through the dehydration of the ketol and subsequent hydrolytic cleavage of a carbon to carbon bond in the unsaturated ketone.

3. The reaction has been applied to other ketols and unsaturated ketones.

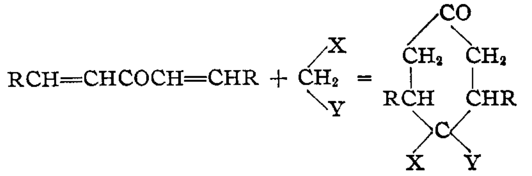
EMERYVILLE, CALIFORNIA RECEIVED MAY 6 1940

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF ROCHESTER]

Some Michael Condensations Involving Benzyl Cyanide

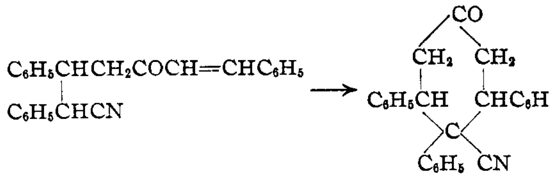
BY R. W. HELMKAMP, LEO J. TANGHE AND JOHN T. PLATI

Kohler and co-workers[1,2] have shown that methyl cyanoacetate and methyl malonate under the influence of a small amount of sodium methylate add readily to dibenzalacetone and similar pentadienones to form cyclohexanone derivatives



We have found that an analogous cyclic ketone is formed with similar ease when benzyl cyanide and dibenzalacetone are brought together in the presence of the same condensing agent

$C_6H_5CH{=}CHCOCH{=}CHC_6H_5 + C_6H_5CH_2CN \longrightarrow$



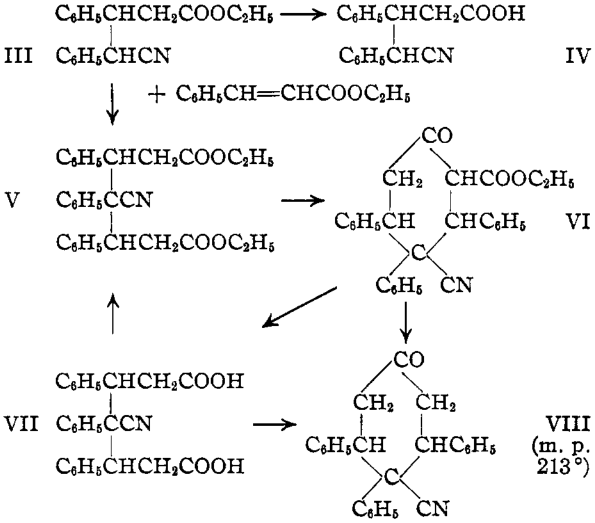
I

II (m. p. 191°)

From the reaction mixture it is possible to isolate, in addition to the cyclohexanone derivative, two compounds isomeric with it. These substances are evidently stereoisomers having the open-chained structure I, for they readily reduce permanganate and are transformed, when dissolved in hot ethyl alcohol containing a trace of sodium hydroxide, into the saturated cyclic compound II. No open-chained addition products have ever been detected in the reactions of methyl cyanoacetate with pentadienones irrespective of the condensing agent used. Similarly, when methyl malonate adds to pentadienones in the presence of sodium methylate, the only condensation products which can be isolated, unless special precautions are taken, are the cyclohexanone derivatives.

Our object in condensing benzyl cyanide with dibenzalacetone was to compare the cyclohexanone II with the structurally identical ketone VIII formed in the following reaction sequence.

$C_6H_5CH{=}CHCOOC_2H_5 + C_6H_5CH_2CN \longrightarrow$



III IV V VI VII VIII (m. p. 213°)

The formation of the products III and VI by the action of sodium ethylate on a mixture of benzyl cyanide and ethyl cinnamate was first reported by Erlenmeyer[3] and the structures of these compounds were later investigated by Avery.[4] Although the trimolecular open-chained addition product V has not been isolated from the condensation reaction, it can be assumed, as has been suggested by Avery, to be the precursor of the β-keto ester VI. He prepared V by the esterification of the pimelic acid VII, obtained by hydrolysis of VI, and he showed that the ester is reconverted into VI when treated with sodium ethylate.

