

LEAD TETRAACETATE OXIDATION OF BRIDGED
BICYCLIC ALCOHOLS*1,*2

Keizo Kitahonoki and Akio Matsuura

Shionogi Research Laboratory, Shionogi & Co., Ltd.
Fukushima-ku, Osaka, Japan

(Received 30 June 1964)

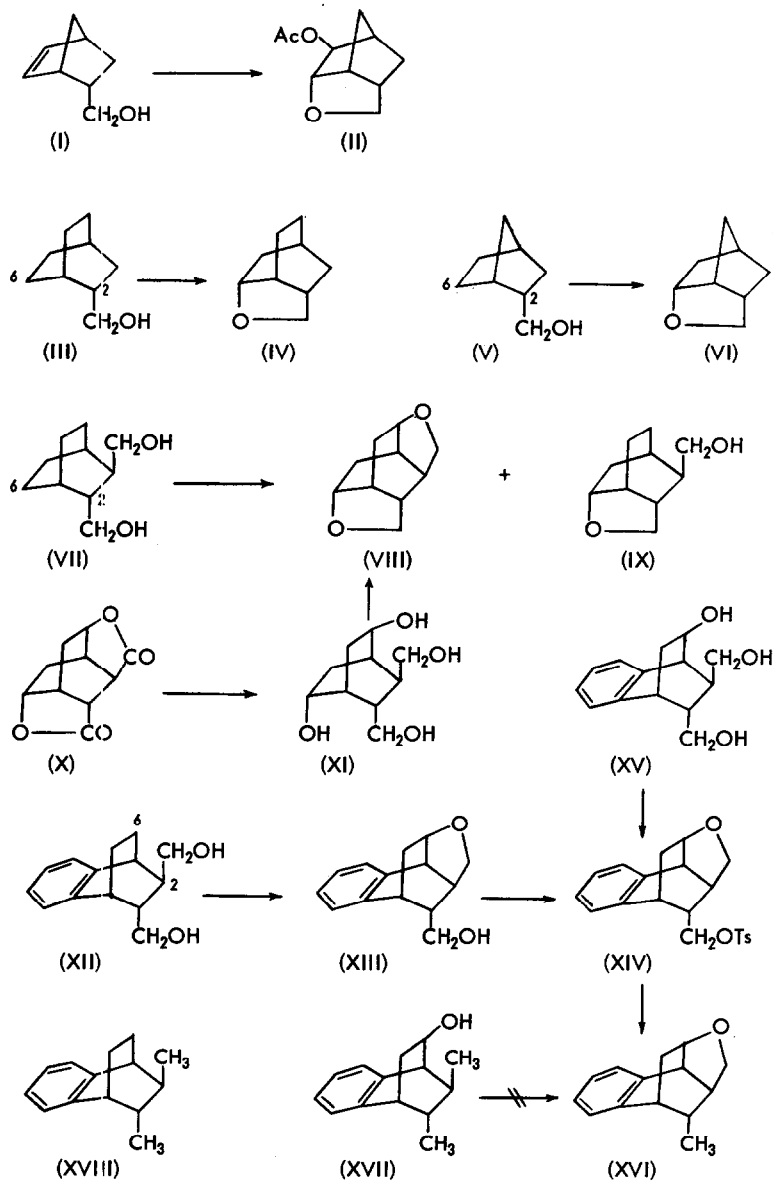
IN recent years, the oxidation of monohydric alcohols to tetrahydrofuran derivatives by lead tetraacetate has been studied extensively in steroids and used successfully to functionalize the "unactivated" C₁₈ or C₁₉ angular methyl group (1,2). We have applied this type of reaction in the bridged ring compounds. Quite recently, Mariarty and Kapadia (3) reported on the oxidation of bicyclo[2.2.1]hept-5-ene-2-methanol (I) to the ether-acetate (II) by lead tetraacetate. The report prompts us to describe our results on the oxidation of saturated bridged alcohols by the same reagent.

When a solution of bicyclo[2.2.2]octane-2-methanol (III) and lead tetraacetate in benzene was heated under reflux for 12 hours until the starting material could no longer be detected, perhydro-3,6-methanobenzofuran (IV), m.p. 147-148°, was obtained in 42.9% yield*3 along with the acetate of the starting alcohol

*1 Bridged Ring Compounds, Part II; Part I of this series: K. Kitahonoki and Y. Takano, Tetrahedron Letters, No. 24, 1597 (1963).

*2 Satisfactory elemental analyses were obtained for all new compounds described.

