Stereochemistry of Carbanions Derived from 1,3-Dioxanes

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Abstract: Proton abstraction from 4-methyl-1,3-dioxane (**1**), 2-phenyl-1,3-dioxane (**4**), 4-phenyl-1,3-dioxane (**5**), *trans*-4-methyl-2-phenyl-1,3-dioxane (**7**), and *cis*- (**12**) and *trans*-2-methyl-4-phenyl-1,3-dioxane (**6**) by means of BuLi/KO-*t*-Bu ("Lochmann-Schlosser base") gave the corresponding carbanions as shown by subsequent deuteronation with EtOD. In contrast, attempted proton abstraction from *cis*-2-phenyl-4-methyl-1,3-dioxane (**3**) under the same conditions was unsuccessful, as was abstraction from phenylcyclohexane. Competitive experiments showed that abstraction of the equatorial hydrogen from **7** was about 4 times faster than corresponding abstraction from **6** and that abstraction of the equatorial hydrogen in **6** was well over 25 times faster than abstraction of the axial hydrogen in **12**. Deuteronation of the 2-phenyl carbanion from **7** gave the trans isomer **8** in a 70:1 or greater ratio. Deuteronation of the carbanion derived from **6** or **12**, in contrast, produced the axial and equatorial 4-phenyl compounds **10** and **11** in a ratio of only about 2:1. The preliminary conclusion that the carbanion derived from 2-phenyl-1,3-dioxane is largely pyramidal, similar to that from 2-phenyl-1,3-dithiane,[8] whereas the 4-phenyl-1,3-dioxanyl carbanion is planar, similar to the phenylcyclohexyl (benzylic) carbanion,[13] was confirmed by ^{13}C NMR study of these carbanions. The ion derived from 4-phenyl-1,3-dioxane is red and shows the large upfield shifts of the ortho and para ring carbons also seen in the phenylcyclohexyl carbanion[13] and characteristic of planar benzylic carbanions.[12] In contrast, the orange carbanion derived from 2-phenyl-1,3-dioxane (which was very unstable and easily oxidized), to the extent that measurement was possible, showed the smaller upfield para carbon shift characteristic of pyramidal benzylic carbanions.[8b,12] It is concluded that, while two adjacent oxygen atoms mildly stabilize equatorial carbanions (presumably inductively), the destabilizing effect of antiperiplanar lone pairs prevents the 2-phenyl carbanion from becoming planar and inhibits abstraction of the axial hydrogen in compound **3**. Reprotonation of the pyramidal ion is stereoselective from the equatorial side. In contrast, in the 4-phenyl carbanion, benzylic resonance stabilization overrides the antiperiplanar effect of one neighboring oxygen atom: Both axial and equatorial hydrogen atoms at C(4) can be abstracted and the carbanion is planar; accordingly reprotonation is essentially nonstereoselective.

Carbanions are key intermediates in many synthetic transformations which result in the formation of new carbon-carbon bonds. Carbanion geometry is of interest because it may affect the stereochemistry of the products of such transformations and because it throws light on the manner in which substituents may stabilize carbanions. Also of interest is the ease with which carbanions can be formed, i.e. the kinetic and thermodynamic acidity of their C-H precursors. In the work here reported we have investigated carbanions next to ether or acetal functions, $RO-C^-$ and $(RO)_2C^-$.

It is well-known[2] that carbon acids next to oxygen, H-C-O- (sp^3 hybridized carbon) are weaker, by several powers of 10, in both kinetic[3] and thermodynamic[4] acidity than corresponding carbon acids next to sulfur, H-C-S-. In fact, organometallic derivatives of the type M-CRR'-O- cannot, in general, be prepared by proton abstraction from the H-CRR'-O- precursor by strong bases, unless R or R' is a carbanion stabilizing group, such as C=O, C_6H_5, CH_2=CH-, CN, RS-, etc., but must be made by indirect methods.[5,7]

It is also known that, in acids of the H-C-S- type, there is strong dependence of kinetic and, a fortiori, thermodynamic acidity on the relative orientation of the acidic hydrogen and the lone pairs on sulfur. Thus in conformationally locked 1,3-dithianes (chair conformation), the equatorial hydrogen is abstracted by butyllithium about ten times as fast as its axial neighbor, with the difference in thermodynamic acidities being even much greater.[8a] In the case of 2-phenyl-1,3-dithiane, there is ample evidence from NMR spectra,[8b] chemical behavior,[8a] and most conclusively X-ray structure[9] that the carbanion partner of the ion pair is pyramidal, with the phenyl being axial. The preference of the unshared electron pair of the carbanion for the equatorial position has been explained on quantum chemical grounds, in terms of favorable and unfavorable orbital overlap, respectively.[10]

Other benzylic carbanions, however, tend to be planar or near planar.[11] Grutzner,[12] having established NMR criteria to assess the planarity of carbanions in the 7-phenylnorbornyl case, found that in 7-phenylnorbornylpotassium and -cesium the benzylic carbanion partner is planar whereas in the corresponding lithium compound it is pyramidal, perhaps because of more covalent

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(2) E.g.: Beak, P.; Reitz, D. B. *Chem Rev.* **1978**, *78*, 275. See also ref 10.

(3) Yakovleva, E. A.; Tsvetkov, E. N.; Lobanov, D. I.; Kabachnik, M. I.; Shatenshtein, A. I. *Tetrahedron Lett.* **1966**, 4161.

(4) E.g.: Bordwell, F. G.; Van Der Puy, M.; Vanier, N. R. *J. Org. Chem.* **1976**, *41*, 1885. See also: Streitwieser, A.; Juaristi, E.; Nebenzahl, L. L. Equilibrium Carbon Acidities in Solution In *Comprehensive Carbanion Chemistry*; Buncel, E., Durst, T., Eds.; Elsevier: New York, 1980; Part A, p 323.

(5) (a) E.g.: Cohen, T.; Matz, J. R. *J. Am. Chem. Soc.* **1980**, *102*, 6900. (b) A notable exception in the anion derived by treatment of $(CH_3)_3CCOCH_3$ with the Lochmann-Schlosser base:[6] Corey, E. J.; Eckrich, T. M. *Tetrahedron Lett.* **1983**, *24*, 3165.

(6) Lochmann, L.; Popfšil, J.; Lím, D. *Tetrahedron Lett.* **1966**, *257*. Schlosser, M. *J. Organomet. Chem.* **1967**, *8*, 9.

(7) See also: Shiner, C. S.; Tsunoda, T.; Goodman, B. A.; Ingham, S.; Lee, S.-h.; Vorndam, P. E. *J. Am. Chem. Soc.* **1989**, *111*, 1381.

(8) (a) Eliel, E. L.; Hartmann, A. A.; Abatjoglou, A. G. *J. Am. Chem. Soc.* **1974**, *96*, 1807. (b) Abatjoglou, A. G.; Eliel, E. L.; Kuyper, L. F. *J. Am. Chem. Soc.* **1977**, *99*, 8262.

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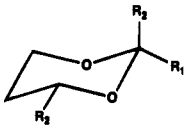
Scheme 1



1, $R_1 = R_2 = H$, $R_3 = CH_3$

2, $R_1 = D$, $R_2 = H$, $R_3 = CH_3$

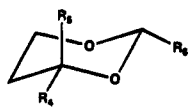
3, $R_1 = C_6H_5$, $R_2 = H$, $R_3 = CH_3$

4[a], $R_1 = C_6H_5$, $R_2 = R_3 = H$ or $R_2 = C_6H_5$, $R_1 = R_3 = H$

7, $R_1 = H$, $R_2 = C_6H_5$, $R_3 = CH_3$

8, $R_1 = D$, $R_2 = C_6H_5$, $R_3 = H$

9, $R_1 = C_6H_5$, $R_2 = D$, $R_3 = CH_3$



5[a], $R_4 = C_6H_5$, $R_5 = R_6 = H$ or $R_5 = C_6H_5$, $R_4 = R_6 = H$

6, $R_4 = H$, $R_5 = C_6H_5$, $R_6 = CH_3$

10, $R_4 = D$, $R_5 = C_6H_5$, $R_6 = CH_3$

11, $R_4 = C_6H_5$, $R_5 = D$, $R_6 = CH_3$

12, $R_4 = C_6H_5$, $R_5 = H$, $R_6 = CH_3$

[a] This compound is conformationally mobile.

