[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, OHIO STATE UNIVERSITY]

CONDENSATIONS OF SECONDARY AMINES WITH ALDEHYDES AND NAPHTHOLS[1]

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In a study of resolving agents for the preparation of optically active compounds, 1-(α-aminobenzyl)-2-naphthol[2,3] was prepared, as well as a number of substituted derivatives which will be described in a later paper. Betti in an earlier article[4] observed that secondary amines did not undergo this condensation with β-naphthol and benzaldehyde to form a compound similar to that formed by ammonia and primary amines. Betti's explanation for the condensation between β-naphthol, benzaldehyde and ammonia or a primary amine involved first the formation of a benzylidine-amine such as $C_6H_5CH{=}NR$, followed by addition between the double bond of this compound and the activated H in the α-position in β-naphthol. By such an explanation condensation with secondary amines is precluded.

In our experiments condensations with secondary amines, benzaldehyde and β-naphthol were attempted and definite condensation products were isolated, particularly with dimethylamine, diethylamine and piperidine. These compounds are similar to the condensation products of the mono-amines and ammonia and gave correct analyses for 1-(α-dimethylaminobenzyl)-2-naphthol, 1-(α-diethylaminobenzyl)-2-naphthol, and 1-(α-1-piperidylbenzyl)-2-naphthol.

Since the isolation of these compounds Dilthey and Stallman[5] have reported on the addition of aldehydes and secondary amines to active methylene compounds of the dibenzyl ketone type, which is undoubtedly capable of enolization into an enol form, $—CH{=}C(OH)—$, and which would be equivalent to the α- and β-groups in β-naphthol. This latter work confirms the possibility of the condensation of secondary amines with aldehydes and active methylene groups and necessitates a revision in the theory of Betti's condensations, which should also fit the theory of Dilthey and Stallman's reaction, as well as similar condensations such as Dimroth's[6] condensation of amides and phenols, Knoevenagel's reaction,[7] Claisen's acid condensation, Perkin's synthesis, etc. The same

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[1] An abstract of a portion of a thesis submitted by Joseph B. Littman in partial fulfilment of the requirements for the degree of Doctor of Philosophy at The Ohio State University.

[2] Betti, *Gazz. chim. ital.*, **31**, I, 385 (1901).

[3] "Organic Syntheses," John Wiley and Sons, Inc., New York, 1929, Vol. IX, p. 60.

[4] Betti, *Gazz. chim. ital.*, **30**, II, 310 (1900).

[5] Dilthey and Stallman, *Ber.*, **62**, 1603 (1929).

[6] Dimroth, *ibid.*, **35**, 995 (1902).

[7] Knoevenagel, *ibid.*, **37**, 4446 (1904).

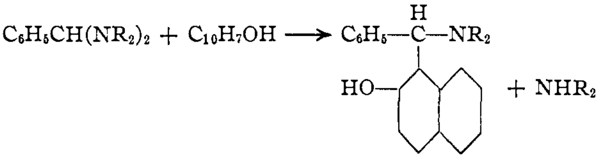
mechanism should hold in all cases where similar compounds are formed from similar reagents.

Dilthey and Stallman confirmed the structure of their condensation compound by treating $(C_6H_5CH_2)_2CO$ with benzylidene dipiperidine, with which they obtained the same compound as before, together with an equivalent amount of piperidine. Using this same reagent with β-naphthol, the condensation took place with the formation of the same compound that was obtained by the direct interaction of the three original materials. While this does not confirm the existence of benzylidene dipiperidine as an intermediate in the condensation, it furnishes additional data on the mechanism of the reaction.

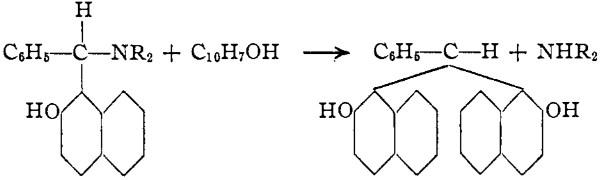
The reaction of the amine with the aldehyde is admitted by Betti and others as the first step in the condensation, and after this addition or dehydration, the second condensation or addition of the naphthol, phenol or active methylene takes place.

