Then the contents of the cylinder were dissolved in warm 5% sodium hydroxide, charcoal was added to the warm yellow solution, and the mixture was allowed to stand 15 minutes. The filtered solution was cooled to 5° in ice and cold dilute hydrochloric acid was added dropwise with stirring until the solution was neutral to litmus. (Ammonium chloride solution was preferred for an acid near the end-point.) The 4,4-dimethyl-2-thiothiazolidone, collected on a buchner funnel, weighed 8.0 g. after drying. By extracting the water solution with ether, 0.66 g. more was obtained; total yield 8.66 g., 83.5%, m.p. 87–91°. An analytical sample was obtained by recrystallization from 95% ethanol and sublimation at 60–75° (0.4 mm.), m.p. 93.4–93.8°.

By the procedure just described 9.5 g. of 2-methyl-2-amino-1-propanol was sealed with 20 g. of carbon disulfide in the stainless steel cylinder. After working up the resulting product in the same way, 11.25 g. of 4,4-dimethyl-2-thiothiazolidone, m.p. 112–116°, was obtained. An analytical sample obtained in the same way as that just described gave a m.p. 117.8–118.3°.[8,13]

The anomaly in the melting points of the two samples of 4,4-dimethyl-2-thiothiazolidone appears to be a case of dimorphism in which the two crystalline forms have nearly the same stability. The mixed melting point was 93–116°. Upon recrystallizing 1 g. of a 1:1 mixture of the two forms from 95% ethanol, 0.80 g. was obtained of m.p. 94–115° and a second crop by adding a few drops of water, of 0.12 g., m.p. 91–93°. The higher melting, less soluble crystals were almost spheroidal in shape, bounded by numerous surfaces while the lower melting form may be described as elongated plates. Seeding the melt of the lower melting crystals with the higher gave only a partial conversion to the second form, with a new m.p. 93–110°. The two samples gave the same 3-benzoyl derivative, the same 3-*p*-nitrobenzoyl derivative, and identical infrared spectra in carbon tetrachloride solution.

The acyl derivatives described in Table II were prepared by the standard Schotten–Baumann procedure and recrystallized from 95% ethanol in which they were all sparingly soluble. The thiothiazolidones except 4-ethyl-2-thiothiazolidone were easily sublimed at low pressure for analytical samples. The thioöxazolidone decomposed upon sublimation.

[13] J. P. English, American Cyanamid Co., reports m.p. 115–116°; private communication.

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Substituted Menthofurans

BY RICHARD H. EASTMAN AND ROSS P. WITHER

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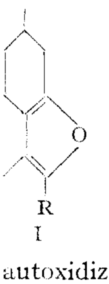
In continuing the study of the autoxidation of menthofuran[1] (I, R = H) we have prepared piperidinomethylmenthofuran (I, R = $CH_2NC_5H_{10}$), menthofuroic acid (I, R = COOH) and its anilide (I, R = $CONHC_6H_5$), and menthofurfuryl alcohol (I, R = CH_2OH) to determine whether the presence of the α-hydrogen atom on the furan nucleus is requisite for the production of the remarkable deep blue color that develops in solutions of menthofuran undergoing autoxidation. The piperidinomethyl compound and menthofurfuryl alcohol are readily autoxidized but do not show the blue color phenomenon. Menthofuroic acid and its anilide are stable towards autoxidation.



I

Experimental

Piperidinomethylmenthofuran (I, R = $CH_2NC_5H_{10}$).—A solution of 5.1 g. of menthofuran,[2] 1.5 g. of piperidine hydrochloride and 1.5 g. of paraformaldehyde in 50 ml. of absolute alcohol was heated under reflux for 1 hour. Removal of most of the solvent under reduced pressure caused the separation of 4.4 g. of white solid of m.p.[3] 202–204° (dec.). Crystallization from an alcohol–hexane–ethyl acetate mixture gave 4.1 g. of piperidinomethylmenthofuran hydrochloride of m.p. 208.5–209° (dec.). An additional 3.0 g. of pure material was isolated from the reaction liquor by concentration, bringing the yield to 84% of the theory.

Anal.[4] Calcd. for $C_{16}H_{26}ClNO$: C, 67.70; H, 9.23; Cl, 12.50. Found: C, 67.45; H, 9.13; Cl, 12.17.