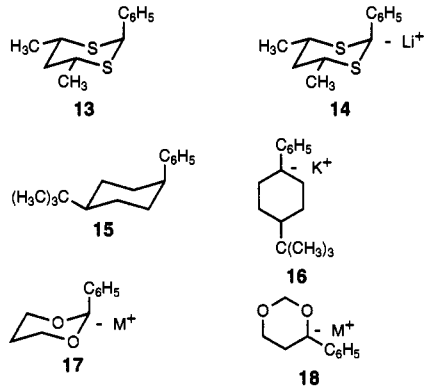
character in the latter. Using both Grutzner's NMR criteria and chemical behavior (absence of stereoselectivity in protonation) it had previously been established[13] that the 1-phenylcyclohexyl carbanion (formed by indirect methods[5a,7,14]) is planar as well.

It was the purpose of the present study to find out the following: (1) whether, using the very strong Lochmann–Schlosser base (BuLi/*t*-BuOK),[6] 1,3-dioxanes, either with or without phenyl substituents at C(2) or C(4)—α to oxygen—could be deprotonated, and if so, what the stereochemistry of subsequent reprotonation would be; (2) using NMR[12] as well as chemical criteria, to establish if the 2-phenyl- and 4-phenyl-1,3-dioxanyl carbanions are planar, like most other benzylic carbanions, or pyramidal, in analogy with the 2-phenyl-1,3-dithianyl carbanion; (3) to assess the relative kinetic acidity of the axial and equatorial hydrogens in anancomeric (conformationally biassed) 2-phenyl- and 4-phenyl-1,3-dioxanes; (4) to assess the relative kinetic acidity of ether, ROC–H, vs acetal, $(RO)_2C$–H, protons in conformationally similar situtations. With respect to the first point, although it was reported in 1969[15] that treatment of 2-phenyl-1,3-dioxane with butyllithium–tetramethylethylenediamine followed by D_2O failed to produce H/D exchange, in later work[16] it was found possible to prepare the carbanion from the same compound as well as from an anancomeric axial 2-phenyl-1,3-dioxane but not from an anancomeric 2-phenyl-1,3-dioxane in which the phenyl group was constrained to an equatorial position.

Results

Treatment of the anancomeric 4-methyl-1,3-dioxane (**1**) with Lochmann–Schlosser base,[6] followed by reprotonation with EtOD, led to the incorporation of 35 ± 5% of deuterium at the equatorial 2-position to give **2**, as evidenced by ^1H and ^2H NMR spectroscopy, showing that deprotonation with the very strong base was at least partially successful, that redeuteronation occurred exclusively from the equatorial side, and hence that the carbanion or ion pair formed was presumably pyramidal, with the lone pair on the equatorial side. Thus it was not surprising that the attempted deprotonation of *cis*-2-phenyl-4-methyl-1,3-dioxane (**3**) at C(2) was unsuccessful, with only 2% of deuterium incorporated at that position even though 94% of one deuterium was incorporated into the phenyl ring (^2H NMR evidence; see also ref 16). As one might expect, the problem is not in the phenyl substituent *per se*, but in its equatorial position: the axial proton at C(2) can evidently *not* be removed by the Lochmann–Schlosser base. Thus 2-phenyl-1,3-dioxane itself (**4**), which is conformationally mobile and exists, at least part of the time, with axial phenyl, was deprotonated at C(2); after quenching the reaction with EtOD, a total of 69% of one deuterium was incorporated, 66% at C(2) and 3% in the ring (some rearrangement apparently occurred as well, judging from the proton NMR spectrum). The carbanion formed was quite unstable and the orange (not deep-red, the color of the carbanion derived from phenylcyclohexane[13]) solution had to be manipulated at −78 °C and, on contact with even traces of air, turned green, presumably through oxidation to the much more stable radical at C(2). (See below for NMR study of this carbanion.) 4-Phenyl-1,3-dioxane (**5**) was similarly deprotonated; quenching with EtOD resulted in the incorporation of 62% of one D, very largely at C(4). This red carbanion was considerably more stable than its C(2) isomer and could be studied by ^{13}C NMR (see below and Table 1).

Table 1. Carbon-13 Chemical Shifts and Shift Differences in ppm



13 **14** **15** **16** **17** **18**

	13	14	15	16	4	17[c]	5	18[c]
δ_{ortho}	129.0	122.5	127.7	105.6	126.6	114	126.3	102.3, 100.9[b]
δ_{para}	127.1	113.4	125.1	88.8	128.9	112	128.2	92.3
$\Delta\delta_{ortho}$[a]	−6.5		−22.1		−12.6		−24, −25.4[b]	
$\Delta\delta_{para}$[a]	−13.7		−36.3		−16.9		−35.9	

[a] Upfield shift of carbanion relative to parent compound indicated: **13/14** (in THF at −25 °C),[8b] **15/16** (in THF at −40 °C),[13] **4/17**, **5/18** (see Experimental Section). [b] Two signals, indicating anisochronous ortho carbons, due to restricted rotation of the phenyl substituent on the NMR time scale. [c] See ref 31 for comments on the counterion(s) designated "M" in the structures.

We next studied the deprotonation and redeuteronation of appropriate anancomeric 1,3-dioxanes. Both *trans*-2-methyl-4-phenyl-1,3-dioxane (**6**) and *trans*-2-phenyl-4-methyl-1,3-dioxane (**7**) were examined. The former compound is very largely in the conformation with axial Ph(4): $\Delta G°$ for 2-Me is 4.0 kcal/mol,[17,18] whereas $\Delta G°$ for 4-Ph is 2.85 kcal/mol;[19] thus the axial preference of the phenyl substituent in **6** amounts to 1.15 kcal/mol (assuming additivity for the substituents) or 87.5:12.5 at 25 °C. The situation in **7** is not as favorable, inasmuch as $\Delta G°$

(10) (a) Lehn, J.-M.; Wipff, G. *J. Am. Chem. Soc.* **1976**, *98*, 7498. (b) Bernardi, F.; Csizmadia, I. G.; Mangini, A.; Schlegel, H. B.; Whangbo, M.-H.; Wolfe, S. *J. Am. Chem. Soc.* **1975**, *97*, 2209. (c) Epiotis, N. D.; Yates, R. L.; Bernardi, F.; Wolfe, S. *J. Am. Chem. Soc.* **1976**, *98*, 5435. (d) Krief, A. *Tetrahedron* **1980**, *36*, 2531. (e) Schleyer, P. v. R.; Clark, T.; Kos, A. J.; Spitznagel, G. W.; Rohde, C.; Arad, D.; Houk, K. N.; Rondan, N. G. *J. Am. Chem. Soc.* **1984**, *106*, 6467.

(11) Patterman, S. P.; Karle, I. L.; Stucky, G. D. *J. Am. Chem. Soc.* **1970**, *92*, 1150. See also: Brooks, J. J.; Stucky, G. D. *J. Am. Chem. Soc.* **1972**, *94*, 7333.

(12) Peoples, P. R.; Grutzner J. B. *J. Am. Chem. Soc.* **1980**, *102*, 4709.

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(14) Screttas, C. G.; Micha-Screttas, M. *J. Org. Chem* **1978**, *43*, 1064; **1979**, *44*, 713.

