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THE STEREOCHEMISTRY OF THE CATHODIC PINACOLIZATION OF CARBONYL COMPOUNDS: THE CONFIGURATION OF BENZOIN PINACOL

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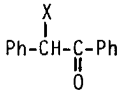
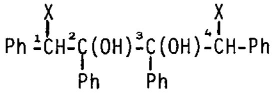
Previous studies have shown that most aldehydes and unsymmetrical ketones produce mixtures of isomeric glycols when subjected to electropinacolization.[1] The degree of reduction stereoselectivity has been ascribed to both solution and cathode surface properties.[1b, 2]

As part of an effort to evaluate the importance of solution vs. electrode effects we studied the electropinacolization of benzoin (1). The reduction of 1 has been shown to be highly stereoselective, giving only one of six possible diastereomeric products.[3] Thus, 24 mmol of 1 was reduced in a basic H_2O/EtOH solution using a mercury-plated copper gauze cathode. The pinacol 4, mp 240° dec., was isolated in 50 % yield, the only other product being hydrobenzoin.



$$\mathrm{Ph{-}\overset{X}{\overset{|}{C}}H{-}\underset{\underset{O}{\|}}{C}{-}Ph}$$

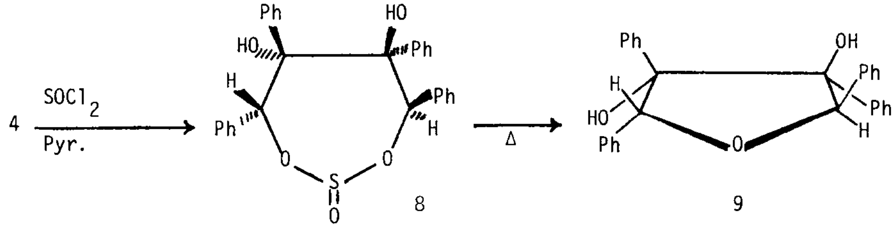


$$\mathrm{Ph\,{-}\overset{X}{\overset{|}{\overset{1}{C}}}H{-}\underset{\underset{Ph}{|}}{\overset{2}{C}}(OH){-}\underset{\underset{Ph}{|}}{\overset{3}{C}}(OH){-}\overset{X}{\overset{|}{\overset{4}{C}}}H{-}Ph}$$

1. X = OH 2. X = NH_2
3. X = CH_3

4. X = OH 5. X = NH_2
6. X = CH_3 7. X = H

The configuration between C-2 and C-3 of the pinacol 4 was established as *threo* by selective hydrogenolysis of the C-1 and C-4 hydroxyls. The sole product was the *threo* isomer[4] of 7. The configuration between C-1 and C-2 as well as C-3 and C-4 was determined to be *erythro* on the basis of the following evidence. Treatment of 4 with $SOCl_2$-pyridine at 0° produced the cyclic sulfite ester 8 in 70 % yield. The latter was quantitatively converted to 9 by heating in vacuo above the melting point.[5]



The facile formation of **8** supports the proposed *erythro* relationship between the C-1, C-2, and C-3, C-4 pairs because the most stable conformation of this isomer places the C-1 and C-4 hydroxyl groups in close proximity.[6] In the contrasting *threo, threo, threo* isomer the terminal hydroxyl groups are positioned at opposite ends of the molecule.

An nmr study of **9** also supports the *erythro, threo, erythro* configuration of **4**.[7] First, the nmr spectrum of **9** showed a single benzylic peak at δ 6.48 (CDCl$_3$), strongly suggesting identical configurations at C-2 and C-5. Secondly, the inability of **9** to complex with Eu(FOD)$_3$ (ΔEu_{OH} = 0.02; $\Delta Eu_{H_{2,5}}$ = 0.03, CDCl$_3$)[8] argues for the more sterically restricted hydroxyls of **9** compared to the isomer with inverted configurations at C-2 and C-5.[9]

The cathodic reductions of ketones **2** and **3** were also studied. While the product configurations were not established, **2** produced only a single pinacol **5** and **3** gave two of the six possible disasteromers of **6**.

The above results appear to be best explained by consideration of both steric and intermolecular hydrogen bonding effects in the transition state of pinacolization. In fact, an argument similar to that generated by the facile formation of **8** must also apply to the pinacolization step itself. Models show clearly that the configuration of the radical anions giving rise to **4** is that which simultaneously favors both maximum intermolecular hydrogen bonding and minimum phenyl-phenyl repulsion during dimerization. The importance of hydrogen bonding is further illustrated by the lowered steroselectivity noted for the reduction of **3** to **6**.

Finally, the question of solution vs. electrode effects must remain unsettled. Although the hydrogen bonding phenomena would appear to minimize the importance of the cathode, hydroxyl and amino groups would also be expected to cause stronger adsorption of the radical to the cathode surface. This latter factor might also influence the stereochemistry of dimerization.

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NOTES:

1. (a) R.E. Juday and W. Sullivan, *J. Org. Chem.*, 20, 617 (1955). (b) J. H. Stocker and R.M. Jenevin, *J. Org. Chem.*, 34, 2807 (1969); *Coll. Czeck. Chem. Commun.*, 36, 925 (1971). (c) H. Lund and A.D. Thomsen, *Acta Chem. Scand.*, 23, 3567 (1969). (d) V.J. Puglisi, G.L. Clapper, and D.H. Evans, *Anal. Chem.*, 41, 279 (1969). (e) L. Horner and D. Degner, *Tetrahedron Lett.*, 1241 (1971).

2. K. Korinek and T.F.W. McKillop, *Ann. Reports, B*, 68, 301 (1971).

3. H. Kauffmann, *Z. Elektrochem.*, 4, 461 (1898).

4. J. H. Stocker and D.H. Kern, *J. Org. Chem.*, 33, 1271 (1968).

5. All new compounds gave the appropriate combustion data.

6. Steric assistance seems to be involved in the formation of **8** since the less hindered 1,4-diphenyl -1,4- butanediol failed to give a similar reaction.

7. Hydrogenolysis of **9** produced the *threo* isomer of **7**, showing that configurations at C-2 and C-3 of **4** were unchanged during ring closure to **8** and **9**.

8. For use of ΔEu values see H. Hart and G.M. Love, *Tetrahedron Lett.*, 625 (1971).

9. Eu(FOD)$_3$ was also unable to complex with 2,5-diphenyltetrahydrofuran. In addition, *meso*-deoxybenzoin pinacol exhibited drastically reduced complexation with Eu(FOD)$_3$ compared with the d,l isomer, thereby supporting the *trans* -3,4-dihydroxyl arrangement of **9**. These results are part of a separate study and will be reported soon.