THE USE OF SODAMIDE AS A CONDENSING AGENT IN ORGANIC CHEMICAL SYNTHESIS

by

D. McDougall

Being a -

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Introduction

Before synthetic research seriously occupied the attention of the earlier organic chemists, the old belief, that organic compounds could be formed only in organic beings, by the directing influence of a vital force, had necessarily to be overcome. Similarly the belief that in living nature the elements obeyed laws quite different from those in dead nature, acted as an effective barrier to any investigation of synthetic methods.

These conceptions prevailed for a considerable length of time. Even the preparation of urea from inorganic sources, by Wöhler in 1828, was at first regarded as of small importance, and for a number of years it was the only well known example of its kind. Finally, however, through the work of Kolbé in the synthesis of acetic acid; of Frankland in building up of hydrocarbons from substances of simpler composition; and the synthesis of fats by Berthelot, the growing conviction, that organic compounds were formed under the influence of the same forces as the inorganic, was gradually strengthened. When these barriers were finally removed, the value of synthetic research became more and more apparent.

Since that time the application of synthetic methods has met with marked success in every section of the wide field of organic chemistry. The application of these methods has led to the elucidation of the chemical constitution of many complex organic compounds. It is true that much can be deduced from the properties, modes of formation, and decomposition products of the compound. In fact from these observations, the structural formula may be deduced with reasonable certainty, but the proof of the correctness of

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these deductions lies in its synthesis, from its elements, or from substances of known composition. The further application of synthetic methods has led to the production of a vast number of new compounds, many of which are of immense value in the commercial world.

Of the many methods employed in synthetic research, perhaps none has proven of greater value, or wider application, than the condensation method. This method is inseparably connected with the earlier history of organic chemistry.

The fact that the chemical processes taking place in the plant and animal organisms, in the formation of complex organic compounds, is essentially one of condensation, has from earliest times served as a stimulus to the investigation of reactions of this type. (1)

Condensation is defined as "the union of two or more organic molecules, or parts of the same molecule (with or without elimination of component elements) in which the new combination is effected between carbon atoms." (2)

When condensation takes place between two or more different molecules it is referred to as external condensation. When union of the carbon atoms in the same molecule takes place leading to ring formation it is termed internal condensation.

Condensation is effected by the addition of some substance which acts as a condensing agent. A variety of substances are employed for this purpose, e.g. dilute sodium hydroxide solution in Claisen's reaction; ammonia, diethylamine, piperidine and aniline, in Knoevenagel's reaction; hydrogen chloride, potassium carbonate, dilute sodium hydroxide solution, and less frequently sulphuric acid, acetic acid, acetic anhydride, and zinc chloride.

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(1) Practical plant biochemistry, Onslow, pp.3.
(2) Advanced Organic Chemistry, Cohen, Part I, page 195.

in the aldol condensation; sodium ethoxide in the acetoacetic ester condensation.

The following investigations have been undertaken with a view to extending the use of sodamide as a condensing agent in organic chemical synthesis. In addition to investigating its use, in cases where condensation readily takes place in the presence of other reagents, a number of new reactions have been tried, e.g. the action of chloroform, ethyl carbonate and ethyl oxalate on quinoline in the presence of sodamide, also the action of nitro compounds and bases in the presence of sodamide. The results of the latter reactions have proven of considerable interest, and appear to offer opportunities for further investigation.

I wish to express my appreciation to Dr. H. P. Armes of the Department of Chemistry, University of Manitoba, at whose suggestion these investigations were undertaken, for his assistance and advice.

D. McDougall.

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Review of Literature

The literature on this subject reveals a great diversity in the nature of the problems treated in the numerous papers. This review is intended to indicate only the outstanding contributors, with special reference to some of the more important papers.

The amide of sodium was discovered during the early part of the 19th century by Gay Lussac and Thénard, and shortly afterward by Humphrey Davey (1). The amide of potassium was discovered at the same time by these investigators.

Synthesis with derivatives of sodamide were carried out as early as 1893 by Carl Blacher (2).

The earliest account of the action of sodamide as a condensing agent appears to be communicated by Freund and Speyer in 1902. An abstract of this appears in the Journal of the Chemical Society of that year. (3) Since that time a considerable amount of work has been carried out on the use of 'sodamide in organic chemical synthesis'.

The principal contributors are:

Haller and Bauer

Haller and Ramart-Lucas

Haller and Louvrier

Haller and Benoist

Haller and Cormubert

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(1) J. C. S. T. 1894, page 504.
(2) J. C. S. Ai. 1895, page 289. Ber. 1895, 28; 432-37.
(3) J. C. S. Ai. 1902, page 584. Ber. 1902, 35; 2321-22

Titherley, A.W.

Tschitschibabin and Zeide

Tschitschibabin and Oparina

Tschitschibabin and Zoscpina

A. W. Titherley, of University College, Liverpool, has contributed a number of papers on this subject. These appear in the transactions of the Chemical Society. In his communication of 1894 he described:

"1. Preparation, properties, and composition of sodamide, and

2. Experiments, disproving the alleged existence of nitride of sodium; and attempts to prepare disodamide."

The paper also refers to a number of experiments on potassamide and lithamide. (1)

In 1897 he described a number of substitution derivatives of sodamide. A series of derivatives were obtained by the substitution of one or both atoms of hydrogen in $Na\ NH_2$ by radicles. (2)

In a later communication he has described the action of sodamide and of acyl-substituted sodamides on organic esters. (3)

Later investigations of some interest have been carried out by Tschitschibabin and Zascpina and Tschitschibabin and Oparina on the action of sodamide on quinoline, and iso quinoline. (4) With quinoline the main products of the reaction are diquinoline $C_{18}H_{14}N_2$ and diquinolyl $C_{18}H_{12}N_2$ The former is readily oxidised to the latter. The preparation of 2-amino-quinoline by the action of sodamide on quinoline has been re-investigated in an endeavour to improve the yield of the amino compound. This has not been successful. Iso quinoline reacts in a similar way with sodamide, in the presence of neutral solvents, amino iso quinoline being produced. (5)

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(1) J.C.S. T. 1894, 504.
(2) J.C.S. T. 1897, 460
(3) J.C.S. T. 1902, 1520
(4) J.C.S. 1923 Ai page 603, J.Russ. Phys.Chem. Soc. 1920, 50; 553-7
(5) J.C.S. 1923 Ai page 604 " " " " " 1920, 50; 543-8