

form which were purified by recrystallization from alcohol-water solutions. In this way the diol (VI) was obtained from both (I) and (IV) and the diol (VII) from (III).

A 1.5-g. sample of the diol (VI) was refluxed for thirty minutes with 4 ml. of acetic anhydride. The reaction mixture was cooled and poured into 200 ml. of saturated sodium bicarbonate solution. The oily precipitate was removed and crystallized from a mixture of ether and petroleum ether to give 1,3-diphenyl-1,2-diacetoxy-3-piperidinopropane (X).

Preparation of 1,1,3-Triphenyl-3-piperidinopropane-diol-1,2 (VIII).—(a) A suspension of 5.0 g. of the acetoxy compound (I) in 200 ml. of dry ether was added to a dry ether solution containing eight molar equivalents of phenylmagnesium bromide. After refluxing for two hours the reaction mixture was decomposed with ice and ammonium chloride. The product was separated as the hydrochloride from the dried ether solution. The free base was liberated in sodium bicarbonate solution and recrystallized from a mixture of ether and petroleum ether, wt. 3.66 g., colorless crystals.

(b) Five grams of (I) reacted with eight molar equivalents of phenyl lithium in a dry ether solution to give 3.80 g. of (VIII). The procedure for isolating the product was the same as in (a) above.

Preparation of 2,4-Diphenyl-4-piperidinobutanediol-2,3 (IX).—This product was obtained from the reaction of (I) with eight equivalents of methylmagnesium iodide in dry ether solution. The procedure was the same as in method (a) for the preparation of (VIII) as given above.

Summary

Methods have been devised for the synthesis of α -acetoxy and α -benzoxy- β -aminobenzylacetophenones. Some of these have been converted into various new types of aminopropylene glycols by the action of lithium aluminum hydride, Grignard reagents and phenyl lithium.

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α -Hydroxy- β -amino Ketones and Derivatives

BY NORMAN H. CROMWELL AND NORVAL G. BARKER

This study was undertaken as a companion research of that reported in the preceding paper.¹ Although no previous investigation of the reaction of an amine with an epoxyketone has been reported it seemed reasonable that such experiments should result in the formation of either α -hydroxy- β -aminoketones or α -amino- β -hydroxyketones or both. Such products on acetylation might then be expected to give acetoxyaminoketones either identical with or position isomers of those obtained from α -bromo- β -aminobenzylacetophenone as reported in the preceding paper.¹

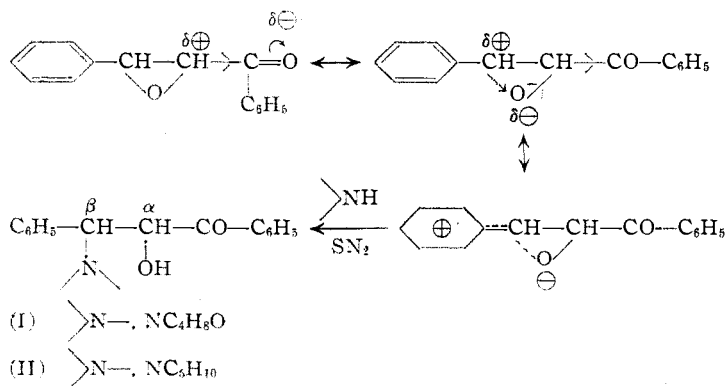
Fourneau and Billeter² have reported that aniline and *p*-phenetidine react with phenyl glycidic ester to give the α -amino products, but with ammonia and aliphatic amines to form the β -amino- α -hydroxy esters.

Our preliminary investigations have now shown that the major products resulting from the reaction of epoxybenzylacetophenone with morpholine and piperidine are the α -hydroxy- β -aminoketones (I) and (II), respectively. The reactions in non-polar solvents such as benzene or ether were extremely slow giving low yields of products. In the absence of solvents these reactions proceeded very rapidly but produced a considerable amount of decomposition products. The best conditions discovered involved the use of methyl alcohol as a solvent at room temperature.

The location of the hydroxy group in these molecules was established by converting them to

the corresponding α -chloro- β -aminoketone hydrochlorides (III) and (IV) which have been reported previously.³ The position of the chlorine was checked through the use of the iodine release method which has been described.³

A kinetic study of the reaction of epoxyketones with amines has been undertaken in this laboratory. The above observed effect of solvent change on the speed of the reaction as well as the established structure of the products points to the mechanism.



The partial positive charge at the β -position should be more favored by resonance than at the α -position. A more detailed discussion of this mechanism must await further experimental results.

The acetylation of the α -hydroxy- β -aminoketones (I) and (II) gave the α -acetoxy- β -aminoketones (V) and (VI). The fact that these products

(1) Cromwell and Starks, *THIS JOURNAL*, **72**, 4108 (1950).

(2) Fourneau and Billeter, *Bull. soc. chim.*, [5] **7**, 593 (1940).

(3) Cromwell and Wankel, *THIS JOURNAL*, **70**, 1320 (1948).

been proposed for these reactions.