On reinvestigating the condensation of benzyl cyanide with ethyl cinnamate, we were able to isolate a hitherto unreported product, which proved to be a stereoisomer of the ester III obtained by Erlenmeyer and Avery. Both compounds yield the same acid IV on hydrolysis.

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(1) Kohler and Helmkamp, THIS JOURNAL, **46**, 1018 (1924).

(2) Kohler and Dewey, *ibid.*, **46**, 1267 (1924).

(3) Erlenmeyer, *Ber.*, **33**, 2006 (1900).

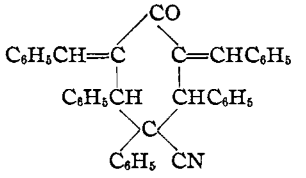
(4) Avery, THIS JOURNAL, **50**, 2512 (1928).

No appreciable ketonic cleavage of the β-keto ester VI occurs by the action of dilute acid or dilute alkali. These reagents cause instead a slow formation of the pimelic acid VII. It is possible to obtain ketone VIII by heating this acid under reduced pressure at 200°. However, a smooth production of the ketone directly from the keto ester takes place in good yield when the latter is heated according to the method of Leuchs[5] with a mixture of hydriodic acid and acetic acid. The use of sulfuric acid in place of hydriodic acid likewise brings about ketonic hydrolysis of VI, but this procedure is less satisfactory.

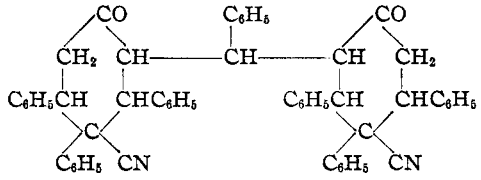
Ketone VIII was found to be stereoisomeric with the cyclic condensation product II from benzyl cyanide and dibenzalacetone. Attempts to transform one stereoisomer into the other were unsuccessful. Ketone II is unaffected by heating with a mixture of hydriodic acid and acetic acid, and neither ketone is converted into the other by the action of a dilute sodium methylate solution. This stability of both ketones is in marked contrast to the ease with which the cyclohexanone first obtained from methyl cyanoacetate and dibenzalacetone is transformed into a stereoisomer by treatment with a dilute solution of sodium hydroxide in methyl alcohol.[1]

Ketones II and VIII show certain noteworthy differences in behavior. Although both ketones readily form oximes,[6] ketone II fails to yield a methyl acetal when subjected to the conditions under which such a derivative is obtainable from ketone VIII. In alkaline medium ketone II reacts with benzaldehyde to form the dibenzal derivative IX, while the only condensation product which could be isolated in a similar experiment with ketone VIII was a compound whose composition and molecular weight correspond to the loss of a molecule of water from two molecules of the ketone and one of benzaldehyde. It has accordingly been assigned the structure X.

It was subsequently found possible to prepare a dibenzal derivative of ketone VIII by the use of hydrogen chloride as a condensing agent, and thus to establish unequivocally that also in this ketone there are two methylene groups adjacent to the carbonyl.

