

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY AND CHEMICAL ENGINEERING, STANFORD UNIVERSITY]

Replacement of Hydrogen at a Tertiary Carbon Atom with OH by Alkaline Permanganate¹

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Oxidation by alkaline potassium permanganate of a number of tertiary alcohols that contain hydrogen attached to a tertiary carbon atom has shown that the hydrogen atom is replaced in 12–60% yield by a hydroxyl group, with retention of configuration.

The use of an alkaline solution of potassium permanganate as an oxidizing agent in organic chemistry is ordinarily reserved for attack on double bonds, easily oxidized functions such as alcohols and aldehydes, and saturated centers which are activated by an attached aromatic ring. We were accordingly surprised at the slow but relatively smooth conversions of the isomeric sabinene hydrates (Ia,b) into the diols IIa,b by the reagent.² Although instances of the oxidation of tertiary hydrogen to hydroxyl are familiar in the chemistry of natural products,³ only one systematic investigation of the replacement of unactivated tertiary hydrogen atoms by the hydroxyl group using alkaline permanganate (and manganate) has been made. Kenyon and Symonds⁴ found that systems of the type $R_1R_2CH(CH_2)_2COOH$ are oxidized to $R_1R_2C(OH)(CH_2)_2COOH$ in 60–90% yields by alkaline manganate or permanganate.

We wish to report preliminary work undertaken to determine the generality of the reaction and its stereochemical course.

As compounds for study we chose first the isomeric dihydro- α -terpineols (IIIa,b)⁵ and were gratified to find that the *cis* isomer IIIa gave *trans*-1,8-terpin (IVa) and the *trans* isomer IIIb gave *cis*-1,8-terpin (IVb) in significant yields^{6,7} on oxidation with dilute, aqueous, permanganate solution during five days at room temperature. It was apparent that the cyclopropane ring, present in the sabinene hydrates (Ia, b) is not a structural necessity for the reaction to proceed and, further, that the replacement of the tertiary hydrogen atom by the hydroxyl group occurred with retention of configuration at the carbon atom involved.⁸ Thus, the process belongs to the class of interposition reactions wherein an oxygen atom appears to be inserted between a carbon atom and an attached hydrogen atom without altering the configuration at the carbon atom.⁹

At this point it became of interest to probe the

(5) It was necessary to prepare pure samples of the isomeric dihydro- α -terpineols, for the literature presents a rather confused picture with regard to them. The preparation of the pure isomers and comparison of their properties with those in the literature is described in the Experimental Part.

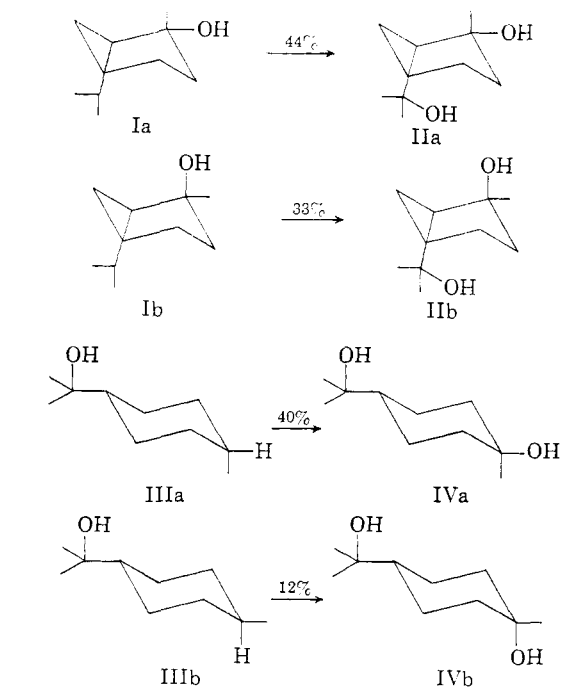
(6) The yields, based upon the amount of starting material not recovered, are stated over the arrows.