In the case of secondary amines no such condensation with benzaldehyde can take place so as to form an imine type of condensation product; rather, a benzylidinediamine or hydroxyamine is formed which splits out a molecular equivalent of amine or water on its condensation with the active methylene.

$$C_6H_5CHO + 2HNR_2 \longrightarrow C_6H_5CH(NR_2)_2 + H_2O \qquad (1)$$



(2)



(3)

The entire condensation is, of course, comparable with the Knoevenagel reaction, the Claisen condensation or other reactions between a carbonyl and active methylene.[8] Knoevenagel showed that amines catalyzed his condensations and he actually carried out the reaction with benzaldehyde, piperidine, and acetoacetic ester as his active methylene compound and explained his reaction in two steps, as above, first, the formation of the benzylidine dipiperidine compound and then, second, its reaction with the active hydrogens in acetoacetic ester to yield $C_6H_5CH = C{<}\genfrac{}{}{0pt}{}{COCH_3}{COOC_2H_5}$. He did not obtain or isolate the intermediate mono secondary amino

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[8] Knoevenagel, *Ann.*, **288**, 321 (1895).

compound. Dilthey and Stallman have in their work carried out the reaction in a way so as to obtain the obvious intermediate product, which must undoubtedly yield on further heating or acid treatment the final product analogous to that obtained by Knoevenagel. Applying the same theory to the naphthol condensation, it is impossible to obtain a compound of the ethylene type since there is only one replaceable H in the α-position in β-naphthol, but with an excess of β-naphthol one should obtain the di-β-naphthol benzal compound, which can be made by direct interaction of benzaldehyde and β-naphthol,[9] and this was actually obtained by heating the dimethyl condensation compound with an excess of β-naphthol in benzene.

In the case of the piperidine condensation product, the melting point of the β-naphthol condensation product was practically the same as that of the above compound, but the latter contained no nitrogen and the mixed melting point of the two gave a depression of nearly 25°.

It is apparent in the above reactions, as well as in the work of Dilthey and Stallman, that we are dealing with possible intermediate products in the more or less standard reaction between a carbonyl and active methylene. The isolation of these intermediate products is best explained on the mild activity of the active methylene groups and the use of an excess of the amine. The use of an excess of the active methylene compound (β-naphthol in our reaction) produced as in the work of Knoevenagel and others the substitution of both of the valences of the carbinol with the methylene radical.

Experimental

Preparation of 1-(α-dimethylaminobenzyl)-2-naphthol.—Ninety-six grams ($^2/_3$ mole) of β-naphthol was dissolved in a mixture of 70.6 g. ($^2/_3$ mole) of benzaldehyde and 100 cc. of 95% ethyl alcohol. Through this solution dimethylamine gas was passed, generated from 140 g. of a 33% methylamine–water solution by heating in a flask attached to a reflux condenser. The solution turned dark brown in color and became very warm. It was necessary to cool the flask with cold water. On standing for twenty-four hours in a tightly stoppered flask, fine white crystals formed which were filtered off and washed twice with small amounts of alcohol. The crude product melted at 148–160°. It was recrystallized thrice from a mixture of benzene and ligroin; m. p. 164–164.5°; yield, 130 g. or 70.7% of the theoretical. The compound is moderately soluble in benzene, slightly soluble in alcohol, and insoluble in water. When dissolved in benzene and treated with an ether solution of ferric chloride it gives an intense violet coloration. The alcohol solution gave a yellow color on heating, and became colorless on cooling.

Anal. Calcd. for $C_{19}H_{19}ON$: C, 82.3; H, 6.86; N, 5.1. Found: C, 81.83; H, 6.91; N, 5.18.

Hydrochloride of 1-(α-Dimethylaminobenzyl)-2-naphthol.—Two grams of 1-(α-dimethylaminobenzyl)-2-naphthol was suspended in 125 cc. of water to which 5 cc. of concentrated hydrochloric acid was added. On warming the solution carefully

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[9] Hewitt and Turner, *Ber.*, **34**, 202 (1901).

the compound went into solution, followed by the precipitation of the hydrochloride in very fine white crystals which were filtered off with suction, and washed a few times with water. The hydrochloride decomposed at 208–210°.

Anal. Calcd. for $C_{19}H_{20}ONCl$: Cl, 11.32. Found: Cl, 11.3%.

1-(α-1-Piperidylbenzyl)-2-naphthol.—Twenty-nine grams (0.2 mole) of β-naphthol was dissolved in a mixture of 21 g. (0.2 mole) of benzaldehyde and 25 cc. of absolute alcohol. To this solution in a small flask, 17 g. (0.2 mole) of piperidine was slowly added, the flask corked and allowed to stand for forty-eight hours. A small amount of heat was evolved. The small white crystals were filtered off and washed twice with alcohol. The crude product melted from 178 to 196°. It was recrystallized thrice from a mixture of benzene and ligroin and melted at 198–198.5°; yield, 46 g., or 72.5% of the theoretical. This compound also gives a violet coloration with ferric chloride in ether–benzene solution and also gives in hot alcohol a yellow coloration which disappears on cooling.

Anal. Calcd. for $C_{22}H_{23}ON$: C, 83.28; H, 7.25. Found: C, 83.01; H, 7.32.

Hydrochloride of 1-(α-1-Piperidylbenzyl)-2-naphthol.—Two grams of 1-(α-1-piperidylbenzyl)-2-naphthol was treated in the same manner as 1-(α-dimethylaminobenzyl)-2-naphthol. The hydrochloride separated as a fine white precipitate. It decomposed at 203–205°.

