TABLE V

RATE OF HYDROLYSIS OF ACETONE SEMICARBAZONE AT 25°, AS A FUNCTION OF ACETIC ACID CONCENTRATION, *P*H 4.60

[HA]	*k*	No. of detns.	Mean deviation, %
0.0550	0.0672	5	1.6
.1375	.124	3	3.2
.311	.226	5	3.1
.535	.379	2	0.8

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Summary

1. Evidence is found that semicarbazide acetate, a salt of the ammonium type, is incompletely dissociated in aqueous solution, from the dependence of the rate of semicarbazone formation on acetic acid concentration.

2. The dissociation constant of this salt into molecules has the approximate value 0.12, both at 25 and at 0°.

3. Consequences of this new equilibrium effect, for semicarbazone preparation and for the mechanism of the reaction are discussed.

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The Betti Condensation. Effect of Substituents on the Stability and Optical Rotation of the Resulting Amines

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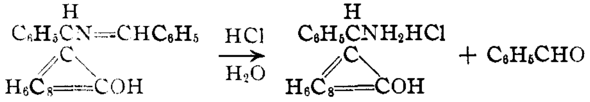
In 1900 Mario Betti first reported the condensation of benzaldehyde, ammonia and β-naphthol to give a Schiff base, I. On hydrolysis with hydrochloric acid phenyl-β-naphtholaminomethane hydrochloride and benzaldehyde resulted,[1] II.



I II

The reaction was extended by the use of primary amines instead of ammonia, and quite recently Littman and Brode[2] have further extended the application to secondary amines.

Betti[3] in a study of optical rotation has condensed his amine with sub-

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(1) Betti, *Gazz. chim. ital.*, **30**, II, 310 (1900); **31**, I, 386 (1901).

(2) Littman and Brode, THIS JOURNAL, **52**, 1655 (1930).

(3) Betti, *Gazz. chim. ital.*, **36**, II, 392 (1906); **37**, I, 63 (1907); **46**, I, 200 (1916); **50**, II, 276 (1920).

stituted aldehydes and measured the rotation of the resulting Schiff base, but, in so far as we have been able to find, no one has investigated the use of substituted benzaldehydes in the original condensation with ammonia and β-naphthol.

This investigation was undertaken to test the general applicability of Betti's condensation. In the present paper the condensation of ortho-, meta- and para-chlorobenzaldehydes with ammonia and β-naphthol is discussed together with a preliminary report on the use of nitrobenzaldehydes.

Betti's amine is readily decomposed, especially in alkaline solution, to give benzaldehyde and β-naphthol. The benzaldehyde thus liberated combines with a molecule of the amine to form the original Schiff base. It was hoped that by the use of substituted benzaldehydes more stable amines would result. Just the opposite has, however, proved to be the case.

The reaction of the three monochlorobenzaldehydes followed closely that of benzaldehyde but the resulting amines were less stable than the amine from the unsubstituted aldehyde. The order of stability was: H > *m*-Cl > *o*-Cl > *p*-Cl.

The chloro substituted amines were also much more difficult to separate into their optical antipodes. Tartaric acid, which effects a satisfactory resolution of the unsubstituted amine, gives with the chloro compounds an insoluble racemic salt. The ortho and meta compounds were finally resolved with the aid of *l*-malic acid but the para resisted all efforts at resolution. The order of optical activity was: *o*-Cl > *m*-Cl > H > *p*-Cl(?).

The *p*-chloro compound could not be resolved. There are two probable explanations: the most usual of which is that the right conditions were not obtained; the other, which we favor, is that the instability of this amine precluded its resolution. While satisfactory resolution of the dextro form of the ortho and meta chloro compounds was possible, it was extremely difficult to obtain the more soluble levo antipodes in a state of purity. Even evaporation of an ether solution at room temperature caused some decomposition and racemization of the amines.

When the nitrobenzaldehydes were mixed with β-naphthol and alcoholic ammonia they reacted to the extent of 90% or more with the ammonia to give the nitrohydrobenzamide. In the case of the *m*-nitrobenzaldehyde in addition to the hydrobenzamide a small amount of a compound melting at 198° was recovered. This is now under investigation and will be the subject of a subsequent paper.

Evidently as the substituents increase in negativity there is less tendency for the β-naphthol to take part in the reaction.

Experimental Part

***m*-Chlorophenyl-β-naphtholaminomethane.**—Eleven grams (1 mol equiv.) of β-naphthol was dissolved in 25 cc. of 95% alcohol to which 20 g. (2 mol equiv.) of *m*-

chlorobenzaldehyde was added. The flask was cooled and saturated with ammonia gas. After standing for twenty-four hours the contents had changed to an almost solid viscous substance which, when treated with a few drops of ether and stirred, changed to fine yellowish crystals. The crystals were washed six times with small portions of alcohol which left 23 g. (82%) of pure white crystals melting at 109°.

Anal. Calcd. for $C_{24}H_{17}Cl_2ON$: C, 70.94; H, 4.19; Cl, 17.47; N, 3.45. Found: C, 70.53; H, 4.25; Cl, 17.30; N, 3.34.

The amine hydrochloride was prepared by steam distilling 15 g. of the condensation product suspended in 20 cc. of 6 *N* hydrochloric acid; 11.5 g. (96%) of the *m*-chlorophenyl-β-naphtholaminomethane hydrochloride was obtained from the acid solution; decomposition temperature, 220 to 230°.

Anal. Calcd. for $C_{17}H_{15}ONCl_2$: Cl, 22.17. Found: Cl, 22.40.

