[Contribution from the Noyes Chemical Laboratory, University of Illinois]

The Structure of the Benzalaniline–Acetic Anhydride Addition Product

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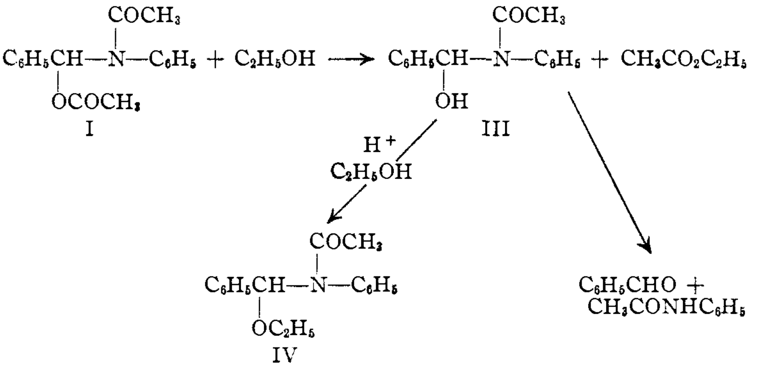
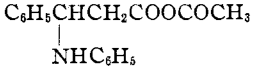
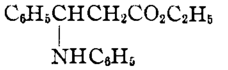
The reaction between benzalaniline and acetic anhydride produces N-(α-acetoxybenzyl)-acetanilide. The reaction of this substance with ethanol yields N-(α-ethoxybenzyl)-acetanilide. The structures of the two substances are proved by their chemical properties and by their infrared absorption spectra. The formation of ethyl cinnamate from the benzalaniline-acetic anhydride addition product in the presence of ethanolic sodium ethoxide occurs through alcoholysis to ethyl acetate, benzaldehyde and acetanilide, followed by a Claisen reaction of the benzaldehyde and ethyl acetate under the influence of the sodium ethoxide.

In earlier studies of reactions between acid anhydrides and anils, conducted in this laboratory,[1] the formulation of the product (I) from benzalaniline and acetic anhydride proposed by Ekeley[2] was considered to be entirely satisfactory. This structure (I) recently has been questioned and an entirely different alternative (structure II) has been suggested.[3] Since the proposal of the new structure was based largely upon the reactions of the addition product with ethanol and with ethanolic sodium ethoxide, the behavior of the compound toward these reagents has been reinvestigated.




$$\underset{\displaystyle NHC_6H_5}{C_6H_5CH}CH_2COOCOCH_3$$

II


$$\underset{\displaystyle NHC_6H_5}{C_6H_5CH}CH_2CO_2C_2H_5$$

V

A substance of structure I might be expected to react with ethanol by alcoholysis, yielding the unstable hydroxyamide (III) which resembles a hemiacetal. In a weakly acidic medium III might react further to give the acetal-like ether (IV). The addition product (I) is readily hydrolyzed by water, and samples which have been exposed to the atmosphere have the odor of acetic acid, which then may be present in sufficient amount to catalyze the etherification (III→IV). However, if a base were added to the ethanolic solution, the etherification should not occur and III would be expected to decompose to benzaldehyde and acetanilide.

A sample of the addition product (I) was dissolved in absolute ethanol and a few drops of a sodium ethoxide solution, sufficient to make the solution alkaline to phenolphthalein, were added. The resulting solution was distilled at room temperature, under reduced pressure and with the addition of absolute ethanol as required to keep the volume approximately constant. The distillate contained ethyl acetate, the presence of which was indicated by the odor and by a positive ester[4] test. Concentration of the residue gave benzaldehyde and acetanilide.