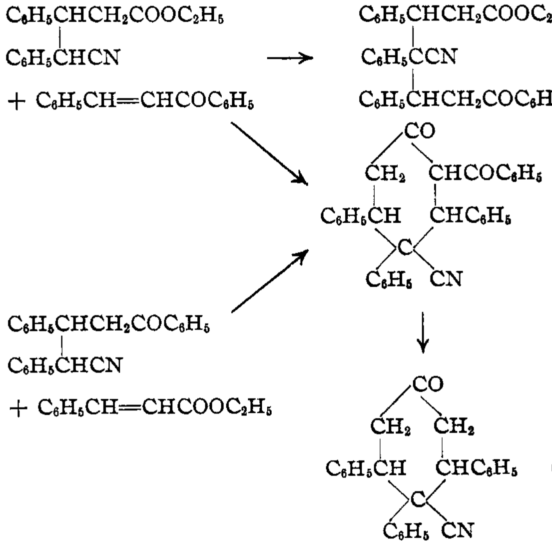


IX



X

Our initial failure to obtain a dibenzal derivative from ketone VIII caused us to consider the possibility that, in spite of rather convincing evidence to the contrary, the condensation of the dimolecular addition product III with a second molecule of ethyl cinnamate might have taken a course different from that indicated, and that consequently the β-keto ester VI and the ketone VIII might possess structures other than those assigned to them. We therefore investigated (a) the condensation of compound III (in both stereoisomeric forms) with benzalacetophenone and (b) the condensation of the addition product of one molecule of benzyl cyanide and one molecule of benzalacetophenone (XI) with ethyl cinnamate.



III

XII

XIII

XI

VIII (m. p. 213°)

The same β-diketone XIII was obtained in each case. In the reaction of benzalacetophenone with the higher melting form of III, it was possible to isolate also the open-chained trimolecular addi-

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(5) Leuchs, Heller and Hoffmann, *Ber.*, **62**, 871 (1929).

(6) *Cf.* Cornubert and Sarkis, *Bull. soc. chim.*, [5] **2**, 215 (1935). These investigators found a striking difference in the tendencies of two of the 3,4,5-triphenylcyclohexanones to form oximes.

tion product XII. If we make the likely assumption that these condensations take place without involving a reversal of the formation of either one of the addition products III and XI, then the production of a common product with the composition of XIII excludes the possibility that the addition reactions leading to its formation have taken any other than the indicated courses. Since hydrolysis of XIII by a mixture of hydriodic acid and acetic acid yields ketone VIII, it follows furthermore that in the reaction of III with ethyl cinnamate the mode of addition is likewise that usually observed in Michael condensations.

Experimental

Condensation of Benzyl Cyanide and Dibenzalacetone.—Thirty grams of benzyl cyanide and 4 cc. of a 5% solution of sodium methylate were added to a suspension of 58.5 g. of dibenzalacetone in 400 cc. of methyl alcohol. The mixture was stirred at room temperature for six hours during which its color became lighter, the dibenzalacetone gradually dissolved and the solid condensation products separated from solution. The precipitate was filtered, and after four extractions in the cold with 100 cc. portions of ether, there remained 40 g. of almost white material. This was separated by fractional crystallization from ethyl alcohol into three isomeric substances which melted at 191, 164, and 144°, respectively. The two lower melting isomers are unsaturated as shown by their reduction of permanganate in acetone solution. When they are dissolved in hot ethyl alcohol containing a small amount of sodium hydroxide, the solutions on cooling deposit the isomer melting at 191°.

γ-Cinnamoyl-α,β-diphenylbutyronitrile (I, m. p. 164°).—*Anal.* Calcd. for $C_{25}H_{21}ON$: C, 85.4; H, 6.0. Found: C, 85.3, 85.0; H, 6.0, 6.0.

γ-Cinnamoyl-α,β-diphenylbutyronitrile (I, m. p. 144°).—*Anal.* Calcd. for $C_{25}H_{21}ON$: C, 85.4; H, 6.0. Found: C, 85.2; H, 6.1.

4-Keto-1,2,6-triphenylcyclohexanenitrile (II, m. p. 191°).—This compound is obtained as a uniform product when the precipitate which is formed in the condensation of benzyl cyanide and dibenzalacetone under the conditions mentioned is recrystallized from ethyl alcohol to which a trace of sodium hydroxide has been added. It was prepared also by the following modification of the original procedure. A sodium methylate solution, made by dissolving a piece of sodium of the size of a small pea in 1 to 2 cc. of methyl alcohol, was added to a mixture of 12 g. of benzyl cyanide, 23.4 g. of dibenzalacetone, and 100 cc. of methyl alcohol. The mixture was refluxed for fifteen minutes, by the end of which a considerable amount of precipitate had formed. After standing for thirty-eight hours at room temperature, the reaction mixture was filtered, and the solid product washed with a small amount of methyl alcohol; yield 18.38 g. (52%). The compound after one recrystallization from ethyl alcohol melted at 187–189°.