To prepare the free racemic amine 10 g. of the amine hydrochloride was treated in an ice mixture with a 25% solution of potassium hydroxide. From 3 to 5 cc. of ether was added and stirred until the amine formed a flocculent precipitate which was immediately filtered and washed free from alkali with water; yield 7 g. (77%) of *m*-chloro-β-naphtholaminomethane melting at 124–125°.

Anal. Calcd. for $C_{17}H_{14}ONCl$: C, 71.94; H, 4.94; Cl, 12.51; N, 4.94. Found: C, 72.12; H, 4.85; Cl, 12.68; N, 5.23.

***o*-Chlorophenyl-β-naphtholaminomethane.**—The condensation product was prepared as described for the meta compound; m. p. 165–167°. After recrystallizing the material once from chloroform and once from benzene it melted rather sharply at 173° (uncorr.).

Anal. Calcd. for $C_{24}H_{17}Cl_2ON$: C, 70.94; H, 4.19; Cl, 17.47. Found: C, 70.87; H, 4.42; Cl, 17.69.

***o*-Chlorophenyl-β-naphtholaminomethane hydrochloride** was prepared by steam distilling 30 g. of the original condensation product with hydrochloric acid as described for the *m*-chloro derivative; 21 g. (88%) of the amine hydrochloride was obtained; decomp. temp. 185 to 190°. Analysis was made from a sample recrystallized twice from hydrochloric acid solution.

Anal. Calcd. for $C_{17}H_{15}ONCl_2$: C, 63.77; H, 4.69; Cl, 22.17. Found: C, 63.93; H, 4.79; Cl, 21.79.

The free amine was prepared as described for the meta derivative. Five and five-tenths g. (62%) of a cream colored amine was obtained, m. p. 129–130°. After recrystallization twice from ether and once from acetone it was almost pure white and melted at 133–134°.

Anal. Calcd. for $C_{17}H_{14}ONCl$: C, 71.97; H, 4.94; Cl, 12.51. Found: C, 72.24; H, 5.22; Cl, 12.76.

***p*-Chlorophenyl-β-naphtholaminomethane.**—The condensation product was prepared as described for the meta compound; m. p. 150°.

Anal. Calcd. for $C_{24}H_{17}Cl_2ON$: C, 70.94; H, 4.19; Cl, 17.47. Found: C, 71.64; H, 4.27; Cl, 17.33.

Six grams of the condensation product was subjected to steam distillation in a suspension of hydrochloric acid; 4.3 g. (91%) of the whitish flaky amine hydrochloride was obtained; decomp. temp. 190 to 195°.

Anal. Calcd. for $C_{17}H_{15}Cl_2ON$: Cl, 22.17. Found: Cl, 22.40.

The free *p*-chloro amine was prepared from the hydrochloride as previously described. The ether extract yielded 2.5 g. (80%) of the white crystalline amine, m. p. 120°.

Anal. Calcd. for $C_{17}H_{14}ClON$: Cl, 12.51. Found: Cl, 12.94.

Resolution of the Racemic Amines

The *m*-chlorophenyl-β-naphtholaminomethane was resolved into its optically active antipodes by treating 5.3 g. (1 mol) of the amine in 130 cc. 95% alcohol with 2.5 g. (1 mol) of *l*-malic acid; 2.7 g. of the salt was obtained. The liquid was further evaporated by an air current and agitated until crystals began to separate which yielded 2.8 g. of the more soluble salt. The salt obtained in the first fraction was hydrolyzed and about 2 g. of the *d*-amine was filtered and washed free of alkali with distilled water; m. p. not sharp at 126°.

In a 1-dm. tube 0.0667 g. of the dry amine in 10 cc. of ethyl ether gave α_D +0.53°, α^{25}_D +79.5°.

The *l*-amine was obtained by hydrolyzing the second fraction to yield 2.1 g. of the *l*-amine; m. p. 122°. This material gave a rotation of −0.37° with 0.0667 g. of the amine dissolved in 10 cc. of ether at room temperature, using a 1-dm. tube, $[\alpha]^{25}_D$ −55.5°.

The last crystalline salt fraction from the above yielded the *l*-amine on hydrolysis with the same specific rotation as that obtained from the salt of the second fraction. An attempt was made to increase the specific rotation of the *l*-amine above −55.5°, first by recrystallizing the salt before hydrolysis, and finally by use of Ingersoll's method,[4] but a more complete resolution was never effected.

Resolution of the *o*-chlorophenyl-β-naphtholaminomethane was carried out as described for the meta compound. Hydrolysis of the salt obtained in the first fraction was accomplished as described above. The optical rotation of the ether solution taken in a 1-dm. tube was +0.65°, and 10 cc. of the solution contained 0.0722 g. of the amine, α^{25}_D +89.8°.

Hydrolysis and extraction of the 0.67 g. of salt from the second fraction was accomplished as described previously: 0.1207 g. in 10 cc. of ether in a 1-dm. tube gave α_D −1.01°, $[\alpha]^{25}_D$ −83.7°.

Attempts to recrystallize the *l*-acid-*l*-base only resulted in a less active amine.

Summary

1. The Betti condensation of aromatic aldehydes, ammonia and β-naphthol has been applied to the mono-chlorobenzaldehydes.

2. Of the three resulting amines the ortho and meta compounds have been resolved into their active forms.

3. The nitrobenzaldehydes gave chiefly the corresponding hydrobenzamides.

4. Due to the instability of the chlorophenyl-β-naphtholamines and the difficulty encountered in their resolution, these bases are less useful as resolving agents than the unsubstituted amine.

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[4] Ingersoll, THIS JOURNAL, 47, 1168 (1925).