Anal. Calcd. for $C_9H_{14}O_3$: C, 63.51; H, 8.29. Found: C, 63.76; H, 8.50.

Ethyl 4-Hydroxybicyclo[2.2.2]octane-1-carboxylate (XV).—The silver salt of the hydroxyacid XIV was prepared in 88% yield by addition of silver nitrate to a solution of XIV in the minimum of dilute aqueous ammonia. The silver salt (0.66 g., 0.0025 mole) was heated under reflux for 14 hours with 0.5 ml. of ethyl iodide in 20 ml. of ether. The mixture was filtered, the ether evaporated and the residue distilled through a semi-micro column.[1] The yield of hydroxyester, b.p. 155° (17 mm.), m.p. 48.5-50.0°, was 0.20 g. (40%).

Anal. Calcd. for $C_{11}H_{18}O_3$: C, 66.64; H, 9.15. Found: C, 66.40; H, 9.11.

CAMBRIDGE 39, MASSACHUSETTS

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

The Synthesis of 2,2-Diphenylcyclopentanone and Some of its Derivatives

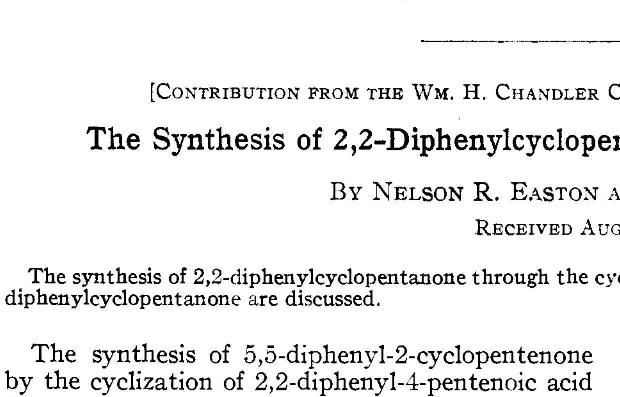
BY NELSON R. EASTON AND SAMUEL J. NELSON[1]

RECEIVED AUGUST 22, 1952

The synthesis of 2,2-diphenylcyclopentanone through the cyclization of the dinitrile is reported. Various reactions of the diphenylcyclopentanone are discussed.

The synthesis of 5,5-diphenyl-2-cyclopentenone by the cyclization of 2,2-diphenyl-4-pentenoic acid has been described[2] and from this 2,2-diphenylcyclopentanone has been prepared[3] by hydrogenation over platinum oxide.

We have also been interested in the preparation of 2,2-diphenylcyclopentanone and have developed an improved preparation of this compound quite different from that described by Craig.[3] We find that 2,2-diphenylcyclopentanone is readily prepared through the reactions

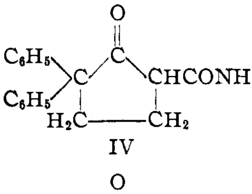


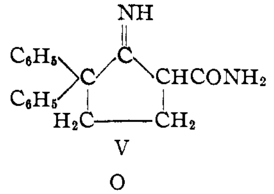
In the preparation of 2,2-diphenyladiponitrile (I) the cyclic product II is sometimes obtained along with the linear product, probably because of the presence of a slight excess of sodium amide. The reaction mixture in these cases is tarry and difficult to purify although yields of about 50% of the cyclized product (II) are obtained. The cyclization of 2,2 - diphenyladiponitrile goes smoothly in virtually quantitative yield when sodium *t*-butoxide in *t*-butyl alcohol is used as the condensing agent. Sodium amide in benzene gives a tarry reaction mixture and a lower yield of product, while sodium ethoxide in absolute alcohol does not catalyze the condensation.

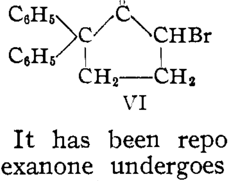
The cyclized product, 5-cyano-2,2-diphenylcyclopentanoneimine, is readily hydrolyzed and decarboxylated with dilute sulfuric acid. A yield of 81% is obtained based on the 2,2-diphenyladiponitrile. When the hydrolysis is incomplete two other products which analyzed for the 2,2-diphenylcyclopentanone-5-carboxamide (IV) and 2,2-diphenylcyclopentanoneimine-5-carboxamide (V) are obtained from the reaction mixture.

