Ponndorf-Verley reduction of (±)-V with (S)-2-octanol affords (−)-VI. Third, the observation[8] that reaction of the phenylglyoxylate of (−)-VI with methylmagnesium iodide yields an excess of the (R)-atrolactate of (−)-VI has furnished supporting evidence for the stated configurational assignment. The (R)-configuration has thus been firmly established for (+)-III.

A Curtius degradation of (−)-(S)-III yielded (−)-I, identified by analysis, melting point, mixture melting point, rotation, and infrared spectrum. It follows that (+)-I has the (R)-configuration, in harmony with the earlier, more tentative conclusions.

EXPERIMENTAL

A mixture of 10 g. of 1,1'-binaphthalene-2,2'-dicarboxylic acid[6] [m.p. 138–145° dec., $[\alpha]_D^{29.5}$ −78.3° (c 0.83, 0.1N NaOH)], 92 ml. of thionyl chloride and 3.6 ml. of anhydrous pyridine was refluxed for 45 min. and the resulting orange solution was evaporated to dryness. The residue was taken up in carbon tetrachloride (100 ml.), the solution was filtered, and the filtrate was evaporated to yield 9.1 g. (82%) of the yellow, crystalline acid chloride, m.p. 173–177°. A solution of 8.05 g. of sodium azide in 20 ml. of water was added dropwise to a swirled solution of 8.05 g. of the acid chloride in 80 ml. of acetone; a precipitate formed on contact. The mixture was cooled in an ice bath and 120 ml. of water was added. The initially formed yellowish brown oil solidified on standing at ice bath temperature to yield a beige solid which was collected by centrifugation, washed with water, and dissolved in 120 ml. of benzene. The benzene solution was dried with calcium sulfate. A vigorous evolution of gas was produced when the solution was heated at 60–70°. After the reaction had subsided, the solution was heated under reflux for 1 hr., 50 ml. of 50% aqueous potassium hydroxide was introduced, and refluxing was continued for 1.5 hr. The benzene layer was separated, ca. 200 ml. of 6N hydrochloric acid was added, and mixture was heated on the steam bath for 15 min. The acid layer was separated, filtered from some gray insoluble material (m.p. >360°), and neutralized with sodium hydroxide. The precipitated amine was washed with water until the washings were neutral to give, after drying, 3.3 g. (40%) of product, m.p. 237–238°. Two recrystallizations from ethanol-benzene yielded a light beige solid, m.p. 242–243.5°, $[\alpha]_D^{30}$ −152.2° (c 1.78, benzene).

Anal.[9] Calcd. for $C_{20}H_{16}N_2$: C, 84.48; H, 5.67; N, 9.85. Found: C, 84.34; H, 5.58; N, 9.81.

A mixture of the product and of authentic[10] (−)-I [m.p. 245°, $[\alpha]_D^{20}$ −156° (c 1.0, benzene); lit.[3] m.p. 243°, $[\alpha]_D^{19}$ 183.8° (benzene)] melted at 242–244°; a mixture of the product and of authentic[10] (+)-I [m.p. 244.5–247°, $[\alpha]_D^{20}$ +154° (c 0.64, benzene)] had m.p. 195–205°. The infrared spectra (KBr pellet) of the product and of authentic (−)-I were identical.

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(8) K. Mislow, V. Prelog, and H. Scherrer. Helv. Chim. Acta, 41, 1410 (1958).

(9) Microanalysis by Schwarzkopf Microanalytical Laboratory, Woodside, N. Y.

(10) We thank Dr. J. H. Rassweiler for providing us with a sample of that substance.

Oxidation of Organic Sulfides with Dimethyl Sulfoxide

SCOTT SEARLES, JR., AND HUGH R. HAYS

In the attempted synthesis of a series of dialkyl and cyclic sulfoxides the usual methods of oxidation of the corresponding sulfides were sometimes found unsatisfactory. One of the difficulties is the relative ease of further oxidation of sulfoxide to sulfone. For example, we were unable to obtain di-t-butyl sulfoxide by oxidation of di-t-butyl sulfide with hydrogen peroxide, nitric acid, or dinitrogen tetroxide, although it was possible to obtain the corresponding sulfone with hydrogen peroxide.

In the hope of finding a mild enough oxidizing agent we attempted the following oxygen exchange reaction, using dimethyl sulfoxide as an oxygen donor:

$$R_2S + Me_2SO \longrightarrow R_2SO + Me_2S$$
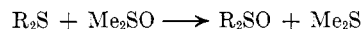
It has been known for some time that sulfoxides may serve as oxidizing agents for several inorganic reagents.[1] Also, Kornblum and collaborators in a recent communication reported the successful oxidation of several phenacyl halides with dimethyl sulfoxide.[2] In the present work, we attempted the dimethyl sulfoxide oxidation of several higher molecular weight sulfides.

Dimethyl sulfoxide was found to oxidize n-propyl, n-butyl, and tetramethylene sulfides to the corresponding sulfoxides in yields of 59, 55, and 58%, respectively. The conditions employed involved heating the sulfide with a 50% molar excess of dimethyl sulfoxide at 160–175° for several hours. Dimethyl sulfide was removed by distillation, as formed.

The structures of the products were shown by identity of melting points and/or boiling points and the infrared spectra with those of authentic samples. It was of interest that the sulfoxides were isolated in high purity by simple distillation, as shown by their melting points and infrared spectra. There was no evidence of any sulfone formation. Unfortunately, several similar sulfides did not react appreciably with dimethyl sulfoxide under these conditions, and attempts to catalyze the reactions with acid were unsuccessful.

