[Contribution from the Research and Development Division, Smith, Kline and French Laboratories]

3,3-Diphenyl-5-methylpyrrolidone-2[1]

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The product of alkaline hydrolysis of the nitrile obtained from diphenylacetonitrile by alkylation with allyl bromide was shown to be 3,3-diphenyl-5-methylpyrrolidone-2, and not the linear amide. Proof of structure was obtained by conversion to the known 1,5-dimethyl-3,3-diphenylpyrrolidone-2 and was substantiated by infrared spectral data. Alkaline hydrolysis of either 2,2-diphenyl-4-pentene-1-carboxamide or the unsaturated nitrile gave both 2,2-diphenyl-4-pentenoic acid and 3,3-diphenyl-5-methylpyrrolidone-2. This ring closure represents the addition of an amide to an isolated carbon-carbon double bond.

Alkylation of diphenylacetonitrile with allyl halides has given good yields of the substituted nitrile (I),[2,3] but the position of the double bond has not been established.[4a] Alkaline hydrolysis of I gave a compound A, $C_{17}H_{17}ON$, m.p. 158°,[2,3] which was considered to be an amide. Because the expected amide, 2,2-diphenyl-4-pentene-1-carboxamide (III)[4] melts at 78°, compound A was tentatively assumed to have the isomeric structure, 2,2-diphenyl-3-pentene-1-carboxamide (II).

A comparison of the chemical properties of these isomers (A and III) brought out the following differences: Compound III was readily reduced to the saturated amide, 2,2-diphenylpentane-1-carboxamide (IV).[5] In contrast, A did not reduce under comparable conditions. While III was readily lactonized to 2,2-diphenyl-4-pentanolactone (V)[2] with sulfuric acid, compound A was not affected by this reagent. Basic hydrolysis of III gave a mixture of 2,2-diphenyl-4-pentenoic acid (VI) and compound A, but compound A could not be further hydrolyzed.

An isomeric structure which is in accord with the chemical properties of compound A is found in 3,3-diphenyl-5-methyl-pyrrolidone-2. Proof of structure was afforded by alkylation to the known N-methyl compound, 1,5-dimethyl-3,3-diphenylpyrrolidone-2 (VII).[6] Confirmatory evidence for the assigned structure of A was found in the infrared spectral data (Table I). The primary amide (IV) has 2 bands assigned to the N—H bonds; alkylation to a tertiary amide removes these bands and shifts the carbonyl band 0.13 μ higher than for the primary amide. The band assigned to the single N—H bond of compound A is eliminated in alkylation to the N-methyl derivative (VI); again the alkylation of the amide results in a shift (0.09 μ) of of the carbonyl band to a higher wave length.

TABLE I

Infrared Data

Compound	Assignment of Bands (μ)	
	N—H	C=O
IV (saturated primary amide)	2.87 3.07	5.97
N,N-Dimethyl-2,2-diphenyl-4-pentenamide (a tertiary amide)[8]	...	6.10
"A"	3.14	5.86
VI (N-methyl analog of A)	...	5.95

The alkaline hydrolysis[2,3] of I was re-examined, and not only A was formed in 16% yield, but a 40% yield of the acid (VI) was obtained. This represents an alternative preparative route for this acid from diphenylacetonitrile by allylation (72% yield) and hydrolysis (40% yield).

The pyrrolidone formation represents the unusual addition of an amide to a carbon-carbon double bond under basic conditions. A similar ring closure recently has been discovered by Brown and van Gulick[7] for the α,α-dimethyl analog. The tendency for this ring closure to occur is greater for the α,α-diphenyl analog than for the α,α-dimethyl analog, as shown by the results of basic hydrolysis of the corresponding nitriles under comparable conditions. The hydrolysis of 2,2-dimethyl-4-pentenonitrile-1[7] by potassium hydroxide in ethylene glycol gave the acid in 90% yield. A similar treatment of the nitrile I gives only 40% of the acid, and 16% of the pyrrolidone is obtained. This result may be ascribed to the

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[1] Presented before the Division of Organic Chemistry at the Minneapolis Meeting of the American Chemical Society, September 12, 1955.

[2] E. M. Schultz, C. M. Robb, and J. M. Sprague, *J. Am. Chem. Soc.*, **69**, 2454 (1947).

[3] N. R. Easton, J. H. Gardner, and J. R. Stevens, *J. Am. Chem. Soc.*, **69**, 2941 (1947).

[4a] The infrared spectrum for I has been analyzed by one of us (ESR), and is in full accord with the structure I ($C_3H_5\equiv$—$CH_2CH=CH_2$). Peaks are found at 6.08, 10.10, 10.99, and 7.06 mμ, which correspond to those expected for a terminal double bond.

