[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

THE SYNTHESIS OF 4-CYANO-4-METHYL-1-KETO-1,4-DIHYDRONAPHTHALENE[1]

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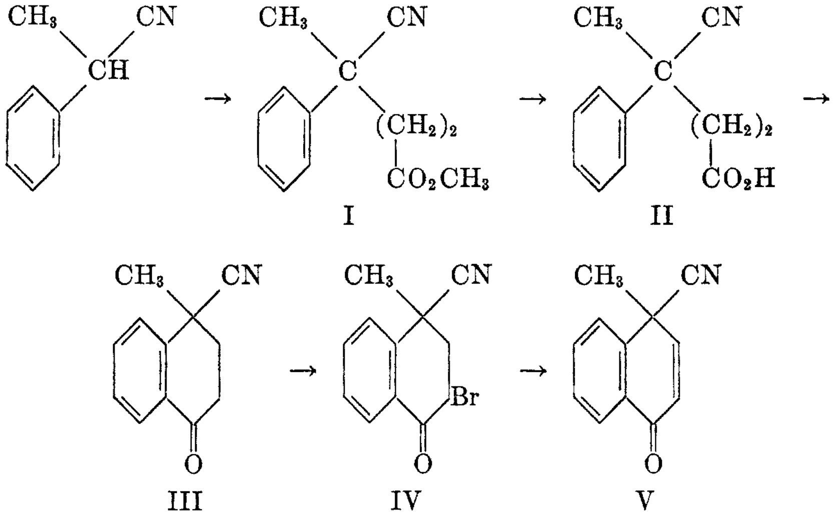
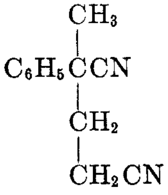
The synthesis of 4-cyano-4-methyl-1-keto-1,4-dihydronaphthalene, undertaken as a part of a study of the von Auwers rearrangement (1), was carried out according to the following scheme.



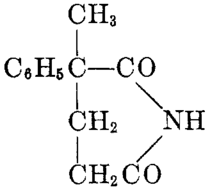
I II III IV V

α-Phenylpropionitrile was condensed with methyl acrylate to produce methyl γ-cyano-γ-phenylvalerate (I). The chloride of the free acid (II) underwent ring closure in the presence of aluminum chloride to form the cyclic cyano ketone (III). Bromination of the cyclic ketone proceeded satisfactorily, and the resulting bromo derivative (IV) was dehydrobrominated with α-picoline to yield the unsaturated ketone (V).

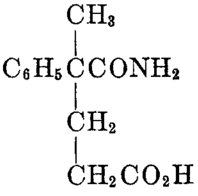
An attempt to prepare the cyano acid (II) by way of α-methyl-α-phenylglutaronitrile (VI) was unsuccessful. Contrary to expectation the primary nitrile


$C_6H_5C(CH_3)(CN)CH_2CH_2CN$

VI


$C_6H_5C(CH_3)(CO)CH_2CH_2CO\text{—}NH$ (cyclic)

VII


$C_6H_5C(CH_3)(CONH_2)CH_2CH_2CO_2H$

VIII

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group could not be hydrolyzed without simultaneous attack of the tertiary cyano group. The dinitrile, made by cyanoethylation of α-phenylpropionitrile, underwent hydrolysis to yield the corresponding imide (VII), and amido acid (VIII).

Syntheses of γ-cyano-2-methyl-α-phenylbutyraldehyde and γ-benzoylvaleric acid, carried out in other unsuccessful attempts to make the desired cyano ketone (V), are described in the experimental section.

EXPERIMENTAL

Methyl γ-cyano-γ-phenylvalerate (I). To 81.6 g. of α-phenylpropionitrile in 200 ml. of dry benzene was added 5.4 g. of dry sodium methoxide. After the solution had been stirred for one hour, 53.3 g. of freshly distilled methyl acrylate was added over a period of 45 minutes. External cooling served to keep the temperature at approximately 25°. The solution was stirred for 18 hours at room temperature, then poured into 500 ml. of water. The aqueous layer was extracted with 150 ml. of ether and the organic layers were combined. The ether solution was washed three times with 100-ml. portions of water and dried over magnesium sulfate. Removal of the ether by distillation left an almost colorless liquid which was distilled through a 10-cm. Vigreux column. A fore-run of 35 g. distilled in the range 66–115° (0.5 mm.). The cyano ester, a colorless liquid, boiled at 117–130° (0.5 mm.); yield 58.2 g. (43%). When redistilled the material boiled at 126–132° (0.5 mm.). An analytical sample was taken at 130° (0.5 mm.); n_D^{20} 1.5057.

