extracted filtrate and the acid washing were combined and neutralized with sodium carbonate. The precipitated solid after crystallization from aqueous alcohol melted at 169–172°. A mixed melting point with an authentic sample of β,N-diphenyl-α-alanine showed no depression.

Anal. Calcd. for $C_{15}H_{15}NO_2$: C, 74.67; H, 6.26; N, 5.81. Found: C, 74.45; H, 6.18; N, 6.13.

Similar results were obtained using 0.1 g. of V instead of 0.1 g. of IV.

2-Benzylidene-3-phenyl-4-*p*-chlorobenzylidene-5-oxazolidone.—A mixture of 8.0 g. of N-phenacetyl-N-phenylglycine, 4.2 g. of *p*-chlorobenzaldehyde, 2.5 g. of freshly fused and powdered sodium acetate and 10 cc. of acetic anhydride was warmed on a steam-bath two hours and then allowed to cool overnight. The crude product was filtered off and washed similarly to the crude mixture of II and III. Fractional crystallization from acetone gave two fractions. The less soluble product was a red solid (IIa), 2.15 g., m. p. 171.5–174°.

Anal. Calcd. for $C_{23}H_{16}ClNO_2$: Cl, 9.49. Found: Cl, 9.41.

The more soluble product, which could be crystallized from aqueous acetone, was a yellow solid (IIIa), 0.75 g., m. p. 140–141.5°.

Anal. Calcd. for $C_{23}H_{16}ClNO_2$: Cl, 9.49. Found: Cl, 9.73.

1,4-Diphenyl-2-benzylidene-3,5-pyrrolidione (IX or X).—To a solution of 0.1 g. of sodium in 5 cc. of anhydrous methyl alcohol (ethyl or benzyl alcohol could also be used) was added 0.2 g. of II and the mixture heated for fifteen minutes on a steam-bath. The alcohol was then distilled off, the residue dissolved in water and the pyrrolidione (IX) precipitated in almost theoretical yield by acidification with 1 *N* hydrochloric acid. IX was crystallized from dilute alcohol and melted at 102–120°.

Anal. Calcd. for $C_{23}H_{17}NO_2 \cdot H_2O$: C, 77.29; H, 5.37; N, 3.93; H_2O, 5.04. Found: C, 77.11; H, 5.50; N, 3.95; H_2O (volatile at 56° at 10 mm.), 5.10.

Similar treatment of III gave X, which was crystallized from alcohol; m. p. 218.5–222°. X was also formed by heating IX at 150° for several hours.

Anal. Calcd. for $C_{23}H_{17}NO_2$: C, 81.39; H, 5.06; N, 4.10. Found: C, 81.34; H, 5.23; N, 4.38.

Ultraviolet absorption curves of IX and X are shown in Fig. 2.

Claisen Condensation of Methyl Ester of V.—To a solution of 0.0735 g. of the methyl ester of V in 1 cc. of absolute ethanol, was added a solution of 0.035 g. of sodium in 1 cc. of absolute ethanol. The reaction mixture

TABLE II

INFRARED ASSAY OF THE PYRROLIDIONES IN NUJOL MULLS

IX, λμ	IXa, λμ	X, λμ	Xa, λμ
3.58	3.52	3.58	3.58
5.98	5.98	6.02	6.03
6.21	6.19	6.12	6.19
6.30	6.27	6.25	6.28
6.71	6.67	6.65	6.7
6.79	7.10	7.16	7.16
7.21	7.55	7.62	7.67
7.52	7.78	8.08	8.10
7.78	8.03	8.44	8.42
8.08	8.26	8.52	8.5
8.50	8.42	9.04	9.04
8.82	8.82	9.13	9.21
9.25	9.20	9.38	9.38
9.74	9.84	9.73	9.71
9.97	10.65	9.99	9.87
10.28	11.47	10.44	10.41
10.69	12.01	10.91	10.91
10.82	12.38	11.58	11.48
11.82	12.83	12.01	11.90
12.01	13.38	12.77	12.08
12.55		13.17	12.30
12.77		13.64	12.78
13.35			13.05
13.61			13.53

was refluxed for five minutes and then allowed to stand for one hour. Upon the addition of water, 0.04 g. of crude X precipitated, which melted at 217–221° after crystallization from alcohol, and showed no depression when mixed with a sample of X prepared from the oxazolidone.

