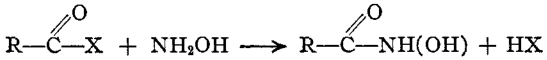
[CONTRIBUTION FROM THE FRICK CHEMICAL LABORATORY OF PRINCETON UNIVERSITY]

Molecular Rearrangements Involving Optically Active Radicals. III. The Lossen Rearrangement of Optically Active Hydroxamic Acids

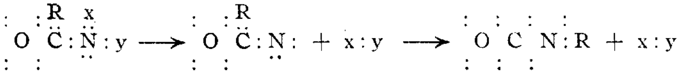
BY EVERETT S. WALLIS AND R. D. DRIPPS

The hydroxamic acids are crystalline compounds which may be prepared by the action of hydroxylamine on esters, acid anhydrides and acid chlorides



$$R{-}\overset{\displaystyle /\!\!/O}{C}{-}X + NH_2OH \longrightarrow R{-}\overset{\displaystyle /\!\!/O}{C}{-}NH(OH) + HX$$

It is a well-known fact that these substances and many of their derivatives are capable of molecular rearrangement. Lossen[1] first observed that the acetyl derivative of a hydroxamic acid when warmed with alkali produced an isocyanate. The metallic salts of these esters are very susceptible to this change. Of the several theories which have been advanced to explain the mechanism of this rearrangement the one which perhaps has received the most attention has been that of Stieglitz[2] which assumes the transient existence of an unstable univalent nitrogen compound. His investigations have made it evident that the Lossen, Curtius and Hofmann rearrangements are fundamentally alike, and he has proposed that all rearrangements of this character take place in a similar manner. In terms of modern valence conceptions Jones and Hurd[3] formulated this theory as follows



$$\overset{:}{\underset{:}{}}O\,\overset{:}{\underset{:}{}}\overset{R}{\ddot{C}}:\overset{x}{\underset{..}{\ddot{N}}}:y \longrightarrow \overset{:}{\underset{:}{}}O\,\overset{:}{\underset{:}{}}\overset{R}{\ddot{C}}:\underset{..}{N}: + x:y \longrightarrow \overset{:}{\underset{:}{}}O\,\overset{:}{\underset{:}{}}C\,\overset{:}{\underset{:}{}}N\overset{:}{}:R + x:y$$

and assumed that the relative ease of rearrangement depends not only upon the groups x and y, and the formation of the univalent nitrogen derivative, but also upon the nature of the radical, R; the greater the tendency of this radical to exist as a free radical the greater the ease of rearrangement. Many facts have been submitted by Jones and his coworkers[4] to support this hypothesis.

In carrying out certain of these investigations Jones and Wallis[5] studied the rearrangement of certain optically active acid azides and optically active hydroxamic acids in which R is an optically active radical. Their experiments with *d*-benzylmethylacetazide, $(C_7H_7)(CH_3)CHCON_3$, showed that this compound on rearrangement gave an optically active isocyanate

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[1] Lossen, *Ann.*, **186**, 1 (1877); **252**, 170 (1889); **281**, 169 (1894).

[2] Stieglitz, *Am. Chem. J.*, **18**, 751 (1896); *ibid.*, **29**, 49 (1903); Stieglitz and Earle, *ibid.*, **30**, 399, 412 (1903); Stieglitz and Slossen, *Ber.*, **28**, 3265 (1895); *ibid.*, **34**, 1613 (1901); Stieglitz and Leech, THIS JOURNAL, **36**, 272 (1914).

[3] Jones and Hurd, THIS JOURNAL, **43**, 2422 (1921).

[4] Jones and Hurd, *ibid.*, **43**, 2422 (1921); Jones and Root, *ibid.*, **48**, 181 (1926); Hurd, *ibid.*, **45**, 1472 (1923).

[5] Jones and Wallis, *ibid.*, **48**, 169 (1926).

which could be converted by ammonia into an optically active monosubstituted urea, and by hydrolysis with concentrated hydrochloric acid into an optically active amine hydrochloride. These results established the fact that regardless of the actual mechanism[6] of this type of rearrangement, the radical, R, in its migration from the carbon atom to the nitrogen atom maintained an asymmetric configuration.

