For purposes of comparison, the monoethyl ether was also prepared with one equivalent of N-chlorosuccinimide and alcoholysis of the resulting unstable, lachrymatory oil. The stable liquid thus obtained exhibited a strong peak in the infrared at 1100 cm.$^{-1}$ consistent with an aliphatic ether.[6] This was verified by elemental analysis.

Experimental[7]

A. **2,3-Dimethylquinoxaline.**—In 2 l. of 2.5% acetic acid, 135 g. of *o*-phenylenediamine (1.25 moles) was dissolved at 65°. A solution of 107.6 g. of biacetyl (1.25 moles) in 750 ml. of water was added, with stirring, over a period of 15 min. The mixture was stirred for an additional 15 min., neutralized with 20% potassium hydroxide, and allowed to stand overnight at 5°. The crude product was filtered, washed with cold water, and recrystallized from aqueous ethanol after treatment with Norit. The product, which crystallizes as the dihydrate, was dried at 60° overnight and was found to weigh 180 g. (91%). It had a melting point of 105.5–106.5° (lit. m.p. 106°).

B. **5,6-Dimethylpyrazine-2,3-dicarboxylic Acid.**—2,3-Dimethylquinoxaline (40 g., 0.253 mole) was dissolved in 2 l. of water at 80° in a 3-l. flask fitted with an efficient stirrer and a thermometer. Potassium permanganate (240 g., 1.52 moles) was added in 3–5-g. portions with vigorous stirring at a rate sufficient to maintain the temperature at 85°. The addition required 1.5–2 hr. The reaction mixture was then stirred at 90° for an additional hour. The hot mixture was filtered and the cake of manganese dioxide washed with hot water until the test washings no longer gave a pink color with 1% ferrous sulfate solution. The combined filtrate and washings were evaporated to about 1 l. under reduced pressure and 126 ml. of 37% hydrochloric acid (1.52 moles) cautiously added with stirring. Evaporation under reduced pressure was continued until 500 ml. remained. The mixture was then cooled and the crude diacid–dihydrate removed by filtration. The filtrate was evaporated to dryness under reduced pressure. Fifty milliliters of water was added followed by 750 ml. of acetone and the mixture refluxed 15 min., filtered, and the filtrate evaporated to dryness. The resulting solid was dissolved by refluxing in 750 ml. of acetone, treated with Norit, filtered, and evaporated to dryness to yield the acid as a light tan crystalline solid. The crude product was recrystallized from water after treatment with Norit and dried in a vacuum desiccator over Drierite. The pure product weighed 34 g. (69%) and had a melting point of 192–193° dec. (lit.[8] m.p. 190°); neut. equiv., 98.51 (theoretical 98.08).

C. **Derivatives of 5,6-Dimethylpyrazine-2,3-dicarboxylic Acid.** 1. **Anhydride.**—Anhydrous acid (4.90 g., 0.025 mole) in 15 ml. of acetic anhydride was heated on a water bath for 4 hr., cooled at 0°, and filtered to yield 2.8 g. of colorless crystals having a melting point of 171–171.5°. Evaporation of the mother liquor followed by treatment with Norit yielded an additional 0.94 g. of anhydride; total yield, 3.74 g. (84%).

Anal. Calcd. for $C_8H_6N_2O_3$: C, 53.94; H, 3.40; N, 15.73. Found: C, 54.00; H, 3.48; N, 15.71.

2. **Methyl Hydrogen Ester.**—One gram of anhydride (0.006 mole) was refluxed in 5 ml. of absolute methanol for 15 min. and evaporated to dryness on a water bath. The residue was recrystallized from benzene–cyclohexane to yield 0.97 g. (82%) of colorless crystals melting at 107–107.5°; neut. equiv., 208.9 (theoretical 210.2).

Anal. Calcd. for $C_9H_{10}N_2O_4$: C, 51.43; H, 4.80; N, 13.33. Found; C, 51.38; H, 4.86; N, 13.31.

D. **2,3-Dimethylpyrazine.**—Anhydrous 5,6-dimethylpyrazine-2,3-dicarboxylic acid (58.9 g., 0.30 mole) was refluxed in 350 ml. of quinoline, under a stream of nitrogen, until no more carbon dioxide was evolved (approximately 4 hr.). The mixture was then carefully fractionated under vacuum to yield 30.2 g. (93%) of 2,3-dimethylpyrazine (I) boiling at 45–46.5° (11 mm.).

Physical properties: b.p. 155.5-156.5° (lit.[9] 156°); n^{20}_D 1.5076; d^{25}_4 1.005.

