Dihydrobenzofuran Derivatives in which $J_{trans\text{-}2,3} > J_{cis\text{-}2,3}$

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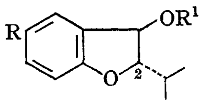
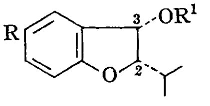
IT is a common assumption that the coupling constants of the C-2 and C-3 protons in 2,3-disubstituted-2,3-dihydrobenzofurans will be larger for *cis*-isomers than for *trans*-isomers.[1] This assumption appears to be based on an estimation of bond angles from molecular models and application of the Karplus equation.[2] While the stereochemical assignments in the literature may be correct, it is quite clear from the data presented below that in the absence of other information such conclusions must be suspect.

During the course of another investigation, we prepared the two families of dihydrobenzofurans (I—III) and (IV—VIII). 5-Bromo-2-hydroxy-(α-bromo-β-methyl)butyrophenone, prepared by bromination of *o*-hydroxyisovalerophenone, on reduction with sodium borohydride in aqueous ethanolic potassium hydroxide gave the *trans*-isomer (I). Acetylation of (I) gave (II), while treatment of (I) with butyl-lithium and then carbon dioxide followed by treatment of the product with methyl-lithium led to (III). The *cis*-isomer (IV) was obtained when 5-bromo-2-hydroxy-(α-bromo-β-methyl)butyrophenone was first reduced with sodium borohydride in the absence of potassium hydroxide and then the product was treated with base. *trans*-Isomers (V—VIII) were prepared from (IV) as described above for the *cis*-isomers. The *trans*-isomers show a coupling constant for the C-2 and C-3 protons of 6 c./sec. while the *cis*-isomers show a smaller coupling constant of 4 c./sec.

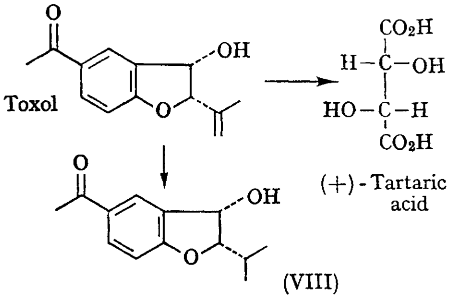


	$J_{2,3}$
(I) R=Br, R^1=H	6 c./sec.
(II) R=Br, R^1=Ac	6
(III) R=Ac, R^1=H	6



(IV) R=Br, R^1=H	4 c./sec.
(V) R=Br, R^1=Ac	4
(VI) R=CO_2H, R^1=H	4
(VII) R=R^1=Ac	4
(VIII) R=Ac, R^1=H	4

The configuration of (VIII) is firmly established since racemic (VIII) was identical in i.r. and n.m.r. spectra with optically active dihydrotoxol[3] prepared by hydrogenation of toxol; toxol yields (+)-tartaric acid on ozonolysis.[3] Thus, the configurations of (IV—VII) and *ipso facto* (I—III) are known (all structures were supported by elemental analyses, i.r. and mass spectra). The observed low value for $J_{2,3}$ in the *cis*-isomers may be due to the stereochemical dependence of the electronegativity effect pointed out by Booth[4] for six-membered rings. Thus, in the *cis*-isomers, as the C-2 and C-3 substitutents bend away from each other to remove steric compression, the angle between the H-3 and the 2-OH or heterocyclic oxygen approach 180°, the angle of maximum electro-negativity effect and minimum $J_{2,3}$.



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