(15) Seebach, D. *Angew. Chem., Int. Ed. Engl.* **1969**, *8*, 639.

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(17) Eliel, E. L.; Knoeber, M. C. *J. Am. Chem. Soc.* **1968**, *90*, 3444.

(18) Nader, F. W.; Eliel, E. L. *J. Am. Chem. Soc.* **1970**, *92*, 3050.

(19) Anteunis, M.; Tavernier, D.; Swaelens, G. *Recl. Trav. Chim. Pays-Bas* **1973**, *92*, 531.

for 4-Me is only 2.9 kcal/mol[17] whereas that for 2-Ph is 3.12 kcal/mol,[18] suggesting an actual preference for equatorial 2-Ph of about 0.22 kcal/mol, i.e. only about 41% of the molecules at room temperature exist with axial Ph(2). However, since we had already established (vide supra) that the cis isomer **3** with equatorial phenyl does not react with the Lochmann–Schlosser base, we did not consider this somewhat unfavorable equilibrium in **7** to constitute a major problem.

Treatment of **7** with Lochmann–Schlosser base followed by EtOD quench led to the incorporation of 73% of one D as evidenced by the ^{2}H NMR spectrum. Of this, 32% were in the 2e position, 8.7% in the 2a position, 28% in the phenyl ring, and the remaining 4.3% in other positions. Thus the ratio of deuterated trans isomer (**8**) to deuterated cis isomer (**9**) was 3.6:1. However, proton and ^{13}C analysis of the reaction mixture showed that the total trans to cis ratio, (**7** + **8**)/(**3** + **9**) was 61:39 (1.6:1). Since the ratio of **7** to **3** in the starting material was 86:14, presumably 14% of the cis product was derived from cis starting material (**3**). Taking this into account, the trans-to-cis ratio in the reaction product is 61:25 or 2.4, considerably less than the ratio of the corresponding deuterated products. This suggests an increase in proportion of the undeuterated cis isomer over that present in the starting material. The most likely explanation for this discrepancy was isomerization of unreacted trans isomer (**7**) to cis (**3**) during workup, since it is know that such isomerization occurs with extreme ease in the presence of even traces of acid. Indeed, when the product was submitted to the workup procedure a second time, the percentage of cis isomer increased by about 5%, confirming that trans isomer was converted to cis in the workup. To avoid the probable concomitant isomerization of **8** to **9**, the quenching EtOD was partially (to the extent of 10%) converted to EtONa by the addition of an appropriate amount of sodium prior to quench. When the experiment was repeated using this solution, the ratio of **8** to **9** changed to 70:1 (trans:cis). This ratio must be considered a minimum since some small amount of conversion of **8** to **9** during workup even under these conditions cannot be excluded. In any case, the result shows that deuteronation of the 2-phenyl-4-methyl-1,3-dioxanyl carbanion at C(2) is highly stereoselective and occurs almost entirely from the equatorial side.

A quite different result was observed in the case of the carbanion derived from *trans*-2-methyl-4-phenyl-1,3-dioxane (**6**). Treatment of **6** with Lochmann–Schlosser base followed by EtOD quenching led to a total of 56% deuterium incorporation. The ^{2}H NMR spectrum indicated that 19% of D was situated at the 4e position and 10.5% at the 4a position (of the remainder, 19% was in the phenyl ring). Thus the ratio of **10**:**11** in the product was 1.8:1. A very similar ratio (2.5:1) was obtained from the epimeric *cis*-2-methyl-4-phenyl-1,3-dioxane (**12**), suggesting hydrogen abstraction at C(4) can occur from either the equatorial or axial position, that the two reactions pass through the same carbanion, and that the deuteronation of that carbanion is not stereoselective.

Competition Experiments. We next carried out competition experiments to gauge the relative kinetic acidities of hydrogen positioned in the equatorial 2-position of **7**, the equatorial 4-position of **6**, and the axial 4-position of **12**. (Earlier experiments, vide supra, had already indicated that the axial H(2) in **3** is totally unreactive.)

In the first competition experiment, a 1:1 mixture of **7** and **6** was treated with 1 equiv of Lochmann–Schlosser base. The product, after EtOD quench (no ethoxide added), was analyzed by ^{1}H, ^{2}H, and ^{13}C NMR spectroscopy. The total deuterium incorporation was 67%. Of this a total of 40% was incorporated in the 2-phenyl compound [38.5% to give **8** and 1.5% to give **9**—the ratio (**8**:**9**) of 26 is less than that of 70 previously observed for **7** by itself, presumably because of epimerization during quenching] and 26% was incorporated in the 4-phenyl compound [18% to give **10** and 8% to give **11**, ratio 2.2, slightly higher than the 1.8 seen for pure **6** as starting material]. Thus the ratio of incorporation of deuterium in **7** vs **6** was 40:26 or 1.5:1. However, in interpreting this ratio, one must take into account that, whereas **6** is 95% in the conformation with axial phenyl, only 36% of **7** exists in that conformation.[20] The relative rate of hydrogen abstraction from conformer **6** is therefore 0.95/0.36, the observed total relative rate of abstraction from *trans*-2-phenyl-4-methyl-1,3-dioxane.[21] The true ratio of reactivity [$H_e(2)$:$H_e(4)$] is therefore 1.5 × 0.95/0.36 or 4.0.[22]

In the second competition experiment a mixture of 1 equiv of **6** and 1 equiv of **12** was allowed to compete for 1 equiv of Lochmann–Schlosser base. The resulting anion was then quenched into EtOD/EtONa so that products could be distinguished from unconsumed starting materials. ^{13}C NMR spectroscopy of the product suggested that almost all the recovered trans isomer was deuterated, since the C(4) signal for the mixture of **6** and **10** (equatorial H or D) was invisible (suggesting that the position was almost totally deuterated, i.e. that the product was nearly entirely **10**) whereas that for the mixture of **12** and **11** (axial H or D) was clearly evident. The ^{2}H NMR spectrum showed 27% deuterium in the 4e position (**10**) and 16% in the 4a (**11**), for a ratio of 1.7:1 very close to the 1.8 ratio observed for the individual diastereomers **6** and **12**. Proton spectroscopy showed that 86% of the H(4) in **12** was left whereas the proton signal in the recovered **6** + **10** was not visible, suggesting that less than 2% of starting **6** was left. Thus the final mole fraction of **12** is 86% of 0.5 or 0.43 (assuming no interconversion of the initial cis and trans isomers under the conditions of the experiment) and the maximum final mole fraction of **6** is 2% of 0.5 or 0.01. Using the kinetic expression[23]

$$k_{trans}/k_{cis} = (\ln t_0/t_t)/(\ln c_0/c_t)$$

where t and c stand for the mole fractions of trans and cis isomer, respectively, at time zero (beginning of reaction) and t (end of reaction) one obtains k_{trans}/k_{cis} = ln (0.5/0.01)/ln (0.5/0.43), i.e. the equatorial H(4) in **6** is at least[24] 26 times more reactive than the axial H(4) in **12**.

NMR Spectroscopy. As implied in Table 1, the planarity or nonplanarity of benzylic carbanions can be gauged from the ^{13}C shifts of the ortho and para carbon nuclei in the benzene

(20) This is on the assumption that the reported[17–19] $\Delta G°$ values are applicable at −78 °C, which may not be strictly correct since $\Delta S°$ for phenyl may not be zero.