This conclusion has been further substantiated by Wallis and Nagel[7] in their studies on the rearrangement of optically active amides. When *d*-benzylmethylacetamide, $C_7H_7(CH_3)CHCONH_2$, was treated with a cold strongly alkaline solution of sodium hypobromite and the mixture warmed to 70–80° in order that rearrangement might take place, the amine so obtained in the form of its hydrochloride was found to be optically active. This fact makes it evident that in the Hofmann rearrangement of an optically active amide, as well as in the Curtius rearrangement of an optically active azide, the radical, R, during its migration from the carbon atom to the nitrogen atom, maintains its asymmetry.

However, in their investigations on the Lossen rearrangement of *d*-benzylmethylacethydroxamic acid, $C_7H_7(CH_3)CHCONHOH$, Jones and Wallis[5] found that the final product which they isolated gave no appreciable rotation. Three possible explanations of this apparent exception were offered. (1) In this rearrangement the radical, R, might actually racemize during its migration from the carbon atom to the nitrogen atom. (2) Inasmuch as the first product of the rearrangement, benzylmethylmethylisocyanate was not isolated as such but was converted by hydrolysis with water at 80–90° to the *sym*-di-benzylmethylmethyl urea, racemization might take place during this second stage of the reaction. (3) Since this symmetrically disubstituted urea was found not to be very soluble in the common organic solvents at room temperature and, therefore, available in solution only in small concentration, it would not be possible to obtain an appreciable polarimetric reading if the urea actually possessed a low specific rotation. Two experimental facts were observed which gave some indication of the true explanation. (a) The melting points of the urea prepared from the *d*, *l*, and *dl* forms of the hydroxamic acid were found to

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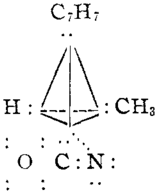
[6] It should be recalled that the nature of this migrating radical, R, has been considered as positive by Jones [*Am. Chem. J.*, **50**, 441 (1913)] and as negative by Stieglitz [THIS JOURNAL, **36**, 280 (1914); *ibid.*, **38**, 2047 (1916)] and more recently by Whitmore [*ibid.*, **54**, 3274, 3436 (1932)]. Jones and Wallis in their discussion of the results stated above pointed out, however, that another interpretation was possible, namely, "that the rearranging group does not exist as a free radical but that in some way, before the group actually parts company with its carbon neighbor, the univalent nitrogen atom has begun already to exercise its influence on the radical, in such a manner that when cleavage actually does take place, a change in the configuration of the groups about the asymmetric carbon atom is prevented." They stated that this influence could be imagined to be of the nature of a partial valence and they pictured the univalent nitrogen derivative on this assumption as indicated. This interpretation has recently received experimental support in this Laboratory and will be discussed in Part IV of this series of papers.



[7] Wallis and Nagel, THIS JOURNAL, **53**, 2787 (1931).

be the same. This would perhaps indicate that racemization at some stage in the process was the more plausible. (b) *d*-Benzylmethylmethylisocyanate prepared from the Curtius rearrangement of the *d*-acid azide gave on hydrolysis with water at 90° a urea of the same composition and melting point which showed no appreciable rotation. This makes it evident that it is unnecessary to assume that in the rearrangement of the hydroxamic acid derivative racemization takes place during the migration of the radical from the carbon atom to the nitrogen atom.

We have continued these investigations on the Lossen rearrangement of hydroxamic acids in order to determine more definitely the true nature of the first products of the rearrangement, and to see whether in this rearrangement as well as in the Hofmann and Curtius rearrangements the radical actually maintains an asymmetric configuration during its transfer from the carbon atom to the nitrogen atom. For this purpose we again prepared *d*-benzylmethylacethydroxamic acid in the form of its benzoyl derivative and converted it into its potassium salt by the method previously described by Jones and Wallis.[8] Rearrangement of this compound was carried out in such a manner as to enable us to obtain the isocyanate, first formed. A benzene solution of this isocyanate was found to be dextrorotatory. Ammonia gas reacted with the *d*-isocyanate to form the monosubstituted urea, $C_7H_7(CH_3)CHNHCONH_2$, a crystalline compound melting at 136.5–137°. Its specific rotation in acetone at 20° was found to be +10.1°.