I was identified by preparation of a picrate, m.p. 149.5–150.5° (lit.[9] 150°).

A methiodide was prepared by a method given by Shriner, Fuson, and Curtin[10] which had m.p. 183–184°.

Anal. Calcd. for $C_7H_{11}N_2I$: N, 11.22. Found: N, 11.21.

E. **2-(α-Chloromethyl)pyrazines.** 2-(α-Chloromethyl)-3-methylpyrazine and 2,3-bis(α-chloromethyl)pyrazine (II) were prepared by the reaction of N-chlorosuccinimide with an equimolar quantity of 2,3-dimethylpyrazine (I), using a catalytic amount of benzoyl peroxide (procedure A). In addition, 2,3-bis(α-chloromethyl)pyrazine (II) was also prepared by treatment of I with chlorine in the presence of ultraviolet light (procedure B).

These α-chloromethylpyrazines are unstable, lachrymatory oils, which decompose on standing, and could not be purified by fractional distillation. Accordingly, after isolation, they were immediately used in the preparation of the corresponding pyrazinylmethyl ethyl ethers.

Procedure A. All (α-Chloromethyl)pyrazines.—I (5.4 g., 0.05 mole) in 250 ml. of carbon tetrachloride containing 1 or 2 equivalents of N-chlorosuccinimide and 0.1 g. of benzoyl peroxide was refluxed 12 hr., cooled to 0°, filtered, and the residue washed with two additional 25-ml. portions of carbon tetrachloride. The combined filtrate and washings were evaporated under vacuum at room temperature. The residual oils were immediately used for the preparation of the corresponding ethyl ethers. The yields of these oils ranged from 75–80% (assuming the oils to be pure).

Procedure B. 2,3-Bis-(chloromethyl)pyrazine.—To 250 ml. of carbon tetrachloride was added 10.8 g. of I (0.1 mole). Chlorine was rapidly bubbled in through a sintered glass gas addition tube while the flask was irradiated with ultraviolet light (Burdick-Type QA-250N). A white precipitate formed after only a few minutes. The passage of chlorine was continued for 2 hr. The mixture was then filtered and the residue washed with two 50-ml. portions of fresh carbon tetrachloride. The filtrate and washings were evaporated under reduced pressure leaving 4.0 g. II as a yellow oil which was immediately used in the preparation of the corresponding ethyl ether. A 23% conversion to II was obtained, based on recovery of 5.6 g. I from its hydrochloride. The yield was 48% (assuming the oil to be pure).

F. **2,3-Bispyrazinylmethyl Ethyl Ether.**—To 0.12 mole of sodium ethoxide in 200 ml. of absolute ethanol was added 0.035 mole of II (6.2 g.) in 25 ml. of absolute ethanol and the mixture refluxed 12 hr., cooled, filtered, and the residue of sodium chloride washed with several portions of absolute ethanol. The combined filtrate and washings were diluted with 25 ml. of water and concentrated on a water bath until most of the alcohol had been removed. The residual oil was then extracted from the alkaline, aqueous layer with diethyl ether. The ether extracts were dried over anhydrous magnesium sulfate and concentrated on a water bath. The residual oil was then carefully fractionated to yield 1.4 g. (20%) of the bisethyl ether which had a boiling point of 115–116° (10 mm.), n^{20}_D 1.4890.

Anal. Calcd. for $C_{10}H_{16}N_2O_2$: C, 61.20; H, 8.22; N, 14.27. Found; C, 61.15; H, 8.31; N, 14.41.

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(7) All melting points are corrected. Infrared spectra were determined on a Perkin-Elmer Infracord spectrophotometer. Microanalyses were performed by Spang Microanalytical Laboratory, Ann Arbor, Mich., or by Schwarzkopf Microanalytical Laboratory, Woodside, N. Y.

(8) K. A. Böttcher, *Ber.*, **46**, 3084 (1913).

(9) Jorre, Dissertation, Kiel, 1897; Beilstein's "Handbuch der organischer Chemie," 4th Ed., Springer Verlag, Berlin, 23, p. 59.

(10) R. L. Shriner, R. C. Fuson, and D. Y. Curtin, "The Systematic Identification of Organic Compounds," 4th Ed., John Wiley and Sons, Inc., New York, N. Y., 1956, p. 228.

