As examples, nitrogen in AgNCO displaces iodine in PI_3 to give $P(NCO)_3$[6] and nitrogen in AgNCO displaces either chlorine or sulfur in $SiCl_3(SH)$ to give $Si(NCO)_4$.[6]

In contrast, the molar volume of the whole group such as isocyanate or isothiocyanate is no criterion, since the smaller chlorine does not replace either,[6] whereas the larger isothiocyanate[9] or isocyanate[8] actually replaces chlorine. Likewise, the strength of the corresponding acids, such as hydrofluoric or isocyanic, is no criterion.

This interpretation explains the lack of interchange between $Si(NCO)_4$ and AgNCS,[6] or between $Si(NCS)_4$ and AgNCO, since nitrogen is the key atom in all cases, and will not replace itself. Moreover, it explains the 1–2% yield of $SiCl_3(SH)$ from $SiCl_4$ and H_2S at 600°,[4] in contrast to the high yield of $SiBr_3(SH)$ from $SiBr_4$ and H_2S.[4]

Obviously, this interpretation is useful in predicting the outcome of untried reactions.

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The Preparation of Ethylhydrazine by Direct Ethylation[1]

BY ROBERT D. BROWN AND ROBERT A. KEARLEY

Previous attempts to prepare monoalkylhydrazines by the direct alkylation of hydrazine have met with little success,[2,3] more highly substituted derivatives accounting for the bulk of the products. A general method proposed by Whitmore[4] has now been used successfully in this Laboratory for the preparation of ethylhydrazine from hydrazine, using ethyl sulfate as the alkylating agent, potassium hydroxide as the base, alcohol as the solvent and diluent and hydrazine in excess.[5]

Experimental

Since hydrazine and its derivatives are corrosive, an all-glass apparatus was used. An air-cooled reflux column was fitted to a 500-ml. flask by means of a ground glass joint, and a wide-mouthed piece of tubing with a stopcock in its lower end was sealed onto the side of the flask. Sealed to the top of the reflux column was a water-cooled condenser, sloping downward to a receiver.

A mixture of 35 g. of potassium hydroxide, 30 ml. of anhydrous hydrazine and 60 ml. of absolute alcohol was placed in the flask. Acid-free ethyl sulfate, 33 ml., was introduced slowly through the side arm while the mixture was cooled with an ice-bath and stirred mechanically. The reflux column and condenser were then attached and the mixture heated to a bath temperature of 165° by means of a glycerol-bath on an electric hot-plate. The distillate was a colorless liquid.

Concentrated hydrochloric acid was added cautiously to the distillate until the solution was strongly acidic, giving a precipitate of hydrazine hydrochloride which was filtered while the solution was still hot. The filtrate was then heated on a water-bath until the volume was halved, a little concentrated hydrochloric acid was added and the solution was allowed to cool. The precipitated crystals were filtered, washed with small portions of concentrated hydrochloric acid, alcohol and ether, and then placed in a vacuum desiccator over calcium chloride. A second crop of product was obtained by concentrating the wash liquids and mother liquor. The total yield of product was 21 g., a 32% yield. Carbon, hydrogen, nitrogen and chlorine analyses, as well as iodate titration[6] and alkali titration agree with the calculated values for the dihydrochloride of ethylhydrazine, $C_2H_5N_2H_3 \cdot 2HCl$.

The free base was prepared in 80% yield from the hydrochloride essentially as described by Fischer,[5] the anhydrous compound being obtained by distillation from excess barium oxide. The properties of the base are those reported by Fischer.

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[1] From a thesis submitted in June, 1949, by Robert A. Kearley to the Graduate School of the University of Alabama in partial fulfillment of the requirements for the degree of Master of Science.

[2] Wieland, "Die Hydrazine," F. Enke, Stuttgart, 1913, p. 14.

[3] Westphal, *Ber.*, **74B**, 759 (1941).

[4] Whitmore, "Organic Chemistry," D. Van Nostrand Co., New York, N. Y., 1937, p. 201.