(21) Cf.: Winstein, S.; Holness, N. J. *J. Am. Chem. Soc.* **1955**, *77*, 5562. The total specific rate of hydrogen abstraction from the conformationally heterogeneous *trans*-4-methyl-2-phenyl-1,3-dioxane is $k = n_a k_a + n_e k_e$ where the k's are rate constants, the n's mole fractions, the quantities with subscript a refer to conformer **7**, and the quantities with subscript e refer to the alternate conformer with equatorial phenyl and axial methyl. However, since the rate of hydrogen abstraction from the analog **3** is essentially zero, it may be assumed that $k_e = 0$. Hence $k_7 = k_a = k/n_a = k/0.36$; similarly $k_6 = k'/0.95$ where k, k' are the experimental specific rates of equatorial hydrogen abstraction.

(22) In order to obtain accurately measurable proportions of deuterated compounds, conversion was made greater than customary in competition experiments. This causes some depletion of the faster reacting component; thus the true ratio may be somewhat greater. Fortunately the error is small, since the raw ratio of consumption of the 2- and 4-phenyl compounds is close to unity.

(23) Cf.: Lee, T. S.; Kolthoff, I. M. *Ann. New York Acad. Sci.* **1951**, *53*, 1093.

(24) The true ratio is probably considerably greater since the trans isomer **6** was almost entirely consumed, so that, toward the end of the reaction, the cis isomer **12** reacted by default, in contrast to the situation discussed in footnote 22.

ring, as established for ions of known geometry by Grutzner.[12] Thus in the 2-phenyl-1,3-dithianyl carbanion, which, because of its highly stereoselective protonation and methylation from the equatorial side,[8a] is deemed to be pyramidal with axial phenyl and equatorial lone pair, the shifts in going from the axial parent compound (*r*-2-phenyl-*t*-4,*t*-6-dimethyl-1,3-dithiane, **13**) to the ion **14** are[8b] ortho carbon −6.5 ppm and para carbon, −13.7 ppm (in THF). In contrast, the corresponding shifts for the anion **16** derived from 1-phenyl-*cis*-4-*tert*-butylcyclohexane (**15**) are (in THF) ortho carbon −22.1 ppm and para carbon −36.3 ppm (K salt).[13] We therefore examined the ^{13}C NMR spectra of the carbanions derived from **4** and **5** and compared them with the corresponding spectra of the parent compounds. (Because of the very minor effects of substituents on the dioxanyl ring on the phenyl shifts, we chose to work with the more accessible parent compounds rather than with the conformationally more rigid **6** and **7**.) Carbanion **18** from **5** was readily prepared at −40 °C; it was red and displayed the following upfield shifts relative to the starting material: ortho carbon, −24.0 and −25.4 ppm; para carbon, −35.9 ppm. These shifts strongly suggest that the 4-phenyl-1,3-dioxanyl carbanion **18** at C(4) is planar. The appearance of two signals in the ortho-phenyl position of the carbanion indicates slow rotation about the C(4)−C(ipso) partial double bond on the NMR time scale at −40 °C.

Unfortunately we were not able to obtain a good ^{13}C NMR spectrum for the carbanion **17** derived from **4**. The solution of this anion prepared at −78 °C (the ion was not stable at −40 °C) was bright orange but all efforts to transfer the solution to an NMR tube resulted in it turning dark (sometimes green); the spectrum recorded from this sample tended to be noisy, perhaps because of the presence of radical impurities. To the extent that signals could be observed, the shift was 12.5 ppm upfield for the ortho carbon and 17 ppm for the para carbon, values which are closer (vide supra) to those for the pyramidal 2-phenyl-1,3-dithianyl **14** than to those for the planar phenylcyclohexyl carbanion **16**.

Discussion

Even though the precision of the data obtained may not always be high (e.g. because of impurity in the starting materials, uncertainties in analysis, complications introduced by isomerization of starting materials, etc.), the following points are clear:

(1) Whereas in our hands phenylcyclohexane could not be appreciably deprotonated at the benzylic position by the Lochmann−Schlosser base, 2-phenyl-1,3-dioxane and even 4-methyl-1,3-dioxane do give the anion at C(2) under these conditions, confirming the known fact that carbanions are stabilized by adjacent oxygen atoms (presumably inductively), though not as much as by adjacent sulfur (1,3-dithianes, which can be readily deprotonated with butyllithium, are clearly much more acidic than 1,3-dioxanes).

(2) In anancomeric systems, only the 2-phenyl-1,3-dioxane with axial phenyl (**7**) can be deprotonated; the diastereomer with equatorial phenyl (**3**) was inert to the Lochmann−Schlosser base.[16] Thus there is a very large ratio in relative kinetic acidities between equatorial and axial hydrogens at C(2), much larger than the ratio of about 10 found in anancomeric 1,3-dithianes.[8a]

(3) In the 4-phenyl-1,3-dioxane system, both compounds with axial phenyl and those with equatorial phenyl can be deprotonated. However, in the anancomeric system **6** and **12**, the kinetic acidity of the equatorial proton is at least 26 times as great as that of the axial proton (the ratio may be considerably larger than that).

(4) The carbanion derived from 4-phenyl-1,3-dioxane appears to be planar or nearly so, similar to the carbanion derived from phenylcyclohexane.[13] Thus, once the carbanion is formed, delocalization of charge into the benzene ring appears to be more important than pyramidalization enforced by the lone pairs of the adjacent oxygen. However (and, because of experimental difficulties, this is less certain), when there are two adjacent oxygen atoms, as in the anion derived from 2-phenyl-1,3-dioxane, the stereoelectronic effect of the lone pairs on oxygen is sufficiently strong to force the ion to become at least somewhat nonplanar, resembling, in that respect, the anion derived from 2-phenyl-1,3-dithiane.

(5) The kinetic acidity of the equatorial proton at C(2) in anancomeric 2-phenyl-1,3-dioxane (**7**) is only 4 times as great as that of the corresponding equatorial proton at C(4) in the 4-phenyl analog **6**. Presumably the additional inductive acidifying effect of the second oxygen in **7** is largely offset by the inability of the incipient benzylic carbanion to become planar, because of stereoelectronic impedance by the lone pairs on the two oxygen neighbors. Nonetheless the overall acidifying inductive effect of oxygen is manifested by the greater kinetic acidity of H_e in **7** as compared to **6** and of **4** and **5** as compared to phenylcyclohexane.

Experimental Section

General. 4-Phenyl-1,3-dioxane (**5**), 4-methyl-1,3-dioxane (**1**), and *n*-butylithium were purchased from Aldrich. Potassium *tert*-butoxide was purchased from Alpha. Thin-layer chromatography was performed on silica gel 60 aluminum plates from EM Science. Basic alumina TLC plates were purchased from Universal Co. Flash chromatography was performed according to Clark Still's specifications.[25] Tetrahydrofuran (THF) was dried over sodium and benzophenone (dried in a solvent pistol) and refluxed prior to use. ^1H, ^2H, and ^{13}C nuclear magnetic resonance spectra were recorded on Bruker AC200 and WM250, or on Varian XL400 instruments. Samples were dissolved in deuteriochloroform (chloroform for ^2H NMR), unless otherwise noted, and tetramethylsilane was used as an internal standard. Signals are reported in parts per million (ppm). The following abbreviations indicate coupling patterns: s = singlet, d = doublet, t = triplet, q = quartet, and m = multiplet. Preparative gas chromatography was performed on a Varian Aerograph, Moduline 2700 series, which has a thermal conductivity detector.