The Cleavage of Aryl Ethers by Alkali Metals in Aliphatic Ether Solvents. Detection by Electron Spin Resonance[1]

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The cleavage of aryl ethers by alkali metals in inert solvents at room temperature was detected by electron

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spin resonance techniques. Some aryl ethers have previously been cleaved by alkali metals,[3] but only under extreme conditions and with no immediate indication of products. In the present research, the cleavage of several types of aromatic ethers was investigated in a variety of inert aliphatic ether solvents employing the alkali metals lithium, sodium, potassium, rubidium, and cesium (Table I). The reaction was first detected in a study of spin exchange in the singly and doubly charged anions of biphenylyl ether.[4]

TABLE I

PRODUCT ANALYSES

Aryl ether	Alkali metal	Products, %		
		ArOH	ArH	ArAr
$(p\text{-PhC}_6H_4)_2O$	Li, Na, K, Rb	60.2	36.0[a]	6.6
$(\beta\text{-C}_{10}H_7)_2O$	Na, K	56.2	42.2[a]	13.8
$(\alpha\text{-C}_{10}H_7)_2O$	Na, K	43.1	6.3[a]	31.9
$(p\text{-NO}_2C_6H_4)_2O$	Na, K, Cs	Negative ion, no cleavage		
$C_6H_5OCH_3$	Na, K	9.7	[c]	[a,b]
$(C_6H_5)_2O$	Na	7.6	[c]	[a,b]

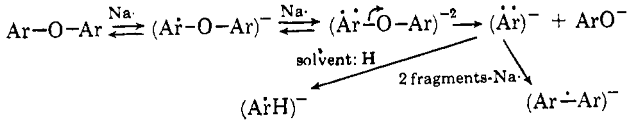
[a] Product detected as negative ion. [b] Incomplete cleavage, yields based on 100% ether initially. Solvents used were 1,2-dimethoxyethane, tetrahydrofuran, tetrahydropyran, and 2-methyltetrahydrofuran. [c] Not detected.

The products of the reaction were, in each case examined, the arylphenol, the aryl hydrocarbon, and small amounts of unidentified high melting neutral material. Product yields and reactivity were greatest with the larger aryl groups—60% *p*-phenylphenol from biphenylyl ether to *ca.* 8% phenol from diphenyl ether. In the case of anisole and diphenyl ether, some unchanged material was recovered. Bis-(*p*-nitrophenyl) ether formed a mononegative ion which failed to cleave and decomposed (losing radical activity) on standing several days. Even the most rigorous conditions, cesium and dimethoxyethane did not succeed in cleaving this ether.[5] Anisole remained completely inert to sodium in tetrahydrofuran, even after standing one week and after subjection to temperatures from −80 to 50°, but reacted readily with potassium in dimethoxyethane. A transient deep yellow color was observed initially in the latter experiment, but, if this species was paramagnetic, it could not be detected, since the immediate formation of biphenyl negative ion covered any other species with its strong signal. Diphenyl thioether (diphenyl sulfide) in dimethoxyethane under treatments similar to those of anisole, yielded no paramagnetic products. The reaction rate depended in some measure upon the solvent in the approximate order dimethoxyethane > tetrahydrofuran > tetrahydropyran ≥ methyltetrahydrofuran[6,7]; however, solvent variation alone did not appear to change significantly the relative product ratios of per cents. The alkali metals were found to be reactive in the order expected: lithium < sodium < potassium < rubidium ≤ cesium.

Several color changes were evident during the reaction stages. In general, the singly charged negative ion was amber or orange, whereas the dinegative ion (detected only with the larger aryl groups) was a greenish color. The color of the product mixture was generally very dark green or blue, owing to the predominant color of the aryl hydrocarbon or the diaryl negative ions.

Stages of reaction were easily followed with e.s.r. signals typical of the compounds under study.[4,8] In the carefully studied case of β-naphthyl ether, increasing reduction of the ether to the orange paramagnetic ion resulted in increasing signal amplitude until the formation of green diamagnetic dinegative ion caused a decrease in signal strength. Further reduction of the mixture resulted in immediate cleavage of the ether and appearance of a strong naphthalene negative ion spectrum. An attempt to produce a paramagnetic negative ion of sodium β-naphtholate resulted only in a diamagnetic and very fluorescent material; therefore, it is not likely that the presence of phenolate anions in the product mixtures would interfere with the hydrocarbon spectra.

Product analysis and the e.s.r. spectra indicate that the reaction proceeds through a heterolytic cleavage of the aryl carbon–oxygen bond of the dinegative ion. During cleavage the two paired electrons are most likely localized in the aryl, rather than the aryloxy, fragment. The aryl fragment may then extract a hydrogen atom from the solvent or combine with another aryl fragment to form the products obtained.



