[CONTRIBUTION NO. 757 FROM THE DEPARTMENT OF CHEMISTRY OF INDIANA UNIVERSITY]

Solid Derivatives of Aldehydes. II. A Specific Reagent for Aldehydes: 1,2-bis(*p*-Chlorobenzylamino)ethane

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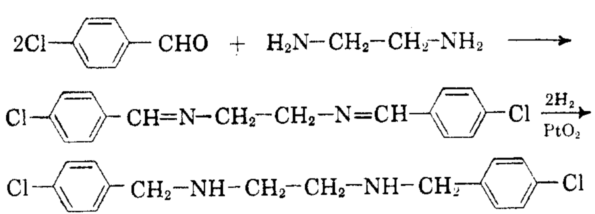
Received November 26, 1956

1,2-Bis(*p*-chlorobenzylamino)ethane, has been found to be a specific reagent for the characterization of aldehydes. This reagent, unlike the corresponding methoxy, derivative does not react with acetone. A series of 2-substituted-1,3-bis(*p*-chlorobenzyl)imidazolidines have been prepared from 1,2-bis(*p*-chlorobenzylamino)ethane and numerous aldehydes. Treatment of the imidazolidines with acid regenerates the diamine and aldehyde in nearly quantitative yields. *N,N'*-Diacetyl-1,2-bis(*p*-chlorobenzylamino)ethane has been prepared.

In an earlier publication[2] it has been shown that 1,2-bis(*p*-methoxybenzylamino)ethane forms satisfactory solid derivatives for the identification of most of the common aldehydes. However, since a few of the aldehydes produce oils or resinous products and the reagent also forms a solid derivative with acetone it was decided that other reagents containing different substituents in place of the methoxyl groups should be prepared in an attempt to find a better and more specific reagent.

Since halogen atoms affect the nature of other substituents attached to a benzene ring in a somewhat different way than the methoxyl group, it seemed of interest to prepare 1,2-bis(*p*-chlorobenzylamino)ethane and to test it as a reagent for aldehydes. In order to make this compound a method similar to that employed for the synthesis of the corresponding methoxy-reagent was used:

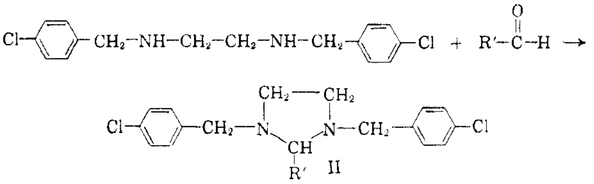


I

Catalytic hydrogenation of the Schiff base was affected without loss of the chlorine atoms. This was a more satisfactory method than reduction with alcohol and sodium because of the low solubility of the Schiff base in alcohol.

The free diamine is an oil and is thus more conveniently isolated, purified, stored, and used in the form of a salt, such as the diacetate.

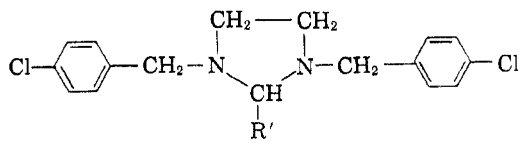
Almost all of the common aldehydes give good solid derivatives when treated with 1,2-bis(*p*-chlorobenzylamino)ethane (I) according to the following reaction:



(R′ = Alkyl or aryl groups)

A list of the 2-substituted 1,3-bis(*p*-chlorobenzyl)imidazolidines (II) (tetrahydroimidazoles) which were prepared are to be found in Table I.

TABLE I



(R′ = ALKYL OR ARYL GROUPS)