***cis*-4-Methyl-2-phenyl-1,3-dioxane (3).** 1,3-Butanediol (9.01 g, 0.10 mol), benzaldehyde (10.61 g, 0.10 mol), a catalytic amount of *p*-toluenesulfonic acid, and 70 mL of benzene were reacted and worked up as per the thermodynamic control method described previously.[17] The clear liquid isolated (15.4 g, 87%) was fractionally distilled to give pure product with a bp of 138−140 °C at 2.6 mm. ^1H NMR: δ 1.30 (d, 3 H, J = 6.7 Hz, 4-Me), 1.53 (d of dAB, 1 H, J = ca. 3, 13 Hz, H_{5e}), 1.80 (d of d of dAB, 1 H, J = 5.2, 10.7, 13 Hz, H_{5a}), 3.93 (d of d of dAB, 2 H, J = ca. 3, 5.2, 12 Hz, H_{6a} and underlying m for H_{4a}), 4.25 (d of d of dAB, 1 H, J = ca. 1.5, 5.2, 12 Hz, H_{6e}), 5.52 (s, 1 H, H_{2a}), 7.35 (m, 3H, Ar(m + p)), 7.5 (m, 2H, Ar(o)). [lit. ^1H NMR values:[26] ca. 3.51 (H_{4a}), 5.24 (H_{2a}) and lit. bp 131 °C (7 mm).] ^{13}C NMR:[27] δ 21.8 (4-Me), 32.9 (C-5), 67.0 (C-6), 73.4 (C-4), 101.3 (C-2), 126.1, 128.2, 128.3, 128.6, 138.8 (Ar-C).

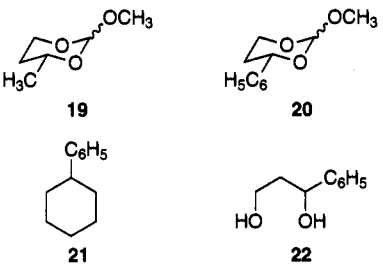
Lochmann Base Treatment of *cis*-4-Methyl-2-phenyl-1,3-dioxane (3) with Inverse Deuterioethanol Quench. In an Ar-flushed, 25-mL, round-bottomed flask fitted with a stirbar, Ar inlet, and wired-on septum, *cis*-2-phenyl-4-methyl-1,3-dioxane (1.78 g, 10.0 mmol), potas-

(25) Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.

(26) Lezina, V. P.; Stepanyants, A. U.; Alimirzoev, F. A.; Zlotskii, S. S.; Rakhmankulov, D. L. *Izv. Akad. Nauk SSSR, Ser. Khim.* **1976**, 792; *Bull. Acad. Sci. USSR Ser. Chem. Sci.* **1976**, *25*, 772. Our data for the proton spectrum are in good agreement, except for a systematic shift difference of about 0.3 ppm [cf. the shift given for H(2) by Grindley (see ref 27) which is within 0.1 ppm of the one reported here] and except that we found the signal for H(5e) downfield of the for Me, as one might expect.

(27) These shifts are very close to those reported in ref 26 and by: Grindley, B.; Gulasekharam, V. *Carbohydr. Res.* **1979**, *74*, 7.

Chart 1



sium *tert*-butoxide (1.25 g, 11.0 mmol), and 20 mL of dry THF were cooled to −78 °C with stirring and under Ar. Then *n*-BuLi (1.11 mL of 10 M in hexanes, 11.1 mmol) was added dropwise via syringe. The mixture was stirred at −78 °C for 2.25 h. Another Ar-flushed two-necked round-bottomed flask was charged with 5 mL of dry THF, and 3 mL of EtOD was added via syringe. The EtOD−THF solution was cooled to −78 °C with stirring. The carbanion solution was transferred via cannula dropwise into the EtOD quench solution. After addition was complete, the resulting solution was warmed to room temperature. Then 25 mL of brine and 10 mL of ether were added to the reaction mixture which was transferred to a separatory funnel. The organic layer was isolated, and the aqueous layer was extracted with three 25-mL portions of ether. The combined organic layers were dried over Mg_2SO_4. After filtration, the solvent was removed under reduced pressure to yield a yellow oil (1.39 g, 78%). ^{1}H NMR: δ 1.305 (d, J = 6.2 Hz, 4-Me), 1.37−1.555 (m, H_{5e}), 1.80 (ddd, 1 H, J = 5.0, 11.1 Hz, H_{5a}), 3.93 (dt, 2 H, J = 2.7, 3.4, 11.5 Hz, $H_{6a\&4a}$), 4.21 (dd, 0.96 H, J = 1.3, 5.0 Hz, H_{6e}), 5.50 (s, 0.87 H, H_{2a}), 7.23−7.52 (m, Ar-H). ^{13}C NMR: δ 21.8 (4-Me), 32.9 (C-5), 67.0 (C-6), 73.4 (C-4), 101.3 (C-2), 126.0, 126.1, 128.1, 128.2, 128.5, 128.6, 138.7 (Ar-C). ^{2}H NMR (acetone-d_6 reference): 103.76% total D incorporation: δ 1.18 (4-Me, 5.26% of total), 1.82,1.68 (D-5a&e, 1.65%), 4.23 (D-6e, 0.33%), 5.53 (D-2a, 0.62%, **9**), 6.01 (D-2e, 2.04%, **8**), 7.475, 7.685 (Ar-D, 93.86%).

Lochmann Base Treatment of 2-Phenyl-1,3-dioxane (4) with Inverse Deuterioethanol Quench. The procedure for the treatment of **3** was followed for 2-phenyl-1,3-dioxane[28] (368 mg, 2.24 mmol) with potassium *tert*-butoxide (251 mg, 2.24 mmol), 4.5 mL of dry THF, and *n*-BuLi (0.450 mL of ca. 5 M in hexanes, 2.25 mmol). The orange carbanion solution was quenched inversely with 1 mL of EtOD in 2 mL of dry THF. A yellow liquid (330 mg, 89%) was isolated. ^{1}H NMR: δ 0.917 (t, byproduct), 1.25 (s, byproduct), 1.17−1.66 (m, H_{5e}), 1.71−2.10 (m, byproduct), 2.23 (m, J = 5.1 Hz, 12.4 Hz, H_{5a}), 3.61 (t, J = 6.4 Hz, byproduct), 3.69−3.91 (m, byproduct), 3.98 (dt, J = 2.5, 12.2 Hz, $H_{4a\&6a}$), 4.26 (ddd, J = 1.4, 5.1, 11.9 Hz, $H_{4e\&6e}$), 5.50 (s, H_{2a}, 0.08 H), 7.24−7.49 (m, Ar-H), 7.55−7.66 (m, byproduct), 7.85−7.90 (m, byproduct), 8.01−8.12 (m, byproduct). ^{13}C NMR: δ 25.8 (C-5), 29.9 (impurity), 67.3 (C-4,6), 101.7 (C-2), 126.0, 128.1, 128.7, 138.7 (Ar), 129.6 (impurity). ^{2}H NMR (acetone-d_6 reference): 68.9% total deuterium incorporation: δ 5.46 (D-2, 65.8% of total), 7.55 (Ar-D, 3.1%).

Lochmann Base Treatment of 4-Phenyl-1,3-dioxane (5) with Inverse Deuterioethanol Quench. The procedure for the treatment of **3** was followed for 4-phenyl-1,3-dioxane (1.64 g, 10.0 mmol) with potassium *tert*-butoxide (1.12 g, 10.0 mmol), 20 mL of dry THF, *n*-BuLi (1.4 mL of ca. 7 M in hexanes, 9.8 mmol), and 2 mL of EtOD in 5 mL of dry THF. A yellow oil (1.26 g, 76%) was isolated. ^{1}H NMR: δ 1.72 (d, 1 H, J = 13.6 Hz, H_{5e}), 2.10−2.12 (m, 1 H, H_{5a}), 3.88 (dt, 1H, J = 2.4, 12 Hz, H_{6a}), 4.21 (dd, 1 H, J = 4.8, 11.6 Hz, H_{6e}), 4.65 (dd, 0.27 H, J = 2.4, 11.2 Hz, H_{4a}), 4.91 (d, 1 H, J = 6.4 Hz, H_{2a}), 5.23 (d, 1H, J = 6.4 Hz, H_{2e}). ^{13}C NMR: δ 33.9 (C-5, product), 34.0 (C-5, st. mat.), 67.0 (C-6), 78.8 (C-4, a triplet upfield of this diminished peak is barely visible in the baseline), 94.2 (C-2), 125.8, 127.9, 128.5, 141.4 (Ar-C of st. mat.), 128.3, 128.4 (Ar-C of product). ^{2}H NMR (acetone-d_6 reference): 61.8% total deuterium incorporation: δ 4.69 (D-4, 56.4%), 5.27 (D-2, 4.6%), 7.3, 7.5 (Ar-D, 0.8%).

