

dergoes rapid addition of methyl ketones and cyclopentanone. The reaction affords a convenient method of preparation of certain β -amino ketones.

The addition of methyl ketones to benzaniline in the presence of boron fluoride is not a reversible process.

URBANA, ILLINOIS

RECEIVED JULY 5, 1939

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

Reactions of Anils. III.¹ A New Type of Diels-Alder Reaction

BY H. R. SNYDER, R. B. HASBROUCK AND J. F. RICHARDSON

The reaction of maleic anhydride on compounds containing the structural unit $\begin{array}{c} >C=C-C=N- \\ | \quad | \\ \quad \quad \quad \end{array}$ has now been examined in the course of a general study of the behavior in the Diels-Alder reaction of open-chain unsaturated systems containing nitrogen.² Since 2-ethyl-2-hexenal-aniline (I) is easily available, it was selected for the study.

2-Ethyl-2-hexenal-aniline reacts readily with maleic anhydride in boiling benzene. The product is a monobasic acid of the composition corresponding to one molecule of each reagent. This acid could not be reduced by sodium amalgam; hydrogen and platinum converted it into a dihydro derivative which could not be further hydrogenated. Both the original acid and the dihydro acids are extremely stable to hydrolysis, either with acids or bases. Fusion of the original acid with alkali brought about its decomposition into aniline and an acid of the composition $C_{11}H_{14}O_2$. Oxidation of the latter gave trimesic acid.

Since the condensation product is a monobasic acid, 1,4-addition of maleic anhydride to give the heterocyclic substance (II) is immediately excluded. An acid of the correct composition might be formed by addition to maleic anhydride, as has been observed in the case of certain pyrroles.³ The primary addition product (III), by tautomerization and intramolecular amide formation, could then be transformed into the monobasic acid (IV). However, a substance having the formula (IV) should be reduced by sodium amalgam and should take up four hydrogen atoms on catalytic reduction. Furthermore, this formula does not account for the formation of an acid $C_{11}H_{14}O_2$ which can be oxidized to trimesic acid.

The formation of the condensation product and all its properties can be accounted for readily on the basis of an aldimine-enamine tautomerism, involving a 1,5-shift of hydrogen, in the original anil (I \rightleftharpoons V). This transformation is not surprising, since the system $-CH_2-C=C-C=N-$ is a vinylog of $-CH_2-C=N-$ in which tautomerism is well known. Addition of maleic anhydride to the diene system of the tautomer gives the substance (VI) which, since it is at once an anhydride and a secondary amine, rearranges to form the bicyclic amido acid (VII).

A compound of the formula (VII) would be expected to resist the action of sodium amalgam and to give only a dihydro derivative on hydrogenation. Vigorous hydrolysis with alkali opens the amide ring to give the β -anilino acid salt (VIII). Loss of a molecule of aniline results in the formation of the dihydrobenzene derivative (IX). The latter is unstable; by expelling a molecule of potassium formate it is converted into the salt of 3,5-diethylbenzoic acid, $C_{11}H_{14}O_2$, (X). Oxidation of the latter gives trimesic acid (XI).