(7) While our work was in progress, Professor W. A. Mosher, University of Delaware, was kind enough to inform us of some earlier pilot experiments on the permanganate oxidation of the dihydro- α -terpineols. He observed formation of the terpins but was not satisfied as to the stereochemical specificity of the reactions. Evidence for the stereochemical specificity is reported in the Experimental Part.

(8) Of course the truth of this statement depends upon the correctness of the assignments of configurations to the alcohols and diols involved. Assignment of configuration to the dihydro- α -terpineols is on the basis of the von Auwers-Skita rule, and since they belong to the class of 1,4-disubstituted cyclohexanes the application of the rule in its simple form would appear justified (*cf.* K. S. Pitzer and W. G. Dauben in "Steric Effects in Organic Chemistry," edited by M. S. Newman, John Wiley and Sons, Inc., New York, N. Y., 1956, p. 16 ff). To eliminate the possibility of proton-bonding effects which might invalidate application of the rule, the nitrites of the dihydro- α -terpineols were prepared. Their physical constants were in accord with their sources and the von Auwers-Skita rule (*cf.* Experimental Part).

The configurations of the terpins are those accepted in the literature [A. Ginsburg, *Chem. Zentr.*, **68**, **II**, 420 (1897)]. 1,8-Cineole is produced by the action of dehydrating agents on *cis*-1,8-terpin but not from the *trans* isomer ["The Terpenes," Vol. I, 2nd Ed., J. L. Simonsen and L. N. Owen, Cambridge, 1947]. The formation of *cis*-1,8-terpin (IVb) by the action of methylmagnesium iodide on ethyl 4-cyclohexanonecarboxylate reported by W. H. Perkin, Jr., and F. W. Key [*J. Chem. Soc.*, **91**, 372 (1907)] would be predicted to result from equatorial attack of the methyl group of the Grignard reagent on the keto group of ethyl cyclohexanonecarboxylate in the chair conformation with the carbethoxyl group in the equatorial orientation [D. J. Cram and F. A. Abd Elhafez, *THIS JOURNAL*, **74**, 5828 (1952)].

(9) The oxidation of *cis*-decalin to *cis*-decalol by ozone (J. R. Durland and H. Adkins, *ibid.*, **61**, 429 (1939)) and the enzymatic introduction of OH stereospecifically (*inter alia*, E. J. Corey, G. A. Gregorius and D. H. Peterson, *ibid.*, **80**, 2338 (1958)) appear to be reactions of this class.



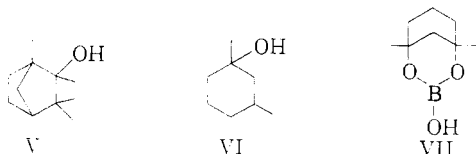
(1) Taken from the Doctoral Dissertation of Ross A. Quinn in the Department of Chemistry and Chemical Engineering at Stanford University.

(2) R. H. Eastman, F. C. Green and J. W. Daly, *THIS JOURNAL*, **80**, 6330 (1958).

(3) P. Lipp, *Ber.*, **56**, 2098 (1923); H. McPhillarny and C. Scholz, *ibid.*, **74**, 5512, 5506 (1952); E. H. Rodd, "Chemistry of Carbon Compounds," Elsevier Press, Houston, Tex., 1951, p. 780.

(4) J. Kenyon and M. C. R. Symonds, *J. Chem. Soc.*, 2129 (1953). Recently, work with a related system has been reported by H. Kwart and G. O. Null, *THIS JOURNAL*, **82**, 2348 (1960).

significance of the hydroxyl group already present in the molecules oxidized to the course of the reaction. Although our findings are by no means conclusive, it would appear that the hydroxyl group plays some necessary part other than that of conferring solubility in the aqueous phase. Thus, whereas 2,2,4-trimethylpentane was not attacked by permanganate during months,¹⁰ and four months was required for the reduction of an equimolar amount by methylcyclohexane,¹¹ both $(\text{CH}_3)_2\text{C}(\text{OH})\text{CH}_2\text{CH}_2\text{CH}(\text{CH}_3)_2$ and $(\text{CH}_3)_2\text{C}(\text{OH})\text{CH}_2\text{CH}(\text{CH}_3)_2$ were converted in 30–50% yield to the corresponding ditertiary glycols during five days under the same conditions. One other observation, the significance of which is not understood at present, is the failure of permanganate to produce a diol from tertiary methylphenyl alcohol (V) in which the tertiary hydrogen atom is attached to a bridge-head carbon atom. After thirty-seven days of reaction an equal number of moles of permanganate had been reduced, 82% of the alcohol was recovered unchanged and the remainder of the material was in the form of oxalic acid.