2. The α -hydroxy- β -aminoketones are readily converted to the corresponding α -chloro and α -acetoxy- β -aminobenzylacetophenones. The latter are identical with the products from the reactions of α -bromo- β -aminobenzyl-

acetophenones with acetate salts.¹

3. The α -hydroxy- β -aminobenzylacetophenones react with lithium aluminum hydride and with phenylmagnesium bromide to produce aminopropylene glycols.

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An Experimental Study of Chromatography on Silicic Acid-Celite. The Applicability of the Theory of Chromatography^{1,2}

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Introduction

Although the theory of the simple adsorption chromatogram has been discussed extensively during the past decade,⁵⁻¹⁰ comparatively few experimental tests of the predictions of the proposed theories have been reported. Furthermore, those experimental studies which have been described present a somewhat incomplete and conflicting picture. The importance of the simple adsorption chromatogram, not only as a practical laboratory tool in its own right, but also as the fundamental chromatographic experiment, prompted the present investigation, which was designed to provide quantitative experimental data suitable for testing the various theories which may be applied to the simple Tswett chromatogram, in particular in their application to chromatograms on columns of silicic acid-Celite.

The first careful experimental study of the fundamental factors involved in simple adsorption chromatography was made by Weil-Malherbe¹¹ who investigated a few simple systems on alumina and silica gel by means of analyses of the filtrate from the column and found in general fairly good agreement with the theory proposed by Weiss.⁷ Likewise, DeVault⁶ was able to explain reasonably well on the basis of his theory the rather limited data of Cassidy and Wood¹² on the development of

lauric acid on carbon. On the other hand, Le-Rosen¹³ could obtain no more than partial qualitative agreement with theory in his experiments with *o*-nitroaniline in benzene on silicic acid, and similarly Thomas¹⁰ found at best only rough qualitative agreement with his kinetic theory of chromatography in experiments with anthracene in cyclohexane on alumina. Jacobs and Tompkins¹⁴ encountered some difficulty in reconciling with theory the results of their studies of the development of certain inorganic ions on alumina, but the more recent experiments of Glueckauf and Coates have almost completely resolved these difficulties. Indeed, as a result of the excellent work of the latter investigators and of Boyd and his co-workers,¹⁵ and Mayer and Tompkins,¹⁶ the theoretical treatment of the special field of ion-exchange chromatography now rests on a firm experimental foundation. Similarly, the theories which have been developed for the special adsorption analysis techniques of Tiselius have been tested extensively and found entirely adequate.¹⁷ Although much of the theory applicable to ion-exchange columns may be considered to apply also to the closely analogous Tswett adsorption chromatogram, the theories of frontal analysis and displacement development¹⁷ are of no direct aid in consideration of the simple adsorption chromatogram; however, their success does demonstrate that straightforward reasoning on the basis of measured adsorption isotherms can for many systems lead to the correct predictions of the chromatographic behavior of mixtures under particular conditions. Several earlier attempts¹⁸ to find a correlation between the adsorption isotherms and relative

(1) Presented in part before the Division of Physical and Inorganic Chemistry at the 115th National Meeting of the American Chemical Society in San Francisco, April 1, 1949.

(2) Aided by a grant from the National Foundation for Infantile Paralysis.

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(5) J. N. Wilson, *THIS JOURNAL*, **62**, 1583 (1940).

(6) D. DeVault, *ibid.*, **65**, 532 (1943).

(7) J. Weiss, *J. Chem. Soc.*, 297 (1943).

(8) A. C. Offord and J. Weiss, *Nature*, **155**, 725 (1945); **156**, 570 (1945).

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(10) H. C. Thomas, *Ann. N. Y. Acad. Sci.*, **49**, 161 (1948).

(11) H. Weil-Malherbe, *J. Chem. Soc.*, 303 (1943).

(12) H. G. Cassidy and S. E. Wood, *THIS JOURNAL*, **63**, 2628 (1941),

(13) A. LeRosen, *ibid.*, **69**, 87 (1947).

(14) P. W. M. Jacobs and F. C. Tompkins, *Trans. Faraday Soc.*, **41**, 388, 395, 400 (1945).

(15) (a) G. E. Boyd, J. Schubert and A. W. Adamson, *THIS JOURNAL*, **69**, 2813 (1947); (b) G. E. Boyd, A. W. Adamson and L. S. Myers, Jr., *ibid.*, 2836; (c) G. E. Boyd, L. S. Myers, Jr., and A. W. Adamson, *ibid.*, 2849; (d) B. H. Kettle and G. E. Boyd, *ibid.*, 2800.

(16) S. W. Mayer and E. R. Tompkins, *ibid.*, **69**, 2866 (1947).

(17) S. Claesson, *Arkiv. Kemi Mineral. Geol.*, **23A**, No. 1 (1946).

(18) See for example (a) A. Lottermoser and K. Edelmann, *Koll. Z.*, **83**, 262 (1939); (b) H. G. Cassidy, *THIS JOURNAL*, **62**, 3073, 3076 (1940).