[Contribution from the Chemical Laboratory of Tufts College]

SOME REACTIONS OF DELTA KETONIC NITRILES. II

By Charles F. H. Allen

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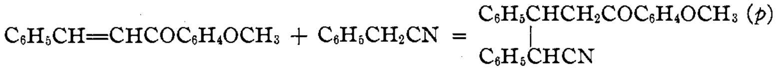
In a paper dealing with the study of 1,5 diketones, Knoevenagel[1] described the treatment of benzal-*p*-methoxy-acetophenone with (a) desoxybenzoin, (b) malonic ester and (c) benzyl cyanide, in the presence of two equivalents of sodium in alcoholic solution, whereby a solid addition product was obtained with the first substance, and oils with the others. The oils were hydrolyzed directly to solid acids which were analyzed. In view of the more recent work on this type of addition reactions by Kohler[2] and his students, it seemed that the product formed by addition of benzyl cyanide should have been a solid, since the unsubstituted ketone gives two isomeric solid δ-ketonic nitriles,[3] and that perhaps by modifying the conditions such a result could be realized experimentally.

This has been found to be the case, and once a crystalline addition product was secured to use for inoculation, a solid could always be obtained under a great variety of conditions. Only one of the two possible isomeric nitriles was formed, but the yield under the best conditions was over 90%.



$$C_6H_5CH{=}CHCOC_6H_4OCH_3 + C_6H_5CH_2CN = \begin{array}{l} C_6H_5CHCH_2COC_6H_4OCH_3\ (p) \\ \quad | \\ C_6H_5CHCN \end{array}$$

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This isomer corresponds to the lower-melting addition product obtained with the unsubstituted ketone, as would be expected;[3] in all previous cases, when but one isomer was produced on addition of cyano compounds, it was the one that readily gave pyridine derivatives with hydrogen bromide and bromine.

This nitrile gives all the usual reactions of this type of compound. It is readily hydrolyzed by Knoevenagel's method to the corresponding acid (II), the latter being easily esterified by methyl alcoholic hydrogen chloride. A solution in glacial acetic acid, when saturated with hydrogen bromide, is transformed into the isomeric tetrahydropyridine derivative (V). It has been possible to isolate the intermediate amide (IV), which has not been done before in this type of reaction except by the use of concd. sulfuric acid instead of hydrogen bromide.[4] Upon bromination, it forms a mixture consisting of the 2-bromopyridine derivative (VII) and the intermediate hydroxy-dihydropyridine derivative (VI).

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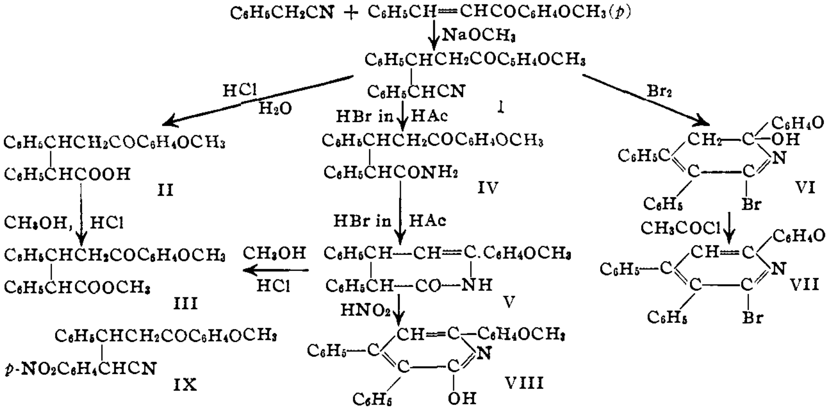
[1] Knoevenagel, *Ann.*, **281**, 62 (1894).

[2] (a) Kohler, This Journal, **38**, 889 (1916); (b) **41**, 764, 995 (1919); (c) **44**, 843, 2540, 2906 (1922).

[3] Kohler and Allen, *ibid.*, **46**, 1522 (1924).

[4] Allen, *ibid.*, **47**, 1733 (1925).

The relation between the various substances is shown by the following outline.



Since most of these substances were prepared by essentially the same methods as reported in the earlier papers[3,4] the experimental details are omitted except where they have been altered.

The Addition Reaction

α,β-Diphenyl-γ-(*p*-methoxybenzoyl)butyronitrile, I.—Forty-seven and six-tenth g. of benzal-*p*-methoxy-acetophenone and 24 g. of benzyl cyanide were dissolved in 145 cc. of dry methyl alcohol on the steam-bath, and enough sodium methylate solution was added to obtain a faint but definite alkaline reaction to litmus. The solution was slightly turbid. The whole was kept hot for two hours, a crystal of solid nitrile added and the mixture allowed to cool. (Rapid cooling resulted in the separation of an oil, from which the solid addition product separated very slowly, in an impure condition.) The next day a first crop of 63.6 g. had formed. A further 3–4 g. was recovered from the mother solution by distilling off some of the alcohol, but it was of poor quality and hardly worth the time it took. Including this, the total yield was 93–94%. It was purified by recrystallization from glacial acetic acid, treating once with Nuchar to remove a slight brownish color.