*3 The yields of the ethers (IV) and (VI) were determined by gas chromatography, comparing the peak area with those of known amounts of the pure samples.



(19.8%). Similar treatment of bicyclo[2.2.1]heptane-2-methanol (V) by lead tetraacetate afforded the ether (VI) in 38.3% yield. The ethers (IV) and (VI) (4) were identical with the respective authentic samples obtained from the corresponding bicyclo[2.2.2]oct- and bicyclo[2.2.1]hept-5-ene-2-methanol by the action of sulfuric acid.

Oxidation of the diol (VII) (5) by lead tetraacetate afforded, after hydrolysis and chromatography on alumina, the diether (VIII), m.p. 164-167° (14.5%), and the ether-alcohol (IX) (hygroscopic crystals, 25.3%). The diether (VIII) was found to be identical with the cyclization product of the di-*p*-toluenesulfonate of the tetraol (XI), m.p. 184-186°, which was obtained by lithium aluminum hydride reduction of the dilactone (X) (6).

Oxidation of the diol (XII) prepared by lithium aluminum hydride reduction of the corresponding *trans*-dimethylester (7) afforded also the ether-alcohol (XIII), oil, whose *p*-toluenesulfonate (XIV), m.p. 161-162°, was identified with the cyclization product of the di-*p*-toluenesulfonate of the triol (XV).^{*4}

These results indicate that the methylol group at C₂ and C₆-methylene in compounds (III), (V) (VII) and (XII) are suitably situated for this radical reaction (8), forming a tetrahydrofuran ring.

When, however, the dimethyl-alcohol (XVII),^{*4, *5} m.p. 128-129°, was treated with lead tetraacetate, thin layer chromatography of the product with an authentic sample of the expected ether (XVI) prepared by lithium aluminum hydride reduction of (XIV) did not show any evidence of the formation of (XVI), but some

^{*4} The triol (XV) and dimethyl-alcohol (XVII) were synthesized starting from the *endo*- β -naphthol-maleic anhydride adduct (7).

^{*5} The *exo* configuration of the hydroxyl group in (XVII) was based on its deshielding effect upon the *exo*-methyl protons observed in the NMR spectra (*exo*-CH₃ of (XVII), (XVII)-acetate and (XVIII): 8.65, 8.73 and 8.91 τ); see Ref. 10.

unidentified carbonyl compounds. The products formed might be due to fragmentation or oxidation of the bicyclic secondary alkoxy-radical. A similar example (9) can be seen on the oxidation of isoborneol, which did not give a tetrahydrofuran derivative.

Consequently, formation of the ether bridge between the methyl and secondary alcohol group on the bicyclic ring by lead tetraacetate seems to be difficult, even though the geometrical situation of both groups is suitable.

Our present results may provide an useful method to introduce a functional group on a bridge carbon by utilization of a methylol group on another bridge.

We thank Dr. Shinzaburo Sumimoto and Miss Mutsuko Sato for the gas chromatography.

REFERENCES

1. cf. e.g. G. Cainelli, M. Lj. Mihailović, D. Arigoni, and O. Jeger, Helv. Chim. Acta **42**, 1124 (1959), and other papers cited in reference 8 (b).
2. Oxidation of saturated aliphatic alcohols to cyclic ethers by lead tetraacetate was recently reported; V. M. Micović, R. I. Mamuzić, D. Jeremić, and M. Lj. Mihailović, Tetrahedron Letters No. 29, 2091 (1963).
3. R. M. Moriarty and K. Kapadia, Tetrahedron Letters No. 19, 1165 (1964).
4. U.S.P. 2,440,220.
5. L. P. Kuhn, P. von R. Schleyer, W. F. Battinger, Jr., and L. Ebersson, J. Am. Chem. Soc. **86**, 650 (1964).
6. R. C. Cookson and N. S. Wariyar, J. Chem. Soc. **1957**, 327.
7. K. Takeda, K. Kitahonoki, M. Sugiura, and Y. Takano, Chem. Ber. **95**, 2344 (1962).
8. cf. e.g. (a) K. Heusler, J. Kalvoda, G. Anner, and A. Wettstein, Helv. Chim. Acta **46**, 352 (1963); (b) J. Kalvoda and K. Heusler, Chem. & Ind. **1963**, 1431.
9. R. E. Partch, J. Org. Chem. **28**, 276 (1963).
10. Y. Kawazoe, Y. Sato, M. Natsume, H. Hasegawa, T. Okamoto, and K. Tsuda, Chem. Pharm. Bull. **10**, 338 (1962).