Acetylation of 1,4-Diphenyl-2-benzylidene-3,5-pyrrolidione.—A mixture of 0.1 g. of IX, 0.1 g. of fused sodium acetate and 1 cc. of acetic anhydride was warmed for three hours on a steam-bath. Addition of a 5% sodium bicarbonate solution destroyed the excess acetic anhydride and caused a yellow precipitate to form, which melted at 167–169° after crystallization from ethyl alcohol.

Anal. Calcd. for $C_{25}H_{19}NO_3$: C, 78.73; H, 5.00. Found: C, 77.40; H, 5.14.

The acetyl derivative of X prepared in a similar manner melted at 165–167°, but a mixture of the two acetates showed a marked depression in melting point.

Anal. Calcd. for $C_{25}H_{19}NO_3$: C, 78.73; H, 5.00; N, 3.67. Found: C, 78.41; H, 5.28; N, 4.08.

Alkylation of 1,4-Diphenyl-2-benzylidene-3,5-pyrrolidione.—The methyl ether of X was prepared by treatment of X with methyl sulfate in alkaline medium. The ether, crystallized from alcohol as yellow needles, melted at 167–169°.

Anal. Calcd. for $C_{24}H_{19}NO_2$: C, 81.59; H, 5.42. Found: C, 81.11; H, 5.36.

Benzoylation of 1,4-Diphenyl-2-benzylidene-3,5-pyrrolidione.—Two hundred milligrams of X was suspended in 1 cc. of pyridine and 0.2 cc. of benzoyl chloride added. The reaction mixture was warmed for fifteen minutes on the steam-bath. Addition of water caused 0.225 g. of the crude benzoate to precipitate and, after crystallization from alcohol, the compound melted at 207–209°.

Anal. Calcd. for $C_{30}H_{21}NO_3$: C, 81.26; H, 4.77. Found: C, 80.79; H, 4.68.

Phenylhydrazone of 1,4-Diphenyl-2-benzylidene-3,5-pyrrolidione.—A mixture of 0.1 g. of X, 0.2 g. of phenylhydrazine and 2 cc. of 50% acetic acid was warmed for one hour on a steam-bath. Addition of water caused the crude phenylhydrazone to precipitate. The solid, 0.15 g., was washed with 10% acetic acid, and after crystallization from alcohol, melted at 216–217.5°.

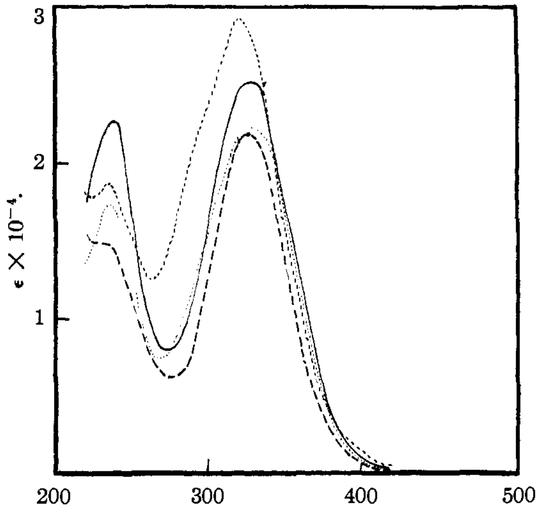


Fig. 2.—Ultraviolet absorption spectra of 1,4-diphenyl-2-benzylidene-3,5-pyrrolidiones: IX in anhydrous ether, —; IX in absolute alcohol, ...; X in anhydrous ether, — — —; X in absolute alcohol, - - - -.

Anal. Calcd. for $C_{29}H_{22}N_3O$: N, 9.82. Found: N, 9.98.