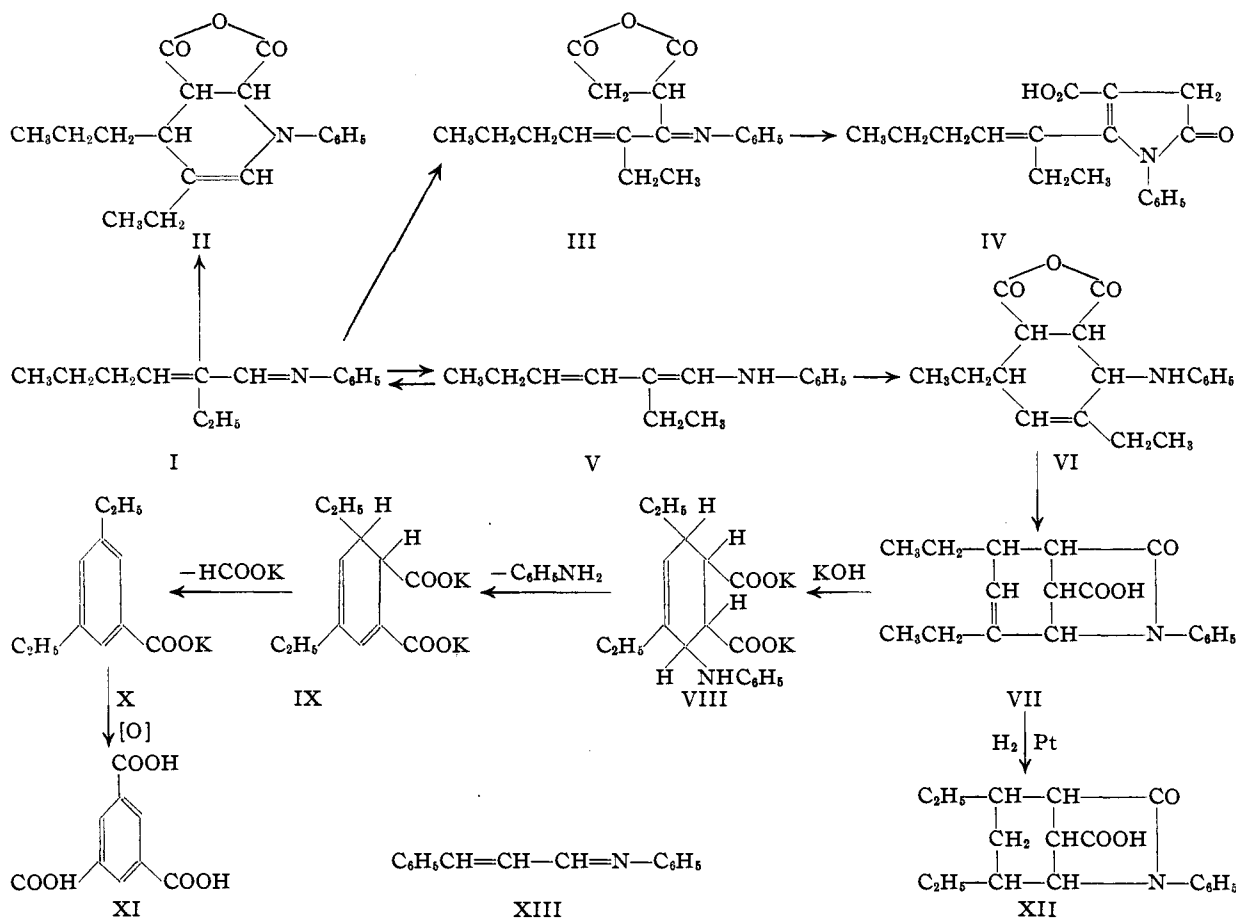
When this work was nearly complete, Bergmann⁴ reported that cinnamalaniline (XIII) and maleic anhydride give only maleanilic acid and cinnamaldehyde. We have carefully reexamined this case; the results have been in harmony with those of Bergmann, except that under highly anhydrous conditions the yield of maleanilic acid was negligible, as might have been expected from the observation² that, in reactions of this kind, the first step is addition of water to the carbon-nitrogen double bond. The failure of cinnamalaniline to undergo condensation supports the formulation given for the reaction of 2-ethyl-2-hexenal-aniline; because the ϵ -carbon atom is part of the benzene ring, cinnamalaniline is unable to undergo the initial tautomerization.

(1) For the preceding paper in this series see Snyder, Kornberg and Romig, *THIS JOURNAL*, **61**, 3556 (1939).

(2) Snyder, Levin and Wiley, *ibid.*, **60**, 2025 (1938).

(3) Diels and Alder *Ann.*, **486**, 211 (1931).

(4) Bergmann, *THIS JOURNAL*, **60**, 2811 (1938).



