Stereochemistry of the Zinc–Acetic Acid Debromination of α-Bromocamphor

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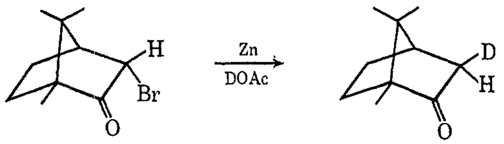
A study of the zinc–acetic acid debromination of α-bromocamphor (**1**) was undertaken with the objective of evaluating the potential of this reaction for the stereospecific syntheses of α-deuteriocamphors. This was to be accomplished by examination of the stereochemistry of the reduction of α-bromocamphor with zinc–acetic acid-*O-d* and of the reduction of α-deuterio-α-bromocamphor (**3**) with zinc–acetic acid. It was anticipated that use of this method might circumvent one of the disadvantages of the exchange methods,[2-4] namely, the continual regeneration of the enols.[5,6]

Experimentally, it was found that treatment of α-bromocamphor with zinc and acetic acid-*O-d* led to the formation of a deuterated camphor which was composed of the following mixture: 88% d_1 and 12% d_0. Structure **2** is assigned to the monodeuterated material on the basis of an analysis of the nmr spectrum (see below).



1 **2**

Similarly, α-deuterio-α-bromocamphor (**3**) was prepared by exchange and subjected to debromination with zinc–acetic acid. The isolated camphors showed the following deuterium distribution: 8.3% d_0, 91% d_1, and ~0.5% d_2. The monodeuterated material was assigned structure **4**.

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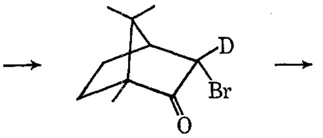

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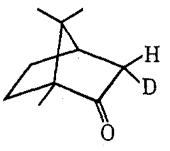

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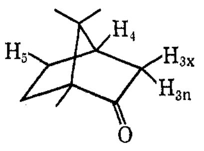

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Since Corey and Sneen[5] had presented an example of a debromination which did not proceed *via* an enol, it was felt that assignment of the stereochemistry of these reactions by analogy[2-4] was not warranted. On examination of the 100-MHz nmr spectra of **2**, **4**, and camphor (**5**), it was possible to make a consistent set of assignments for the α protons 3_x and 3_n based on the expected coupling constants in this system.[7] In camphor itself these protons are the AB part of a complex spin system with $J_{AB} = 17.5$ Hz. The 3_n proton appeared at δ 1.83 as the upfield wing of the quartet and was not further split as expected from the geometry of the system.[7] The downfield wing of the quartet appeared at δ 2.35 and was assigned to absorption by the 3_x proton. Each line of this multiplet was further split into four lines as a result of coupling to the vicinal bridgehead proton (H_4) and the exo proton on C_5.[7,8]

The presence of deuterium in **2** and **4** would be expected to result in the disappearance of one of the wings of the original quartet and alteration of the appearance of the remaining one. The latter expectation is a consequence of the difference in the magnitude of the coupling constants between hydrogen:deuterium and hydrogen:hydrogen interactions and of the fact that deuterium has a nuclear spin number of 1.[9] The nmr spectrum of the monodeuteriocamphor assigned structure **2** was consistent with the above generalization in that the downfield absorptions disappeared and the resonance attributed to 3_n collapsed to a closely spaced triplet at δ 1.79 (J = 2.5 Hz). In compound **4**, the upfield multiplet vanished and the low field resonance at δ 2.28[10] appeared at a septet with 2.5-Hz spacings. In both cases, the two isomers appeared to be essentially free of each other.

Thus, these debromination reactions provide convenient syntheses of **2** and **4** with little concurrent dideuteration. It is not known with certainty at which point in the experimental procedure the undeuterated material is formed, but it is not unlikely that exchange could have occurred during the work-up procedure.

Experimental Section

Melting points were determined on a Mel-Temp apparatus and are uncorrected. Nmr spectra were determined on either a Varian Model A-60 or HA 100 spectrometer in chloroform solutions and tetramethylsilane as an internal standard. Mass spectra were determined on an Hitachi RMU-7 mass spectrometer at 70 eV.