The high-melting neutral products (unidentified) noted earlier are compounds which probably result from combination with aryl fragments of solvent radicals generated by hydrogen atom extraction.

$$(\ddot{\mathrm{Ar}})^- \xrightarrow{\text{solvent:H}} (\dot{\mathrm{Ar}}\mathrm{H})^- + (\text{solvent}\cdot)$$

In the cleavage of 1-naphthyl ether only the strong signal of naphthalenide ion was detected in the product mixture; however, product analysis indicated that 1,1′-dinaphthyl was the more abundant product. Consequently, experiment proved that somewhat less of an equivalent of naphthalene added to one equivalent of 1,1′-dinaphthylide ion indeed resulted in exchange of the electrons to naphthalene. Studies are being undertaken to determine the reason for this anomaly, since generally, the larger aryl system possesses the greater electron affinity.[9]

Experimental

General Remarks.—All samples were prepared in a glass apparatus described previously[7] for use in an instrument described earlier.[10] In those experiments in which the major products were separated and examined, 1 g. of sample was used; in those in

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[3] P. P. Shorygin, *Ber.*, **57B**, 1627 (1924); *Comp. rend. acad. Sci. URSS*, **14**, 505 (1937) [*Chem. Abstr.*, **31**, 5777 (1937)]; M. Tomita, Y. Inubushi, and H. Niwa, *J. Pharm. Soc. Japan*, **72**, 206 (1952) [*Chem. Abstr.*, **47**, 6428g (1955)]; A. A. Morton and A. E. Brachman, *J. Am. Chem. Soc.*, **76**, 2973 (1954).

[4] D. H. Eargle, Jr., and S. I. Weissman, *J. Chem. Phys.*, **34**, 1840 (1961).

[5] Splitting by cesium (I = 7/2) was detected in the negative ion spectrum, which was much broader (47.8 gauss) than the potassium spectrum (30.9 gauss), but not quite so broad as the spectrum of cesium–nitrobenzene (53.9 gauss).

[6] N. D. Scott, J. F. Walker, and V. L. Hansley, *J. Am. Chem. Soc.*, **58**, 2442 (1936).

[7] D. E. Paul, D. Lipkin, and S. I. Weissman, *ibid.*, **78**, 116 (1956).

[8] N. M. Atherton and S. I. Weissman, *ibid.*, **83**, 1330 (1961); M. G. Townsend, *J. Chem. Soc.*, 51 (1962).

[9] G. J. Hoijtink, in private communication, reports noting this behavior of α-dinaphthyl.

[10] R. L. Ward and S. I. Weissman, *J. Am. Chem. Soc.*, **79**, 2086 (1957).

which the reaction was examined only by means of the e.s.r. signal, samples of 2–3-mg. size were used. The alkali metals, except for lithium, were distilled into the sample tubes under a vacuum of about 10^{-6} torr; lithium metal was carefully melted (with partial reaction with the glass) in a side-arm tube.

Cleavage of β-Naphthyl Ether.—As a typical example, the cleavage by sodium and subsequent work-up of β-naphthyl ether is described. After introduction of β-naphthyl ether (1.00 g., 0.0037 mole) into the sample tube, the system was outgassed and a small chunk (*ca.* 0.2 g.) of freshly cut sodium was distilled three times through constrictions in a side tube, each constriction being sealed off after use. About 4 cc. of dimethoxyethane was distilled into the sample tube (using liquid nitrogen as coolant), and the sample and solvent were thoroughly degassed. The sample tube was then sealed from the vacuum system and shaken two or three times to allow the solution to contact the metal mirror. An orange color immediately developed, which was found to be the color of the mononegative ion. Subsequent shaking caused the mixture to turn a dark blue-green, indicative of the formation of naphthalene negative ion. The mixture was shaken 1 hr. longer, and the sample tube was broken open and the contents exposed to air, whereupon the blue-green color rapidly disappeared. The mixture was neutralized with dilute sulfuric acid and 20 cc. of ether added to it. Extraction of the products was accomplished, first with sodium bicarbonate solution, then with sodium hydroxide, the neutral material remaining unchanged. The acidified bicarbonate extract in this case, as in all others, yielded only a very thin film (after evaporation of the ether solvent) having an odor of aliphatic acids. The acidified sodium bicarbonate extract yielded a white material, which, after sublimation, weighed 0.30 g., m.p. 122°. The melting point upon admixture with authentic β-naphthol was unchanged; yield, 56%. The ether was removed from the neutral material, which was fractionally sublimed. The first and easiest obtained fractions were of an aromatic white material, 0.20 g., m.p. 80–83°, mixture melting point with authentic naphthalene unchanged. Subsequent fractions yielded a white compound, 0.13 g., m.p. 181–183.5 (mixture melting point with β-dinaphthyl unchanged), and a small amount (0.01 g.) of very high-melting material which was not identified. We assume some product loss occurred during the work-up and sublimation procedure; the product yields are all based on pure material recovered.