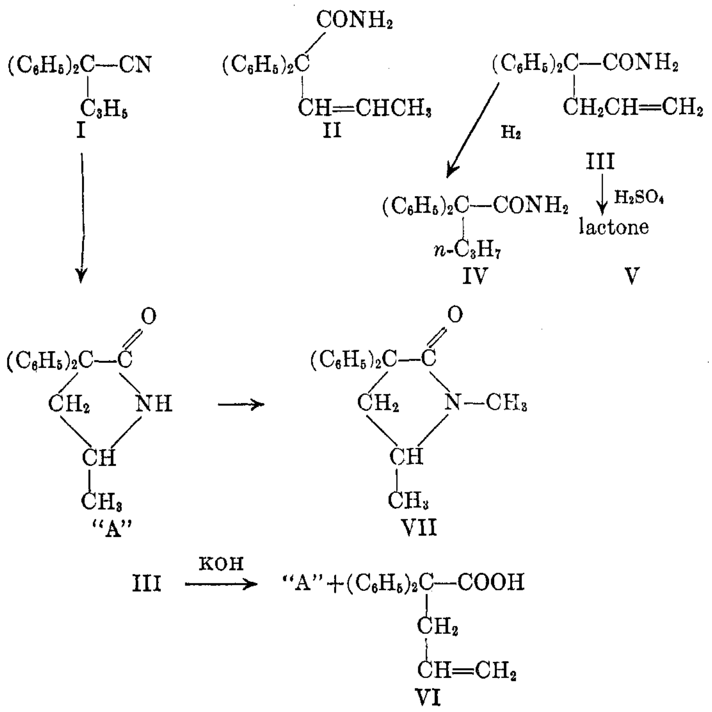
[4] P. N. Craig and I. H. Witt, *J. Am. Chem. Soc.*, **72**, 4925 (1950).

[5] Danilow, *Beilstein's Handbuch der organischen Chemie*, IV Ed., Erganz. II, Vol. 9, p. 480.

[6] (a) J. H. Gardner, N. R. Easton, and J. R. Stevens, *J. Am. Chem. Soc.*, **70**, 2906 (1948). (b) E. Walton, P. Ofner, and R. H. Thorp, *J. Chem. Soc.*, 648 (1949). (c) W. Wilson, *J. Chem. Soc.*, 3524 (1952).

[7] R. F. Brown and N. M. van Gulick, *J. Am. Chem. Soc.*, **77**, 1092 (1955).

[8] P. N. Craig, *J. Am. Chem. Soc.*, **74**, 129(1952).



greater steric hindrance afforded to the carbonyl group of the amide by the phenyl groups than by the methyl groups. This effect would not interfere with the removal of a proton from the amide nitrogen, nor with the subsequent steps involved in the intramolecular reaction.

EXPERIMENTAL

Reactions of 2,2-diphenyl-4-pentene-1-carboxamide (III) (a) Reduction of 1 g. amide in 25 ml. ethanol with platinum oxide occurred at 50 lb. pressure of hydrogen in 15 min. The amide crystallized on dilution with water m.p. 101–102°. (Danilow reports 102°.[5])

(b) Hydrolysis of 1 g. amide by a mixture of 4 g. potassium hydroxide, 4 ml. water, and 20 ml. ethylene glycol was run for 2 hr. at reflux. The mixture was diluted to 100 ml. with water and was extracted twice with 20 ml. benzene and once with ether. Acidification of the aqueous layer, followed by ether extraction, gave 150 mg. of 2,2-diphenyl-4-pentenoic acid, m.p. 137–138°. One recrystallization from acetone-water gave 130 mg., m.p. and mixed m.p. 140–141°. The benzene layer was evaporated and the oil was taken up in 15 ml. hot hexane and cooled; 150 mg. crude 3,3-diphenyl-5-methylpyrrolidone-2 crystallized, m.p. 148–155°. One recrystallization from alcohol–water gave 100 mg., m.p. 161–162°.[2] The residue was an oily mixture of unchanged amide and pyrrolidone which was again hydrolyzed to give more of both products.

Reactions of 3,3-diphenyl-5-methylpyrrolidone-2 (Compound A). (a) The pyrrolidone was recovered unchanged after a solution in conc. sulfuric acid was warmed 15 min. on the steam bath. (b) Treatment with ethylene glycol, water, and potassium hydroxide did not affect the compound. (c) Hydrogenation under the conditions reported above for the unsaturated amide did not take place. (d) Alkylation was accomplished by stirring a mixture of 1 g. compound A, 1 g. sodium hydride, 5 g. methyl iodide, and 25 ml. benzene for 1 hr. The methylated product was obtained on concentration of the filtered benzene solution, followed by addition of petroleum ether; crystals, m.p. 122°. (Lit. reports 122°.[6b])

Hydrolysis of 2,2-diphenyl-4-pentene-1-nitrile. The nitrile was obtained in 72% yield using sodium hydride, allyl bromide, and diphenylacetonitrile. It was distilled through a 40-inch column 30 mm. in diameter, packed with 1/4-inch glass helices; b.p. 136°/0.8 mm., n_D^{25} 1.5724.[2]

Hydrolysis of 5 g. nitrile in a mixture of 50 ml. ethylene glycol, 5 ml. H_2O, and 10 g. potassium hydroxide was accomplished by refluxing for 24 hr. After dilution with water, benzene was added to the mixture. Acidification of the aqueous layer gave 3.0 g. of 2,2-diphenyl-4-pentenoic acid, m.p. 138–140°, undepressed by a sample of pure acid. Two recrystallizations from acetone and water gave 2.0 g., m.p. 142–143°. Evaporation of the benzene solution gave a solid, which was recrystallized from benzene-petroleum ether to give 0.8 g. compound A, m.p. 158–159.5°.[2,3]

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