Anal.[3] Calc'd for $C_{13}H_{15}NO_2$: C, 71.86; H, 6.96; N, 6.45.
Found: C, 72.06; H, 6.97; N, 6.45.

γ-Cyano-γ-phenylvaleric acid (II). To a hot solution of 24 g. of potassium hydroxide and 24 ml. of water in 105 ml. of methanol was added, with swirling, 58.2 g. of methyl γ-cyano-γ-phenylvalerate. The solution was allowed to stand overnight at room temperature. The alcohol was evaporated by a current of air and the residue diluted with water to a volume of 150 ml. Acidification of this solution caused the separation of a colorless oil which was taken up in 200 ml. of ether. The ether solution was washed with water and dried over sodium sulfate. Removal of the ether by distillation and crystallization of the remaining oil from a benzene-high-boiling petroleum ether mixture gave 54 g. (the theoretical amount) of shining white needles melting at 71–73°. An analytical sample crystallized from the same solvent mixture melted at 74–74.5°. The infrared spectrum of this compound contained bands which can be assigned to cyano and carboxyl groups.[4]

Anal. Calc'd for $C_{12}H_{13}NO_2$: C, 70.91; H, 6.45; N, 6.89.
Found: C, 71.24; H, 6.49; N, 6.89.

4-Cyano-4-methyl-1-keto-1,2,3,4-tetrahydronaphthalene (III). A mixture of 23.3 g. of γ-cyano-γ-phenylvaleric acid and 17.4 g. of thionyl chloride was allowed to stand until the spontaneous reaction stopped, then warmed on the steam-bath for 15 minutes. The excess thionyl chloride was removed by vacuum-distillation, and 150 ml. of dry, high-boiling petroleum ether containing no unsaturated components was added to the residual acid chloride. The mixture was chilled and 20 g. of aluminum chloride added, with stirring, in one lot. External heat was then applied and the stirring continued at reflux temperature until the precipitated complex became solid. After the mixture had been heated under reflux for 4 hours, the petroleum ether was decanted and the solid complex decomposed with ice-water. The organic material was taken up in 150 ml. of ether and the solution washed twice with 50-ml. portions of water. A small amount of starting material was removed by extracting the ether solution with two 75-ml. portions of 5% sodium hydroxide

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[3] The microanalyses were carried out by Miss Emily Davis, Miss Rachel Kopel, and Mrs. Jean Fortney.

[4] The infrared absorption spectra were observed and interpreted by Miss Elizabeth Petersen.

solution. After the solution had been dried over magnesium sulfate, the ether was removed and the dark residual oil distilled. The distillate, 10–12 ml. of yellow oil boiling at 105–125° (0.3 mm.), yielded 6.9 g. (33%) of white prisms from a benzene-petroleum ether mixture; m.p. 53–54°. An analytical sample, crystallized from the same solvent, melted at 57.5–58°.

Anal. Calc'd for $C_{12}H_{11}NO$: C, 77.81; H, 5.98; N, 7.57.
Found: C, 77.64; H, 6.02; N, 7.47.

The carbonyl character of the compound is proved by its reaction with 2,4-dinitrophenylhydrazine. The infrared spectrum contains absorption bands at 1682 cm.$^{-1}$ and 2240 cm.$^{-1}$ which can be assigned, respectively, to the carbonyl and cyano groups. The benzene ring is also represented by a band at 1598 cm.$^{-1}$.

2-Bromo-4-cyano-4-methyl-1-keto-1,2,3,4-tetrahydronaphthalene (IV). This procedure is essentially that previously used for the bromination of acetophenone (2). To 6.7 g. of compound III in 70 ml. of dry ether was added 0.05 g. of aluminum chloride. The mixture was cooled in an ice-bath, and 5.8 g. of bromine in 20 ml. of carbon tetrachloride was added, with stirring, over a period of 45 minutes. As the addition of the bromine progressed a white solid separated from the solution. The solvents were removed at reduced pressure and the residue was triturated with 20 ml. of water and dried in a vacuum. Crystallization of this material from a high-boiling petroleum ether-benzene mixture gave 7.9 g. (83%) of white needles. The compound does not have a sharp melting point, but softens over a wide range with melting completed at 133.5°. Presumably it is a mixture of two racemic forms.