The addition product crystallizes in large, nearly rectangular prisms; m. p., 116°. It is very sparingly soluble in methyl and ethyl alcohols and ether, but readily soluble in the following warm reagents: glacial acetic acid, chloroform, carbon tetrachloride, benzene, ethyl acetate, acetone and carbon disulfide.

Anal. Calcd. for $C_{24}H_{21}O_2N$: C, 81.1; H, 5.9. Found: C, 81.0; H, 6.0.

The first time the addition reaction was carried out, one mole of sodium methylate was used; on cooling, a thick oil separated, doubtless the same as Knoevenagel observed. The whole was cooled in a mixture of ice and hydrochloric acid and the methyl alcoholic solution poured off; it was from the latter that the first solid was obtained; after allowing it to stand for two days, one or two crystals were noticed in the bottom of the containing beaker; these were removed, found to be insoluble in water (hence not sodium acetate) and when the oil above was inoculated with them a large part of it slowly crystallized. As the use of so much sodium methylate was found to result in a large amount of oily product, the recommended procedure using a trace of alkalinity was worked out. Rapid cooling was also found to be inadvisable for the same reason. No other solid was found at any time.

α-*p*-Nitrophenyl-β-phenyl-γ-(*p*-methoxybenzoyl)butyronitrile, IX.—After the reaction had been carried out for the first time and an oil obtained, it seemed advisable to try a similar reaction, adding *p*-nitrobenzoyl cyanide to benzal-*p*-methoxy-acetophenone, as the latter would be expected to give a solid of much higher melting point. The result was surprising; an oil was formed from which no solid separated for three months. Then the addition product slowly formed in a yield of 65%. It crystallizes in white plates and is insoluble in alcohol and ether, but readily soluble in glacial acetic acid; m. p., 151°.

Anal. Calcd. for $C_{24}H_{20}O_4N_2$: C, 72.0; H, 5.0. Found: C, 72.0; H, 5.1.

Reactions of the Addition Product

The nitrile is unaffected by hours of boiling with sodium methylate or alcoholic potassium hydroxide. Detectable traces of ammonia are not formed. By heating in a sealed tube for two hours with concentrated hydrochloric acid, it is readily hydrolyzed to the acid.

α,β-Diphenyl-γ-(*p*-methoxybenzoyl)butyric Acid, II.—Five g. of the nitrile and 25 cc. of concd. hydrochloric acid were heated in a sealed tube at 130–140° for two hours. There was very little pressure on opening. The solid filtered off was completely soluble in potassium carbonate, and was recrystallized from glacial acetic acid or a mixture of acetone and methyl alcohol, from which it separated as warty aggregates; m. p., 200–201°. It is insoluble in water, carbon disulfide and petroleum ether, moderately soluble in methyl alcohol and chloroform, and quite soluble in acetone, acetic acid, ether and benzene.

Anal. Calcd. for $C_{24}H_{22}O_4$: C, 77.0; H, 5.9. Found: C, 76.8; H, 6.1.

Methyl-α,β-diphenyl-γ-(*p*-methoxybenzoyl)butyrate, III.—Five g. of the acid was dissolved in 300 cc. of warm methyl alcohol, and hydrogen chloride was passed in to saturation (the solution boiled.) After two days the flask was full of long, silky needles that felted together on filtration. The yield was quantitative. After several recrystallizations from methyl alcohol, the ester melted at 169°. It is only moderately soluble in methyl alcohol, but easily soluble in ether.

Anal. Calcd. for $C_{25}H_{24}O_4$: C, 77.3; H, 6.2. Found: C, 77.2; H, 6.2.

2-Keto-3,4-diphenyl-6-(*p*-methoxyphenyl)-tetrahydropyridine, V.—Thirty-eight g. of the nitrile was dissolved in 260 cc. of glacial acetic acid and the solution saturated with hydrogen bromide. After four days it was poured into water, the precipitate filtered and boiled with 100 cc. of acetone to remove a little oily product and most of the water. On cooling, this acetone solution deposited 5 g. of the desired product. The remainder was dissolved in 100 cc. of boiling aniline, filtered and allowed to crystallize. When cold, the hydropyridine was filtered and washed with successive portions of ether until the washings were colorless. Further purification was brought about by several equally effective methods. Portions were recrystallized from acetic acid, carbon tetrachloride and xylene. The use of a Soxhlet extractor, placing the solid in the cup and refluxing until all had dissolved and siphoned off, was found to be very useful as it avoided the bumping prevalent when the solid was simply suspended in the solution, and a much smaller amount of solvent could be used. From all solvents, this tetrahydropyridine crystallizes in very fine, long plates; m. p., 199°; yield, 91%.