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The Conversion of 2-Acetoxypulegone to Menthofuran. Terpenes. V.[1]

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Menthofuran, II, has been prepared from isopulegone, I, and from pulegone, Ia, as shown in Diagram I.[4,5,6]

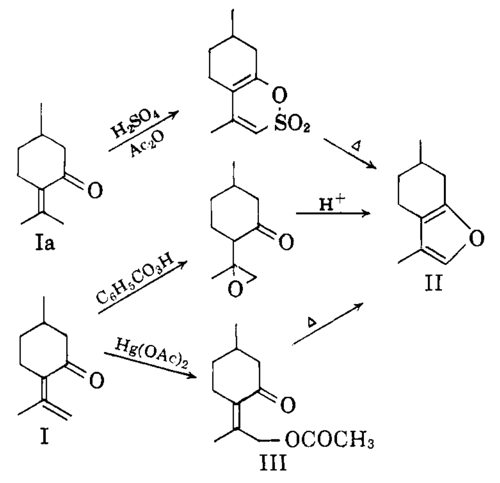
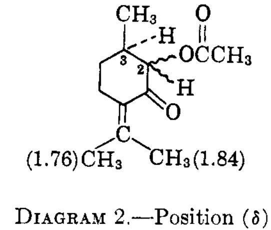


DIAGRAM I

We now report the isolation of optically pure menthofuran as the major product of the pyrolysis of 2-acetoxypulegone, V (Diagram 2). This unusual reaction prompted us to reinvestigate the structure of the product obtained by treating pulegone with mercuric acetate; structure V was assigned to this product by earlier workers.[7] Structure III previously had been assigned to the product obtained by treating isopulegone with mercuric acetate; on pyrolysis III gave menthofuran.

The product isolated on treatment of pulegone with mercuric acetate according to the procedure of Reitsema[7b] was found to have physical properties identical with those previously reported. However, gas chromatography (hydrogen flame detector) showed that it was a mixture containing approximately equal amounts of two components; attempts to separate these two compounds using column chromatography failed. Nevertheless, an examination of the n.m.r. spectrum of the product showed that III was not one of these components, and that the mixture consisted of the *cis* and *trans* isomers of 2-acetoxypulegone, V. The methyl protons of the isopropylidene group in V (*cis* and *trans* isomers) appeared at δ 1.76 (3 protons) and at δ 1.84 (3 protons). In both the *cis* and *trans* isomers the methyl protons of the isopropylidene group *cis* to the carbonyl group would be expected to show a paramagnetic shift compared with the methyl protons *trans* to the carbonyl group (see Diagram 2).[8] Structure III would be expected to show only three protons in this region of its n.m.r. spectrum. The protons of the C-3 methyl group in V ap-



Va *cis* (acetoxy group up)
CH_3 at C_3: δ 0.96; doublet $J = 7$ c.p.s.
H at C_2: δ 5.10; doublet, $J = 5.5$ c.p.s.
Vb *trans* (acetoxy group down)
CH_3 at C_3: δ 1.05; doublet $J = 5.5$ c.p.s.
H at C_2: δ 4.64; doublet $J = 10.5$ c.p.s.

DIAGRAM 2.—Position (δ) of protons in n.m.r. spectrum of 2-acetoxypulegone.

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[1] Terpenes. IV. Constitution and Absolute Configuration of Eremophilenolide, *Tetrahedron*, in press. Terpenes. III, *Chem. Ind.* (London), 38 (1962). Terpenes. II, *J. Org. Chem.*, **27**, 3535 (1962). Terpenes. I, *ibid.*, **26**, 981 (1961).

[2] Holder of National Science Foundation Summer Fellowship for Graduate Teaching Assistants, Summer, 1962. National Institutes of Health Fellow, 1962–63.

[3] Participant in National Science Foundation College Chemistry Teachers Research Participation Program at Oklahoma State University, Summer, 1962.

[4] W. Treibs, *Ber.*, **70**, 85 (1937).

[5] H. Fritel and M. Fetizon, *J. Org. Chem.*, **23**, 481 (1958).

[6] W. Treibs, G. Lucius, H. Kogler, and H. Breslauer, *Ann.*, **581**, 59 (1953).

[7] (a) W. Treibs and H. Bast, *ibid.*, **561**, 165 (1949); (b) R. H. Reitsema, *J. Am. Chem. Soc.*, **79**, 4465 (1957).

[8] L. M. Jackman, "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry," Pergamon Press, New York, N. Y., 1959.