(0.3 mole) of sodium hydride in 50 ml. of dimethoxyethane. To the suspension which was obtained was added 3.0 g. (0.036 mole) of 3-pentanone. The mixture was then stirred at room temperature for 30 min. and cooled, and the sticky precipitate was filtered and washed with dimethoxyethane. The filtrate was then fractionated. In addition to dimethoxyethane, a small amount of O-ethyldiethylketoxime was obtained, b.p. 131–134°.[11] The infrared spectrum of this liquid was identical with that of authentic O-ethyldiethylketoxime.

Acknowledgment.—We are indebted to Merck and Company, Inc., for a grant which supported part of this work.

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Reduction of N-Alkoxyphthalimides

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Orndorff and Pratt have reported that the interaction of phthalic anhydride and hydroxylamine gave two compounds, one white and the other yellow.[1] These authors were unable to assign definite structures to these substances. Pratt and Gibbs later made the methyl ethers of the white compound and of the yellow compound but also were uncertain as to the structures of these compounds.[2]

More recently, Roderick and Brown found that there was no detectable difference between the infrared spectra of the white and yellow forms of Orndorff and Pratt's products.[1] Also, they found that the yellow color of the "yellow form" was due to a slight amount of impurity that could be removed by several methods. They concluded that both so-called forms were N-hydroxyphthalimide.[3]

The findings of Kühler and Wegler[4] confirmed the conclusions of Roderick and Brown.

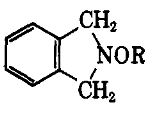
It occurred to the present authors that a new class of isoindoline derivatives, N-alkoxyisoindolines (I), might be made by the reduction of N-alkoxyphthalimides, provided that the alkoxy group was not removed during the reduction.

The methyl and ethyl ethers of N-hydroxyphthalimide were prepared by the interaction of an aqueous solution of sodium bicarbonate and the appropriate alkyl sulfate with N-hydroxyphthalimide. Hydrolysis of the resulting N-alkoxyphthalimide with boiling dilute hydrochloric acid gave alkoxyamine hydrochlorides.[5]

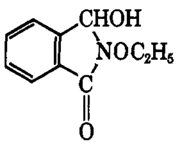
N-Alkoxyisoindolines (I) were indeed obtained on the reduction of the methyl and ethyl ethers of N-hydroxyphthalimide with lithium aluminum hydride. The correctness of the N-alkoxyisoindoline structure for the reduction products was confirmed by elemental analysis, infrared spectra, and n.m.r. spectra.

Reduction of N-ethoxyphthalimide with the weaker reducing agent, sodium borohydride, did not yield N-ethoxyisoindoline but rather 2-ethoxy-3-hydroxyphthalimidine (II). This structure for the reduction product was demonstrated by elemental analyses, infrared spectra, and n.m.r. spectra. Horii, Iwata, and Tamura have shown that the analogous compounds, N-alkylphthalimides, were reduced by sodium borohydride to 2-alkyl-3-hydroxyphthalimidine.[6]

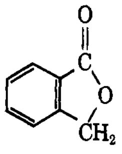
However, reduction of N-methoxyphthalimide with sodium borohydride did not yield a phthalimidine derivative. The only organic product which was isolated was phthalide (III). The same compound was obtained by Horii, Iwata, and Tamura in varying amounts by the reduction of N-alkylphthalimides.[6] The formation of phthalide on reduction of N-methoxyphthalimide may be accounted for in a way analogous to that suggested by Horii, Iwata, and Tamura.[6] It is suggested that the N-methoxyisoindoline which was formed, first was reduced further to a borohydride complex of *o*-hydroxymethyl-N-methoxybenzamide which was later hydrolyzed to phthalide. It would appear that in the case of N-ethoxyphthalimide that the more bulky N-ethoxy group interfered with a similar reduction to *o*-hydroxymethyl-N-ethoxybenzamide.



I



II



III

Experimental[7]

N-Alkoxyphthalimides.—N-Hydroxyphthalimide (0.64 mole) was dissolved in a solution of 120 g. of sodium bicarbonate in 300 ml. of water. To this solution was slowly added 0.7 mole of dialkyl sulfate with stirring. In the case of diethyl sulfate the addition took place at room temperature for 8 hr. while in the case of dimethyl sulfate the addition took place at approximately 15° for 90 min. The precipitate of N-alkoxyphthalimide was filtered and recrystallized from 95% ethanol and then from 1-butanol; yield, 60–64%.

N-Methoxyphthalimide.—The infrared spectrum (KBr) showed important bands at 3.4 (w), 5.8 (s), 6.8 (m), 7.2 (m), 8.4 (s), 8.8 (s), 9.2 (m), 9.8 (s), 10.0 (s), 11.0 (s), 11.3 (s), 12.6 (m), and 14.2 (s) μ; m.p. 133°.[2]

Anal. Calcd. for $C_9H_7NO_3$: C, 61.0; H, 3.98. Found: C, 61.37; H, 4.11.