R′	M.P. (Corr.), °C.	Yield, %	Nitrogen, % Calcd.	Nitrogen, % Found
Methyl	57–58	57	8.36	8.40
2-Methoxyphenyl	63–64	64	6.56	6.58
4-Methylphenyl	67–68	60	6.82	6.94
n-Butyl	72–73	58	7.43	7.62
n-Propyl	75–75.5	51	7.72	7.82
3,4-Diethoxyphenyl	76.5–77.5	80	5.76	5.85
Isopropyl	79–80	30	7.72	7.51
2-Furfuryl	80–81	63	7.24	7.15
3,4-Dimethoxyphenyl	79.5–80.5	52	6.13	5.94
Benzyl	82.5–83	45	6.83	6.85
Ethyl	84–85	56	8.02	7.84
2,3-Dimethoxyphenyl	87.5–88	65	6.13	6.39
3,4-Dichlorophenyl	89.5–90	75	6.01	6.17
2,4-Dichlorophenyl	89.5–90	83	6.01	6.14
2-Chlorophenyl	91–92	80	6.48	6.44
Phenyl	98–99	74	7.05	7.27
3,4-Dioxymethylenephenyl	106–107	21	6.35	6.20
3-Nitrophenyl	110–110.5	30	9.50	9.47
3-Thienyl	118–118.5	53	6.95	7.15
4-Chlorophenyl	122–123	44	6.49	6.74
4-Methoxyphenyl	122–123	75	6.56	6.61
2-Phenylethenyl	131.5–132.5	66	6.60	6.79
4-Hydroxy-3-methoxyphenyl	140–140.5	76	6.32	6.35
2-Hydroxyphenyl	164–165.5	85	6.78	6.59
2,4-Dihydroxyphenyl	167–171 dec.	50	6.53	6.68
4-Hydroxyphenyl	200–201	48	6.78	7.04

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[2] J. H. Billman, J. Y. C. Ho, and L. R. Caswell, *J. Org. Chem.* 17, 1375 (1952).

Under the experimental conditions used, formaldehyde and hydrocinnamaldehyde gave derivatives which were oils. The α,β-unsaturated aldehydes, such as acrolein and α-ethyl-β-propylacrolein, gave oils or resinous products. In such cases the diamine reagent probably reacts with the double bond in the alpha-beta position to give a different type of product.

Unlike the *p*-methoxy-substituted diamine, the 1,2-bis(*p*-chlorobenzylamino) ethane (I) did not react with acetone under the experimental conditions used. Other ketones such as cyclohexanone, methyl ethyl ketone, diethyl ketone, acetophenone, diisopropyl ketone, and benzophenone were likewise tested and failed to react. From this evidence, it appears that 1,2-bis(*p*-chlorobenzylamino)ethane can be used as a specific reagent for aldehydes in the presence of ketones.

The variance in behavior of the two diamines toward acetone could be caused by the difference in the electronegativity of the chloro and methoxyl groups. Since the methoxyl group is such a strong electron releasing group it might increase the electron density about the nitrogen atoms to such an extent that the attractive forces between the nitrogen atoms and the carbon atom of the carbonyl group are sufficiently great to overcome the steric effect of the methyl groups of acetone. On the other hand, the chloro groups would not impart such a high electron density to the nitrogen atoms with the result that the attraction of the nitrogen atoms for the carbonyl group would not be sufficient to overcome the steric factor.

Like the methoxy derivatives, the 2-substituted 1,3-bis(*p*-chlorobenzyl) imidazolidines (II) are readily decomposed by dilute mineral acid to yield the original aldehyde and the salt of the diamine in nearly quantitative yields.

$$\text{II} + 2\text{HCl} + \text{H}_2\text{O} \longrightarrow \text{I}\cdot 2\text{HCl} + \text{RCHO}$$

Work is under way on the preparation of other substituted diamines as well as a study of the behavior of these compounds with carbonyl- and potential carbonyl-containing compounds of a more complex nature.

EXPERIMENTAL

1,2-Bis(p-chlorobenzylideneamino)ethane. To 250 g. of *p*-chlorobenzaldehyde partially dissolved in 350 ml. of absolute ethanol in a 1-l. three-neck flask, to which was attached a reflux condenser and a one-liter dropping funnel, was added dropwise 75 ml. of dry ethylenediamine. The mixture was stirred and refluxed for a period of 1 hr. at the end of which time the hot solution was poured into a 1-l. Erlenmeyer flask. Colorless crystals formed when the solution was cooled to room temperature. Recrystallization from absolute ethanol gave the Schiff base, with a melting point of 144–145° (uncorr.), in a yield of 264.5 g. or 98% of the theory.

Anal. Calcd. for $C_{16}H_{14}N_2Cl_2$: N, 9.18. Found, N, 9.13.

