Preliminary Experiments.—These were carried out using aniline and acetaldehyde with a variety of reduction and condensation catalysts. The results are summarized in Table I.

The products were identified by their physical properties and picrates.

Alkylanilines.—Six alkylanilines were prepared using the procedure developed in preliminary experiment 6. In Table II are summarized the compounds prepared, the yields, and the method of identification. In the case of the first four alkylanilines up to 10% of the tertiary amines were produced, but no tertiary amines were found in the case of N,*n*-heptylaniline and N-benzylaniline. The reduction mixture always contained some aniline indicating the equation given above is reversible. This probably accounts for the fact that the yields range from 47 to 65%.

Summary

A procedure has been developed for the reductive alkylation of primary aromatic amines, using aldehydes in the presence of Raney nickel, hydrogen, and sodium acetate. By this method six alkylanilines have been synthesized in 47 to 65% yields.

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

The Reaction of Acid Anhydrides with Anils

BY H. R. SNYDER, R. H. LEVIN AND P. F. WILEY

Conjugated systems of the type —CH=N—N=CH— have not been shown to undergo the Diels–Alder condensation, but observations have been reported[1,2] which suggest that this type of reaction might be brought about under proper conditions. A study of the reaction between benzalazine and maleic anhydride was undertaken to test this idea. Heterocyclic compounds were not isolated, but the study has revealed certain facts which are of interest in connection with the general question of the reaction between acid anhydrides and anils.

When a solution of benzalazine and maleic anhydride in ordinary ether was refluxed, benzalmaleinhydrazine (I) and benzaldehyde were slowly formed. The use of ether containing dissolved water resulted in more rapid formation of the same products. With anhydrous ether solutions only a trace of benzalmaleinhydrazine was produced. The reaction therefore appears due to hydrolysis of benzalazine followed by reaction with maleic anhydride.

$$\begin{aligned} \text{(A)}\ & C_6H_5CH{=}N{-}N{=}CH{-}C_6H_5 + H_2O \rightleftarrows \\ & C_6H_5CH{=}N{-}NH{-}CH(OH)C_6H_5 \rightleftarrows \\ & C_6H_5CHO + C_6H_5CH{=}N{-}NH_2 \xrightarrow{C_4H_2O_3} \\ & C_6H_5CH{=}N{-}NHCOCH{=}CH{-}CO_2H \\ & \text{(I)} \end{aligned}$$

Ekeley and Lefforge[3] recently reported the displacement of one or both of the benzal groups of benzalazine by treatment with acetic anhydride. By analogy with the previous interpretation of the reaction of acetic anhydride with anils,[4] they assumed the initial reaction to be the addition of acetic anhydride yielding $C_6H_5CH{=}NN(COCH_3)CH(C_6H_5)OCOCH_3$ (II). La Parola[5] used this mechanism to account for the reaction of maleic anhydride with anils in the presence of water. In the present investigation it has been found that the rate of formation of the supposed addition product from benzalaniline and acetic anhydride is considerably increased when small amounts of acetic acid are added. The primary reaction, contrary to the assumption of Ekeley and Lefforge, is therefore addition of acetic acid. In the second step a molecule of acetic acid is liberated and may renew the cycle (B).

$$\begin{aligned} \text{(B)}\ & C_6H_5CH{=}N{-}C_6H_5 + CH_3COOH \rightleftarrows \\ & C_6H_5CH(OCOCH_3)NHC_6H_5\ \text{(III)} \xrightarrow{(CH_3CO)_2O} \\ & C_6H_5CH(OCOCH_3)N(COCH_3)C_6H_5\ \text{(IV)} + \\ & CH_3COOH \end{aligned}$$

Compounds formed by addition of acetic acid and thioacetic acid to anils have been reported.[6–8] These substances have been formulated as containing the groupings $—N(COCH_3)CH(OH)—$ and $—N(COCH_3)CH(SH)—$. The cyclization of benzalanthranilic acid, discussed later in this report, indicates the alternate mode of addition (B).

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[1] Wagner–Jauregg obtained small amounts of a crystalline substance thought to be a *bis*-pyrazolidine by refluxing a benzene solution of maleic anhydride and benzalazine [*Ber.*, **63**, 3219 (1930)].

[2] W. W. Moyer observed the formation of an apparently neutral solid by heating a mixture of benzalazine and maleic anhydride to the boiling point (private communication).

[3] Ekeley and Lefforge, THIS JOURNAL, **58**, 562 (1936).

[4] Ekeley, *et al.*, *ibid.*, **34**, 161 (1912); **35**, 282 (1913); **36**, 603 (1914); **37**, 582 (1915); **44**, 1756 (1922); *Gazz. chim. ital.*, **62**, 81 (1932).

[5] La Parola, *ibid.*, **64**, 919 (1934).