Therefore it must be concluded that in the Lossen rearrangement of an optically active hydroxamic acid as well as in the Hofmann rearrangement of an acid amide, and the Curtius rearrangement of an acid azide, the radical actually maintains an asymmetric configuration during the rearrangement. The fact that the *sym*-di-benzylmethylmethyl urea, $C_7H_7(CH_3)CHNHCONHCH(CH_3)C_7H_7$, prepared by Jones and Wallis showed no appreciable rotation must be attributed to explanations 2 or 3 as stated above.

It is also to be noted that the value of the specific rotation of the monosubstituted urea prepared by the rearrangement of the hydroxamic acid derivative is of the same magnitude as the value of the specific rotation of the same urea prepared by rearrangement of the acid azide. A similar fact was observed by Wallis and Nagel[7] in their studies on the Hofmann rearrangement. The amine hydrochloride prepared from the acid azide, and from the acid amide, gave the same value for its rotatory power. They reasoned from their experiments that if partial inversion (racemization) took place, it could be detected inasmuch as the conditions of the rearrangement are very different. It is improbable that the amount of inversion would be the same. The above results on the monosubstituted

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(8) Jones and Wallis, THIS JOURNAL, **48**, 176 (1926).

urea justify with an added certainty their conclusions that in rearrangements of this type the radical, R, has either the same configuration as it had originally or that it undergoes complete inversion. Partial inversion seems unlikely. If we take into account the sign of the rotatory power perhaps the first conclusion is more probable.

Experimental Part

Preparation of the Benzoyl Ester of *d*-Benzylmethylacethydroxamic Acid, $C_7H_7(CH_3)CHCONHOCOC_6H_5$.—This compound was prepared from *d*-benzylmethylacetic acid. The acid used in these experiments was prepared from ethyl acetoacetate according to the method of Conrad,[9] with a few modifications described by Jones and Wallis.[5] It was resolved into its optically active isomers by the method of Kipping and Hunter.[10] Its rotation α_D at 20° without solvent in a 100-mm. tube was +20.12°. The methyl ester of this acid was prepared and converted into the hydroxamic acid according to the method of Jones and Wallis.[5] The benzoyl derivative was prepared according to the method of Jacobs and Heidelberger,[11] a modification of the Schotten–Baumann reaction. This ester melted at 115.5–116.5° after recrystallization from ethylacetate and petrolether (30–60°). 0.2079 g. of this compound dissolved in ethyl alcohol (95%), total volume 5.00 cc., gave the following rotations at 20° in a 200-mm. semi-micro tube: $\alpha_{6563} = +4.95$; $\alpha_{6893} = +6.37$; $\alpha_{5463} = +7.68$; $\alpha_{4861} = +10.30$. $[\alpha]^{20}_{6563} = +59.5$; $[\alpha]^{20}_{5893} = +76.7$;[12] $[\alpha]^{20}_{5463} = +92.1$; $[\alpha]^{20}_{4861} = +120.2$.

Preparation of *d*-Benzylmethylmethyl Urea, $C_7H_7(CH_3)CHNHCONH_2$.—One gram of the *d*-benzoyl ester was converted into the potassium salt by the method described by Jones and Wallis.[8] The salt which precipitated as a white material was filtered quickly and suspended immediately in dry benzene. This suspension was refluxed for fifteen minutes on the water-bath and after cooling to room temperature was filtered. The residue, which was mostly potassium benzoate, was discarded. The benzene solution possessed a sharp penetrating odor characteristic of isocyanates and was dextrorotatory. Dry ammonia gas was bubbled through the solution for ten minutes and a white precipitate soon formed. The suspension was allowed to stand in the ice box for a short time and then filtered; yield 0.5 g. Recrystallization from alcohol and water gave a solid which melted at 136.5–137°. The melting point of *d*-benzylmethylmethyl urea as reported by Jones and Wallis was 136°. 0.0824 g. of this urea dissolved in pure acetone, total volume 5.00 cc., gave the following rotations at 20° in a 200-mm. semi-micro tube: $\alpha_{6563} = +0.26$; $\alpha_{5893} = +0.33$; $\alpha_{5463} = +0.40$; $\alpha_{4861} = +0.48$. $[\alpha]^{20}_{6563} = +7.9$; $[\alpha]^{20}_{5893} = +10.1$; $[\alpha]^{20}_{5463} = +12.1$; $[\alpha]^{20}_{4861} = +14.2$. The specific rotation $[\alpha]^{20}_D$ for the *d*-benzylmethylmethyl urea prepared from the *d*-acid azide and the isocyanate was reported by Jones and Wallis to be +10.7°.