Anal. Calc'd for $C_{12}H_{10}BrNO$: C, 54.56; H, 3.82; N, 5.30.
Found: C, 54.77; H, 3.84; N, 5.34.

4-Cyano-4-methyl-1-keto-1,4-dihydronaphthalene (V). A solution of 6.9 g. of the bromo compound (IV) in 35 ml. of dry α-picoline was heated under reflux for 1.3 hours, cooled, acidified, and extracted with 100 ml. of ether. The ether solution was washed with water, dried over sodium sulfate, treated with Darco, and filtered. Evaporation of the ether and crystallization of the residue from a high-boiling petroleum ether-benzene mixture gave 3.0 g. (64%) of fluffy white needles, m.p. 82–83°. Recrystallization of the compound from the same solvent provided an analytical sample, m.p. 86–86.5°.

Anal. Calc'd for $C_{12}H_9NO$: C, 78.67; H, 4.95; N, 7.65.
Found: C, 78.71; H, 5.03; N, 7.60.

Infrared evidence for the structure of this compound is provided by bands at 1665 cm.$^{-1}$, 2240 cm.$^{-1}$, and 1603 cm.$^{-1}$ which may be assigned to the twice-conjugated carbonyl group, a cyano group, and the benzene ring, respectively.

α-Methyl-α-phenylglutaronitrile (VI). A solution of 37.1 g. of acrylonitrile in 40 ml. of *tert*-butyl alcohol was added, with stirring, over a period of 45 minutes to a mixture of 75.7 g. of α-phenylpropionitrile, 188 ml. of *tert*-butyl alcohol, and 6 g. of a 30% solution of potassium hydroxide in methanol. Cooling was employed throughout the addition to keep the temperature at 15–25°. The reaction mixture was stirred for an additional 2 hours at 20°, then poured into 750 ml. of water. The water layer was extracted three times with 100-ml. portions of ether, and the combined organic layers were washed twice with 400-ml. portions of water. The solution was dried over magnesium sulfate and the solvents were removed by distillation. The clear oil remaining was fractionated through a 10-cm. Vigreux column. A fore-run of 15 ml. distilled at 37–65° (0.3 mm.). The main fraction consisted of 57.6 g. (55%) of a clear liquid boiling in the range 151° (0.3 mm.)–165° (2 mm.). Approximately 30 ml. of resinous material remained in the distilling flask. A portion of the main fraction was redistilled twice through the same column and a sample for analysis taken at 159° (1.2 mm.); n_D^{20} 1.5202.

Anal. Calc'd for $C_{12}H_{12}N_2$: C, 78.23; H, 6.57; N, 15.21.
Found: C, 78.37; H, 6.81; N, 15.26.

γ-Methyl-γ-phenylglutaramic acid (VIII). *First procedure.* To a warm mixture of 1 g. of sodium chloride and 25 ml. of 75% sulfuric acid was added, with shaking, 5 g.

of α-methyl-α-phenylglutaronitrile. The solution was heated for 2 hours on the steam-bath, then poured with stirring on 100 g. of cracked ice. The gummy solid which precipitated was separated by decantation and dissolved in 30 ml. of 5% sodium hydroxide. The solution was extracted with 20 ml. of ether, then acidified with concentrated hydrochloric acid. The precipitated acid was collected and dried. After three recrystallizations from nitromethane the compound, in the form of tiny white prisms, melted at 163.5–164.5°. The infrared spectrum had bands assignable to the carboxyl and amide groups. Although the relative positions of the two functional groups have not been proved, it is not unreasonable to assume that complete hydrolysis occurred at the less hindered position. The neutralization equivalent is 223 (calc'd 221).

Anal. Calc'd for $C_{12}H_{15}NO_3$: C, 65.14; H, 6.83; N, 6.33.
Found: C, 65.44; H, 6.95; N, 6.44.

Second procedure. A solution of 2 g. of the nitrile (VI) in 15 ml. of concentrated sulfuric acid was allowed to stand for 12 hours at 35°, then poured on 50 g. of cracked ice. This solution was neutralized with 20% potassium hydroxide and evaporated to a small volume on a hot plate under a current of air. Acidification of the remaining liquid gave a white precipitate which was collected and triturated with 20 ml. of hot absolute alcohol. The insoluble inorganic material was removed. When chilled, the alcohol solution deposited 0.7 g. (29%) of the acid monoamide; m.p. 164–165°.