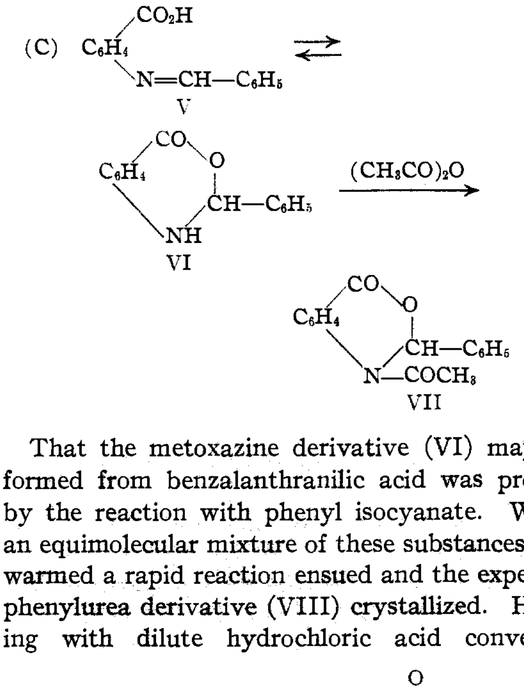
[6] Von Auwers, *Ber.*, **50**, 1599 (1917).

[7] Eibner, *ibid.*, **34**, 659 (1901).

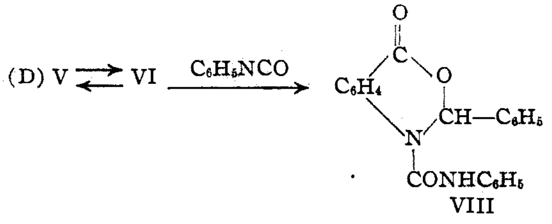
[8] Galatis. *ibid.*, **66**, 1774 (1933).

Preliminary experiments indicate that a similar addition of acetic acid to the double bond in benzalazine does not occur to the same extent as in the case of benzalaniline. Thus we have so far been unable to obtain the compound (II) from benzalazine and acetic anhydride even when acetic acid was added to the mixture. However, addition of water to such a mixture brought about rapid reaction, with the production of *sym*-diacetylhydrazine and benzalacetylhydrazine in good yields. It is indicated, therefore, that the reaction observed by Ekeley and Lefforge was due to atmospheric moisture.

The behavior of benzalanthranilic acid is of particular interest. When this compound is heated with acetic anhydride the metoxazine derivative (VII) is formed.[4] The production of this substance might be accounted for on the basis of initial addition of acetic anhydride[4] or of acetic acid as discussed above. However, *intra*molecular addition of carboxyl group to the double bond might occcur yielding the oxazine VI which would be converted to VII by acetic anhydride.



That the metoxazine derivative (VI) may be formed from benzalanthranilic acid was proved by the reaction with phenyl isocyanate. When an equimolecular mixture of these substances was warmed a rapid reaction ensued and the expected phenylurea derivative (VIII) crystallized. Heating with dilute hydrochloric acid converted VIII into benzaldehyde and N-phenylcarbamylanthranilic acid.



Confirmation of the existence of the cyclic form of benzalanthranilic acid has been obtained by Rodebush, Buswell and Roy[9] in this Laboratory from measurement of the infrared absorption. The absorption curve of a solution of the substance in carbon tetrachloride indicated the presence of both —COOH and $>$N—H groups.

The reaction of benzalanthranilic acid with acetic anhydride therefore involves ring closure followed by acetylation (C). On the basis of this mechanism it might be expected that maleic anhydride, succinic anhydride or phthalic anhydride would react with benzalanthranilic acid under anhydrous conditions. However, attempts to induce such reactions under conditions similar to those employed with acetic anhydride have been unsuccessful, both in this work and that of La Parola.[5]

The production of the oxazoline observed by Galatis[8] in the reaction between *o*-benzalaminophenol and acetic anhydride may be explained on the basis of a similar cyclization.[10] The infrared absorption curve of *o*-benzalaminophenol in carbon tetrachloride solution at room temperature shows that under these conditions the compound exists entirely as the cyclic form.[9]

Experimental

Benzalmaleinhydrazine.—To 75 cc. of ether saturated with water in a glass-stoppered flask were added 5.2 g. of benzalazine and 2.5 g. of maleic anhydride. After four days the benzalmaleinhydrazine, 4.2 g. or 78% of the theoretical, was collected and washed with ether. This substance is almost insoluble in the common solvents. After purification from acetonitrile it melted at 183°.

Anal. Calcd. for $C_{11}H_{10}O_3N_2$: C, 60.55; H, 4.58; N, 12.84; neut. equiv., 218. Found: C, 60.11; H, 4.88; N, 13.06; neut. equiv., 221.

Extraction of the ethereal mother liquor with sodium bisulfite solution, followed by regeneration of benzaldehyde and treatment with phenylhydrazine gave 2.7 g. or 55% of benzalphenylhydrazine; m. p. 156–157°. Similar treatment of an ether solution of benzalazine gave no benzalphenylhydrazine.

In a parallel experiment in which no water was added to the ether employed as the solvent a very small amount, estimated as less than 0.05 g., of benzalmaleinhydrazine, was formed.

Degradation of Benzalmaleinhydrazine.—A mixture of 0.805 g. of benzalmaleinhydrazine and 150 cc. of water was heated to reflux for two hours. On cooling benzalazine

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[9] Rodebush, Buswell and Roy, unpublished work.

