# Conversion of Steroidal δ-Lactones into Dihydropyrans or Tetrahydropyrans[1]

By GEORGE R. PETTIT* and JERRY R. DIAS

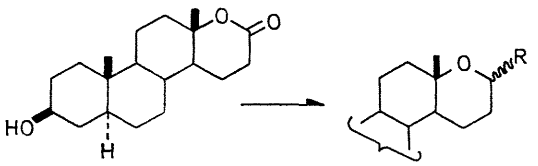
(*Department of Chemistry, Arizona State University, Tempe, Arizona* 85281)

*Summary* By varying experimental conditions, diborane has been found useful for converting certain δ-lactones into either hemiacetal, tetrahydropyran, or dihydropyran derivatives.

REAGENTS prepared from, *e.g.*, sodium borohydride–boron trifluoride or more directly from diborane–boron trifluoride have been employed for reduction of various esters and lactones to the corresponding ethers.[2] In the absence of a boron halide, reduction of lactones by diborane has been shown to yield hemiacetals.[3] We now report that certain δ-lactones can be converted by diborane into di- or tetrahydropyrans. Also, we have observed that the corresponding acetal and hemiacetal derivatives can be reduced to the tetrahydropyran stage by sodium borohydride–boron trifluoride etherate. Accordingly, diborane can be usefully employed for reduction of various lactones and esters, particularly those derived from secondary or tertiary alcohols, to hemiacetal, ether, or vinyl ether derivatives.

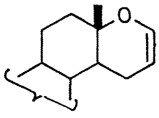
Reduction reactions proceeding from lactone (I)[4] are illustrative. With approximately 1 mole equiv. of borane–tetrahydrofuran (0·5 hr. at room temperature), lactone (I) yielded (82%, m.p. 159—194°) epimeric hemiacetal (IIa).[5]

Extending the reaction period to 3—4 days (vitreous gel becomes fluid) afforded (52%, m.p. 144—147°)† vinyl ether (III). Repeating the reduction with 1 mole equiv. of borane–tetrahydrofuran (0·5 hr.) and then adding an additional 2 mole equiv. of the same reagent gave (55%), after 4 days, ether (IIb).[4] Treating methyl acetal (IIc) (m.p. 115—125°) with sodium borohydride–boron trifluoride etherate in refluxing (2 hr.) tetrahydrofuran–diglyme also yielded (47%) tetrahydropyran (IIb).[6]

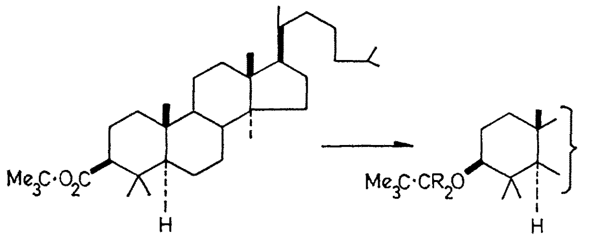


(I)

(II)a; R = OH
b; R = H
c; R = OMe



(III)



(IV)

(V) a; R = H
b; R = D

With lack of the requisite substituents for vinyl ether formation, diborane reduction can offer a practical route to the corresponding ether. For example, with three or more mole equiv. of borane–tetrahydrofuran at room temperature for 3 days, pivalate ester (IV) (m.p. 185—186°) was converted in 70% yield into neopentyl ether (Va) (m.p. 182—183°). Reduction of ester (IV) using sodium borodeuteride–boron trifluoride etherate (2 days, reflux) provided (70%) the dideuterio-counterpart (Vb). Introduction of two deuterium atoms was verified by mass spectral and n.m.r. measurements and provides some additional justification for our earlier assumption that both newly introduced hydrogens emanate from the boron hydride reagent.[7] The scope of these new diborane reactions is being studied.

This investigation was supported by Public Health Service Research Grants from the National Cancer Institute. We are also grateful to the National Institutes of Health for the award of a predoctoral fellowship to J.D.

(*Received, April 1st, 1970; Com. 438.*)

---

† The structure assigned each new compound has been confirmed by results of mass, $^{1}$H n.m.r., and i.r. spectral data and elemental analyses. The purity of each compound was substantiated by preparative layer and thin-layer chromatography.

[1] Previous paper: G. R. Pettit, D. C. Fessler, K. D. Paull, P. Hofer, and J. C. Knight, *Canad. J. Chem.*, 1969, **47**, 2511.

[2] See for example, G. R. Pettit and W. J. Evers, *Canad. J. Chem.*, 1966, **44**, 1293.

[3] G. R. Pettit, J. C. Knight, and W. J. Evers, *Canad. J. Chem.*, 1966, **44**, 807.

[4] G. R. Pettit and T. R. Kasturi, *J. Org. Chem.*, 1960, **25**, 875. In this regard it should be noted that propyl ethers have been detected following reaction between borane–tetrahydrofuran and propionyl derivatives of alginic acid: J. H. Manning and J. W. Green, *J. Chem. Soc. (C)*, 1967, 2357.

[5] G. R. Pettit, T. R. Kasturi, B. Green, and J. C. Knight, *J. Org. Chem.*, 1961, **26**, 4773. Presumably, lactol (IIa) is predominantly the $17\alpha$-isomer: J. S. Baran, *J. Org. Chem.*, 1965, **30**, 3564.

[6] Reduction of certain acetals to ethers has previously been accomplished using a lithium aluminium hydride–aluminium chloride reagent or by isobutyl aluminium hydride. For example, consult U. E. Diner and R. K. Brown, *Canad. J. Chem.*, 1967, **45**, 2547 and L. I. Zakharkin and I. M. Khorlina, *Izvest. Akad. Nauk S.S.S.R., Otdel. khim. Nauk*, 1959, 2255 (*Chem. Abs.*, 1960, **54**, 1087).

[7] G. R. Pettit and T. R. Kasturi, *J. Org. Chem.*, 1961, **26**, 4557.