N-Ethoxyphthalimide.—The infrared spectrum (KBr) showed bands at 3.4 (w), 5.8 (s), 6.8 (m), 7.1 (m), 7.3 (m), 8.4 (s), 8.9 (s), 9.2 (m), 9.8 (s), 10.2 (s), 11.3 (s), 12.6 (m), and 14.2 (s) μ; m.p. 97–98°.[1]

Alkoxyammonium Chlorides.—The N-alkoxyphthalimides were refluxed with an excess of 6 *N* hydrochloric acid for 2 hr. On cooling, phthalic acid precipitated. The filtrate from this mixture was evaporated under reduced pressure. The residue was recrystallized from ethanol–ether; yield, 56–60%. Meth-

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[1] W. R. Orndorff and D. S. Pratt, *Am. Chem. J.*, **47**, 89 (1912).

[2] D. S. Pratt and H. D. Gibbs, *Phillippine J. Sci.*, **8A**, 165 (1913).

[3] W. R. Roderick and W. G. Brown, *J. Am. Chem. Soc.*, **79**, 5196 (1957).

[4] E. Kühler and R. Wegler, *Ann.*, **616**, 183 (1958).

[5] J. Petraczek, *Ber.*, **16**, 827 (1883).

[6] Z. Horii, C. Iwata, and Y. Tamura, *J. Org. Chem.*, **26**, 2273 (1961).

[7] All infrared spectra reported were determined on a Perkin-Elmer Infracord. N.m.r. spectra were obtained on a Varian A-60 instrument.

oxyamine hydrochloride had m.p. 150–151°[5]; ethoxyamine hydrochloride had m.p. 129–131°.[8]

N-Alkoxyisoindolines.—Over a period of 90 min. a solution of 0.05 mole of N-alkoxyphthalimide in dry ether was slowly added with stirring to a slurry of 0.13 mole of lithium aluminum hydride in ether. After the mixture had been stirred at room temperature for 8 hr., the reaction mixture was cooled and the complex present was decomposed by successive additions dropwise of 6.5 ml. of water, 4.5 ml. of 20% potassium hydroxide, and 10 ml. of water. The inorganic salts were removed by filtration. The filtrate was dried with magnesium sulfate and then fractionated.

N-Ethoxyisoindoline Picrate.—A colorless liquid, b.p. 145–152° (5 mm.), was obtained which became dark red on standing. The infrared spectrum of the freshly distilled, colorless liquid (neat) showed important absorption bands at 3.5 (m), 6.8 (m), 7.3 (m), 9.5 (s), 11.2 (m), and 13.4 (s) μ and no carbonyl absorption. A few drops of the freshly distilled liquid was added to a saturated solution of picric acid in 95% ethanol. The mixture was warmed over steam for a few minutes and then cooled. The yellow crystalline precipitate was filtered and recrystallized from ethanol, m.p. 170° dec. The n.m.r. spectrum of this picrate (in deuterated dimethyl sulfoxide) showed a singlet at τ 1.7 with a relative area of 2, a singlet at 2.7 with an area of 4, a singlet at 5.35 with an area of 4, a quartet at 6.0 with an area of 2, and a triplet at 9.0 with an area of 3.

Anal. Calcd. for $C_{16}H_{16}N_4O_8$: C, 48.98; H, 4.11; N, 14.27. Found: C, 48.85; H, 4.38; N, 14.78.

N-Methoxyisoindoline Picrate.—Fractionation gave a light yellow liquid, b.p. 135–140° (15 mm.), which became colorless on repeated distillations; yield, 72% of theory. On standing in the cold, the color quickly changed to dark red. The infrared spectrum (neat) had bands at 3.4 (s), 3.55 (m), 9.5 (s), 6.8 (m), and 13.4 (s) μ but no carbonyl bands. The picrate was prepared by the addition of a few drops of the freshly distilled liquid to a saturated solution of picric acid in 95% ethanol. After the solution had been warmed, it was cooled and a yellow crystalline precipitate appeared. This was filtered and recrystallized from ethanol, m.p. 104–105°.

Anal. Calcd. for $C_{15}H_{14}N_4O_8$: C, 47.63; H, 3.73; N, 14.80. Found: C, 47.66; H, 3.97; N, 14.61.