Anal. Calcd. for $C_{24}H_{21}O_2N$: C, 81.1; H, 5.9. Found: C, 80.8; H, 6.1.

It is insoluble in the alcohols, ether, nitrobenzene and carbon disulfide, slightly soluble in chloroform, benzene, cymene, acetone and ethyl acetate, moderately soluble in carbon tetrachloride, xylene and acetic acid, and easily soluble in aniline and pyridine.

It decolorizes bromine instantly and also permanganate in acetone. A concentrated solution in methyl alcohol, saturated with hydrogen chloride, deposits the ester above, on long standing. It was oxidized to the hydroxypyridine by concd. sulfuric acid, as well as by nitrous acid; the latter acid was produced in an acetic acid solution of the hydropyridine by the use of butyl nitrite, which proved much more satisfactory than sodium nitrite, used in the earlier papers. Sulfuric acid, however, gives a product of better quality.

2-Hydroxy-3,4-diphenyl-6-(*p*-methoxyphenyl)pyridine, VIII.—Five g. of the tetrahydropyridine derivative, 9 cc. of butyl nitrite and 50 cc. of glacial acetic acid were warmed until evolution of gas began; when this slackened, the mixture was refluxed for two hours. After one and a half hours the suspended solid had entirely dissolved. The next day the crude hydroxypyridine had separated, was filtered, washed with alcohol, and recrystallized several times from glacial acetic acid. It is only sparingly soluble in the alcohols, chloroform, xylene and acetone, and moderately soluble in acetic acid. It crystallizes in fine, white prisms; m. p., 249°.

Anal. Calcd. for $C_{24}H_{19}O_2N$: C, 81.6; H, 5.4. Found: C, 81.5; H, 5.4.

α,β-Diphenyl-γ-(*p*-methoxybenzoyl)butyramide, IV.—When the acetic acid solution of the nitrile, saturated with hydrogen bromide, was poured into water after one day, a small amount of the amide was separated from the tetrahydropyridine by fractional crystallization. It is slightly more soluble than the latter in acetic acid, but insoluble in chloroform. It crystallizes in fine rods; m. p., 248–250°.

Anal. Calcd. for $C_{24}H_{23}O_3N$: C, 77.2; H, 6.2. Found: C, 77.0; H, 6.5.

This amide does not decolorize bromine nor reduce permanganate.

Solutions of the nitrile in chloroform or acetic acid readily react with bromine, evolving hydrogen bromide. From chloroform solutions, a mixture separated, largely bromopyridine, but containing a small amount of the intermediate hydroxydihydropyridine. The latter was separated by extraction with methyl alcohol; yield, 10%.

2-Bromo-3,4-diphenyl-6-(*p*-methoxyphenyl)-6-hydroxy-dihydropyridine (VI) crystallizes in rods; m. p., 119°.

Anal. Calcd. for $C_{24}H_{20}O_2NBr$: C, 66.4; H, 4.6. Found: C, 66.1; H, 4.8.

It dissolves easily in acetyl chloride with loss of water, and on evaporation the bromopyridine crystallizes out.

2-Bromo-3,4-diphenyl-6-(*p*-methoxyphenyl)pyridine, VII.—This substance is obtained in a yield of 80% by bromination of the nitrile. It crystallizes in large, white prisms; m. p., 152°.

Anal. Calcd. for $C_{24}H_{18}ONBr$: C, 69.2; H, 4.3. Found: C, 68.7; H, 4.3.

It is very slightly soluble in methyl alcohol, but readily soluble in acetone, ethyl acetate, acetic acid, acetyl chloride, *n*-butyl alcohol, pyridine and chloroform.

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Summary

1. In the presence of a small amount of sodium methylate, benzyl cyanide adds readily to benzal-*p*-methoxy-acetophenone. The δ-ketonic nitrile formed is a solid.

2. This addition product forms pyridine or tetrahydropyridine derivatives when treated with bromine or hydrogen bromide.

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[Contribution from the Case School of Applied Science]

"SATURATION" OF THE PETROLEUM LUBRICANT HYDROCARBONS AS SHOWN BY THEIR REACTION WITH BROMINE[1]

By Charles F. Mabery

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Since a complete description of the method employed was given in the first paper,[1] it seems to be only necessary to present here all the results, and they are brought together in Table I. Most of the oils are distillates; some are solvent fractions such as the Ohio D and H, the Mecca and the Russian oils.