Anal. Calcd. for $C_{25}H_{21}ON$: C, 85.4; H, 6.0; mol. wt., 351. Found: C, 85.2; H, 5.9; mol. wt. (cryoscopic method in benzene), 339; mol. wt. (Rast), 363.

Oxime.—Five grams of hydroxylamine hydrochloride and 6.2 g. of sodium hydroxide, each dissolved in the minimum amount of water, were added to a mixture of 5 g. of compound II and 250 cc. of dry ethyl alcohol. After six days the solvent was evaporated under an air blast; yield, 4 g. Recrystallization from ethyl alcohol, in which the oxime is much more soluble than the ketone from which it is derived, gave a product melting at 196–198°.

Anal. Calcd. for $C_{25}H_{22}ON_2$: C, 82.0; H, 6.1. Found: C, 82.2; H, 6.0.

Dibenzal Derivative (IX).—To a suspension of 19 g. of compound II in 700 cc. of alcohol were added 19 cc. of benzaldehyde and 10 cc. of 6 *N* sodium hydroxide solution. The mixture was kept at room temperature and shaken occasionally. The ketone gradually went into solution, and after three days crystals of the condensation product began to appear on the walls of the flask. After eight days the product was filtered; yield, 8.3 g. (30%). The compound was purified by recrystallization from ethyl alcohol; m. p. 196°.

Anal. Calcd. for $C_{39}H_{29}ON$: C, 88.8; H, 5.5; mol. wt., 527. Found: C, 88.9, 88.2, 88.6; H, 5.7, 5.5, 5.5; mol. wt. (cryoscopic method in benzene), 496.

Ethyl γ-Cyano-β-γ-diphenylbutyrate (III, m. p. 101.5° and m. p. 59–60.5°).—Both inactive forms of this ester were isolated by a procedure somewhat different from that by which Avery[7] obtained the higher melting isomer. A solution of 45 cc. of benzyl cyanide and 64 cc. of ethyl cinnamate was added during one and one-half hours to a stirred ice-cold mixture of 800 cc. of dry ether and an amount of sodium ethylate corresponding to 9.2 g. of sodium. Stirring and cooling were continued for five hours. After standing overnight in a refrigerator, the mixture was acidified with dilute hydrochloric acid. The ether layer was then separated and washed with water. Removal of the ether by distillation left a residue from which on crystallization from ethyl alcohol 37.2 g. of the higher melting isomer (m. p. 98–100°) was obtained. The alcoholic filtrate was concentrated and cooled in an ice-bath. Water was added dropwise until a slight permanent precipitate formed. On standing for several hours in the ice-bath, the solution yielded 14 g. of crystals (m. p. 56–60°). The product, after several recrystallizations in this manner, melted at 59–60.5°.

Anal. Calcd. for $C_{19}H_{19}O_2N$: C, 77.8; H, 6.5. Found: C, 77.6, 77.5; H, 6.6, 6.5.

Hydrolysis.—The lower melting isomer was hydrolyzed by the same procedure as that used by Avery[7] for the hydrolysis of the higher melting isomer. The same acid (IV) is obtained from both esters.

Ethyl 3-Cyano-6-keto-2,3,4-triphenylcyclohexanecarboxylate (VI).—The procedure followed for the preparation of this compound was essentially that given by Avery[8] except that one atom of sodium per molecule of benzyl cyanide was used. The yield (m. p. 208–209°) was 66% of the theoretical.

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(7) Avery, This Journal, **50**, 2516 (1928).

(8) Avery, *ibid.*, **50**, 2517 (1928).