2-Benzyl-1,4-diphenyl-3,5-pyrrolidione (XI).—A mixture of 0.05 g. of IX, 0.1 g. of red phosphorus, 0.5 cc. of 56% hydriodic acid and 0.5 cc. of acetic anhydride was refluxed gently for two hours and then concentrated under reduced pressure. The residue was suspended in water, and dilute sodium hydroxide solution added to dissolve the white solid. The unreacted phosphorus was filtered off, and the filtrate acidified with hydrochloric acid. The product, after crystallization from aqueous alcohol, melted at 220–223°.

Anal. Calcd. for $C_{23}H_{19}NO_2$: C, 80.94; H, 5.62; N, 4.10. Found: C, 81.19; H, 5.90; N, 4.37.

Identical results were obtained when X was used instead of its isomer IX. Upon catalytic reduction of either IX or X in acetic acid using palladium black, one mole of hydrogen was absorbed, and XI was isolated.

Oxidation of 1,4-Diphenyl-2-benzylidene-3,5-pyrrolidione (X).—A solution of 0.9 g. of potassium permanganate in 20 cc. of water was added slowly to a solution of 1.0 g. of X in 30 cc. of 0.1 *N* sodium hydroxide to which had been added 20 g. of ice. Oxidation took place immediately with the formation of a precipitate of manganese dioxide and the reaction was complete in ten minutes. The reaction mixture was then acidified with dilute sulfuric acid and 1.0 g. of sodium bisulfite added to dissolve the manganese dioxide. The solution was extracted twice with benzene, then neutralized with sodium carbonate and extracted with ether.

Concentration of the ether extract gave 0.05 g. of benzaldehyde identified as phenylhydrazone, m. p. 153–155°.

The benzene extracts were washed with water and then extracted twice with 2% sodium bicarbonate solution. Upon acidification of the bicarbonate extracts a yellow precipitate was obtained. The portion (0.05 g.) of this precipitate which was soluble in hexane was identified as benzoic acid by melting point and mixed melting point. The portion (0.45 g.) of the precipitate which was insoluble in hexane melted at 176.5–178.5° (dec.). The acid was purified by crystallization from dilute alcohol and then melted at 185–187° (dec.).

Anal. Calcd. for $C_{23}H_{17}NO_4$: C, 74.38; H, 4.62; N, 3.78. Found: C, 74.06; H, 5.45; N, 4.00.

Upon heating to 190° it decomposed to give one equivalent of carbon dioxide. The compound was not investigated further and was assumed to be XII. The benzene layer was evaporated to dryness and the residue fractionally sublimed. The first fraction was apparently benzaldehyde, but a second fraction, subliming at 150° at 25 mm. pressure was a yellow crystalline solid, which melted at 62–63°, after resublimation.

Anal. Calcd. for $C_{14}H_{11}NO_2$: C, 74.80; H, 4.93; N, 6.23. Found: C, 75.00; H, 5.19; N, 6.44.

The oxime of this compound melted at 205–207°. Beckmann and Köster have reported a m. p. of 63° for phenylglyoxylanilide and a m. p. of 205–206° for the oxime.[6] A similar oxidation of 1,4-diphenyl-2-*p*-chlorobenzylidene-3,5-pyrrolidione also gave phenylglyoxylic acid anilide.

1,4-Diphenyl-2-*p*-chlorobenzylidene-3,5-pyrrolidione (IXa, Xa).—These compounds were prepared similarly to the unchlorinated compounds IX and X. IXa melted at 196–199°.

Anal. Calcd. for $C_{23}H_{16}ClNO_2$: Cl, 9.49. Found: Cl, 9.40.

Xa melted at 200–205°.

Anal. Calcd. for $C_{23}H_{16}ClNO_2$: Cl, 9.49. Found: Cl, 9.64.

A mixed melting point of IXa and Xa was 196–204°; however, the infrared spectra of the compounds showed marked differences and thus proved their dissimilarity.

Summary

The condensation of N-phenacetyl-N-phenylglycine with benzaldehyde or with *p*-chlorobenzaldehyde in the presence of acetic anhydride has been shown to give geometric isomers of the expected oxazolidones.