[10] Cyclization of a corresponding thiophenol derivative has been demonstrated by Lankelma, THIS JOURNAL, 53, 2654 (1931).

separated and was collected. The filtrate was diluted to 250 cc. in a volumetric flask. A 50-cc. portion required 16.2 cc. of 0.0502 N sodium hydroxide for neutralization to phenolphthalein. The neutralized solution was shaken with 2 cc. of benzaldehyde, causing the formation of more benzalazine. The solution became acid and required an additional 16.2 cc. of the alkali for neutralization. These values are in accordance with the equations below.

$$\begin{aligned}&2C_6H_5CH{=}N{-}NHCOCH{=}CHCO_2H + H_2O \longrightarrow \\ &\quad C_4H_4O_4(\text{maleic acid}) + C_6H_5CH{=}N{-}N{=}CHC_6H_5 \\ &\qquad + NH_2NH_2{\cdot}C_4H_4O_4 \qquad (1)\end{aligned}$$

$$\begin{aligned}&NH_2NH_2{\cdot}C_4H_4O_4 + 2C_6H_5CHO \longrightarrow \\ &\qquad C_6H_5CH{=}N{-}N{=}CHC_6H_5 + C_4H_4O_4 \qquad (2)\end{aligned}$$

Catalysis of the Reaction between Benzalaniline and Acetic Anhydride by Acetic Acid.—In each of two 25-cc. flasks were placed 4.5 g. of benzalaniline and 2.5 cc. of pure acetic anhydride. To one mixture was added 0.5 cc. of glacial acetic acid. The flasks were closed with corks and allowed to stand at 55–65° for eighteen hours. They were then stored at +5° in a refrigerator overnight. The reaction mixture containing acetic acid was allowed to come to room temperature and was filtered. The solid was washed with two 5-cc. portions of cold ether. The weight of the supposed addition compound (IV) was 5.0 g.; m. p. 131–132°. An attempt to recover unchanged benzalaniline from the filtrate failed. Similar treatment of the reaction mixture to which acetic acid was not added gave 1.8 g. of IV. From the mother liquor there was recovered 1.6 g. of impure benzalaniline.

The Reaction of Benzalazine with Acetic Anhydride and Water.—Attempts to prepare the addition compound (II) from benzalazine and acetic anhydride by the method used with benzalaniline failed even when the reaction period was seven days.

A mixture of 10.4 g. of benzalazine and 15.3 g. of acetic anhydride was stirred over the steam-bath and 2.5 cc. of water was added in one portion. Heating and stirring were continued for thirty minutes. From the mixture, by a modification of the procedure of Ekeley and Lefforge,[3] there was obtained 2.0 g., 34% of the theoretical, of *sym*-diacetylhydrazine and 3.0 g., 37% of the theoretical, of benzalacetylhydrazine.

Benzalanthranilic Acid and Phenyl Isocyanate.—A mixture of 5.6 g. of benzalanthranilic acid and 3.0 g. of phenyl isocyanate, protected by a calcium chloride tube, was warmed. A reaction occurred and most of the material separated as transparent crystals. The mixture was cooled and washed with about 50 cc. of benzene. The yield of crude material (VIII) was quantitative. After purification from toluene or chloroform it melted at 171°.

Anal. Calcd. for $C_{21}H_{16}O_3N_2$: N, 8.14. Found: N, 8.12.

A mixture of 0.2 g. of the oxazine (VIII), 1 cc. of concentrated hydrochloric acid and 5 cc. of water was heated to the boiling point for about five minutes. The odor of benzaldehyde was clearly evident. The insoluble solid material was separated and shaken with 5 cc. of 5% sodium hydroxide solution. Acidification of the filtered extract gave N-phenylcarbamylanthranilic acid, m. p. 180–181°.

Benzalanthranilic Acid and Maleic, Succinic and Phthalic Anhydrides.—Anhydrous equimolecular mixtures of benzalanthranilic acid and one of these anhydrides heated on the steam-bath alone or in dioxane solution, or refluxed in benzene solution, did not react. When access of moisture was not prevented, for instance, when a benzene solution of benzalanthranilic acid, with maleic anhydride or succinic anhydride, was allowed to stand in an open beaker, an almost quantitative yield of *o*-carboxymaleanilic acid or of *o*-carboxysuccinanilic acid, respectively, was obtained as demonstrated by mixed melting points made with authentic samples. The mother liquor in each case smelt strongly of benzaldehyde.

Summary

In anhydrous ether solutions benzalazine and maleic anhydride do not react. If water is present the benzalazine undergoes hydrolysis, followed by reaction with maleic anhydride to form benzaldehyde and benzalmaleinhydrazine.

The reaction between benzalaniline and acetic anhydride is catalyzed by acetic acid.

Benzalanthranilic acid undergoes cyclization by addition of the carboxyl group to the nitrogen–carbon double bond. The cyclic form reacts with phenyl isocyanate.

Certain reactions previously formulated as *direct* addition of acetic anhydride to the nitrogen–carbon double bond are better interpreted as involving (1) addition of water or carboxylic acid to the double bond followed by (2) acetylation by acetic anhydride.

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