4-Keto-1,2,6-triphenylcyclohexanenitrile (**VIII,** m. p. 213°).—To 20 g. of the β-keto ester VI were added 150 cc. of glacial acetic acid and 150 cc. of freshly distilled hydriodic acid (b. p. 127°). A production of carbon dioxide was noted after mixing of the reagents, and a smooth evolution of the gas occurred when the mixture was refluxed. By maintaining the reflux condenser at 60° and a declining condenser connected to it at 15°, the ethyl iodide was removed as formed without loss of acetic acid from the reaction flask. After boiling for one and one-half hours, the mixture was cooled and extracted with benzene. After the benzene extract had been washed with a dilute solution of alkali and then with water, the benzene was removed by distillation and evaporation. The residue was crystallized from ethyl alcohol; yield, 12.4 g. (75%); m. p. 213°.

Anal. Calcd. for $C_{25}H_{21}ON$: C, 85.4; H, 6.0; mol. wt., 351. Found: C, 85.3; H, 6.2; mol. wt. (cryoscopic method in benzene), 337.

Oxime.—The procedure was similar to that followed in the preparation of the oxime of the isomeric ketone II; m. p. 218–220°.

Anal. Calcd. for $C_{25}H_{21}ON$: C, 82.0; H, 6.1. Found: C, 82.1; H, 6.0.

Methyl Acetal.—A solution of 1.5 g. of compound VIII in 300 cc. of methyl alcohol was saturated with dry hydrogen chloride and then allowed to stand for forty hours at room temperature. The crystals which had separated were filtered and an additional crop was obtained on concentration of the filtrate; yield, 1.2 g. Recrystallization from methyl alcohol gave a product melting at 192–194°.

Anal. Calcd. for $C_{27}H_{27}O_2N$: C, 81.6; H, 6.8. Found: C, 81.3, 81.2; H, 6.8, 6.9.

A practically quantitative reconversion into the ketone occurred when 0.1 g. of the acetal was heated for one-half hour in a boiling mixture of 5 cc. of concentrated hydrochloric acid and 5 cc. of glacial acetic acid.

When the attempt was made to form the methyl acetal of the isomeric cyclohexanone II likewise by treatment with a methyl alcohol solution of hydrogen chloride, the ketone was recovered unchanged.

Dibenzal Derivative.—A current of dry hydrogen chloride was passed for an hour into a mixture of 3.3 g. of compound VIII, 2.5 g. of benzaldehyde, and 18 cc. of absolute alcohol; after about twenty minutes, during which the mixture was shaken, the ketone was completely dissolved; by the end of the hour the solution had set to a mass of crystals. The solid was loosened by the addition of 15 cc. of alcohol, filtered, and dried on a steam-bath. It weighed 3.7 g. and melted not very sharply at approximately 170°. Purification by recrystallization from ethyl alcohol gave a product melting at 237–238°. The compound decolorizes permanganate and bromine solution and gives an intense red color with concentrated sulfuric acid.

Anal. Calcd. for $C_{39}H_{29}ON$: C, 88.8; H, 5.5; N, 2.7. Found: C, 88.9; H, 5.7; N, 2.6.

Condensation with Benzaldehyde in Alkaline Medium.—A mixture of 16 g. of ketone VIII, 15 cc. of benzaldehyde, 500 cc. of ethyl alcohol, and 10 cc. of 6 *N* sodium hydroxide solution was allowed to stand for three weeks. The ketone gradually went into solution and another compound separated. The product was filtered and recrystallized from acetone; yield, 4.8 g.; m. p. 299–301° (decomposition). The analytical data indicate that the compound is formed by the loss of a molecule of water from two molecules of the cyclohexanone and one molecule of benzaldehyde.

Anal. Calcd. for $C_{57}H_{46}O_2N_2$: C, 86.5; H, 5.9; mol. wt., 791. Found: C, 86.4, 86.9; H, 6.0, 5.9; mol. wt. (Rast), 780.