Anal. Calcd. for $C_{22}H_{24}ONCl$: Cl, 10.04. Found: Cl, 10.4.

Preparation of 1-(α-Diethylaminobenzyl)-2-naphthol.—Thirty-six grams (0.25 mole) of β-naphthol and 27 g. (0.25 mole) of benzaldehyde were dissolved in 50 cc. of absolute alcohol. To this solution 28 g. (0.25 mole + 10 g. excess) of diethylamine was added and the solution became slightly warm. Considerable difficulty was experienced in getting the compound to crystallize out. After five weeks' standing crystals started to form. They were filtered and washed with alcohol. The crude product melted at 101–106°. Recrystallization from alcohol raised the melting point to 117–118°; yield, 15.5 g., or 20.8% of the theoretical. This compound, like the other two, gives a violet coloration with ferric chloride in benzene–ether solution and also gives a yellow coloration in hot alcohol, which disappears on cooling.

Anal. Calcd. for $C_{21}H_{23}ON$: N, 4.6. Found: N, 4.64.

Preparation of 1-(α-1-Piperidylbenzyl)-2-naphthol from β-Naphthol and Benzylidine Dipiperidine.—Benzylidine dipiperidine was prepared according to the method of Laun.[10] Ten and four-tenths grams of benzylidine dipiperidine was dissolved in 75 cc. of 95% ethyl alcohol. To this solution 6 g. of β-naphthol dissolved in 15 cc. of alcohol was added. After forty-eight hours the mixture yielded 3 g. of 1-(α-1-piperidylbenzyl)-2-naphthol. The crude product melted at 195–197°. Recrystallization from a mixture of benzene and ligroin gave a melting point of 197–198°. A mixed melting point with the 1-(α-1-piperidylbenzyl)-2-naphthol did not vary from this temperature.

Preparation of Benzal-di-β-naphthol from β-Naphthol and 1-(α-Dimethylaminobenzyl)-2-naphthol.—Five and one-half grams of 1-(α-dimethylaminobenzyl)-2-naphthol and 3 g. of β-naphthol were dissolved in the minimum amount of benzene. The solution was slowly heated on a hot-plate and as the benzene evaporated dimethylamine was evolved until a sticky transparent yellow mass was obtained. The sticky substance was dissolved in hot alcohol and on cooling a white crystalline compound separated. It was triturated with warm benzene and filtered. This treatment removed the unreacted 1-(α-dimethylaminobenzyl)-2-naphthol. The compound was then recrystallized twice from alcohol and gave a melting point of 197–198°. A mixed

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[10] Laun, *Ber.*, 17, 678 (1884).

melting point with benzaldi-β-naphthol prepared according to the method of Hewitt and Turner[9] did not vary.

The dimethyl, diethyl and piperidyl derivatives are only slightly basic. They are quite stable and are not affected by light or oxidation. Further work on these compounds including attempts at their resolution is contemplated.

Summary

A study has been made of the condensation of secondary amines with benzaldehyde and β-naphthol and intermediate products in the condensation have been isolated.

It has been shown that the use of amines as catalysts in condensations of a carbonyl with an active methylene may yield first an amine or diamine followed by addition to the active methylene with the formation of a substituted amine, which on further treatment yields the free amine and the final condensation product.

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[CONTRIBUTION FROM THE CONVERSE MEMORIAL LABORATORY OF HARVARD UNIVERSITY]

POLYMERIZATION REACTIONS UNDER HIGH PRESSURE. I. SOME EXPERIMENTS WITH ISOPRENE AND BUTYRALDEHYDE

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In a preliminary paper[1] on the irreversible transformations of organic compounds under high pressure, some experiments were reported on the polymerization of isoprene and other unsaturated compounds at room temperature by the application of pressures of the order of magnitude of 9000 atmospheres. This work has been continued with the aim of discovering the factors which control the rate of polymerization under high pressures and the nature of the products formed. A great majority of the experiments were performed with isoprene since this substance polymerizes more rapidly than any other substance of this general type which is readily available; furthermore, the early observations showed that very erratic results were obtained with different samples of isoprene and we desired, if possible, to discover the catalytic substances which seemed to be responsible for the peculiar behavior. A few experiments also were performed with some other compounds and they will be discussed at the end of this communication. The pressure apparatus employed was kindly lent us by Professor Bridgman. We wish to express our appreciation of his kind coöperation, and the courtesy extended to us by the Director of the Jefferson Physical Laboratory of Harvard University in which the physical part of the experiments was actually performed. Manipulation of the

[1] P. W. Bridgman and J. B. Conant, *Proc. Nat. Acad. Sci.*, **15**, 680 (1929).