Finally, we investigated the application of the reaction to the isomeric 1,3-dimethylcyclohexanols (VI), to which configurations had been assigned¹² on the basis of the von Auwers-Skita rule. From each of the isomers a diol was indeed obtained in 30% yield, but, contrary to elementary expectations, it was the diol derived from the isomer assigned¹² the *trans* CH_3/CH_3 configuration which gave a stable ester with boric acid. The diol from the isomer assigned¹² the *cis* CH_3/CH_3 configuration gave dehydration products. On the basis of models, a *cis* arrangement of the hydroxyl groups is favorable to the formation of the borate (formulated as VII). It follows then, assuming that the introduction of the hydroxyl group proceeds with retention of configuration in this case as in that of the dihydro- α -terpineols, that assignment of configurations to the 1,3-dimethylcyclohexanols on the basis of the von Auwers-Skita rule is incorrect. The failure of the rule in its simple form to apply to 1,3-disubstituted cyclohexane derivatives is expected on the basis of conformational analysis¹³ and is well documented¹⁴ experimentally, so our results are consistent with the assumption that the replacement of H by OH proceeds stereospecifically with retention of configuration.

(10) Failure of reaction to occur was judged by the failure of manganese dioxide to form in detectable amount.

(11) S. N. Iyer and J. L. Simonsen [*J. Chem. Soc.*, 2049 (1926)] and E. R. Alexander [THIS JOURNAL, **172**, 3796 (1947)] report that *p*-menthane (which contains three tertiary hydrogen atoms) is not attacked by boiling alkaline permanganate solutions. In contrast, the dihydro- α -terpineols reduce hot, dilute, alkaline permanganate solutions in a few minutes.

(12) G. Chiurdoglu, *Bull. soc. chim. Belg.*, **47**, 241 (1938).

(13) F. Rossini and K. Pitzer, *Science*, **106**, 147 (1947).

(14) See D. S. Noyce and R. I. Nagel, THIS JOURNAL, **75**, 127 (1953), for examples and a bibliography.

Although our data to date shed little light on the mechanism of the reaction, it may be pointed out that there is a formal similarity between the attack of permanganate on a π -bond to give a glycol which is *cis* and attack on a σ -C-H bond to give a tertiary alcohol with retention of configuration.

Experimental Part¹⁵

Preparation of the Dihydro- α -terpineols.—The solid portion of practical grade α -terpineol (Eastman Kodak Co.) was separated by centrifugation and crystallized from methanol (final temperature -15°) to yield purified α -terpineol of m.p. 34.5 – 36.9° , n_D^{20} 1.4810 (supercooled); reported¹⁶ 34 – 35° , n_D^{20} 1.48131. Two moles (308 g.) of α -terpineol was dissolved in 150 ml. of alcohol and hydrogenated at 100° and a hydrogen pressure at 2000–1000 p.s.i. during 8 hours in the presence of 9.0 g. of Raney nickel catalyst prepared according to the method of Mozingo.¹⁷ The catalyst was filtered off, most of the alcohol removed by distillation and the residual oil was fractionated on a 1 m. \times 20 mm. Steadman column (70-TP, theoret. plates) at 90 mm., reflux ratio of 100:1. Cuts 3–13, comprising 96.0 g. of material of b.p. range 136.3 – 137.3° at 90 mm. and n_D^{20} (supercooled) range 1.4623 – 1.4632 , partly solidified on being cooled to 0° , and centrifugation yielded crystalline *trans*-dihydro- α -terpineol. Sublimation yielded the pure *trans* isomer of m.p. 34.5 – 35.0° , n_D^{20} 1.4630 (supercooled). Cuts 25–28, comprising 39.0 g. of material of b.p. range 137.7 – 138.0° at 90 mm. and n_D^{20} (supercooled) range 1.4658 – 1.4665 , had m.p. 46.7 – 47.0° , n_D^{20} (supercooled) 1.4664, and were taken to be essentially pure *cis*-dihydro- α -terpineol.¹⁸ A mixture of equal amounts of the two isomers was liquid at room temperature. Subsequently, it was found advantageous to employ Adams platinum oxide catalyzed hydrogenation of α -terpineol for the preparation of *trans*-dihydro- α -terpineol. Whereas Raney nickel hydrogenation yielded only 33% of material of n_D^{20} 1.4634 or less, the platinum-catalyzed reaction yielded 80% of such material. From the platinum-catalyzed hydrogenation of 77 g. of α -terpineol, 38 g. of crystalline *trans*-dihydro- α -terpineol of m.p. 31 – 34.6° was obtained on fractional distillation.