Summary

Evidence is submitted in this paper to show that the Lossen rearrangement of an optically active hydroxamic acid yields an optically active rearrangement product. This result is similar to those previously communicated in this series of papers on the Hofmann rearrangement of an

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[9] Conrad and Bischoff, *Ann.*, **204**, 177 (1880); Conrad, *Ber.*, **11**, 1055 (1878).

[10] Kipping and Hunter, *J. Chem. Soc.*, **83**, 1005 (1903).

[11] Jacobs and Heidelberger, THIS JOURNAL, **39**, 1441 (1917).

[12] The value of the specific rotation of this compound and the mixed levo form reported by Jones and Wallis in their experiments is not correct due to a clerical error. Their data should have read—a solution of 1.5400 g. in alcohol, total volume 50 cc., gave a rotation of +4.40 in a 200 mm. tube at 20°; $[\alpha]^{20}_D = +71.4$. This correction should be noted.

optically active amide, and the Curtius rearrangement of an optically active acid azide. The fact that optically active products were not obtained in the experiments described by Jones and Wallis on *d*-benzylmethylacethydroxamic acid is shown to be due to secondary causes and not to racemization of the compound during rearrangement.

d-Benzylmethylacethydroxamic acid in the form of its benzoyl ester was allowed to rearrange in such a manner as to enable us to study the first product of the rearrangement, benzylmethylmethylisocyanate, and to observe its behavior toward polarized light. A benzene solution of this compound was dextrorotatory. *d*-Benzylmethylmethyl urea was prepared from this isocyanate and its specific rotation was found to be of the same value as the urea prepared from *d*-benzylmethylacetazide.

These facts point to the conclusion stated in part II of this series that in rearrangements of this type the radical, R, has either the same configuration as it had before rearrangement or that it undergoes complete inversion during its migration from the carbon atom to the nitrogen atom. Partial inversion seems unlikely.

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The Synthesis of Acenaphthene-*peri*-metathiazines and of Some Dyes Derived Therefrom[1]

BY MARSTON TAYLOR BOGERT AND RICHARD B. CONKLIN

Introductory

Having completed in these laboratories the synthesis of the naphthalene-*peri*-metathiazines[2] (I), we turned our attention to the analogously constituted and hitherto unknown acenaphthene-*peri*-metathiazines (II), and this contribution records their successful synthesis from the 4-nitroacenaphthene-3-sulfonchloride (IV). This synthesis supplies further corroboration of the constitution assigned to that nitrosulfo acid, as well as to those ascribed to the 3-nitro and 3-sulfo derivatives of acenaphthene.

The general plan of this synthesis involved the preparation of the 4-amino-3-acenaphthenylmercaptan (V) from the *peri*-nitrosulfonchloride (IV) and, by treatment of this *peri*-aminomercaptan with acid chlorides, effecting ring closure and thiazine formation, as described by Reissert,[3] and by Bogert and Bartlett,[2] in the naphthalene-*peri*-metathiazine group.

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[1] The completion of this work was made possible by a generous grant from the Trustees of the Joseph Henry Fund of the National Academy of Sciences, to whom we wish to express our gratitude.—M. T. B. and R. B. C.

[2] Bogert and Bartlett, THIS JOURNAL, **53**, 4046 (1931).

[3] Reissert, *Ber.*, **55**, 858 (1922).