Each of the oxazolidones have been isomerized to a mixture of the two forms.

The isomeric oxazolidones have been rearranged upon treatment with a sodium alcoholate to isomeric pyrrolidiones.

NEW BRUNSWICK, N. J. RECEIVED MARCH 20, 1950

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[6] Beckmann and Köster, *Ann.*, **274**, 9 (1893).

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF DELAWARE]

The Oxidation of Benzpinacolyl Alcohol

BY WILLIAM A. MOSHER AND HOWARD A. NEIDIG[1]

Recent reports from this laboratory have indicated the generality of the cleavage of aliphatic secondary alcohols on oxidation with chromic anhydride.[2] Concurrent with studies of aliphatic compounds, oxidation of analogous aromatic structures has been underway. Benzpinacolyl alcohol (phenyltriphenylmethylcarbinol) is analogous to methyl-*t*-butylcarbinol, one of the first examples of the cleavage reaction. On oxidation with chromic anhydride, in 70% aqueous acetic acid, this compound yielded 61% benzopinacolone, 22% triphenylcarbinol, 7% tetraphenylethylene and 6% benzaldehyde, all calculated on a molar basis. Benzoic acid has been obtained in some runs in amounts closely equivalent to triphenylcarbinol. The 22% cleavage here obtained is in contrast to a maximum of 7% found with methyl-*t*-amylcarbinol.[2]

Delacre[3] found that benzpinacolyl alcohol could be cleaved by alkali in high yield to triphenylmethane and benzaldehyde. Triphenylmethane is readily oxidized to triphenylcarbinol so that additional evidence was necessary to determine whether the cleavage reaction was entirely oxidative or caused by some other mechanism followed by oxidation. Identical oxidative conditions with triphenylmethane gave only 34% oxidation. A competitive reaction using equimolar amounts of benzpinacolyl alcohol and triphenylmethane was carried out: 88% of the triphenylmethane was recovered and a 50% yield of benzopinacolone was obtained, comparable with 61% when the secondary alcohol was oxidized alone. Under similar conditions the ketone benzopinacolone did not oxidize. It would appear that the cleavage is a direct result of oxidative attack on the secondary alcohol.

Other oxidizing agents have been studied. Potassium permanganate in acetic acid gave 54% triphenylcarbinol and 57% benzaldehyde. Potassium permanganate in boiling acetic acid gave no oxidation with benzopinacolone and gave a 57% yield of benzophenone with triphenylmethane. No benzophenone was found in the oxidation of benzpinacolyl alcohol. Neutral permanganate in acetone gave no oxidation of benzpinacolyl alcohol whereas oxidation was rapid in acetone containing acetic acid even at 40°. This may be a significant fact in elucidating the mechanism of permanganate oxidations.

Selenium dioxide in acetic acid was without effect on benzpinacolyl alcohol at 70° or 100°.

Lead tetraacetate has been postulated as oxidizing through a free radical mechanism[4] and to be rather specific for 1,2-glycols and related compounds.[5] At 50° this agent gave 70% triphenylcarbinol and 4% tetraphenylethylene; at 120°, where more free radical type reactions should be apparent, the products were 51% tetraphenylethylene, 35% benzaldehyde, and 33% triphenylcarbinol. The same reaction was repeated in the presence of air. Had any tri-

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[1] From a thesis submitted by Howard A. Neidig in partial fulfillment of the requirements for the degree of Doctor of Philosophy, University of Delaware, September, 1948. Complete experimental details may be obtained from this thesis.

[2] Mosher, THIS JOURNAL, **70**, 2544 (1948); **71**, 286 (1949).

[3] Delacre, *Bull. Acad. Roy. Belgique*, [3] **20**, 109 (1890).

[4] *Cf.* Waters, "The Chemistry of Free Radicals," second edition, Oxford Press, New York, N. Y., 1948, p. 227 *et seq.*

[5] *Cf.* Baer, THIS JOURNAL, **64**, 1416 (1942), for references to recent studies.