The phenylurethans¹⁸ of the isomeric dihydro- α -terpineols were prepared by allowing the alcohol to stand for one week with an equivalent quantity of phenyl isocyanate in a sealed tube. Extraction of the crystal mass with pentane, followed by crystallization from aqueous methanol of the residue left on evaporation of the pentane, gave phenylurethans which in the case of both isomers melted at 114 – 116° . Repeated crystallizations did not improve the melting range. A mixture of the urethans had m.p. 91 – 97° , and more than one hundred crystallizations from various solvents failed to give a separation.

The nitrites of the *cis*- and *trans*-dihydro- α -terpineols were prepared by treating 5.0 g. of the alcohol suspended in a solution of 7.2 g. of sodium nitrite cooled in ice with 30 ml. of concd. sulfuric acid in 20 ml. of water. The yellow oil which resulted was taken up in ether, the ether solution was dried and the product was distilled through a glass helices-

(15) Melting points are not corrected. Analyses by Microchemical Specialties, Berkeley, Calif.

(16) "Berichte Schimmel and Co.," Oct. 1905, p. 46; *Chem. Zentr.*, **76**, II, 1341 (1905).

(17) L. Mozingo, *Org. Syntheses*, **21**, 15 (1932).

(18) The "Encyclopedia of Chemical Technology," Interscience Publishers, Inc., New York, N. Y., 1954, Vol. 13, p. 732, lists the following properties for the isomers: *cis*, m.p. 45° , n_D^{20} 1.4663; *trans*, m.p. 34° , n_D^{20} 1.4630. These values had been supplied through a private communication from the Hercules Powder Co. and were not found reported elsewhere in the literature. G. H. Keats [*J. Chem. Soc.*, 2004 (1937)], by the Grignard process of W. H. Perkin and S. S. Pickles [*ibid.*, 650 (1905)], had converted the *cis*- (n_D^{20} 1.4429) and *trans*- (n_D^{20} 1.4392) ethyl hexahydro-*p*-toluolates into the corresponding *cis*- and *trans*-dihydro- α -terpineols for which he found melting points of 25 and 35° , respectively. The *cis* isomer is reported by O. Zeitschel and H. Schmidt [*Ber.*, **60**, 1376 (1927)] to be a liquid giving a phenylurethan of m.p. 94 – 95° . The phenylurethan prepared by Keats melted at 114° (*cis*) and 115° (*trans*). Since the phenylurethans (see above) of both of our isomers melted at 114 – 116° , while their mixture melted at 91 – 97° , it is apparent that Zeitschel and Schmidt's liquid isomer was a mixture. It seems probable that Keats's *cis* isomer also may have been slightly contaminated.

filled fractionating column (10 mm. \times 18 cm.) at 1 mm. After a small fore-run, the esters distilled smoothly at a constant temperature. The nitrite of *cis*-dihydro- α -terpineol had b.p. 53° at 1 mm. and n_D^{20} 1.4594, while that from the *trans* isomer had b.p. 51.5° and n_D^{20} 1.4491. The infrared spectrum of each contained a strong band at 6.3 μ , assigned to the N=O stretching vibration,¹⁹ and samples left exposed to the air reverted to the original alcohols in a few days through hydrolysis by the moisture in the air.

