formation of addition compounds between certain benzoins has been observed.

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[CONTRIBUTION FROM THE FRICK CHEMICAL LABORATORY, PRINCETON UNIVERSITY]

# MOLECULAR REARRANGEMENTS INVOLVING OPTICALLY ACTIVE RADICALS. II. THE HOFMANN REARRANGEMENT OF OPTICALLY ACTIVE ACID AMIDES

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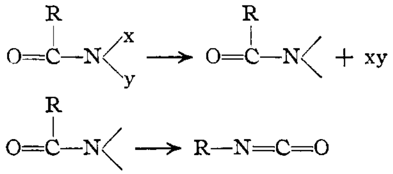
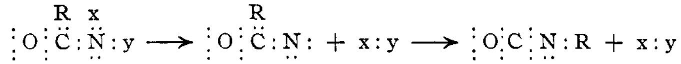
It has long been known that aliphatic and aromatic acid amides are converted into amines by treatment with chlorine or bromine and an alkali. Hofmann discovered this reaction[1] and detected among the products an isocyanate. It has since been shown, however, that the first product formed is a halogen amide. Of the several theories which have been advanced to explain this rearrangement, perhaps the most fruitful has been the interpretation of Stieglitz and his students[2] developed from the suggestion of Tiemann[3] that an acid amide is converted into an amine through the formation of an unstable intermediate univalent nitrogen compound. Their investigations have made it evident that the Lossen, Curtius and Hofmann rearrangements are fundamentally alike and they have proposed that all rearrangements of this character take place as follows



$$O{=}\overset{R}{\overset{|}{C}}{-}N\!\left\langle{}^{x}_{y}\right. \longrightarrow O{=}\overset{R}{\overset{|}{C}}{-}N\!\left\langle\right. + xy$$

$$O{=}\overset{R}{\overset{|}{C}}{-}N\!\left\langle\right. \longrightarrow R{-}N{=}C{=}O$$

In terms of modern valence relationships Jones and Hurd[4] suggested an interpretation of this mechanism based on the Lewis conception of chemical bonds and electrons:



$$\vdots O \vdots \overset{R}{\ddot{C}} : \overset{x}{\ddot{N}} : y \longrightarrow \vdots O \vdots \overset{R}{\ddot{C}} : \ddot{N} : + x:y \longrightarrow \vdots O \vdots C \vdots \ddot{N} : R + x:y$$

From this interpretation it was assumed that the radical, R, in its wandering from the carbon atom to the nitrogen atom existed momentarily as a free radical, and that the ease of the rearrangement of such types of compounds depended upon the tendency of the radical, R, in the univalent

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[1] Hofmann, *Ber.*, **15**, 407 (1882).

[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).

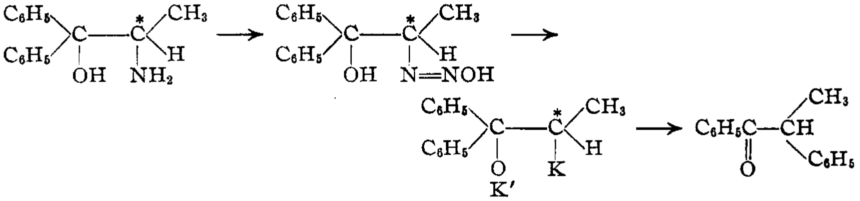
[3] Tiemann, *Ber.*, **24**, 4162 (1891).

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

nitrogen derivative to exist as a free radical. This hypothesis has since been tested in this Laboratory by Jones and his co-workers[4,5] and many facts have been found which are wholly in agreement.

In carrying out certain of these investigations Jones and Wallis[6] studied the nature of the products formed by the rearrangement of certain optically active acid azides and optically active hydroxamic acids in which the radical, R, is an optically active radical. From the viewpoint of the above hypothesis three possibilities suggested themselves: (1) the radical might racemize during rearrangement and yield inactive products; (2) it might retain its activity and its configuration; (3) it might retain its activity but change its configuration, that is, undergo Walden inversion. The first possibility was excluded by their experiments with *d*-benzylmethylacetazide, $(C_7H_7)(CH_3)CHCON_3$. This compound was found to give on rearrangement an optically active isocyanate, which could be converted by aniline into an optically active monosubstituted urea, and by hydrolysis into an optically active amine hydrochloride. These facts suggested two possible interpretations, one based on the theory of partial valence, the other based on the assumption of carbonium ions. A survey of the properties of optically active compounds described in the literature led them to suggest that the second interpretation was perhaps the more probable; that in such rearrangements the radical, R, if existing momentarily as a free radical must do so in such a way as to maintain a configuration required to produce an optically active rearrangement product, that is, it is a positive radical which is of the nature of a carbonium ion, and that in its migration from the carbon atom to the nitrogen atom it leaves behind the electron it shared with the carbon atom.