2-Ethoxy-3-hydroxyphthalimidine.—To 10.0 g. (0.05 mole) of N-ethoxyphthalimide suspended in 90% methanol was added a solution of 3.7 g. of sodium borohydride in methanol over a period of 1 hr. After the mixture had been stirred at room temperature for 18 hr., 5 ml. of glacial acetic acid was added. The methanol was partially removed by evaporation under reduced pressure. Water was added; the white solid which formed was filtered and then recrystallized from water: m.p. 120–121°; yield, 62% of theory. Characteristic infrared absorption bands (KBr) were found at 3.2 (s), 3.5 (m), 6.0 (s), 6.8 (m), 9.35 (s), and 13.3 (s) μ. The n.m.r. spectrum (in $CDCl_3$) showed a singlet at τ 2.0 (area 4), a doublet at 3.7 (area 1), a doublet at 6.45 (area 1), a quartet at 5.5 (area 2), and a triplet at 8.6 (area 3).

Anal. Calcd. for $C_{10}H_{11}NO_3$: C, 62.15; H, 5.74; N, 7.25. Found: C, 62.12; H, 5.71; N, 7.21.

Phthalide.—To 3.9 g. (0.022 mole) of N-methoxyphthalimide suspended in 90% ethanol was added a solution of 1.9 g. (0.05 mole) of sodium borohydride in 100 ml. of ethanol over a period of 1 hr. The mixture was then stirred at room temperature for 6 hr. The bases were neutralized with glacial acetic acid. The ethanol was partially removed by evaporation under reduced pressure. Water precipitated a white solid which was recrystallized from water: m.p. 73–74°; lit.[9] m.p. 73°; yield, 67% of theory. The infrared absorption spectrum (KBr) of this solid showed characteristic bands at 3.5 (w), 5.7 (s), 6.8 (m), 6.9 (m), 7.2 (m), 7.5 (m), 7.7 (m), 8.1 (m), 9.4 (s), 9.85 (s), and 13.3 (s) μ.

Anal. Calcd. for $C_8H_6O_2$: C, 71.61; H, 4.52. Found: C, 71.15; H, 4.44.

Acknowledgment.—We are indebted to Merck and Company, Inc., for a grant in support of this research.

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An Improved Method for the Preparation of Volatile Epoxides

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The synthesis of the isomeric 2-butene oxides has been reported previously[2,3] and involves the conversion of *cis-* and *trans-*2-butene to the corresponding epoxides *via* the halohydrins. The halohydrins are isolated and purified before treatment with strong aqueous base to give the epoxides. The over-all yields average 44–48%.

The first one-step preparation of the isomeric 2-butene oxides was reported by Eliel and Delmonte.[4] The *trans* epoxide was prepared by treating the monotosylate (not isolated) of *meso*-2,3-butanediol with strong aqueous base. The reported yield of epoxide in this procedure is 28%.

Various investigators who have used the 2-butene oxides in research have prepared the compounds by the methods outlined above. It is of interest to note that no direct oxidations of the olefins with peracids seem to have been reported. We have observed that direct epoxidation of *cis-* or *trans-*2-butene with *m*-chloroperbenzoic acid in dioxane gives the corresponding *cis-* and *trans-*2-butene oxides in a high state of stereochemical purity and in good yield (52–60%). The experimental procedure is much simpler in that the epoxide is distilled directly from the reaction mixture without prior removal of the *m*-chlorobenzoic acid. Under these conditions the epoxides are stable in the presence of the carboxylic acid.

The general method also appears to be applicable to the preparation of higher boiling epoxides. Treatment of 1-hexene with *m*-chloroperbenzoic acid in diglyme (b.p. 162°) followed by direct distillation of the 1-hexene oxide at 116–119° gives the epoxide in 60% yield.

The greater simplicity in the experimental procedure used and the saving in time and effort makes this procedure very attractive for the preparation of volatile epoxides.

Experimental

Preparation of *cis-* and *trans-*2-Butene Oxides.—In a three-necked 1000-ml. round-bottom flask equipped with a delivery tube, magnetic stirrer, and Dry Ice–acetone reflux condenser was placed 500 ml. of anhydrous dioxane and 65.3 g. (0.322 mole) of *m*-chloroperbenzoic acid (FMC Corp., 85% minimum purity). After dissolution of the acid, the contents of the flask was cooled to 0°; 18.1 g. (0.322 mole) of *cis-* or *trans-*2-butene (Matheson Coleman and Bell, 99.0% minimum purity) was added *via* the delivery tube. The contents of the flask was stirred for 10 hr. under the Dry Ice–acetone condenser. At the end of this period of time the butene stopped refluxing. The flask was stoppered and placed in a refrigerator overnight. The mixture was subjected to distillation, collecting the fraction up to 100°. This fraction was fractionated through a 2-ft. helices-packed column giving a 52–60% yield of *cis*-2-butene oxide, b.p. 58.0–59.0° (748 mm.), and *trans*-2-butene oxide, b.p. 52.0–53.0° (748 mm.).

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