The infrared spectra of *cis*- and *trans*-dihydro- α -terpineol were very similar, differences being due mainly to differences in intensity of bands in the region of skeletal vibrations.

Permanganate Oxidation of the Dihydro- α -terpineols.—Since the procedure used in the oxidations was essentially the same in all cases, it will be described in some detail here, and referred to subsequently as the standard procedure.

To 3.0 g. (0.0192 mole) of pure *cis*-dihydro- α -terpineol suspended in 90 ml. of water was added 0.548 g. (0.0035 mole) of powdered potassium permanganate. The flask was shaken by hand until the permanganate had dissolved and then allowed to stand at room temperature for 2 days at which point the color of permanganate ion had disappeared. Potassium permanganate was then added in approximately half-gram portions as each portion was reduced (approximately 2 days) until a total of 4.22 g. (0.0266 mole) of permanganate had been added. The whole reaction mixture then was extracted in a separatory funnel with three 50-ml. portions of ether. The ether extract was dried and the solvent was removed, finally at reduced pressure, leaving 1.92 g. of crystalline material identified as starting material by its melting point and infrared spectrum.

The aqueous layer then was filtered to remove the manganese dioxide, and the filtrate was continuously extracted for 4 days with ether. Evaporation of the ether extract after drying it over anhydrous sodium sulfate left a crystalline residue which on crystallization from a small volume of ethyl acetate yielded 0.47 g. (0.0027 mole) of *trans*-1,8-terpin, m.p. 157.4–157.6°. The yield was 39% based on the amount of *cis*-dihydro- α -terpineol consumed (1.08 g.) and identity was established in a mixed melting point (m.m.p. 156.0–157.1°) with an authentic sample of *trans*-1,8-terpin²⁰ of m.p. 156.5–157.5° and by infrared absorption spectroscopy.

The aqueous layer from the continuous ether extraction was then acidified strongly with concentrated hydrochloric acid and continuously extracted with ether for several days. Evaporation of the ether left a gummy residue which crystallized on being seeded with terpenylic acid, and crystallization from ether yielded a small amount of terpenylic acid, m.p. 87.0–88.7°, undepressed by mixture with an authentic sample²¹ of m.p. 87.3–89.2°.

By the same procedure, pure *trans*-dihydro- α -terpineol was converted in 12% yield (based on starting material consumed) to *cis*-1,8-terpin which was characterized as its hydrate, m.p. 116–117°, and identified by comparison with an authentic sample in mixed melting point and infrared absorption spectra determinations.

Oxidation of the Terpins.—In order to be certain that the stereospecificity observed in the oxidations of the isomeric dihydro- α -terpineols was not simply the result of preferential further oxidation of one of the 1,8-terpins by permanganate, it was felt to be necessary to show that the attacks on the terpins by permanganate go at comparable rates. The terpin sample (60 mg.) was combined with potassium permanganate (5 mg.) in 2 ml. of water. Manganese dioxide was first apparent in the case of the *cis* isomer in 4 days and in the case of the *trans* in 10 days. Complete bleaching of the color of permanganate required 17 days in the case of the *cis* isomer and 19 days in the case of the *trans*. Thus, the terpins are oxidized at comparable rates which are slow relative to the rates of oxidation of the isomeric dihydro- α -terpineols under the same conditions. These observations render it unlikely that the oxidations of either of the isomeric dihydro- α -terpineols lead to a mixture of the isomeric 1,8-terpins that is simplified by a more rapid destruction of one of the terpins giving only the appearance of stereospecificity to the reaction.

(19) P. Tarte, *J. Chem. Phys.*, **20**, 1570 (1952).

(20) Prepared from dipentene dihydrobromide by the method of J. von Baeyer, *Ber.*, **26**, 2865 (1893).