Camphor-*3-exo-d* (2).—A solution of 3.0 g (0.013 mol) of α-bromocamphor[11] in 50 ml of acetic acid-*O-d*[12] was heated for 14.5 hr (90°) with 1.68 g (0.0256 g-atom) of zinc dust. The reaction mixture was diluted with ether and the zinc was removed by decantation. The ether was washed with 5% sodium hydroxide solution until neutral. Evaporation of the dried ether solution gave a residue which was sublimed at 75° (0.25 mm). The yield of **2**, mp 169–174°, was 1.50 g (75%): mass spectrum *m/e* (rel intensity, average of four runs) 154 (12.2), 153 (100), and 152 (13.5). Camphor showed the following relative intensities (average of five runs): 154 (O), 153 (13.8), and 152 (100).

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(2) (a) A. F. Thomas and B. Willhalm, *Tetrahedron Lett.*, 1309 (1965); (b) J. M. Jerkunica, S. Borčić, and D. E. Sunko, *ibid.*, 4465 (1965).

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(5) This gives rise to dideuterated products. For example,[3] an exchange reaction of α-dideuteriocamphor with H_2O produced the following distribution of camphors: 21% d_2, 64% d_1, and 15% d_0.

(6) E. J. Corey and R. A. Sneen, *J. Amer. Chem. Soc.*, **78**, 6269 (1956), have shown that debromination of steroidal bromo ketones with deuterated acids does not lead to polydeuterated products.

(7) For recent data and a summary of earlier literature, see A. P. Marchand and J. E. Rose, *ibid.*, **90**, 3725 (1968).

(8) For a summary of long-range coupling, see M. Barfield and B. Chakrabarti, *Chem. Rev.*, **69**, 757 (196)9.

(9) F. A. Bovey, "Nuclear Magnetic Resonance Spectroscopy," Academic Press, New York, N. Y., 1969, p 90.

(10) Substitution of deuterium for hydrogen in a methyl or methylene group has been observed to cause small shifts in the absorptions of the remaining proton(s); see ref 9, p 86.

(11) This material was purchased from the Matheson Coleman and Bell Co.

(12) Acetic acid-*O-d* was prepared by warming an equimolar solution of deuterium oxide and acetic anhydride.

α-**Bromocamphor-*3-d*** (**3**).—A solution of sodium ethoxide in ethanol-*O-d* was prepared by the reaction of 0.020 g (0.008 g-atom) of sodium with 20 ml of ethanol-*O-d*.[13] *α*-Bromocamphor (2.3 g, 0.001 mol) was added and the mixture was heated for 66 hr on a steam bath. The solvent was removed by evaporation and the residue was sublimed to yield 2.0 g (87%) of crystals, mp 78° (lit.[14] mp 76° for *α*-bromocamphor). The nmr spectrum revealed the presence of *ca.* 14% of the undeuterated material based on the integrated area of the HCBr doublet at δ 4.84.

Camphor-*3-endo-d* (**4**).—The above material was debrominated by the same procedure as before except that unlabeled acetic acid was used. There was obtained an 89% yield of **4**, mp 170–177°: mass spectrum *m/e* (rel intensity, average of five runs) 154 (14.0), 153 (100), and 152 (26.3). The calculated deuterium distribution[15] for these ratios was 21.1% d_0, 78.5% d_1, and 0.4% d_2. Upon correction for the unlabeled starting material, the following distribution of label was calculated: d_0, 8.3%; d_1, 91%; and d_2, 0.5%. The errors in peak height measurement limit the accuracy of these percentages to ±1% (absolute error).

Registry No.—**1,** 1925-58-2; **2,** 27808-88-4.

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[14] T. M. Lowry, V. Steele, and H. Burgess, *J. Chem. Soc.*, **121**, 633 (1922).