The addition product (I) is reported[3] to yield ethyl cinnamate in yields up to 45% when allowed to stand in the presence of two equivalents of sodium ethoxide in ethanol. The observations reported above suggest that this ester arises from the Claisen[5] reaction of benzaldehyde and ethyl acetate. To test this possibility, a mixture of equimolar amounts of benzaldehyde and ethyl acetate in absolute ethanol containing two equivalents of sodium ethoxide was allowed to stand for sixteen hours at room temperature. Presumably this reaction mixture differs from that made from the addition product and ethanolic sodium ethoxide only in that it does not contain acetanilide. The mixture was treated as described,[3] and cinnamic acid was obtained in 36% yield. Accordingly, the formation of cinnamic acid is readily explicable on the basis of formula I.

A sample of the addition product was converted to the ether (IV) by heating with ethanol.[3] When the product was heated with 1% hydrochloric acid in an apparatus arranged for steam distillation, it was converted rapidly and nearly quantitatively to benzaldehyde and acetanilide. The reduction of the substance with sodium and ethanol gave benzylaniline as the only isolable product. The course of the reduction, the sensitivity to dilute acid and the stability to alkaline hydrolysis[3] clearly show it to have the acetal-like structure (IV), rather than the proposed[3] amino ester structure (V).

The assignment of structure I to the addition product and of structure IV to the material obtained from it by alcoholysis might have been made on the basis of infrared absorption alone.

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[1] H. R. Snyder, R. H. Levin and P. F. Wiley, This Journal, **60**, 2025 (1938).

[2] J. B. Ekeley, M. C. Swisher and C. C. Johnson, *Gazz. chim. ital.*, **62**, 81 (1932).

[3] H. S. Angel and A. R. Day, This Journal, **72**, 3874 (1950).

[4] D. Davidson, *J. Chem. Ed.*, **17**, 81 (1940). This test depends upon the reaction of an ester with hydroxylamine to give a hydroxamic acid, which is detected with ferric chloride. Since the solution being tested here may have contained benzaldehyde, the color produced was compared to the colors observed when ethanolic solutions of ethyl acetate and benzaldehyde were employed. The color in the test on the distillate closely resembled that from ethyl acetate and was quite dissimilar to that from benzaldehyde. The ethanol employed gave no color in a blank determination.

[5] In Claisen's method metallic sodium was employed as the condensing agent and ethyl acetate was used in excess [L. Claisen, *Ber.*, **23**, 977 (1890)].

The spectrum of the addition product (I), determined in chloroform solution, shows a strong absorption band at 1745 cm.$^{-1}$ (ester carbonyl) and another at 1671 cm.$^{-1}$ (disubstituted amide carbonyl); there is no absorption in the regions of —OH and >NH groups and of anhydride carbonyl groups. Similarly, the spectrum of the ether (IV), determined in chloroform solution, shows an absorption band at 1650 cm.$^{-1}$ (disubstituted amide carbonyl) and lacks absorption in the —OH and >NH region.[6]

The addition product I may be regarded as a derivative of benzaldehyde diacetate, one of the oxygen atoms being replaced by a phenylimino group. A substance of structure II, containing a reactive secondary amine group and a reactive acid anhydride linkage, could not be expected to exist; such a substance undoubtedly would change extremely rapidly to the acetylamino acid. The addition product actually is quite stable thermally. It melts at 131–132° with no apparent decomposition; temperatures above 200° are required for its pyrolysis,[3] which proceeds with the regeneration of benzalaniline and acetic anhydride rather than with the formation of an amide.

Experimental

N-(α-Acetoxybenzyl)-acetanilide.—(I) was prepared as previously described.[1] Its reaction with ethanol (to give **N-(α-ethoxybenzyl)-acetanilide**, IV) was effected by the procedure of Angel and Day.[3,7]