(21) O. Wallach, *Ann.*, **277**, 118 (1893).

Oxidation of Tertiary Methyl Fenchyl Alcohol (V).—Tertiary methyl fenchyl alcohol was prepared by the procedure of Bredt-Savelsberg and Bruchkremer²² starting with fenchone. From 80 g. of fenchone we obtained 30 g. of the desired alcohol, b.p. 95.5–96.5° at 15 mm. in a 13 TP glass-helices packed column, and m.p. 67.8–68.2°; reported²² m.p. 61°.

The oxidation with permanganate was conducted on a 1.0 g. sample of the alcohol following the procedure described above for the dihydro- α -terpineols. A total of 0.940 g. of permanganate was reduced during 37 days. A total of 82% of the unreacted alcohol was recovered, the continuous ether extract of the alkaline, aqueous solution yielded no product when evaporated; and the acidic fraction was small and composed mainly of oxalic acid.

Preparation and Oxidation of 2,5-Dimethyl-2-hexanol.—The alcohol was prepared by the Grignard synthesis using isoamyl bromide and acetone. A good yield of product of n_D^{20} 1.4209 (reported²³ n_D^{20} 1.42085) was obtained. A 3.0-g. sample reduced a total of 1.81 g. of potassium permanganate over a 5-day period following the standard procedure. Recovered starting material comprised 1.93 g., and the continuous ether extract of the alkaline layer yielded a crystalline solid which after crystallization from ethyl acetate and sublimation at reduced pressure comprised 0.44 g. of white crystals, m.p. 89.2–90.2°. The anhydrous form of 2,5-dimethyl-2,5-hexanediol is reported²³ to melt at 92–93° and to form an unstable hexahydrate, m.p. 41–42°. Crystallization of our sample of the anhydrous form from water gave the hydrate, m.p. 39–42°. The yield of diol was 37% based on the amount of the alcohol consumed.

Preparation and Oxidation of 2,4-Dimethyl-2-pentanol.—The alcohol was prepared by the Grignard synthesis using isobutyl chloride and acetone. The crude product was distilled in a Claisen flask and a middle cut, b.p. 49.0–50.0° at 24 mm., n_D^{20} 1.4168 (reported²⁴ n_D^{20} 1.4172), was collected. A 4.00-g. sample of the alcohol was oxidized using the standard procedure, 5.45 g. of potassium permanganate being reduced in a 2-day period. Recovered starting material amounted to 2.97 g., and a neutral liquid fraction (0.90 g.) of n_D^{20} 1.4330 was obtained on continuous ether extraction of the aqueous layer from the oxidation. The expected product, 2,4-dimethyl-2,4-pentanediol, is reported²⁵ to have m.p. 7°, n_D^{20} 1.4327 and to form a crystalline borate of m.p. 102°. When the neutral liquid fraction (above) was treated in a sublimation apparatus with an excess of boric anhydride at 100° and 30 mm. pressure, the sublimate had m.p. 99.8–101.3° after crystallization from hexane. This material was concluded to be the borate reported by Hermans.²⁵ The yield of 2,4-dimethyl-2,4-pentanediol was 52% based on the amount of starting material not recovered.

Preparation of the 1,3-Dimethylcyclohexanols.—A mixture of the isomeric 1,3-dimethylcyclohexanols was prepared by the action of methylmagnesium iodide on 3-methylcyclohexanone (160 g.). The crude product was fractionated (13 TP) while monitoring the fractionation by infrared spectroscopy. The first 40 g. of distillate, which contained some 3-methylcyclohexanone, was rejected. The next 36 g. of distillate, b.p. 68.5–68.8° at 15 mm., n_D^{20} 1.4504, was taken as the lower-boiling 1,3-dimethylcyclohexanol, the *cis* CH₃/CH₃ isomer according to the results reported herein. Fractions taken during the distillation of the next 32 g. showed a gradual but significant change in the profile region on infrared analysis. The last 40 g. of distillate, b.p. 75° at 15 mm., n_D^{20} 1.4545, was taken as the higher-boiling 1,3-dimethylcyclohexanol, the *trans* CH₃/CH₃ isomer according to the results reported herein. This material solidified on being chilled.