4 - Hydroxy - 4 - methyl - 1,2,6 - triphenylcyclohexanenitrile.—A solution of methylmagnesium iodide prepared from 2 cc. of methyl iodide, 0.75 g. of magnesium turnings, and 22 cc. of dry ether was added during a period of forty-five minutes to a cooled and stirred solution of 8 g. of ketone VIII in 50 cc. of dry benzene. An additional 20 cc. of dry ether was then added, and the stirring continued for thirty minutes. The reaction mixture was thereupon thoroughly shaken with dilute sulfuric acid. The benzene–ether layer was separated and washed with sodium bicarbonate solution and then with water. The residue after evaporation of the solvent was taken up in methyl alcohol. Crystals were obtained by cooling the solution in an ice-and-salt mixture and adding sufficient water to produce a slight precipitation; yield of crude product, 5.4 g.; m. p. after recrystallization from ethyl alcohol, 155–158°.

Anal. Calcd. for $C_{26}H_{25}ON$: C, 85.0; H, 6.8. Found: C, 84.9, 85.0; H, 7.0, 6.8.

3 - Benzoyl - 4 - keto - 1,2,6 - triphenylcyclohexanenitrile (**XIII**). (1) **From γ-Benzoyl-α,β-diphenylbutyronitrile and Ethyl Cinnamate.**—A mixture of 3.3 g. of γ-benzoyl-α,β-diphenylbutyronitrile (XI),[9] 1.7 cc. of ethyl cinnamate, and a solution of sodium ethylate prepared from 0.3 g. of sodium and 5 cc. of dry ethyl alcohol was heated on a hot-plate and stirred with a thermometer until the temperature reached 100°. The brown mass was then treated with 25 cc. of chloroform and 1 cc. of glacial acetic acid. After extraction of the mixture with water, the chloroform layer was separated, and the solvent was allowed to evaporate. The residue was crystallized from ethyl alcohol; yield of the β-diketone, 0.2 g.

(2) **From Ethyl γ-Cyano-β,γ-diphenylbutyrate and Benzalacetophenone.**—(a) A mixture of 2.9 g. of ethyl γ-cyano-β,γ-diphenylbutyrate (III m. p. 101.5°), 2.1 g. of benzalacetophenone, and a solution of sodium ethylate prepared from 0.23 g. of sodium and 5 cc. of ethyl alcohol was treated in practically the same way as the reaction mixture in (1); yield of the β-diketone after crystallization from methyl alcohol, 0.3 g. (b) A repetition of procedure (a) in which the ester (III, m. p. 101.5°) was replaced by its lower melting isomer (III, m. p. 59–60.5°) gave a similar result. (c) Two grams of granulated sodium and 5 cc. of absolute ethyl alcohol were heated in 75 cc. of dry toluene under a reflux condenser. After all the sodium had been converted into the ethylate, a solution of 17.8 g. of benzalacetophenone, 25.2 g. of ethyl γ-cyano-β,γ-diphenylbutyrate (III, m. p. 101.5°), and 25 cc. of toluene was added. The mixture was refluxed for thirty minutes and then acidified by the addition of 6 cc. of glacial acetic acid. The residue obtained after evaporation of the solvent under an air blast was extracted with 70 cc. of ether and a moderate quantity of water. The undissolved solid yielded on crystallization from 1600 cc. of ethyl alcohol 3.5 g. of the β-diketone.

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[9] Kohler and Allen, This Journal, **46**, 1526 (1924).

The identity of the products obtained by these procedures was established by mixed melting points. The purified compound melted at 237–237.5°.

Anal. Calcd. for $C_{32}H_{25}O_2N$: C, 84.4; H, 5.5; mol. wt., 455. Found: C, 84.2, 84.1; H, 5.6, 5.5; mol. wt. (Rast), 426.

Ethyl ε-Benzoyl-γ-cyano-β,γ,δ-triphenylcaproate (XII).—This compound was isolated on concentration and cooling of the alcohol filtrate from the crystallization of the β-diketone in (2c); yield of crude product (m. p. 135–140°), 6.4 g.; m. p. after recrystallization from ethyl alcohol, 142–143°.

Anal. Calcd. for $C_{34}H_{31}O_3N$: C, 81.4; H, 6.2. Found: C, 81.5; H, 6.3.