1,2-Bis(p-chlorobenzylamino)ethane diacetate. Fifty g. of 1,2 - bis(*p* - chlorobenzylideneamino)ethane partially dissolved in 150 ml. of absolute ethanol was hydrogenated by using 0.5 g. of platinum oxide and an initial hydrogen pressure of 45 lb./sq. in. The theoretical amount of hydrogen was adsorbed in an hour. The solution was filtered and concentrated under reduced pressure to remove all of the alcohol. To the dark, oily residue was added about 50 ml. of glacial acetic acid. The white solid diacetate which formed was filtered and combined with a small amount of diacetate which resulted when the filtrate was neutralized with a 20% sodium hydroxide solution. The product after recrystallization from boiling water melted at 139–140° (uncorr.). The yield was 28.5 g. (70.4%).

Anal. Calcd. for $C_{20}H_{26}Cl_2N_2O_4$: N, 6.53; Cl, 16.55. Found, N, 6.84; Cl, 16.65.

2-Substituted-1,3-bis(p-chlorobenzyl)imidazolidines (II). (*a*) *General procedure for the identification of aldehydes.* To 2.5 g. of the acetate of 1,2-bis(*p*-chlorobenzylamino)ethane in a test tube was added 15 ml. of 20% NaOH solution. The mixture was warmed on a steam bath until an oil formed and the heating continued for 15 min. The mixture was cooled preferably in an ice bath in order to convert the diamine to a semisolid. The aqueous layer was rejected and the residue washed with three 15-ml. portions of water to remove the excess alkali. As much of the water as possible was decanted and the free amine dissolved in a minimum amount of absolute alcohol. To this alcoholic solution was added approximately 1 g. or 1 ml. of the aldehyde. (If the aldehyde was a solid, it was first dissolved in a minimum amount of absolute alcohol.) The test tube was stoppered and shaken occasionally for 10 to 15 min. If, in this time, the solid derivative did not form, the mixture was heated to about 65° for 10 min. and then cooled to room temperature. Occasionally it was necessary to cool this solution in ice in order to cause the derivative to precipitate. The solid was removed by filtration and recrystallized from a minimum amount of absolute alcohol.

(*b*) *Specific procedure for making imidazolidines.* Procedure (a) is followed except that a small excess of the known aldehyde is used.

N,N'-Diacetyl-1,2-bis(p-chlorobenzylamino)ethane. One g. of the acetate of 1,2-bis(*p*-chlorobenzylamino)ethane was treated with 2 ml. of 20% NaOH solution. The mixture was stirred and warmed on a water bath for 10 to 15 min. until an oil formed. After cooling in an ice bath the aqueous solution was rejected. A few ice chips were added to the test tube containing the diamine. To this mixture was added 3 ml. acetic anhydride and 1 ml. of a 10% sodium acetate solution. The oil which formed solidified to a colorless solid which was recrystallized from absolute alcohol. Its melting point was 135–135.5° (uncorr.).

Anal. Calcd. for $C_{20}H_{22}Cl_2N_2O_2$: N, 7.13. Found: N, 7.27.

Hydrolysis of the 2-substituted-1,3-bis(p-chlorobenzyl)-imidazolidines (recovery of aldehydes). Three g. of 1,3-bis(*p*-chlorobenzyl)-2-(*p*-chlorophenyl)imidazolidine was treated with 20 ml. of a 10% hydrochloric acid solution. The mixture was stirred for 10 min., then 50 ml. of ether were added and the flask was stoppered and shaken for a few minutes. The white precipitate which formed was collected on a weighed sintered glass crucible and washed several times with 10-ml. portions of ether. The precipitate was dried at 100° for an hour, cooled to room temperature; it weighed 2.66 g. The calculated weight of dihydrochloride of the diamine should be 2.64 g.

The water-ether filtrate from the ether treatment was concentrated to remove the ether. The solid which formed in the aqueous portion after evaporation of the ether was found to be *p*-chlorobenzaldehyde.

Acknowledgment: We wish to thank the Eli Lilly Company for analyzing a large number of the reported compounds. We are also indebted to Mr. William Wright for his assistance in the laboratory.

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