The physical properties reported¹² for the low and high-boiling isomers are, respectively, b.p. 77.6° and 84.0° at 25 mm., n_D^{20} 1.4507 and 1.4575.

Oxidation of the High-boiling 1,3-Dimethylcyclohexanol.—Under the standard conditions, the high-boiling 1,3-dimethylcyclohexanol reduced an equimolar amount of potassium permanganate within 2 days. Following the standard procedure there was obtained a 30% yield (based on the

(22) M. Bredt-Savelsberg and J. Bruchkremer, *Ber.*, **64**, 605 (1931).

(23) P. Bruylants, *Chem. Zentr.*, **80**, II, 797 (1909).

(24) G. Edgar, G. Calingaert and R. Marker, *THIS JOURNAL*, **51**, 1483 (1929).

(25) P. Hermans, *Z. anorg. Chem.*, **142**, 101 (1925).

amount of starting material not recovered) of a neutral, crystalline product of m.p. 87–103°. A sample after being dried at 90° over anhydrous calcium chloride, then crystallized from anhydrous ethyl acetate, had m.p. 100.4–103°.

Anal. Calcd. for $C_8H_{16}O_2$: C, 66.63; H, 11.8. Found: C, 65.66; H, 10.94.

After standing exposed to the air for a few days the analytical sample showed m.p. 87–97°, whereupon it was suspected that the large melting point range of the crude material was due to the formation of an unstable hydrate. Accordingly a sample of the crude material was crystallized once from water to yield crystals of m.p. 87–97°. This material was analyzed.

Anal. Calcd. for $(C_8H_{16}O_2)_2 \cdot H_2O$: C, 62.71; H, 11.18. Found: C, 63.00; H, 11.61.

This compound is assigned the structure of *trans*-1,3-dimethyl-1,3-cyclohexandiol on the basis of its behavior toward boric acid (see below). The possibility that the large melting-point range of this diol was due to contamination by *cis*-1,3-dimethyl-1,3-cyclohexandiol was disposed of by comparison of infrared spectra. Both the crude oxidation product (m.p. 87–103°) and the analytical samples of the anhydrous form (m.p. 100.4–103°) and the hemihydrate (m.p. 87–97°) showed distinctive, strong bands at 10.87 and 9.05 μ which were not present in the spectrum of pure *cis*-1,3-dimethyl-1,3-cyclohexandiol (see below). The only absorption bands near these positions in the *cis* isomer were at 11.05 and 9.14 μ ; the minima associated with which fell at 10.70 and 9.02 μ , respectively, close to the positions of the strong bands in the *trans* isomer.

When a 0.20-g. sample of anhydrous *trans*-1,3-dimethylcyclohexandiol (m.p. 100.4–103°) was heated with an excess of boric anhydride at 90° and 30 mm. in a micro-sublimation apparatus, an oil collected on the cold-finger. This oil did not give a qualitative test for boron, reduced permanganate solution instantly, showed a band at 6.2 μ in the infrared indic-

ative of unsaturation, and gave analytical figures indicating that partial dehydration had occurred. It was not further investigated.

Anal. Calcd. for $C_8H_{14}O$: C, 76.14; H, 11.18. Found: C, 74.78; H, 10.98.

Oxidation of the Low-boiling 1,3-Dimethylcyclohexanol.—Under the standard conditions the low-boiling 1,3-dimethylcyclohexanol reduced an equimolar amount of permanganate in 3 days. After separating unreacted starting material, a continuous ether extract of the aqueous reaction mixture yielded 31% (based on unrecovered starting material) of crystalline material which melted at 88.9–90.0° after crystallization from petroleum ether (b.p. 35–36°)-ethyl acetate.

Anal. Calcd. for $C_8H_{16}O_2$: C, 66.63; H, 11.18. Found: C, 66.55; H, 11.09.