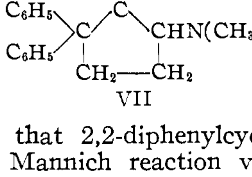
Although Burger[4] has reported that 2,2-diphenylcyclohexanone is brominated readily with bromine in carbon tetrachloride, we find that 2,2-diphenylcyclopentanone gives a variety of products which are very difficult to separate when brominated in this manner; however, excellent yields of VI are obtained when this bromination is carried out using the complex of ether and bromine. When this substance, which is an ether-insoluble oil, is added to an ether solution of the ketone, the bromo compound is obtained in 76% yield.

The amination of 5-bromo-2,2-diphenylcyclopentanone with dimethylamine is carried out in 95% alcohol. Yields of VII of about 33% are obtained when four moles of the amine are used, but these are increased to 81% when 20 moles are used.


IV


V


VI


VII

It has been reported[4] that 2,2-diphenylcyclohexanone undergoes the Mannich reaction very readily when formaldehyde and dimethylamine are used. We were unable to obtain any basic product under these conditions with 2,2-diphenylcyclopentanone.

Experimental

2,2-Diphenyladiponitrile.—A mixture of 110 ml. of sodium dried benzene, 18.4 g. (0.0953 mole) of diphenylacetonitrile and 3.90 g. (0.100 mole) of finely powdered

---

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

[2] P. N. Craig and I. H. Witt, THIS JOURNAL, **72**, 4925 (1950).

[3] Personal communication from P. N. Craig.

[4] A. Burger and W. B. Bennet, THIS JOURNAL, **72**, 5415 (1950).

sodium amide was refluxed rapidly with stirring until the precipitate of the sodium salt of diphenylacetonitrile made stirring difficult (1–2 hr.). The flask was cooled and 10 g. (0.0965 mole) of γ-chlorobutyronitrile in 20 ml. of benzene was added in 0.5 hour. The temperature rose slowly, the semi-solid mass dissolved and a precipitate of sodium chloride appeared. Refluxing was continued for 6 hours.

The reaction mixture was washed twice with water; the benzene–ether layer was distilled and the oily residue allowed to stand on ice overnight. The oil crystallized and after two recrystallizations from methyl alcohol, the 2,2-diphenyladiponitrile (12.3 g., 50%) melted at 65–67°.

In this preparation the cyclized product described below was sometimes formed, and occasionally was the only product. A sample was prepared for analysis by sublimation; m.p. 66–67°.

Anal. Calcd. for $C_{18}H_{16}N_2$: N, 10.76. Found: N, 10.82.

5-Cyano-2,2-diphenylcyclopentanoneimine.—To a solution of 0.2 g. of sodium in carefully dried *t*-butyl alcohol was added 27.9 g. of 2,2-diphenyladiponitrile, which was dissolved by heating and swirling and the solution was refluxed for 3.5 hours. The *t*-butyl alcohol was distilled, initially at atmospheric pressure and finally under reduced pressure. The flask was cooled and the residue crystallized forming a solid gray cake. The dried product melted at 136–146° and after three recrystallizations from methyl alcohol the melting point was 149–150°.

Anal. Calcd. for $C_{18}H_{16}N_2$: C, 83.04; H, 6.20; N, 10.76. Found: C, 83.32; H, 6.13; N, 10.80.

2,2-Diphenylcyclopentanone.—To a solution of 48 ml. of water in 140 ml. of concentrated sulfuric acid at room temperature was added 27.5 g. of the crude, finely powdered 5-cyano-2,2-diphenylcyclopentanoneimine. The imine was added slowly with manual stirring to give a smooth dispersion. The resulting paste was heated on the steam-bath until the iminonitrile was all dissolved and then for 15 minutes more. The flask was cooled in ice and 250 ml. of water added all at once. The mixture was then refluxed for 18 hours with vigorous stirring, preferably using a Hershberg stirrer. The warm mixture was treated with benzene and the water layer was separated and extracted twice with ether, and the combined ether benzene solutions were evaporated, and the distillate (20.1 g., 81% based on diphenylacetonitrile) melted at 87.5–89.5°.

Anal. Calcd. for $C_{17}H_{16}O$: C, 86.40; H, 6.84. Found: C, 86.71; H, 6.84.

Its 2,4-dinitrophenylhydrazone after three recrystallizations from a benzene–alcohol mixture, melted at 182.0–182.5°.

Anal. Calcd. for $C_{23}H_{20}O_4N_4$: C, 66.33; H, 4.84. Found: C, 66.64; H, 5.00.