The presence of nitrogen was established by sodium fusion; and the ultraviolet absorption spectrum showed $\lambda_{\max}^{\text{alc.}}$ 233 mμ (4.01) which is expected on the basis that menthofuran shows $\lambda_{\max}^{\text{alc.}}$ 219.5 mμ (3.78).

The free base was generated by treating the hydrochloride with an excess of 20% sodium carbonate solution. It was obtained as a colorless, water-insoluble oil of b.p. 189.5–191.5° at 20 mm.

Anal. Calcd. for $C_{16}H_{25}NO$: C, 77.68; H, 10.19; N, 5.66; neut. equiv., 247. Found: C, 77.72; H, 10.20; N, 5.68; neut. equiv., 236.

The ultraviolet absorption showed $\lambda_{\max}^{\text{alc.}}$ 228 mμ (4.10) and 294 mμ (1.28). The weak absorption at 294 mμ is ascribed to an autoxidation product of the base since the intensity of absorption at this wave length increased to log ϵ 2.30 on exposure of the free base to air during 14 days.

The picrate of the base constituted bright-yellow crystals of m.p. 139.5–140° after crystallization from aqueous alcohol.

Anal. Calcd. for $C_{22}H_{28}N_4O_8$: C, 55.45; H, 5.92. Found: C, 55.48; H, 5.85.

Menthofuroylanilide (I, R = $CONHC_6H_5$).—Menthofuran (28 g.) and phenyl isocyanate (45 g.) were heated with protection from moisture at 160° for 24 hours. Upon cooling the reaction mixture 25 g. of yellowish crystals separated which were crystallized from aqueous alcohol to give 24 g. of white needles of m.p. 156–156.5°.

Anal. Calcd. for $C_{17}H_{19}NO_2$: C, 75.84; H, 7.11. Found: C, 75.56; H, 6.89.

This substance is assigned the structure of menthofuroyl anilide on the basis of its analysis, insolubility in acid and base, and its ultraviolet absorption which showed $\lambda_{\max}^{\text{alc.}}$ 292 mμ (4.40) and great similarity to that of furoyl anilide, $\lambda_{\max}^{\text{alc.}}$ 276 mμ (4.27).

In subsequent experiments, using carefully purified phenyl isocyanate, it was discovered that the Friedel-Crafts reaction did not proceed well unless a trace of hydrogen chloride was added to the reaction mixture. The quantity of hydrogen chloride in ordinary samples of phenyl isocyanate was sufficient to catalyze the reaction.

Menthofuroic Acid (I, R = COCH).—Attempts to hydrolyze menthofuroyl anilide using 6 *N* hydrochloric acid, 10% aqueous or alcoholic potassium hydroxide, and the methods of Baum[5] and of Marquis[6] for furoyl anilide returned the anilide unchanged. Hydrolysis of the anilide (1.0 g.) with barium hydroxide octahydrate (4.7 g.) in 25 ml. of ethylene glycol at 140° for 4 hours gave a 76% yield (0.55 g.) of a white acidic solid of m.p. 179–179.5° (dec.) which is assigned the structure of menthofuroic acid on the basis of its analysis, decomposition into menthofuran by heat, and ultraviolet absorption spectrum which showed $\lambda_{\max}^{\text{alc.}}$ 270 mμ (4.24) to be compared with that for furoic acid $\lambda_{\max}^{\text{alc.}}$ 246 mμ (4.05).

Anal. Calcd. for $C_{11}H_{14}O_3$: C, 68.02; H, 7.27. Found: C, 67.98; H, 7.44.

Menthofurfuryl Alcohol (I, R = CH_2OH).—Ten grams of menthofuroic acid in 150 ml. of dry ether was added dropwise to 130 ml. of ether containing 2.42 g. of lithium aluminum hydride. Following the addition, stirring was continued for 15 minutes. The unreacted hydride was decomposed by the addition of water and then 80 ml. of 10% sulfuric acid was added. The ether layer was separated, washed with dilute sodium bicarbonate solution and dried

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[1] R. B. Woodward and R. H. Eastman, THIS JOURNAL, **72**, 399 (1950).