[5] Ethylhydrazine was originally prepared from 1,3-diethylurea by Fischer, *Ann.*, **199**, 282 (1879).

[6] Kolthoff, THIS JOURNAL, **46**, 2009 (1924).

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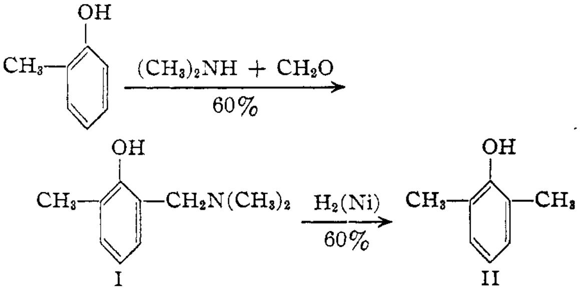
A New Synthesis of 2,6-Xylenol[1]

BY ROBERT B. CARLIN AND HAROLD P. LANDERL[2]

A practicable synthesis of 2,6-xylenol (II) was required for the preparation of a supply of 2,6-dimethylcyclohexanone. The following synthesis of II, which was suggested by the work of Caldwell and Thompson,[3] offers a considerable advantage in cost of starting materials over the commonly employed preparative method which starts with 2,6-xylidine.[4]



The hydrogenolysis of the dimethylaminomethylcresol to II demonstrates that the structure I, assigned by Décombe[5] without direct proof to the product of the first reaction represented above, is correct. Although Caldwell and Thompson showed[3] that certain phenols with available ortho positions undergo para substitution in the Mannich reaction, there was no evidence that 2-methyl-4-dimethylaminomethylphenol was present in reaction mixtures from which I was isolated.

Despite the fact that I is converted to II by

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[1] Abstracted from part of a doctor's thesis by Harold P. Landerl.

[2] Institute Graduate Fellow in Organic Chemistry, 1947–1948.

[3] Caldwell and Thompson, THIS JOURNAL, **61**, 765, 2354 (1939).

[4] *Cf.* Karrer and Leister, *Helv. chim. acta.*, **27**, 678 (1944).

[5] Décombe, *Compt. rend.*, **196**, 866 (1933).

means of essentially the same procedure which has been used for the hydrogenation of II to 2,6-dimethylcyclohexanol,[6] the conversion of I to 2,6-dimethylcyclohexanol in one operation could not be accomplished in good yield in the presence of this catalyst. Better yields of the dimethylcyclohexanol were realized from I when the intermediate II was isolated and purified before its hydrogenation was attempted.

For purposes of identification, some samples of 2,6-dimethylcyclohexanol produced from I in a single operation and some samples obtained by the hydrogenation of II were converted to their phenylurethans, all of which melted at 158°. Application of the same hydrogenation procedure to a sample of II obtained from the Shell Development Co. has been observed[6] to give a 2,6-dimethylcyclohexanol, whose phenylurethan melts at 132°. Anziani and Cornubert[7] have shown that the 132° and 158° phenylurethans are derived from stereoisomeric forms of 2,6-dimethylcyclohexanol. The foregoing observations indicate that small changes in reaction conditions, the nature of the Raney nickel catalyst and small amounts of impurities present in the xylenol may exert a profound effect upon the stereochemical course of the reaction. There appears to be no recorded evidence that mixtures of stereoisomeric modifications of 2,6-dimethylcyclohexanol ever have been formed by any of the several available preparative methods. One isomer always is produced to the exclusion of the other.[6,7,8]

Experimental

2-Methyl-6-dimethylaminomethylphenol (I).—A stirred mixture of 60 g. of *o*-cresol (Eimer and Amend, Technical) and 90 g. of 25% aqueous dimethylamine (du Pont, Technical) was kept at 15–20° while 50 g. of 30% formalin was added. The aqueous layer was saturated with sodium chloride, separated and extracted with three 60-ml. portions of ether. The ether extracts were combined with the organic layer from the reaction mixture, and the temperature of the resulting solution was maintained below 30° during extraction with two 500-ml. portions of 15% hydrochloric acid. Neutralization of the ice-cold acid extracts to *p*H 9 with 25% aqueous sodium hydroxide effected the separation from the solution of an oil. The aqueous layer was extracted with three 60-ml. portions of ether, and the extracts were combined with the oil. Removal of the ether left 54 g. (60%) of crude Mannich base (I), which gave 39 g. (44%) of distillate, b. p. 91–95° (2 mm.), n^{25}_D 1.5195. The reported b. p. is 110–112° (13 mm.).[5]

