

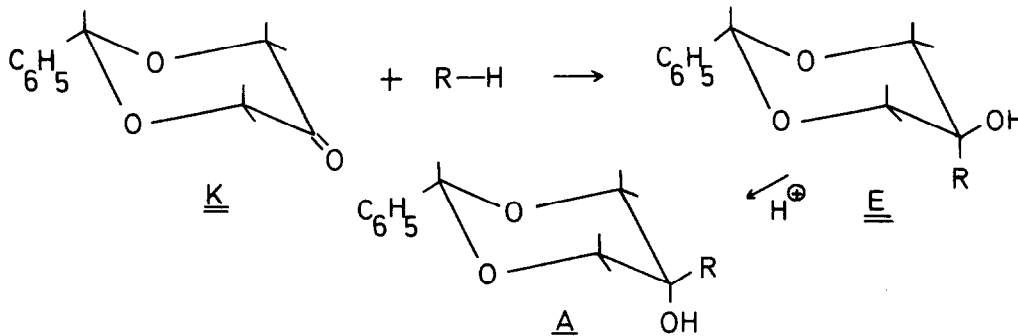
STEREOSPECIFIC SYNTHESIS OF 5-SUBSTITUTED 1,3-DIOXANES
BY APPLICATION OF DIMROTH'S PRINCIPLE

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Grignard reagents and LiAlH_4 add to 2-phenyl-1,3-dioxan-5-one (K)¹⁾ exclusively through axial attack²⁾ to give the pure alcohols E of Table 1.

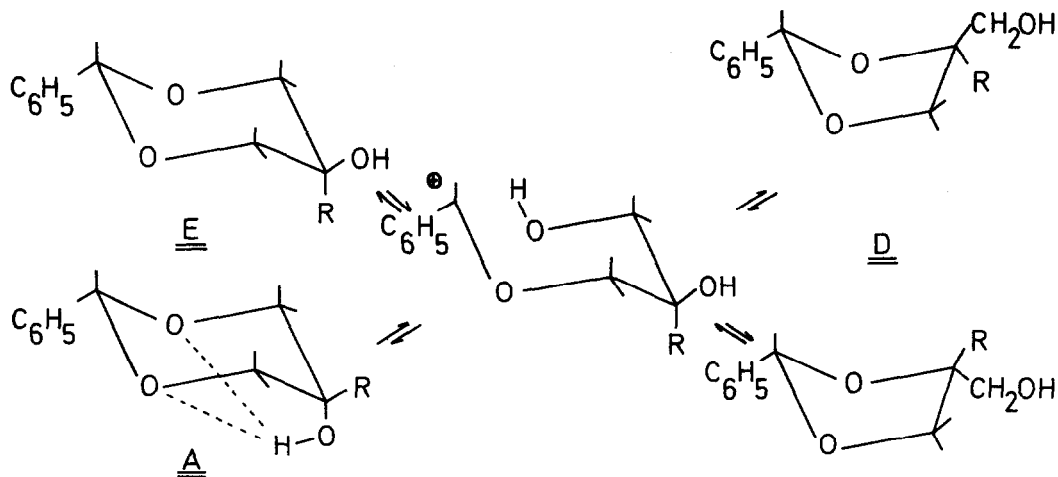


If the crystals of E are kept in a dry atmosphere of HCl gas³⁾, they melt and soon (1 h - 3 days at 5°) crystallize again consisting then entirely of the spectroscopically pure alcohols A with an axial OH group. This quantitative isomerization represents another application of Dimroth's principle⁴⁾ which we recently used successfully in the preparation of some rare 2-deoxy-2-amino-hexoses⁵⁾.

The configurational assignments of E and A follow from the IR-⁶⁾ and NMR-spectra⁷⁾. Only the OH protons of the compounds A are completely intramolecularly hydrogen bonded to the ring oxygens in 0.005 M solutions

in CCl_4 ⁸⁾. The positions of the benzylic H-2 protons and the shifts of the protons at C-4 and -6 have been shown ^{7, 9)} to be characteristic of the conformations. Some physical data of the isomers E and A and of their acetates are given in Table 1.

If one bubbles a little dry HCl gas through the 0.2 M solutions of E or A in CCl_4 , equilibration occurs among four components as shown in the scheme ¹³⁾:



Equilibrium is reached at 25° within several hours and can be followed by integrating the NMR signals of the H-2 protons. The composition of the equilibrium mixture is the same starting either from E or from A. The results are given in Table 2. The acetates also equilibrate under the same conditions leading to acetylated dioxolanes, D, exclusively. These compounds must form through acetyl migration.

The equilibria demonstrate that - at least in solution - the maximum free energy difference of the four isomers is less than 3 kcal/mole ^{10, 11)} indicating that "product development control" ¹²⁾ is not a plausible explanation of both the exclusive formation of E by Grignard addition to K and the exclusive formation of A by the treatment of E with HCl gas.

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Table 1

Isomer	R	mp.	$\delta(\text{H-2})$ ^{a)}	$\delta(\text{R})$ ^{b)}	Acetate: mp.	$\delta(\text{H-2})$	$\delta(\text{R})$ ^{b)}
K	-	70 ¹⁾	5.79	-	-	-	-
E	H	65 ³⁾	5.26	-	118 ³⁾	5.32	-
A	H	83 ⁶⁾	5.39	-	101 ⁶⁾	5.40	-
E	CH ₃	72	5.40	1.36	83	5.34	1.74
A	CH ₃	74	5.30	1.00	40	5.33	1.30
E	CH ₃ CH ₂	68	5.39	1.72	46	5.34	2.24
A	CH ₃ CH ₂	50	5.31	1.36	104	5.32	1.80
E	(CH ₃) ₂ CH	98	5.51	2.09	41	5.41	2.73
A	(CH ₃) ₂ CH	87	5.28	1.58	70	5.32	2.55

a) 90 MHz spectra (Bruker FHX 90) of solutions in CCl₄. Shifts in ppm from TMS.

b) Shifts of the protons of R which are two bonds separated from C-5.

Table 2

Equilibration of the dioxanols E and A in 0.2 M solutions in CCl₄ ^{c)} at 25° under an atmosphere of dry HCl gas.

Starting isomer: R ^{d)}	Equilibrium: % E ^{e)}	% A	% D ^{f)}
H	14	45	41 (23 + 18)
CH ₃	9	73	18 (12 + 6)
CH ₃ CH ₂	6	71	23 (10 + 13)
(CH ₃) ₂ CH	4	70	26 (9 + 17)

c) The equilibrium composition is rather insensitive to the concentration.

d) Starting from pure E gives the same equilibrium mixture as starting from A.

e) The figures are averages of 4 runs, all figures $\pm 2\%$.

f) No configurational assignment has been tried for the dioxolanes.

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