[2] R. H. Eastman, *ibid.*, **72**, 5313 (1950).

[3] Melting points are corrected.

[4] Analyses by Microchemical Specialties Co., Berkeley, California.

[5] E. Baum, *Ber.*, **37**, 2949 (1904).

[6] R. Marquis, *Ann. chim. phys.*, [8] **4**, 279 (1905).

over potassium carbonate. The ether was evaporated to leave a residue of 6.1 g. of a base-insoluble, white, crystalline solid of m.p. 50°.

Anal. Calcd. for $C_{11}H_{16}O_2$: C, 73.30; H, 8.95. Found: C, 73.54; H, 8.95.

This substance is assigned the structure of menthofurfuryl alcohol on the basis of its method of preparation and analysis. Exposure of it to the atmosphere, even momentarily, caused discoloration and rapid liquefaction and tar formation. Hence, the ultraviolet absorption of the material, $\lambda_{\max}^{\text{alc.}}$ 228 mμ (3.96), 294 mμ (2.31) cannot be regarded as indicative of its structure.

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Anomalies in the Vapor Phase Ozonolysis of Cyclohexene

BY RICHARD H. EASTMAN AND R. M. SILVERSTEIN

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Ozonolysis of cyclohexene in the liquid phase has been shown[1] to produce adipic acid and the corresponding half and dialdehydes. The renewed interest in the ozonolysis reaction[2] prompts this preliminary report of a study of the vapor phase ozonolysis of cyclohexene which has been found to produce the abnormal products formic acid and *trans*-1,2-cyclohexandiol in small yield in addition to adipic acid as the major product.

A. **Materials and Method.**—The cyclohexene (Phillips Petroleum) was redistilled 99 mole per cent. material of infrared absorption[3] identical with that reported.[4]

For the preparation of cyclohexene ozonide a stream of dry nitrogen flowing at a rate of 50 ml. per minute was passed through a thermostated hydrocarbon bubbler to carry cyclohexene vapor into a reaction tube at 0.16 millimole per minute. Ozone entered the reaction tube at the rate of 0.10 millimole per minute in a dry, ozonized oxygen stream flowing at the rate of 150 ml. per minute. At the confluence of the streams an aerosol was produced as a heavy smoke. As the reaction proceeded, a viscous, colorless condensate appeared on the walls of the reactor tube and slowly ran down into a trap provided for its collection.

The ultraviolet absorption spectrum of the ozonide showed only general absorption of low intensity in the 220–310 mμ region. Absorption in the carbonyl region (270–300 mμ) was specifically absent in samples taken with precaution to avoid moisture but appeared in samples exposed to laboratory air or treated with water.

The infrared absorption of the ozonide showed strong bands at 2.95, 3.40 and 5.82 μ which are attributed to OH, CH and C=O[5] vibrations, respectively. The 6–13 μ region showed only general absorption with a suggestion of discrete bands at 8.5 and 9.1 μ.

As the ozonide stood, crystals of adipic acid were slowly deposited. The yield of adipic acid never exceeded 50% in a number of experiments, the remainder of the material being an intractable, alkali-soluble, viscous oil.

Titration of the ozonide with sodium hydroxide against phenolphthalein gave neutral equivalents of 269, 261 and 243. A Zerewitinoff determination in cineole as solvent showed 0.75 active H per $C_6H_{10}O_3$ unit. Iodometry showed an active oxygen content of 1.8%. Analysis of the ozonide gave: C, 52.0, 52.2, 52.4; H, 7.9, 8.5, 8.9. Calcd. for $C_6H_{10}O_3$: C, 55.4; H, 7.7.

B. **Isolation of Formic Acid.**—Cyclohexene ozonide (10.6 g.) was distilled into two traps in series, one at 0° and the second at −78°. The pressure was slowly lowered to 2 mm. as the pot temperature was raised to 90°. The contents of the traps were found to be aqueous formic acid solutions. Identity was established by infrared absorption and by the hydroxamic acid–ferric ion color reaction. The quantity of formic acid was determined by titration and corresponded to 10% of the theoretical based upon one mole per mole of $C_6H_{10}O_3$ (0.37 g.).