Anal. Calcd. for $C_{10}H_{15}NO$: C, 72.69; H, 9.15. Found: C, 72.95; H, 8.96.[9]

Picrate, yellow needles from methanol, m.p. 153–154°. *Anal.* Calcd. for $C_{16}H_{18}N_4O_8$: C, 48.73; H, 4.60; N, 14.21. Found: C, 48.91; H, 4.60; N, 13.78.[9]

Because distillation of crude I was always attended by the evolution of dimethylamine and the formation of resins (through intermolecular condensations of I), greater overall yields of II were realized when crude I was used without purification.

2,6-Xylenol (II).—A mixture of 54 g. of crude I and about 8 g. of Raney nickel was treated at 200° with hydrogen at 1800 lb./sq. in. pressure until one mole of hydrogen per mole of I had been consumed. A benzene solution of the reaction mixture was shaken with 15% hydrochloric acid and then with five 100-ml. portions of 15% aqueous sodium hydroxide. Acidification of the cold alkaline extract with 20% hydrochloric acid brought about the separation of the xylenol (II) as an oil, which was combined with the ether extracts of the residual aqueous solution and dried over "Drierite." Distillation of the oil remaining after removal of the ether gave 24 g. (60%) of II, b. p. 197–202°.[10] On redistillation, this crude xylenol yielded a solid condensate, m. p. 35–40°,[11] which formed an *α*-naphthylurethan, white needles, m. p. 178°,[12] from petroleum ether (b. p. 66–71°).

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[6] Carlin, This Journal, **67**, 928 (1945).

[7] Anziani and Cornubert, *Compt. rend.*, **217**, 233 (1943).

[8] Skita, *Ber.*, **56B**, 2234 (1923).

[9] These samples were prepared for analysis by Mr. Gerald W. Larson.

[10] Gattermann, *Ann.*, **357**, 327 (1907), gives the b. p. 203°.

[11] Noelting, *Ber.*, **21**, 2829 (1888), reported the m. p. 49°.

[12] Hurd and Pollack, This Journal, **58**, 181 (1936), reported the m. p. 176.5°.

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On Long Range Forces in Solution

By B. Carroll

In looking for long range forces[1] in solution we followed the procedure of trying to coat the bovine serum albumin molecule by the adsorption of simple dye anions. The effect of a proteolytic enzyme on the coated protein was then determined.

Calculations based on such data as molecular weight, diffusion coefficient, viscosity, and dielectric dispersion[2] lead to a value of about 25,000 sq. Å. for the surface area of the serum albumin molecule if a prolate ellipsoid is used as a model. Other models such as a flat disc 20 Å. thick, as suggested by spreading experiments, yield a somewhat smaller value.

Orange I was used for building up the "screen" or "blanket" on the protein molecule. The area covered by this dye molecule may be 60 to 150 sq. Å. depending on whether the dye molecule is cube-shaped, or is spread flat over the surface of the albumin molecule. If the average is taken on these two extreme values, it will be seen that some 250 dye molecules on the surface of an albumin molecule may be considered a unimolecular layer.

We found that the adsorption of (2.0×10^{-5} *M*) Orange I by bovine albumin in 0.01 *M* hydrochloric acid indicated values above 200 dye molecules per protein molecule, when the protein concentration was two parts per million or less. As the protein concentration was increased, the number of dye molecules per protein molecule dropped gradually. At an albumin concentration of 10 parts per million, the number of dye molecules per protein molecule was 110. The

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[1] Rothen, This Journal, **70**, 2732 (1948).

[2] Alexander and Johnson, "Colloid Science," Vol. I, Oxford University Press, 1949.