***trans*-2-Methyl-4-phenyl-1,3-dioxane (6).** A mixture of *cis*- and *trans*-(1:1.4) 2-methoxy-4-phenyl-1,3-dioxane (**20**, 1.00 g, 5.15 mmol) and methylmagnesium bromide (2.00 mL of 3 M solution in ether, 6.00 mmol) was reacted in a manner analogous to a literature procedure.[29] A pale yellow liquid (0.705 g, 77%) was isolated and found to be 65% *trans* product, 34% *cis*-2-methoxy-4-phenyl-1,3-dioxane, and 1% *trans*-2-methoxy-4-phenyl-1,3-dioxane. The mixture, in 10% EtOAc/hexanes, was chromatographed on a base-washed column packed with basic alumina with gravity into base-washed Erlenmeyer flasks containing potassium carbonate. A clear liquid (0.131 g, 14%) was isolated which consisted of 93.5% *trans* product and 6.5% *cis* product (**12**). ^{1}H NMR (toluene-d_8): δ 1.31 (d, 3H, J = 5.1 Hz, 2-Me of **6**), 1.41 (d, J = 5.1 Hz, 2-Me of **12**), 1.58 (dq, 1 H, J = 2.8, 5.6 Hz, H_{5e} of **6**), 2.14 (m, H_{5a} of **6**), 3.55 (dt, 1H, J = 2.7, 11.2 Hz, H_{6a} of **6**), 3.655 (2 dq, J = 0.7, 2.8 Hz, 1H, H_{6e} of **6**), 3.80−3.89 (m, $H_{6e\&a}$ of **12**), 4.31 (dd, J = 2.6, 11.3 Hz, H_{4a} of **12**), 4.62 (q, J = 5.1 Hz, H_{2a} of **12**), 4.83 (q, 1 H, J = 5.1, 10.3 Hz, H_{2a} of **6**), 4.93 (dd, 1 H, J = 2.6, 5.6 Hz, H_{4e} of **6**), 7.01−7.30 (m, 6.38 H, Ar-H of **6** & **12**). ^{13}C NMR (toluene-d_8): δ 21.0 (2-Me, **6**), 23.5 (2-Me, **12**), 27.6 (C-5, **6**), 33.8 (C-5, **12**), 62.4 (C-6, **6**), 66.6 (C-6, **12**), 72.0 (C-4, **6**), 78.6 (C-4, **12**), 93.5 (C-2, **6**), 99.5 (C-2, **12**), 126.0, 127.1, 127.2, 140.9 (Ar-C, **6**).

Lochmann Base Treatment of *trans*-2-Methyl-4-phenyl-1,3-dioxane (6) with Inverse Deuterioethanol Quench. The procedure for the treatment of **3** was modified slightly to protect the extremely acid-sensitive starting material and product. *trans*-2-Methyl-4-phenyl-1,3-dioxane (**6**; 131 mg, 0.735 mmol, contaminated with 6.5% *cis*-2-methyl-4-phenyl-1,3-dioxane) was added to the basic solution of potassium *tert*-butoxide (91.6 mg, 0.82 mmol) in 1.5 mL of dry THF. *n*-BuLi (0.082 mL of 10 M in hexanes, 0.82 mmol) was added, and the solution was quenched into 1.5 mL of EtOD in 2 mL of dry THF. The workup used Na_2CO_3 (aqueous) saturated with NaCl instead of saturated NaCl (aqueous), and benzene was used as the organic solvent instead of ether. Glassware was base washed with Na_2CO_3 (aqueous), and all liquids and solutions were stored over K_2CO_3. An orange-gold oil (134 mg, 102%) was isolated. ^{1}H NMR (toluene-d_8): *cis*: 36.2% and *trans*: 63.8%: δ 1.31 (d, J = 5.1 Hz, 2-Me, **6**), 1.41 (d, J = 5.1 Hz, 2-Me, **12**), 1.51−1.61 (m, H_{5e}), 1.71−1.88 (m, H_{5a}), 3.24−3.98 (m, $H_{6e\&a}$), 4.30 (dd, J = 2.5, 11.4 Hz, H_{4a}, **12**), 4.43−4.86 (m), 4.61 (q, J = 5.0 Hz, H_{2a}, **6**), 4.82 (q, J = 5.1 Hz, H_{2a}, **12**), 4.96−5.40 (m), 7.01−7.38 (m, Ar-H). ^{13}C NMR (toluene-d_8): δ 15.1, 16.6, 17.9 (new), 27.4 (C-5, **6**), 29.0, 30.3, 31.2 (new), 33.6 (C-5, **12**), 36.5, 42.6, 59.9, 60.2, 61.1 (new), 62.4 (C-6, **6**), 63.3, 63.4 (new), 66.6 (C-6 **12**), 75.0 (C-4, **12**; for C-4, **6**, a triplet is barely visible in the baseline at ca. 71 ppm), 93.1, 93.3, 94.1, 94.4 (new), 93.5 (C-2, **6**), 99.5 (C-2 **12**), 125.8, 126.0, 126.9, 127.1, 127.2, 127.5, 127.6, 127.7, 128.5, 128.8 (Ar-C). ^{2}H NMR (in toluene with acetone-d_6 reference): 56.25% total D incorporation: δ 1.12 (2-Me, 0.7% of total), 1.56 (D-5, 7.1%), 4.78 (D-4a, 10.55%, **11**), 5.39 (D-4e, 19.15%, **10**), 7.50, 7.61 (Ar-D, 18.8%).

***trans*-4-Methyl-2-phenyl-1,3-dioxane (7).** This compound was prepared as previously described in the literature[29] and purified as described for **6**. A clear liquid (307 mg, 20%) composed of 87.5% *trans* product, 11.3% epimerized, *cis* product, and 1.2% *trans*-2-methoxy-4-methyl-1,3-dioxane was isolated. ^{1}H NMR (toluene-d_8): δ 1.09 (d, 3H, J = 6.5 Hz, 4-Me of **7**), 1.11 (d, J = 6.2 Hz, 4-Me of **3**), 1.14−1.23 (m, 1H, H_{5e} of **7**), 1.37−1.54 (m, 1H, H_{5a} of **7**), 3.51 (dt, J = 2.7, 11.3 Hz, $H_{6e\&a}$ of **3**), 3.66 (t, 2H, J = 5.6 Hz, $H_{6e\&a}$ of **7**), 3.81−3.98 (m, 1H, H_{4a} of **7**), 5.32 (s, H_{2a} of **3**), 5.915 (s, 1 H, H_{2e} of **7**), 7.01−7.24 (m, 3H, Ar-H of **7**), 7.38−6.43 (m, Ar-H of **3**), 7.50−7.55 (m, 2 H, Ar-H of **7**), 7.57−7.62 (m, Ar-H of **3**). [lit.[29] ^{1}H NMR: ca. 4.0 (H_{4a}), 5.87 (H_{2e}) and lit. bp: 73 °C (0.2 mm).] ^{13}C NMR (toluene-d_8): δ 19.1 (4-Me, **7**), 21.9 (4-Me, **3**), 31.6 (C-5, **7**), 33.3 (C-5, **3**), 61.1 (C-6, **7**), 66.6 (C-4, **7**), 66.9 (C-6, **3**), 73.2 (C-4, **3**), 95.5 (C-2, **7**), 101.5 (C-2, **3**), 126.7, 127.1, 127.5, 139.79 (Ar-C, **7**).