C. **Isolation of *trans*-1,2-Cyclohexandiol.**—Cyclohexene ozonide (8.7 g.) was decomposed by heating under reflux with water (40 ml.) for 2.5 hours. The hydrolysate was brought to *p*H 9 by the addition of standard sodium hydroxide corresponding to 0.8 carboxyl group per $C_6H_{10}O_3$; and, the alkaline solution was continuously extracted with ether for 10 hours. Evaporation of solvent left 1.3 g. of yellowish oil which was distilled to give 0.47 g., b.p. 70–110° at 14 mm. which was presumably largely cyclopentenealdehyde-1 since it showed $\lambda_{\max}^{\text{alc}}$ 235 mμ, and formed a semicarbazone[1] of m.p. 208–209°; and, 0.2 g. b.p. 110–170° at 1 mm. which solidified on being cooled. Three crystallizations of the solid from benzene plus hexane gave 0.1 g. of white plates of m.p. 100–102.5°.

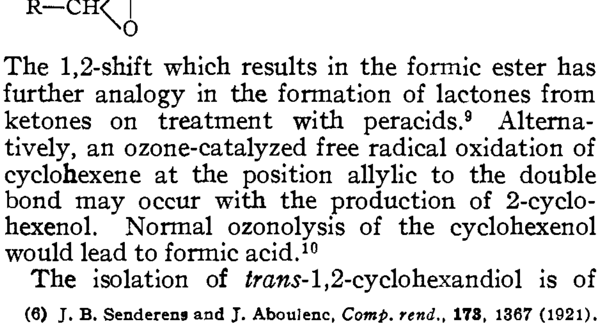
Anal. Found: C, 61.9; H, 10.4. Calcd. for $C_6H_{12}O_2$: C, 62.1; H, 10.4.

The infrared absorption of this material was identical with that of an authentic sample[6] of *trans*-1,2-cyclohexandiol, and no depression was observed in a mixed melting point determination.

Discussion

These results support the earlier observation[7] that the reaction of ozone with olefins in the vapor phase produces "ozonides" having different properties than those produced in condensed systems. Thus, the absence of ketone or aldehyde absorption in the ultraviolet is to be contrasted with the frequent appearance of these groups in liquid phase ozonolyses.[8] Further, in a direct comparison of the infrared absorption of the liquid phase product, prepared according to Harries,[1] and the vapor phase product, although both showed a strong band at 5.82 μ, the band at 2.92 μ was absent in the liquid phase product. In addition there was no correspondence in the 6–13μ region.

A possible source of formic acid in the distillate from the vapor phase reaction product is suggested by application of the mechanism proposed by Criegee[8] as



The 1,2-shift which results in the formic ester has further analogy in the formation of lactones from ketones on treatment with peracids.[9] Alternatively, an ozone-catalyzed free radical oxidation of cyclohexene at the position allylic to the double bond may occur with the production of 2-cyclohexenol. Normal ozonolysis of the cyclohexenol would lead to formic acid.[10]

The isolation of *trans*-1,2-cyclohexandiol is of

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[1] C. Harries and R. Seitz, *Ann.*, **410**, 24 (1915).

[2] B. Witkop and J. B. Patrick, THIS JOURNAL, **74**, 3855, 3861 (1952); references 5 and 8.

[3] Spectra were determined with a Perkin–Elmer model 12-c spectrophotometer in the region 2.5 to 12 μ using rock salt optics.

[4] A.P.I. Index.

[5] E. Briner, *et al.*, have found a band at 5.8 μ in the spectra of a large number of ozonized solutions of hydrocarbons, including cyclohexene; *Helv. Chim. Acta*, **35**, 340, 345, 353 (1952).

[6] J. B. Senderens and J. Aboulenc, *Comp. rend.*, **173**, 1367 (1921).

[7] E. Briner, *Helv. Chim. Acta*, **12**, 154, 529 (1929); E. Briner and S. de Nimitz, *ibid.*, **21**, 748 (1938).

[8] R. Criegee, 120th Meeting of the American Chemical Society, New York, N. Y., Sept. 7, 1951, Abstracts 22M.

[9] W. E. Doering and L. Speers, THIS JOURNAL, **72**, 5515 (1950).

[10] J. E. Leffler, *Chem. Rev.*, **45**, 400 (1949). This alternative was suggested by one of the Referees.