Experimental

Cinnamalaniline and maleic anhydride reacting in ether gave maleanilic acid, m. p. 193–195°, in yields varying from less than 2% (when dry ether was used) to 96% (when the theoretical amount of water was added). Similar results were obtained with benzene and dioxane solutions.

Preparation of 2-Ethyl-2-hexenal-aniline.—To 40.2 g. of 2-ethyl-2-hexenal (Carbide and Carbon Chemicals Corporation) was added 30 g. of aniline. The solution was heated on the steam-bath for one minute and, after cooling, was allowed to stand at room temperature for fifteen minutes. The product was separated from the water layer by extraction with 100 cc. of benzene. After removal of the benzene, 48 g. (75%) of 2-ethyl-2-hexenal-aniline (I) was distilled at 127–128° (2 mm.) (or 139.5–140.5° (6 mm.)); d_{20}^{20} 0.9379; n_D^{20} 1.5596; M_D calcd., 68.77, M_D found, 69.29.

Anal. Calcd. for $C_{14}H_{19}N$: C, 83.52; H, 9.52; N, 6.96. Found: C, 83.58; H, 9.42; N, 7.11.

Maleic anhydride and 2-ethyl-2-hexenal-aniline in equimolecular amounts, were dissolved in anhydrous benzene (1300 cc. per mole of anhydride). After standing for two hours in a closed flask the solution was filtered from a small amount of maleanilic acid. The clear solution was refluxed for three hours, atmospheric moisture being excluded by a calcium chloride tube. After stand-

ing for several days, or immediately after seeding, the solution deposited white crystals. After recrystallization from alcohol the product, 5,7-diethyl-2-phenyl-2-azabicyclo-(2,3,1)-oct-6-ene-3-one-8-carboxylic acid (VII), melting at 145–146°, was obtained in 75–80% yield.

Anal. Calcd. for $C_{18}H_{21}O_3N$: C, 72.24; H, 7.08; N, 4.68; neut. equiv., 299.2. Found: C, 72.46; H, 7.09; N, 4.78; neut. equiv., 302.

Catalytic Reduction of the Condensation Product.—A solution of 55 g. (0.184 mole) of the acid in 200 cc. of absolute alcohol was reduced at three atmospheres pressure over Adams platinum oxide catalyst. The pressure drop corresponded to 0.188 mole of hydrogen. The solution was filtered, treated with fresh catalyst and returned to the apparatus; no further reduction occurred. The dihydro acid (XII) was crystallized from dilute alcohol; yield 50 g. (90%). The air-dried material was a monohydrate; it decomposed at 120–130° and melted again at 177°; the neutral equivalent was found to be 322.5, as compared to a theoretical value of 319.2 for the monohydrate. Samples dried *in vacuo* melted at 177° and were anhydrous.

Anal. Calcd. for $C_{18}H_{23}O_2N$: C, 71.7; H, 7.70; N, 4.65; neut. equiv., 301.2. Found: C, 71.8; H, 7.73; N, 4.60; neut. equiv., 300.

The dihydro acid was converted to the chloride by treatment with thionyl chloride. Dry ammonia was

bubbled through a benzene solution of the crude chloride to give an 80% yield of the amide, recrystallized from alcohol, m. p. 187–188°.

Anal. Calcd. for $C_{18}H_{24}O_2N_2$: N, 9.33. Found: N, 9.33.

Hydrolysis of the Condensation Product (VII).—A number of attempts to hydrolyze the acid and its dihydro derivative by boiling with acids and bases were unsuccessful; the starting materials were recovered even after boiling for ten days with 10% sodium hydroxide.

To a solution of 20 g. of potassium hydroxide in 20 cc. of water in a nickel crucible was added 20 g. of (VII). The crucible was heated over a free flame while the mixture was carefully stirred. As water was driven off the mixture solidified; it then melted again and evolved aniline (identified as the benzoyl derivative from a run carried out in glass apparatus). When the evolution of aniline had stopped the hot mixture again solidified. It was dissolved in water and boiled with charcoal. The filtrate, on acidification, gave a yellow solid. This was dried and extracted with three 25-cc. portions of hot chloroform. The residue from evaporation of the chloroform was decolorized in methyl alcohol; after three recrystallizations from dilute methyl alcohol the product, 3,5-diethylbenzoic acid (X), melting at 133°, weighed 2.5 g.