2,2-Diphenylcyclopentanone-5-carboxamide.—When shorter reflux times (8–10 hr.) were used in the hydrolysis and decarboxylation of 5-cyano-2,2-diphenylcyclopentanoneimine, the flask from which the final distillation was conducted contained a non-volatile residue from which two compounds were separated. The residue was heated with benzene and filtered. A white solid, described below, remained behind. By evaporation of the solvent and cooling, a neutral compound melting at 125–127.5° was obtained. After several recrystallizations from methyl alcohol it melted at 132–133° and analyzed for 2,2-diphenylcyclopentanone-5-carboxamide.

This compound was converted to 2,2-diphenylcyclopentanone by refluxing with stirring in dilute sulfuric acid.

Anal. Calcd. for $C_{18}H_{17}O_2N$: C, 77.39; H, 6.14; N, 5.02. Found: C, 77.63; H, 6.26; N, 4.88.

2,2-Diphenylcyclopentanoneimine-5-carboxamide.—The benzene-insoluble powder filtered from the soluble portion of the residue obtained upon distillation of the partially hydrolyzed 5-cyano-2,2-diphenylcyclopentanoneimine was a high melting compound insoluble in most organic solvents. It was recrystallized twice from glacial acetic acid, m.p. 218–222°, and finally sublimed at 175° and a pressure of 1 mm. or less. The sublimate was a white powder with a slight yellowish cast; m.p. 229–232° (with darkening). This compound was also obtained from a basic hydrolysis of 5-cyano-2,2-diphenylcyclopentanoneimine.

Anal. Calcd. for $C_{18}H_{18}ON_2$: C, 77.67; H, 6.52; N, 10.07. Found: C, 77.65; H, 6.60; N, 10.08.

5-Bromo-2,2-diphenylcyclopentanone.—An addition product of bromine and ether was prepared by slowly adding dry ether to 3.56 g. (0.02222 mole) of ice-cold bromine until a second layer formed above the dark-red insoluble oil. The temperature was not allowed to rise above 20°. The addition product was used immediately and dropped into a stirred solution of 5 g. (0.0211 mole) of 2,2-diphenylcyclopentanone in 50 ml. of dry ether over a period of 15 min. at room temperature.

The faintly yellow solution was evaporated on the steam-bath. The product, 5-bromo-2,2-diphenylcyclopentanone, crystallized upon cooling. After recrystallization from methanol 5.1 g. (76%) was obtained, m.p. 97.5–99.5°. An additional quantity of less pure material was obtained upon evaporation of the mother liquor.

A sample was purified for analysis by five recrystallizations from methyl alcohol, from which it was obtained as brilliant white needles melting at 99.5–100.5°.

Anal. Calcd. for $C_{17}H_{15}OBr$: C, 64.77; H, 4.80. Found: C, 64.62; H, 4.87.

Bromination of 2,2-diphenylcyclopentanone with bromine itself always resulted in the presence of a higher melting impurity that could not be separated by recrystallization. It was present after bromination in carbon tetrachloride or ether solution, after bromination at 10°, and even when only 70% of the theoretical amount of bromine was used. The high melting product was unstable and could not be isolated in pure form, but analysis indicated that it was a dibromo derivative.

5-Dimethylamino-2,2-diphenylcyclopentanone Hydrochloride.—A solution of 5.1 g. (0.016 mole) of 5-bromo-2,2-diphenylcyclopentanone in 50 ml. of ethanol was cooled rapidly in ice with stirring. The ketone then precipitated in finely divided form and to the resulting paste 5.8 g. (0.064 mole) of dimethylamine dissolved in ethanol was added. The flask was heated slowly with stirring to 40° and was held at this temperature for 2.5 hours. The ketone dissolved and the alcohol solution slowly developed a greenish fluorescence. After the period of heating was over, the solution was allowed to stand overnight at room temperature.

The alcohol was evaporated under reduced pressure and water added. A brown oil separated that was taken up in benzene. The water layer was removed and the benzene solution shaken with 5% hydrochloric acid. Shortly after the two layers separated, the amine hydrochloride crystallized from the aqueous layer. The crystals were filtered and washed with hydrochloric acid, and benzene. When dry, the product, 5-dimethylamino-2,2-diphenylcyclopentanone, weighed 1.7 g. (33% yield) and melted at 201–204° with decomposition. Recrystallization from absolute ethanol and ether did not change the melting point.

When the amination was carried out in benzene the same product was obtained in very low yield.

Anal. Calcd. for $C_{19}H_{21}ON{\cdot}HCl$: N, 4.43; Cl, 11.23. Found: N, 4.40; Cl, 11.38.

When a very large excess (20 equivalents) of the dimethylamine was used yields as high as 81% of crude product were obtained.

BETHLEHEM, PA.