Since the publication of these experiments McKenzie and his co-workers[7] have carried out investigations on molecular rearrangements of optically active compounds involving migration of groups from one carbon atom to another adjacent carbon atom. It has been shown by them that under certain conditions optically active tertiary amino alcohols and pinacols can undergo rearrangement to give optically active ketones. They have suggested the following mechanism for the change which takes place in the tertiary amino alcohols



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[5] Jones and Root, THIS JOURNAL, **48,** 181 (1926).

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

[7] McKenzie, Rogers and Mills, *J. Chem. Soc.*, **129,** 779 (1926); *Ber.*, **62B,** 272 (1929).

where K and K′ are electric charges. It is evident from this that their interpretation involves the same assumption as previously expressed by Jones and Wallis[6] for the rearrangement of optically active acid azides, that is, that in the rearrangement it is possible that the optically active radical may exist for a certain length of time as a carbonium ion, and that the asymmetry is retained due to the fact that an electric charge plays the part of the fourth grouping.

We have continued these investigations on carbon to nitrogen rearrangements involving optically active radicals in order to seek an answer to the second and third possibilities suggested by the above interpretation for the rearrangement of acid azides, hydroxamic acids and halogen amides. Does the radical retain its configuration during the rearrangement, or does it change its configuration and undergo Walden inversion? For this purpose *d*-benzylmethylacetamide $(C_7H_7)(CH_3)CHCONH_2$, $[\alpha]_D^{20}$ +38.94°, was prepared, and its rearrangement by bromine and an alkali studied. It was thought that some information could be obtained from a comparison of the specific rotation of the amine hydrochloride produced in the Curtius rearrangement of an optically active acid azide with the same amine hydrochloride produced by the Hofmann rearrangement of an optically active acid amide. The conditions of the rearrangement are very different and if partial inversion (racemization) takes place it can be detected, as it is improbable that in two rearrangements carried out under such different conditions the amount of inversion would be the same in the two instances. McKenzie[7] has found that in the rearrangement of optically active tertiary amino alcohols and pinacols the molecule undergoes partial racemization. In the case of the tertiary amino alcohols there is a change in the sign of the rotatory power. Our experiments with *d*-benzylmethylacetamide show that in the rearrangement and subsequent hydrolysis of the isocyanate the amine hydrochloride which is produced is optically active, $[\alpha]_D^{20}$ +16.8°. It has the same sign for the rotatory power as the acid amide from which it is obtained, and its specific rotation is the same as the specific rotation of the amine hydrochloride produced in the rearrangement of the *d*-benzylmethylacetazide.[6] It seems, therefore, that we can now state with some degree of certainty that in these two rearrangements the amine hydrochloride has either the same configuration as the original acid amide and acid azide, or that during the rearrangement the radical undergoes complete Walden inversion. Partial inversion seems unlikely.

## Experimental Results

**Preparation of *d*-Benzylmethylacetamide,** $(C_7H_7)(CH_3)CHCONH_2$.—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[8] with a

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[8] Conrad, *Ann.*, **204**, 177 (1880).

few modifications as described by Jones and Wallis.[9] It was resolved into its optically active isomers by the method of Kipping and Hunter.[10] Its rotation, $\alpha_D$, at 20° without solvent in a 50-mm. tube was +10.08°. The acid was converted into its chloride by means of thionyl chloride according to the method of Pickard and Yates.[11] The chloride boiled at 120° (15 mm.) and gave a rotation of +12.60° in a 50-mm. tube at 20° without solvent; 15 g. of the chloride was dissolved in 200 cc. of dry ether, and the solution saturated at 0° with dry ammonia gas. A heavy white precipitate of ammonium chloride formed. The mixture was allowed to stand at room temperature for fifteen minutes and then filtered. The ether solution was concentrated to about one-half its volume, and then placed in the ice box overnight. A white crystalline material separated out. This was filtered, washed with petrol ether (30–60°) and dried in a vacuum desiccator. *d*-Benzylmethylacetamide crystallizes from ether in long, beautiful needles. It melts at 104.5°; 0.3916 g. dissolved in ether, and made up to a volume of 50 cc. gave $\alpha_D$ +0.61° at 20° in a 2-dm. tube; $[\alpha]^{20}_D$ +38.94°.

*Anal.* Subs., 0.4270: N, 33.05 cc. (23°, 758 mm.). Calcd.: N, 8.59. Found: N, 8.66.

The filtrates from the fractional crystallization of the quinine salt of benzylmethylacetic acid were worked up and a mixed levo acid was obtained. This acid was converted into the corresponding mixed levo amide by the method described above for the pure dextro modification: 0.3269 g. of this material in 25 cc. of benzene solution gave $\alpha_D$ −0.83° at 20° in a 2-dm. tube; $[\alpha]^{20}_D$ −31.7°.