Table I

Action of Bromine on Petroleum Lubricant Hydrocarbons

	Density		Bromide		Mol. wt.			
	Oil	Bromide	Calcd., %	Found, %	Oil Calcd.	Oil Found	Bromide Calcd.	Bromide Found
West Virginia	0.8819	0.9632	11.19	11.60	636	635	716	717
Pennsylvania	.8662	1.005	16.16	15.87	416	408	491	496
Gulf Coast	.9356	1.130	19.61	19.38	328	331	408	410
Oklahoma	.9010	1.049	17.82	17.38	369	371	449	454
Ohio 8D	.9004	1.007	14.70	14.96	464	462	544	542
Ohio 8H	.9010	1.048	14.62	14.34	468	471	540	548
Illinois	.9047	1.138	18.22	18.16	360	359	439	437
Mecca	.8962	1.007	12.30	12.14	580	575	659	660
Russian	.8726	1.032	13.95	13.83	490	494	574	568
Texas	.9444	1.112	14.00	14.34	492	483	571	563

	Formulas		G. of HBr from 10 g. of oil	
	Oil	Bromide	Calcd.	Found
West Virginia	$C_{46}H_{84}$	$C_{46}H_{83}Br$	1.2	1
Pennsylvania	$C_{30}H_{56}$	$C_{30}H_{55}Br$	2.3	2.3
Gulf Coast	$C_{24}H_{40}$	$C_{24}H_{39}Br$	2.4	2.4
Oklahoma	$C_{27}H_{48}$	$C_{27}H_{47}Br$	2.2	2.2
Ohio 8D	$C_{33}H_{68}$	$C_{33}H_{57}Br$	1.7	1.8
Ohio 8H	$C_{34}H_{60}$	$C_{34}H_{59}Br$	1.7	1.8
Illinois	$C_{26}H_{48}$	$C_{26}H_{47}Br$	2.3	2.3
Mecca	$C_{42}H_{76}$	$C_{42}H_{75}Br$	1.3	1.4
Russian	$C_{36}H_{62}$	$C_{36}H_{61}Br$	1.8	1.7
Texas	$C_{36}H_{60}$	$C_{36}H_{59}Br$	1.6	1.6

With the evidence of these results it is difficult to escape the conclusion as set forth in the first paper that petroleum lubricant hydrocarbons contain no carbon atoms connected by double bonds ordinarily alluded to as unsaturation. It will be observed that the series C_nH_{2n-8} is assumed from former tables, except in the Russian and Texas oils. For the Russian oil the series is C_nH_{2n-10} and for the Texas oil it is C_nH_{2n-12}.

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[1] When the first paper was presented [Mabery, This Journal, **48**, 2663 (1926)], I expected to continue this work, but since I am unable to do it, it seems best to present all the determinations I had made, in order that the fundamental idea set forth in the preliminary paper may have their full support.

In a discussion of polymerization and depolymerization as an explanation of the composition of petroleum lubricants, Thorpe[2] suggested that such changes may result from a condition of unsaturation in the crude oil. But a comparison of the residual hydrocarbons with the composition of the corresponding crude oils as shown by their comprehensive study during the last few years in this Laboratory, precludes the possibility of such decomposition during the process of refining. Thorpe's allusion to the relative ease with which the lubricant loses its oiliness in the engine is not supported by the data of the numerous frictional tests made in this Laboratory, which indicate, in my opinion, that lubricants properly refined from the best crude oils lose very little of their oiliness under strenuous use. Furthermore, the action of bromine on commercial lubricants disproves unsaturation, provided they are properly refined.

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NOTES

The Effect of Ethylene on the Enzymes of Pineapples.—While tasting pineapples which had been ripened with ethylene to improve the flavor and texture, it was noticed that not only were the treated pineapples sweeter but that they seemed to dissolve the mucosa of the mouth more readily than the untreated fruits. Since pineapples are known to be high in proteoclastic enzymes, it was deemed advisable to see if any difference in the activity of these enzymes could be measured quantitatively.

Four pineapples of the same size and degree of ripeness, as judged from external appearances, were selected for each treatment. They were given ethylene or propylene (1:1000) once a day for four days. On the fifth day they were sampled for texture and flavor by a tasting squad. To avoid prejudiced opinions the members of the squad were not told in advance of the treatments administered, but each one was required to give first an opinion of the acidity, sweetness and aroma of the pineapples. There was agreement that the ethylene-treated fruits were much superior to the untreated fruits, and that propylene produced a better flavor than ethylene.

Samples for chemical analysis and for enzyme activity were taken by placing all the fruits of one treatment together, cutting them up in cubes and then, after thorough mixing, removing 100g. samples for chemical analysis and 200g. samples for enzyme study. The samples for enzyme study were immediately ground fine through a Russwin food chopper and the juice pressed out through cheese cloth. The quantity of juice in both cases was 110 cc. out of 200 g. of material so that the juice was not more concentrated in one case than the other, since moisture determinations showed the same total solid content in each sample.

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[2] Thorpe, *Science*, **64**, 236 (1926).