α-Methyl-α-phenylglutarimide (VII). A solution of 2 g. of the nitrile (VI) in 12 g. of 75% sulfuric acid was heated on the steam-bath for 6 hours, then cooled and poured on 30 g. of cracked ice. The precipitated solid was washed with water and crystallized from dilute ethanol. The yield was 1 g. of fluffy, shining, white plates melting at 103–105°. An analytical sample had m.p. 104–105°. The imide is slightly soluble in water, soluble in alcohol and sodium hydroxide, and insoluble in sodium bicarbonate solution.

Anal. Calc'd for $C_{12}H_{13}NO_2$: C, 70.91; H, 6.45; N, 6.89.
Found: C, 71.00; H, 6.57; N, 7.01.

This imide was also prepared from γ-methyl-γ-phenylglutaramic acid as follows: A small amount of the acid monoamide was heated at 180–200° for one-half hour. The product was dissolved in 5% sodium hydroxide solution. Saturation of this solution with carbon dioxide precipitated a white solid which crystallized from dilute ethanol in white plates melting at 104–105°. A mixture of this compound and the imide prepared by hydrolysis melted without depression.

γ-Cyano-α-methyl-α-phenylbutyraldehyde. To a mixture of 48 g. of α-phenylpropionaldehyde (3) and 1 g. of 50% potassium hydroxide was added, with stirring, over a period of 1½ hours 21.2 g. of freshly-distilled acrylonitrile. The temperature of the reaction mixture was held at 55–60° by occasional cooling. After the addition of acrylonitrile was complete, the solution was stirred at room temperature for one-half hour, then at 65° for 1½ hours. The mixture was made acidic to Congo Red with dilute hydrochloric acid and 50 ml. of ether was added. The ether solution was washed three times with 50-ml. portions of water and dried over sodium sulfate. After removal of the ether by distillation, the residual oil was distilled twice through a 10-cm. Vigreux column. The yield was 49.8 g. (74%) of aldehyde boiling at 135–141° (0.6 mm.); n_D^{20} 1.5270. The fuchsin aldehyde reagent, phenylhydrazine, and 2,4-dinitrophenylhydrazine react with the compound. The infrared spectrum has bands ascribable to the aldehyde and cyano groups.

Anal. Calc'd for $C_{12}H_{13}NO$: C, 76.97; H, 7.00; N, 7.48.
Found: C, 76.76; H, 7.22; N, 7.72.

2,4-Dinitrophenylhydrazone. This derivative crystallizes from an ethanol-ethyl acetate mixture in yellow needles melting at 167–168°.

Anal. Calc'd for $C_{18}H_{17}N_5O_4$: C, 58.85; H, 4.67; N, 19.07.
Found: C, 58.93; H, 4.66; N, 19.10.

γ-Benzoylvaleronitrile. To 40.4 g. of propiophenone and 2 g. of Triton B in 75 ml. of dioxane was added over a period of one hour, with stirring, 15.9 g. of freshly-distilled acrylonitrile. External cooling was used to hold the temperature of the reaction mixture at 25–30°. The solution was stirred at room temperature for an additional 5 hours. It was then neutralized with dilute hydrochloric acid and poured into 500 ml. of water. The organic layer was dissolved in 150 ml. of ether, and the solution was washed three times with 100-ml. portions of water. After drying the solution over sodium sulfate, the ether was removed by distillation. Fractionation of the residue through a 10-cm. Vigreux column gave a fore-run of 20 g. boiling at 55–58° (0.4 mm.) and a main fraction, the monocyanoethylated product, distilling in the range 135–143° (0.4 mm.); yield 20 g. (36%). The main fraction was redistilled and a sample for analysis taken at 135° (0.4 mm.); n_D^{20} 1.5265.

Anal. Calc'd for $C_{12}H_{13}NO$: C, 76.97; H, 7.00; N, 7.48.
Found: C, 77.21; H, 7.06; N, 7.59.

The *2,4-dinitrophenylhydrazone* crystallizes from ethanol in orange needles melting at 141–142°.

Anal. Calc'd for $C_{18}H_{17}N_5O_4$: C, 58.85; H, 4.66; N, 19.07.
Found: C, 58.82; H, 4.71; N, 18.99.

SUMMARY

A synthesis of 4-cyano-4-methyl-1-keto-1,4-dihydronaphthalene has been described.

A study was made of the hydrolysis of α-methyl-α-phenylglutaronitrile.

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REFERENCES

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