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Epoxidation by Thallium Triacetate[1]

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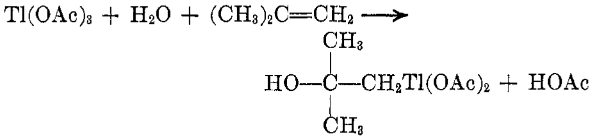
It has been known for several years that the oxidation of olefins with thallium triacetate in aqueous acid medium yields glycols and carbonyl compounds.[2] In acetic acid[3] and methanol,[4] 1,1-and 1,2-acetates and ethers as well as allylic oxidation products are formed. The preparation of σ-bonded oxythallation adducts[4,5] in nonaqueous systems, and kinetic[6] as well as polarographic[7] evidence of their presence in aqueous systems strongly suggest that such adducts are involved in the reaction sequence. Decomposition of these adducts occurs by heterolytic splitting of the metal–carbon bond giving thallous ions and oxidation products which result from neutralization of the incipient carbonium ion by one or more of the following routes: attack of the solvent, hydride shift, or neighboring group participation.[8] In only one favorable case, the oxidation of isobutylene, has neighboring hydroxyl participation been suspected.[6] In that study, conducted in strongly acidic aqueous medium, isobutyraldehyde, which can be formed only by neighboring hydroxyl participation, and isobutylene glycol were the products. Isobutylene oxide, the initial product expected, would decompose under the reaction conditions to the observed products. If hydroxyl participation occurs in aqueous acid, one might expect that in weaker solvating media, which favor this effect, the adducts from other olefins such as propylene may also decompose by this route. Furthermore, in less acidic systems the initial oxide product is more stable and can perhaps be isolated.

This note reports that, indeed, epoxides are obtained in weakly solvating media, not only with isobutylene but also with propylene. Thus, in 50% (v/v) aqueous acetic acid, thallium triacetate oxidized propylene to propylene oxide and acetone in a 1:1 ratio. In addition, by employing a less polar solvent, the ratio of epoxide to carbonyl compound can be changed significantly in favor of the epoxide. For example, in 70% (v/v) tetrahydrofuran, 20% water, and 10% acetic acid, the oxidation products of propylene consisted of 72% propylene oxide, 16% acetone, and 12% 1-acetoxy-2-propanol, giving an epoxide to carbonyl ratio of 4:1. For isobutylene, in the same solvent system, the ratio of isobutylene oxide to isobutyaldehyde was about 25:1, together with 15% 1-acetoxy-2-methyl-2-propanol. The product distribution for isobutylene was less sensitive to solvent composition. Blank experiments for the decomposition of the epoxides under our experimental conditions showed that the glycolic ester, and not the carbonyl compound, was formed from the epoxides. No glycols (<2%) were found under conditions of the experiments. Use of *tert*-butyl alcohol, dioxane, and other weakly solvating cosolvents gave similar results. With ethylene and *cis*- and *trans*-2-butene, only traces of epoxides were detected.

Although the existence of hydroxythallation adducts had been previously demonstrated,[5] by working at low temperatures we have now been able to isolate the hydroxythallation adduct I from thallium(III) triacetate and isobutylene in 80% (v/v) THF, 10% H_2O, and 10% acetic acid according to eq 1. The structure of



$$\mathrm{Tl(OAc)_3 + H_2O + (CH_3)_2C{=}CH_2 \longrightarrow HO{-}\overset{\displaystyle CH_3}{\underset{\displaystyle CH_3}{C}}{-}CH_2Tl(OAc)_2 + HOAc} \qquad (1)$$

I

I has been assigned on the basis of its nuclear magnetic resonance spectra reported in the Experimental Section.

The rate of decomposition of I and the corresponding propylene adduct in aqueous solution was followed by polarographically monitoring the Tl(I), Tl(III), and thallium adduct concentrations as a function of time.

The decomposition of the thallium(III)–isobutylene adduct followed first-order kinetics in aqueous perchlorate solutions. The rate was found to increase with increasing acidity at 25°; for example, the half-life for its decomposition was 23 min at pH 6.4, 15 min at pH 3.0, and much less than 1 min at pH 1. At pH 10.5, an aqueous perchlorate solution containing 10^{-3} *M* I became yellow in color and decomposed at a rate corresponding to a half-life of approximately 2 hr. At

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[7] P. M. Henry, personal communication.

[8] P. M. Henry, *Advan. Chem. Ser.*, **70**, 126 (1968).