Lochmann Base Treatment of *trans*-4-Methyl-2-phenyl-1,3-dioxane (7) with Inverse Deuterioethanol Quench. The procedure for the treatment of **6** was followed for *trans*-4-methyl-2-phenyl-1,3-dioxane (306 mg, 1.72 mmol, contaminated with 14.4% *cis*-4-methyl-2-phenyl-1,3-dioxane), potassium *tert*-butoxide (214 mg, 1.89 mmol) in 3.5 mL of dry THF, *n*-BuLi (0.191 mL of 10 M in hexanes, 1.91

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mmol), and 1 mL of EtOD in 2 mL of dry THF. A yellow liquid (224 mg, 73%) was isolated. ^{1}H NMR (toluene-d_8): δ 1.09 (d, J = 5.2 Hz, 4-Me, **7**), 1.11 (d, J = 5.0 Hz, 4-Me, **3**), 1.14−1.23 (m, H_{5e}), 1.36−1.66 (m, H_{5a}), 3.50 (dt, J = 2.1, 9.9 Hz,$H_{6e\&a}$, **3**), 3.66 (t, J = 4.5 Hz, $H_{6e\&a}$, **7**), 3.81−3.97 (m, H_{4a}), 5.315 (s, H_{2a}, **3**), 5.91 (s, H_{2e} (barely visible)), 7.01−7.28 (m, Ar-H, **7**), 7.37−7.42 (m, Ar-H, **3**), 7.49−7.54 (m, Ar-H, **7**), 7.57−7.61 (m, Ar-H, **3**). ^{13}C NMR (toluene-d_8): δ 19.2 (4-Me, **7**), 21.9 (4-Me, **3**), 31.7 (C-5, **7**), 33.3 (C-5, **3**), 61.1 (C-6, **7**), 66.6 (C-4, **7**), 66.9 (C-6, **3**), 73.2 (C-4, **3**), 101.5 (C-2, **3**), 126.8, 127.1, 127.4, 128.1, 128.2, 139.7 (Ar-H). ^{2}H NMR (in toluene with acetone-d_6 reference): 72.6% total D incorporation: δ 1.13 (Me-D, 1.8%), 3.74, 3.98 (D-6, D-4a, 2.5%), 5.35 (D-2a, 8.7%, **9**), 5.93 (D-2e, 31.9%, **8**), 7.06, 7.19, 7.50, 7.65 (Ar-D, 27.7%)

Lochmann Base Treatment of *trans*-4-Methyl-2-phenyl-1,3-dioxane (7) with Inverse Deuterioethanol/Sodium Ethoxide Quench. The procedure for the treatment of **6** was modified to protect further the extremely acid-sensitive starting material, **7**, and product. *trans*-4-Methyl-2-phenyl-1,3-dioxane (63.5 mg, 0.356 mmol)—contaminated with 15.5% *cis*-4-methyl-2-phenyl-1,3-dioxane (**3**)—was added to the basic solution of potassium *tert*-butoxide (35 mg, 0.30 mmol) in 1.04 mL of dry THF-d_8. *n*-BuLi (0.055 mL of 5.565 M in hexanes, 0.30 mmol) was added. The basic quench was achieved by placing 2 mL of dry THF and 40 mg of sodium metal—enough to convert 10% of the deuterioethanol to sodium ethoxide—in an Ar-flushed round-bottomed flask. Deuterioethanol (1 mL) was added via syringe. The mixture was stirred at room temperature until all the sodium had dissolved. Then the homogeneous mixture was cooled to −78 °C with stirring and under Ar. The carbanion solution was added dropwise via a cannula to the basic quench solution. A pale yellow liquid (42.5 mg, 67%) was isolated. ^{1}H NMR (toluene-d_8): δ 0.68−1.05 (m, byproduct), 1.09 (d, J = 6.1 Hz, 4-Me, **7**), 1.11 (d, J = 6.3, 4-Me, **3**), 1.16−1.59 (m, byproduct, $H_{5e\&a}$), 3.23−3.37 (m, impurity), 3.51 (td, J = 2.9, 11.9 Hz, $H_{6e\&a}$, **3**), 3.66 (dt, 0.4, 5.5 Hz, $H_{6e\&a}$, **7**), 3.79−3.97 (m, H_{4a}), 5.31 (s, H2a, **3**, 0.48 H), 5.91 (s, H_{2e}, **7**, 0.02H), 7.13 (d, J = 0.5, Ar-H, **7**), 7.17−7.22 (m, Ar-H, **7**), 7.39−7.42 (m, Ar-H, **3**), 7.50−7.61 (m, Ar-H, **7**). ^{13}C NMR (toluene-d_8): δ 14.0, 14.4 (byproduct), 19.2 (Me, **7**), 21.9 (Me, **3**), 29.9, 30.3 (byproduct), 31.7 (C-5, **7**), 32.4 (byproduct), 33.3 (C-5, **3**), 39.5, 40.3 (byproduct), 61.0 (C-6, **7**), 66.6 (C-4, **7**), 66.9 (C-6, **3**), 73.2 (C-4, **3**), 101.5 (C-2, **3**), 126.7, 127.1, 139.7 (Ar, **7**), 127.6, 128.3 (Ar, **3**). ^{2}H NMR (toluene, acetone-d_6 as reference): 107.2% total deuterium incorporation: δ 4.02 (D_{6e}, 1.0%), 5.07, 5.15 (impurity, not included in total), 5.81 (D_{2a}, 1.0%, **9**), 6.41 (D_{2e}, 70.9%, **8**), 8.07, 8.14 (Ar-D, 34.3%).

Competition for Lochmann Base by *trans*-4-Methyl-2-phenyl-1,3-dioxane (7) and *trans*-2-Methyl-4-phenyl-1,3-dioxane (6) with Inverse Deuterioethanol Quench. The procedure for the treatment of **6** was followed. *trans*-4-Methyl-2-phenyl-1,3-dioxane (200 mg, 1.12 mmol, contaminated with 13.2% *cis*-4-methyl-2-phenyl-1,3-dioxane) and *trans*-2-methyl-4-phenyl-1,3-dioxane (200 mg, 1.12 mmol, contaminated with 8.5% *cis*-2-methyl-4-phenyl-1,3-dioxane) were added to the basic solution of potassium *tert*-butoxide (126 mg, 1.12 mmol) in 3.5 mL of dry THF. *n*-BuLi (0.202 mL of 5.6 M in hexanes, 1.13 mmol) was added, and the yellow solution turned red. The quench was performed with 1 mL of EtOD in 2 mL of dry THF. A yellow liquid (402.5 mg, 100%) was isolated. ^{1}H NMR (toluene-d_8): δ 1.09 (d, J = 6.5 Hz, 4-Me of **6**), 1.1 (d, J = 6.1 Hz, 4-Me of **3**), 1.15−1.24 (m, H_{5e} of **7**), 1.31 (d, J = 5.2 Hz, 2-Me of **6**), 1.41 (d, J = 5.1 Hz, 2-Me of **12**), 1.53 (t, J = 2.9 Hz, H_{5e} of **6**), 1.60 (t, J = 2.9, H_{5a} of **6**), 1.65−1.83 (m, $H_{5e\&a}$ of **12**), 3.44−3.71 (m, $H_{6e\&a}$ of **6** and H_{6e} of **12**), 3.65 (t, J = 5.6 Hz, $H_{6e\&a}$ of **7**), 3.80−3.98 (m, H_{4a} of **7** and H_{6a} of **12**), 4.30 (dd, J = 2.5, 11.3 Hz, H_{4a} of **3**), 4.61 (q, J = 5.1 Hz, H_{2a} of **6**), 4.82 (q, J = 5.1 Hz, H_{2a} of **12**), 5.32 (s, H_{2a} of **3**), 5.92 (s, H_{2e} of **7**), 7.02−7.30 (m, Ar-H of **6**, **7**, **12**), 7.37−7.43 (m, Ar-H of **3**), 7.49−7.55 (m, Ar-H of **7**), 7.57−7.62 (m, Ar-H of **3**). ^{13}C NMR (toluene-d_8): δ 19.2 (4-Me, **7**), 20.5 (2-Me, **6**), 21.9 (2-Me, **12**), 22.1 (4-Me,**3**), 27.5 (C-5, **6**), 31.7 (C-5, **7**), 33.3 (C-5, **3**), 33.8 (C-5, **12**), 61.0 (C-6, **7**), 62.4 (C-6, **6**), 66.6 (C-6, **12** & C-4, **7**), 66.9 (C-6, **3**), 73.2 (C-4, **3**), 78.6 (C-4, **12**), 93.5 (C-2, **6**), 99.5 (C-2, **12**), 101.5 (C-2, **3**), 126.0 (Ar-C), 126.8 (Ar-C), 127.1 (Ar-C), 128.2 (Ar-C), 129.2 (Ar-C). ^{2}H NMR (in toluene with acetone-d_6 reference): 66.9% total D incorporation: δ 4.35 (s, D-4a, 8.05% of total, **11**), 4.95 (s, D-4e, 18.2%, **10**), 5.33 (s, D-2a 1.5%, **9**), 5.90 (s, D-2e, 38.5%, **8**), 7.04, 7.15 & 7.60 (3 s, Ar-D, 0.7%).