Base-catalyzed Ethanolysis of N-(α-Acetoxybenzyl)-acetanilide.—A solution of 5 g. of the addition product in 50 ml. of absolute ethanol was prepared in a three-necked flask fitted with an ebulliator tube, a dropping funnel and a condenser set for distillation. A few drops of phenolphthalein solution and a few drops of a solution of sodium ethoxide (prepared from 0.5 g. of sodium and 19 ml. of absolute ethanol) were added. The mixture was allowed to distil at 40 mm. pressure for 3 hours, during which time the flask was kept in a bath at 25–30°. During the distillation absolute ethanol was added from time to time to maintain the volume, and a few more drops of the sodium ethoxide solution were added as needed to keep the indicator colored; less than 1 ml. of the sodium ethoxide solution was used. At the end of the three-hour period the solution in the distilling flask was evaporated to dryness, yielding a semi-solid residue. The residue was extracted with carbon tetrachloride, leaving undissolved 1.61 g. (67.4%) of acetanilide melting at 111–113° without recrystallization. As the carbon tetrachloride extract was concentrated, small additional amounts of acetanilide separated and were removed by two filtrations during the concentration. The yellow oily residue of benzaldehyde, weight 0.6 g. (32%), was identified by conversion to the phenylhydrazone (m.p. 154–155.5°). The distillate collected during the first part of the experiment had the odor of ethyl acetate and gave a positive ester test.[4]

Preparation of Cinnamic Acid from Benzaldehyde, Ethyl Acetate and Sodium Ethoxide.—A mixture of 22.8 g. (0.216 mole) of benzaldehyde, 19 g. (0.216 mole) of ethyl acetate and a solution of sodium ethoxide prepared from 10 g. (0.432 atom) of sodium and about 150 ml. of absolute ethanol was allowed to stand at room temperature for 16 hours, during which time it set to a red gel. The mixture was worked up as described[3] for the reaction of I with sodium ethoxide in ethanol. The crude cinnamic acid, weight 11.5 g. (36%), melted at 117–125°; recrystallization from water raised the melting point to 132.5–133.5°, alone or mixed with known cinnamic acid.

Acid Hydrolysis of N-(α-Ethoxybenzyl)-acetanilide.—One gram of IV was mixed with 20 ml. of 1% hydrochloric acid in a distilling flask fitted with an addition funnel. The mixture was boiled over a flame, and water was added from the funnel to keep the volume approximately constant. Benzaldehyde and water distilled immediately; after about 20 minutes the generation of benzaldehyde had subsided. The addition of phenylhydrazine to the distillate produced benzaldehyde phenylhydrazone (m.p. 156–157°) in quantitative yield. Cooling of the dilute acid solution in the distilling flask caused the separation of acetanilide (m.p. 113–114°) in quantitative yield.

Reduction of N-(α-Ethoxybenzyl)-acetanilide.—Five grams of clean sodium was added in small portions to a solution of 6 g. of IV in 125 ml. of absolute ethanol. The heat of reaction caused the solution to reflux. After the dissolution of the last of the sodium the mixture was concentrated by the distillation of about 50 ml. of alcohol and the residue was poured into about 150 ml. of water. The aqueous mixture was acidified with concentrated hydrochloric acid, decolorized, made alkaline and extracted with ether. About 2 ml. of a crude base was obtained by removal of the ether. Portions of this oil were treated with benzenesulfonyl chloride and *p*-toluenesulfonyl chloride to give, respectively, the benzenesulfonyl derivative (m.p. 117–118°) and the *p*-toluenesulfonyl derivative (m.p. and mixed m.p., 136–137°) of N-benzylaniline. The loss of acyl groups from nitrogen during the sodium-ethanol reduction of amides had been observed previously.[8]

URBANA, ILL.

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[6] The authors are indebted to Miss Elizabeth M. Petersen for the determination and interpretation of the spectra.

[7] Because the previously reported analysis (ref. 3) of this compound contained errors, this sample was submitted for analysis; *anal.* calcd. for $C_{17}H_{19}NO_2$: C, 75.81; H, 7.11; found: C, 75.75; H, 7.12. The authors are indebted to Miss Jean Fortney for this analysis.

[8] L. Bouveault and G. Blanc, *Compt. rend.*, **138**, 148 (1904).