EXPERIMENTAL

General procedure. A mixture of 0.1 mole of dialkyl sulfide and 0.15 mole of dimethyl sulfoxide[3] was heated at 160–

(1) R. Connor, in H. Gilman's, Organic Chemistry, John Wiley & Sons, New York, N. Y., 1943, Vol. I, p. 872.

(2) N. Kornblum, J. W. Powers, G. J. Anderson, W. J. Jones, H. O. Larson, O. Levand, and W. M. Weaver, J. Am. Chem. Soc., 79, 6562 (1957).

(3) We are indebted to the Stepan Chemical Co. for a generous gift of dimethyl sulfoxide.

TABLE I

OXIDATION PRODUCTS

| Sulfoxide | Yield | M.P. | | B.P. | |
		Obs.	Lit.	Obs.	Lit.
Di-n-propyl	59%	22–23°	24.5–25.5°	80°/2 mm.	80°/3 mm.
Di-n-butyl	55%	30–31°	32°	106–107°/2 mm.	—
Tetramethylene	58%	—	—	102–105°/15 mm.	105–107°/15 mm.

175° for 8–12 hr. The dimethyl sulfide was allowed to distill through a reflux condenser maintained at about 40°; its boiling point was observed to be 37° (lit. 37.30°).[4] The mixture was observed to turn yellow at first and eventually became black after 2–4 hr. Reduced pressure distillation separated the product from tarry residues and the product was redistilled.

The yields and properties of the products are given in Table I. The melting points were taken without recrystallization.

The infrared spectra of each of these compounds showed very strong absorption between 9.2 and 9.8μ, characteristic of the sulfoxide group. The spectrum of the known sample of n-propyl sulfoxide was identical with that of n-propyl sulfoxide. No bands in the 8.8μ and 7.5μ regions, characteristic of the sulfone group were observed.

Attempts to apply this oxidation to di-t-butyl, diisopropyl-diphenyl, and pentamethylene sulfides and to 3,3-dimethyl, thietane were unsuccessful under the above conditions. Only unreacted starting materials were recovered from these reactions.

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(4) D. T. McAllan, T. V. Cullum, R. A. Dean, and F. A Fidler, *J. Am. Chem. Soc.*, **73**, 3627 (1951).

A Re-examination of Limitations of the Hofmann Reaction[1,2]

ERNEST MAGNIEN AND RICHARD BALTZLY

An implicit tribute to the original study of Hofmann on the rearrangement that bears his name lies in the fact that except for theoretical interpretations, no substantial revision of his work has been made in the course of seventy years.[3] Theoretical considerations, however, led to the belief that the practical limitations of this reaction as set forth by Hofmann, were functions of his experimental conditions and might therefore be extended by variations of these.

In operating with the amides of fatty acids, Hofmann found that yields of amine fell off with the higher members because of two side reactions. From heptanoamide to capramide there was loss from formation of nitrile having one less carbon atom than the starting amide. With the still higher members, loss in yield was due mainly to formation of alkylacyl ureas. When the amide is not derived from a simple fatty acid, the limitations are somewhat different, numerous phenethyl amines being satisfactorily obtained from the corresponding hydrocinnamic amides. Here also, however, a limitation does appear. For example, the late J. S. Buck[4] recovered 3,4-diethoxy-α-methylhydrocinnamamide unchanged from an attempted Hofmann rearrangement. This result was presumably due to the lack of solubility, since the same amide was converted quantitatively to N-carbomethoxy-β-(3,4-diethoxyphenyl)isopropylamine by the Jeffreys modification[5] of the Hofmann. Such a solubility limitation may be expected to be general, especially when an amide is treated with preformed hypohalite, since that reagent cannot long persist after the temperature has been raised above about 40°.

It was our view that the loss from urea formation was largely due to the physical properties of the organic compounds. As molecular weight increases, the isocyanate, the proximate rearrangement product, the product amine and the earlier intermediates have an increasing tendency to extract each other from solution, whereby the isocyanate is increasingly likely to react with other substances than hydroxide ion. Such side reactions should be minimized by use of an inert co-solvent. The obvious substance for that purpose is dioxane.[6]

It also seemed likely that formation of nitrile, observed by Hofmann with amides of intermediate chain length, was due to his technique of adding bromine to a solution or mixture of the other reactants. Where the amide is added to an initially

(1) Abstracted from a thesis submitted by Ernest Magnien in partial fulfillment of the requirement for the M.S. degree at the Polytechnic Institute of Brooklyn, 1958.

(2) The authors express their gratitude to Burroughs Wellcome & Co. (U.S.A.) Inc. for permission to carry out the experimental part of this study in the Wellcome Research Laboratories.

(3) The literature on the Hofmann Reaction has been reviewed by Wallis and Lane up to 1946. [E. S. Wallis and J. F. Lane, *Org. Reactions*, III, 267 (1946)]. Except for special points, references are not made here to literature covered in this review.

(4) J. S. Buck, unpublished work.

(5) E. Jeffreys, *Ber.*, **30**, 898 (1897); *Am. Chem. J.*, **22**, 14 (1899).

(6) The use of dioxane as a co-solvent in Hofmann reactions was mentioned in a preparation of β-2,5-dimethoxy-phenylisopropylamine. R. Baltzly and J. S. Buck, *J. Am. Chem. Soc.*, **62**, 161 (1940).