Anal. Calcd. for $C_{11}H_{14}O_2$: C, 74.20; H, 7.87; neut. equiv., 178. Found: C, 74.05; H, 8.04; neut. equiv., 174.

Trimesic Acid (XI).—To a solution of 1 g. of 3,5-diethylbenzoic acid and 1 g. of potassium carbonate in about 50 cc. of water was added 7.0 g. of potassium permanganate.

The mixture was heated until a vigorous reaction occurred; when the reaction subsided the mixture was heated for about ten minutes longer. The clear solution obtained after treatment with sulfur dioxide was acidified with hydrochloric acid and cooled in ice-salt. The white solid was collected, dissolved in aqueous potassium carbonate, precipitated with hydrochloric acid and dried. It did not melt at 300°. One-half gram of the acid was converted to the methyl ester by treatment with phosphorus pentachloride and methyl alcohol. After three crystallizations from methyl alcohol the ester melted at 146–147°. A sample prepared from authentic trimesic acid melted at 146–147°; mixtures of the two samples melted at 146–147°.

Anal. Calcd. for $C_{12}H_{12}O_6$: C, 57.1; H, 4.76. Found: C, 57.0; H, 4.87.

Summary

2-Ethyl-2-hexenal aniline and maleic anhydride give 75–80% yields of 5,7-diethyl-2-phenyl-2-azabicyclo-(2,3,1)-oct-6-ene-3-one-8-carboxylic acid. The structure of this product has been proved by reduction to the dihydro derivative, and by degradation to 3,5-diethylbenzoic acid which was oxidized to trimesic acid.

The reaction has been shown to occur through tautomerization of the anil and addition of maleic anhydride to the diene system of the resulting enamine.

URBANA, ILLINOIS

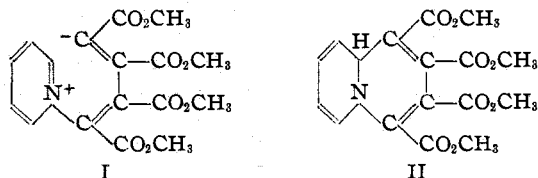
RECEIVED JULY 12, 1939

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

Reactions of Anils. IV.¹ The Reactions of Benzalaniline and Cinnamalaniline with Methyl Acetylenedicarboxylate

BY H. R. SNYDER, HARRY COHEN AND WM. J. TAPP

The behavior of simple anils toward methyl acetylenedicarboxylate is of interest in connection with the novel structure (I) assigned by Diels and Alder² to the labile isomer obtained from pyridine and this reagent. Since only the carbon-nitrogen double bond appears to be involved in the formation of this substance and its stable isomer (II), other compounds containing this linkage might be expected to give similar products.



(1) For the third communication in this series see *THIS JOURNAL*, **61**, 3568 (1939).

(2) Diels and Alder, *Ann.*, **510**, 87 (1934).

It has been found that benzalaniline and the acetylenic ester, reacting in commercial ether, give low yields of a substance (VI) having the composition corresponding to the addition of one molecule of the anil to one of the ester. However, the fact that the yields were greatly improved by the presence of a small amount of water suggested that the reaction involved hydrolysis of the anil. Addition of the liberated aniline to the acetylenic bond of the ester would give (IV), which by tautomerization ($IV \rightleftharpoons V$) and condensation with benzaldehyde would give (VI).

That the compound obtained has the structure (VI) was shown by its formation from methyl oxalacetate, benzaldehyde and aniline. It also could be obtained from methyl oxalacetate and benzalaniline in the presence of a trace of water, and from benzaldehyde, aniline and methyl acetyl-