**Rearrangement of *d*-Benzylmethylacetamide to *d*-Benzylmethylmethylamine Hydrochloride,** $(C_7H_7)(CH_3)CHNH_3Cl$.—Several experiments were carried out in order to determine the best conditions for the rearrangement. It was found that an excess of bromine greatly diminished the yield of the amine hydrochloride. The following procedure gave the best results: 1.5 g. of sodium hydroxide was dissolved in 12 cc. of water and cooled to 0°; 0.5 cc. of liquid bromine was then added in small portions and the contents stirred until homogeneous. To this solution was added 1.0 g. of *d*-benzylmethylacetamide. After it had dissolved the solution was slowly warmed. When the temperature reached about 70–80° rearrangement took place, the solution became suddenly cloudy, and an oil separated out on top of the liquid. The mixture was heated to the boiling point and distilled. Water was added frequently. The oily distillate was strongly alkaline in its reaction toward litmus and had an amine odor. When acidified with dilute hydrochloric acid a clear water-white solution was obtained. This was evaporated to dryness on the water-bath. The white crystalline salt was extracted twice with ether to remove any unchanged amide that might have passed over, and then thoroughly dried in a vacuum desiccator; 1.0 g. was obtained. A portion of it melted at 145°; 0.7810 g. dissolved in water and made up to 25 cc. gave $\alpha_D$ +1.33° at 20°; $[\alpha]^{20}_D$ +21.3°. Experiments showed that the specific rotation of this substance changed with concentration. Therefore for a comparison of the rotatory power with the same amine hydrochloride prepared from the *d*-acid azide the following solution was prepared, and its rotatory power determined: 0.9584 g. was dissolved in water, and made up to 20 cc. This solution gave $\alpha_D$ at 20° in a 2-dm. tube +1.61°; $[\alpha]^{20}_D$ +16.8°. This is the same concentration that was used by Jones and Wallis[6] in their experiments on *d*-benzylmethylmethylamine hydrochloride prepared from *d*-benzylmethylacetazide. The value of the specific rotation reported by them was $[\alpha]^{20}_D$ +16.6°. The mixed levo amide on rearrangement gave the corresponding levo amine hydrochloride; 0.3500 g. in 25 cc. of aqueous solution gave $\alpha_D$ at 20° in a 2-dm. tube −0.28°; $[\alpha]^{20}_D$ −10.0°.

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[9] Jones and Wallis, This Journal, **48**, 174 (1926).

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

[11] Pickard and Yates, *Trans. Chem. Soc.*, **95**, 1019 (1909).

## Summary

Benzylmethylacetamide has been prepared in a pure dextro and a mixed levo modification.

Evidence is submitted to show that when this compound undergoes the Hofmann rearrangement the amine hydrochloride so obtained is optically active. It is further shown that the rotatory power has the same sign as the amide from which it is produced, and that the value of the specific rotation of the *d*-amine hydrochloride produced from the *d*-acid amide is the same as the value of the amine hydrochloride obtained by Jones and Wallis from *d*-benzylmethylacetazide.

A discussion of these results is given with special reference to the Walden inversion.

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[CONTRIBUTION FROM THE WALKER CHEMICAL LABORATORY OF THE RENSSELAER POLYTECHNIC INSTITUTE]

# THE PREPARATION OF CYCLOPROPYL CYANIDE AND TRIMETHYLENE CHLOROBROMIDE[1]

BY J. B. CLOKE, R. J. ANDERSON, J. LACHMANN AND G. E. SMITH

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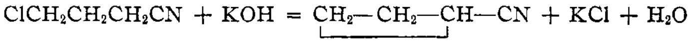
**Cyclopropyl Cyanide.**—During the last few years workers in this Laboratory have found it necessary to prepare quantities of cyclopropyl cyanide as the starting material in a series of investigations on the stability of certain cyclopropane derivatives. Since the ordinary procedures for the preparation of this rather costly reagent have given unsatisfactory yields, a number of attempts have been made to devise a better process.

Cyclopropyl cyanide was first made by Henry in 1898 by the distillation of $\gamma$-chlorobutyronitrile with dry potassium hydroxide,



$$ClCH_2CH_2CH_2CN + KOH = \underbrace{CH_2—CH_2—CH}—CN + KCl + H_2O$$

but its true nature was not recognized until a year later.[2] Although certain workers have claimed that this process gives "satisfactory" results, this has not been the general experience, since losses arise as the result of hydrolysis and polymerization. More recent descriptions of the method have been given by Haller and Benoist, Nicolet and Sattler and by one of us.[3] It is

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[1] The experimental data reported herein have been abstracted from theses on cyclopropane derivatives which have been presented to the Rensselaer Polytechnic Institute by Raymond J. Anderson, John Lachmann and Gustavus E. Smith in partial fulfilment of the requirements for the degree of Chemical Engineer.

[2] M. L. Henry, *Bull. sci. acad. roy. belg.*, [3] **36**, 34 (1898); *ibid.*, [3] **37**, 17–22 (1899).

[3] Haller and Benoist, *Ann. chim.*, [9] **17**, 28 (1922); Nicolet and Sattler, THIS JOURNAL, **49**, 2068 (1927); Cloke, *ibid.*, **51**, 1180–1181 (1929).