Hydrolysis of 3-Benzoyl-4-keto-1,2,6-triphenylcyclohexanenitrile (XIII). (1) In Alkaline Medium.—A solution of 35 cc. of methyl alcohol, 7 g. of potassium hydroxide, and 1 g. of the β-diketone XIII was placed in an ice-bath for thirty hours. The mixture was then treated with a large volume of water and extracted with ether. Acidification of the aqueous layer precipitated 0.4 g. of crude β-cyano-β,γ-diphenylbutyric acid, formed evidently by a reversal of the Michael condensation.

(2) **In Acid Medium.**—A mixture of 1.5 g. of the β-diketone XIII, 10.5 cc. of glacial acetic acid, and 10.5 cc. of constant boiling hydriodic acid was refluxed for one and one-half hours, during which a gradual solution of the diketone occurred. The acid was then neutralized with sodium carbonate, and the mixture was extracted with benzene. Evaporation of the benzene yielded 1.1 g. of the ketone VIII. The identity of the product and that of the oxime formed from it were established by mixed melting points with samples of these compounds prepared from the β-keto ester VI.

Summary

1. Benzyl cyanide and dibenzalacetone condense readily in the presence of a small amount of sodium methylate to form two γ-cinnamoyl-α,β-diphenylbutyronitriles and a 4-keto-1,2,6-triphenylcyclohexanenitrile.

2. Ethyl 3-cyano-6-keto-2,3,4-triphenylcyclohexanecarboxylate obtained by condensation of benzyl cyanide and ethyl cinnamate yields on ketonic hydrolysis a stereoisomer of the 4-keto-1,2,6-triphenylcyclohexanenitrile formed from benzyl cyanide and dibenzalacetone.

3. Condensation of ethyl γ-cyano-β,γ-diphenylbutyrate with benzalacetophenone and condensation of γ-benzoyl-α,β-diphenylbutyronitrile with ethyl cinnamate yield the same 3-benzoyl-4-keto-1,2,6-triphenylcyclohexanenitrile. The 4-keto-1,2,6-triphenylcyclohexanenitrile formed on hydrolysis of this β-diketone is identical with that produced by hydrolysis of the ethyl 3-cyano-6-keto-2,3,4-triphenylcyclohexanecarboxylate.

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[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF WELLESLEY COLLEGE]

A Study of the Configuration of the Nickel Salt of Formyl Camphor

BY H. S. FRENCH AND G. CORBETT[1]

Nickel lends itself especially well to a study of the configuration of its coördination compounds. In common with several other metals, it may have either a square coplanar or a tetrahedral non-coplanar arrangement of bonds in its four coördination number complex. In asymmetric optically active complexes, the metal can be a center of asymmetry, or of optical activity, only in the case of the tetrahedral non-coplanar arrangement of its bonds. Any experimental procedure, therefore, which determines the group governing the optical activity of a molecule determines at the same time the arrangement of bonds around the metallic atom. Pfeiffer[2] and his co-workers recently used the determination of rotatory dispersion as such an experimental procedure, and assumed that the appearance of a Cotton effect indicated the tetrahedral bond arrangement and *vice versa*. Because the rotatory dispersion was determined only for a relatively small portion of the visible region of the spectrum, and because no correlation was made with absorption spectra, inconsistent and unexplainable conclusions resulted. We present therefore in this paper further experimental results on one of the same compounds used by Pfeiffer, namely, the ultraviolet absorption spectrum and the ultraviolet rotatory dispersion of *d*-nickel formyl camphor. Our conclusion for this compound is the opposite from Pfeiffer's conclusion. He found no Cotton effect and therefore concluded that the nickel complex in nickel formyl camphor

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(1) This work is included in a thesis submitted by Miss G. Corbett to the Faculty of Wellesley College in partial fulfillment of the requirements for the degree of Master of Arts.

(2) Pfeiffer, Christelheit, Hesse, Pfitzner and Thielert, *J. prakt. Chem.*, **150**, 261 (1938).