This diol is assigned the structure of *cis*-1,3-dimethyl-1,3-cyclohexandiol. Neither the crude oxidation product nor the analytical sample of the diol showed significant absorptions at 10.87 or 9.05 μ where the *trans* isomer has strong bands.

When 0.20 g. of this diol was heated in a sublimation apparatus with an excess of boric anhydride at 90° and 30 mm., white crystals collected on the cold-finger. These were crystallized three times from petroleum ether (b.p. 35–65°) and dried to yield the borate VII, m.p. 93.4–95.2°. The substance gave a strong test for boron (solution in methanolic sulfuric acid followed by ignition).

Anal. Calcd. for $C_8H_{16}O_3B$: C, 56.50; H, 8.90. Found: C, 56.85; H, 8.82.

Titration curves for the borate (9.0 mg.) and boric acid (1.6 mg.) in 5 ml. of water using sodium hydroxide were identical, so it was concluded that the cyclic borate VII is rapidly hydrolyzed to its components.

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[CONTRIBUTION FROM THE CHEMISTRY DIVISION, OAK RIDGE NATIONAL LABORATORY, OPERATED BY UNION CARBIDE CORP. FOR THE U. S. ATOMIC ENERGY COMMISSION, OAK RIDGE, TENN.]

Studies Involving Isotopically Labeled Formic Acid and its Derivatives.¹ VI. Estimation of the Relative Ionization Constants of Formic Acid and Formic-*d* Acid at $24.0 \pm 0.5^\circ$

BY GUS A. ROPP

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The ratio of the ionization constants of formic acid and formic-*d* acid (DCOOH) in aqueous solution at $24.0 \pm 0.5^\circ$ was found to be $K_a(H)/K_a(D) = 1.06 \pm 0.03$. The value of this secondary equilibrium deuterium isotope effect is not consistent with the suggestion of Halevi⁴ that the previously observed⁵ secondary deuterium isotope effect in the case of the ionization constant of α, α -dideuteriophenylacetic acid is the result of stronger *inductive electron* release from C–D than from C–H bonds.

Introduction

The mechanism of operation of secondary deuterium isotope effects has recently aroused considerable interest.^{2,3} Halevi approached the problem by way of studies of the ionization constants⁴ of deuterated organic compounds.

In connection with studies of ion-molecule reactions (ref. 1 (III) and (IV)) in formic acid and formic-*d* acid (DCOOH) in the mass spectrometer, we have sought information about the effect of deuterium substitution on the electron displacement toward the oxygen atoms in formic acid. An esti-

mate of the effect of deuterium substitution on the ionization constant of formic acid in aqueous solution at $24.0 \pm 0.5^\circ$ has been made.

Halevi and Nussim⁵ reported that the two deuterium atoms in α, α -dideuteriophenylacetic acid, $C_6H_5CD_2COOH$, lowered the ionization constant of phenylacetic acid about 12% at 25°; the ionization constant of α -deuteriophenylacetic acid, $C_6H_5CHDCOOH$, should therefore be about 6% smaller than that of phenylacetic acid. Halevi⁴ suggested that the measured effect⁵ of deuterium on the ionization constant is due to a greater *inductive electron release* of a deuterium atom on the electron displacement toward the oxygen atoms of the carboxyl group as compared with a hydrogen atom. The *inductive effect* of a substituent (in this case a deuterium atom) is well known to increase markedly

(1) Other papers in this series: THIS JOURNAL, (I) **73**, 5573 (1951); (II) **79**, 4944 (1957); (III) **80**, 3509 (1958); (IV) **80**, 5573 (1958); (V) **82**, 842 (1960).

(2) W. H. Saunders, Jr., S. Ašperger and D. H. Edison, *ibid.*, **80**, 2421 (1958).

(3) Symposium on Hyperconjugation, University of Indiana, June, 1958.

(4) E. A. Halevi, *Tetrahedron*, **2**, 175 (1957).

(5) E. A. Halevi and M. Nussim, *Bull. Res. Council Israel*, **5A**, 263 (1956).