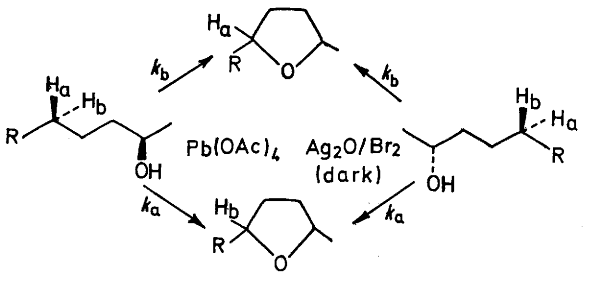
Dynamic Stereochemistry: Mechanistic Controversy in the Silver Oxide–Bromine Induced Cyclizations of Alcohols

By MARK M. GREEN,* J. MICHAEL MOLDOWAN, and JOHN G. MCGREW, II
(*Department of Chemistry, University of Michigan, Ann Arbor, Michigan* 48104)

Summary The abstraction of a diastereotopic hydrogen (1,4) in the silver oxide–bromine catalysed formation of tetrahydrofurans from three acyclic secondary alcohols has been shown to be stereoanalogous to the hydrogen abstraction in lead tetra-acetate generated alkoxy-radicals in the same molecules.

FOLLOWING the observations of Corey and White,[1] cationic oxygen intermediates have been suggested and refuted in the silver oxide–bromine induced (dark) cyclizations of aliphatic alcohols.[2]



SCHEME. R = Ph or C_6H_{11} (cyclohexyl)

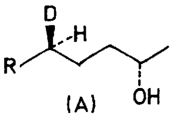
Following earlier work,[3] we have studied the comparative dynamic stereochemistries for the hydrogen abstraction steps (k_a/k_b, Scheme) in the lead tetra-acetate and silver oxide–bromine induced cyclizations of 5-phenylpentan-2-ol and 5-cyclohexylpentan-2-ol. Since the lead tetra-acetate induced reactions proceed *via* alkoxy-radicals,[4] these comparisons potentially offer a solution to the problem. The secondary alcohols deuteriated in turn at H_a and H_b (Scheme) are suitable for this work.[5]

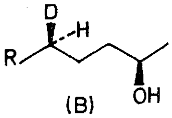
TABLE[a]

	Pb(OAc)$_4$ H/D			Ag$_2$O/Br$_2$ H/D		
R	(A)	(B)	$\Delta\Delta G^{\ddagger c}$	(A)	(B)	$\Delta\Delta G^{\ddagger c}$
C_6H_{11}	19/100	35/100	215	13/100[b]	28/100[b]	225
Ph	16/100	30/100	210	19/100	33/100	219
Me	20/100	27/100	100	17/100[b]	22/100	80

[a] The average deviations are: H/D ratios of the resultant substituted tetrahydrofurans from diastereoisomers (A) and (B) ± 1·0; $\Delta\Delta G^{\ddagger}$ values for the abstraction of the diastereotopic hydrogens (H_a, H_b) in the Scheme ± 20 cal mol^{-1}. The *cis* and *trans* isomers of the substituted tetrahydrofurans were separated by g.c. and analysed by m.s. for deuterium content. The resultant H/D ratios were independent of tetrahydrofuran stereochemistry. H/D ratios for R = Me were taken from ref. 3 and the $\Delta\Delta G^{\ddagger}$ values calculated. [b] Reactions carried out heterogeneously in hydrocarbon solvent at 25°. All other values obtained at 81°. The reactions yielded about 50% (based on starting material) of product tetrahydrofurans with the other major pathway returning starting material. [c] In all cases H_a is preferred over H_b (Scheme).

The deuterium content of the tetrahydrofuran products from the Ag_2O/Br_2 and the $Pb(OAc)_4$ cyclizations of the deuteriated diastereoisomers[5] and the resultant calculated[6,7] $\Delta\Delta G^{\ddagger}$ values are shown in the Table. The data show the essential 1,4-hydrogen abstraction step in the lead tetra-acetate and silver oxide–bromine induced reactions. Thus unless two differing mechanisms show qualitatively and quantitatively identical stereoselectivities for abstraction of the diastereotopic hydrogens in three different compounds (Table), the data demand superimposable transition states.


(A)


(B)

It follows that acceptance of the lead tetra-acetate intermediate as an alkoxy-radical,[4] requires a corresponding intermediate for the hydrogen abstraction step in the formation of 2,5-substituted tetrahydrofurans *via* the reaction of silver oxide–bromine on the compounds studied.

We thank the National Institute of General Medical Science for financial support.

(*Received, 30th March* 1973; *Com.* **444**.)

---

[1] E. J. Corey and R. W. White, *J. Amer. Chem. Soc.*, 1958, **80**, 6686.

[2] R. A. Sneen and N. P. Matheny, *J. Amer. Chem. Soc.*, 1964, **86**, 3905; *ibid.*, p. 5503; M. Akhtar, P. Hunt, and P. B. Dewhurst, *ibid.*, 1965, **87**, 1807; G. Smolinsky, and B. I. Feuer, *J. Org. Chem.*, 1965, **30**, 3216; A. Deluzarche, A. Maillard, P. Rimmelin, F. Schue, and J. M. Sommer, *Chem. Comm.*, 1970, 976; N. Matheny Roscher, *ibid.*, 1971 474; V. Boido and O. E. Edwards, *Canad. J. Chem.*, 1971, **49**, 2664.

[3] M. M. Green, J. G. McGrew, II, and J. M. Moldowan, *J. Amer. Chem. Soc.*, 1971, **93**, 6700.

[4] For general reviews of this reaction class see G. Sosnovsky and D. J. Rawlinson, *Adv. Free-Radical Chem.*, 1972, **4**, 249; M. Lj. Mihailović and Z. Čeković, *Synthesis*, 1970, 209; M. Akhtar, *Adv. Photochem.*, 1964, **2**, 263; K. Heusler and J. Kalvoda, *Angew. Chem. Internat. Edn.*, 1964, **3**, 525.

[5] For the stereospecific preparations of the 5-deuterio-5-phenylpentan-2-ol and 5-cyclohexyl-5-deuteriopentan-2-ol diastereoisomers see, J. M. Moldowan, Ph.D., University of Michigan, 1972.

[6] This calculation allows the isolation of the isotope effect so that k_a/k_b may be obtained directly: D. Y. Curtin and D. B. Kellom, *J. Amer. Chem. Soc.*, 1953, **75**, 6011.

[7] For use of this method in closely related experiments see: M. M. Green, J. M. Moldowan, D. J. Hart, and J. M. Krakower, *J. Amer. Chem. Soc.*, 1970, **92**, 3491, and ref. 3.