***cis*-2-Methyl-4-phenyl-1,3-dioxane (12).** 1-Phenyl-1,3-propanediol (**23**, 1.24 g, 8.14 mmol), acetaldehyde diethyl acetal (0.96 g, 8.1 mmol), 25 mL of cyclohexane, and a catalytic amount of *p*-toluenesulfonic acid were placed in a round-bottomed flask fitted with a one-piece simple distillation apparatus. The flask was heated until no more ethanol−cyclohexane azeotrope distilled over (ca. 2 h). When the solution was cool, potassium carbonate was added, and the resulting mixture was stirred overnight. After filtration and removal of solvent at reduced pressure, a pale yellow liquid (0.984 g, 70%) was isolated. ^{1}H NMR: δ 1.41 (d, 3H, J = 5.1 Hz, 2-Me), 1.67 (m, 1H, H_{5e}), 2.00 (ddd, 1 H, J = 5.0, 12.1 Hz (J_{gem} = J_{anti}), H_{5a}), 3.98 (dt, 1 H, J = 2.6, 11.8 Hz, H_{6a}), 4.195 (ddd, 1H, J = 1.5, 5.0, 11.5 Hz, H_{6e}), 4.7 (dd, 1H, J = 2.6, 11.3 Hz, H_{4a}), 4.90 (q, 1H, J = 5.1 Hz, H_{2a}), 7.25−7.41 (m, 5H, Ar-H). [lit.[30] ^{1}H NMR: 1.2 (d, 2-Me), 1.6 (m, $H_{5a\&e}$), 3.7 (m, $H_{6e\&a}$), 4.4 (m, H_{4a}), 4.6 (q, H_{2a}), 7.1 (s, Ar-H) and lit. bp 108−110 °C (9 mm).] ^{13}C NMR: δ 21.4 (2-Me), 33.2 (C-5), 66.8 (C-6), 78.8 (C-4), 99.4 (C-2), 126.0, 127.5, 128.5, 141.7 (Ar-C).

Lochmann Base Treatment of *cis*-2-Methyl-4-phenyl-1,3-dioxane (12) with Inverse Deuterioethanol Quench. The procedure for the treatment of **3** was followed for 2-methyl-4-phenyl-1,3-dioxane (400 mg, 2.24 mmol) with potassium *tert*-butoxide (277 mg, 2.46 mmol), 8 mL of dry THF, *n*-BuLi (0.25 mL of a 10 M solution in hexanes, 2.5 mmol), and 1 mL of EtOD in 3 mL of dry THF. The orange-gold solution turned deep red upon *n*-BuLi addition. After quenching, the red carbanion solution became light orange. A yellow oil (334 mg, 83%) was isolated. ^{1}H NMR: δ 1.33 (d, J = 5.2 Hz, 2-Me, **12**), 1.41 (d, J = 5.1 Hz, 2-Me, **6**), 1.56−1.70 (m, H_{5e}), 1.88−2.03 (m, H_{5a}), 2.10 (dt, J = 2.9, 14.0 Hz, H_{5e} of 4-D material), 2.44 (ddd, J = 5.3, 11.3 Hz (J_{gem} = J_{anti}), H_{5a}), 3.77−4.02 (m, H_{6a} of **12** & $H_{6e\&a}$ of **6**), 4.18 (ddd, J = 1.4, 5.0, 11.5 Hz, H_{6e}, **12**), 4.67 (dd, J = 2.6, 11.3 Hz, H_{4a}, **12**), 4.89 (q, J = 5.1 Hz, H_{2a}, **12**, **6**), 7.21−7.41 (m, Ar-H). ^{13}C NMR: δ 20.8 (2-Me, **6**), 21.4 (2-Me, **12**), 27.2, 33.0 (C-5, **6**), 33.2 (C-5, **12**), 62.6 (C-6, **6**), 66.8 (C-6, **12**), 78.8 (C-4, **12** (C-4 of **6** probably underneath $CDCl_3$ triplet)), 93.3 (C-2, **6**), 99.4 (C-2, **12**), 126.0, 127.8, 128.5, 141.8 (Ar-H, **12**), 126.8, 127.3, 128.7, 140 (Ar-H, **6**). ^{2}H NMR (acetone-d_6 reference): 37.27% total deuterium incorporation: δ 1.25 (Me-D, 2.54%), 4.71 (D-4a, **11**, 8.29%), 5.23 (D-4e, **10**, 20.77%), 7.30, 7.46 (Ar-D, 5.67%).

Competition for Lochmann Base by *cis*-2-Methyl-4-phenyl-1,3-dioxane (12) and *trans*-2-Methyl-4-phenyl-1,3-dioxane (6) with Inverse Deuterioethanol/Sodium Ethoxide Quench. The inverse deuterioethanol/sodium ethoxide quench procedure described for **7** was used to protect the extremely acid-sensitive starting material, **6**, and product. *trans*-2-Methyl-4-phenyl-1,3-dioxane (134 mg, 0.654 mmol) contaminated with 13% *cis*-2-methyl-4-phenyl-1,3-dioxane (0.974 mmol) and *cis*-4-phenyl-2-methyl-1,3-dioxane (99.3 mg, 0.557 mmol) were added to the basic solution of potassium *tert*-butoxide (73.4 mg, 0.654 mmol) in 3.5 mL of dry THF. *n*-BuLi (0.12 mL of 5.57 M in hexanes, 0.67 mmol) was added, and the gold solution turned red. The basic quench used 2 mL of dry THF and 40 mg of sodium metal. Deuterioethanol (1 mL) was added. The red carbanion solution was added dropwise via a cannula to the basic quench solution. A pale yellow liquid (225 mg, 96%) was isolated. ^{1}H NMR (toluene-d_8): δ 0.76−1.03 (m, byproduct), 1.10−1.14 (m, byproduct), 1.16−1.21 (m, byproduct), 1.30 (d, J = 5.1 Hz, 2-Me, **6**), 1.40 (d, J = 5.1 Hz, 2-Me, **12**), 1.53−1.91 (m, $H_{5e\&a}$), 2.97 (s, byproduct), 3.08−3.16 (m, byproduct), 3.39−3.59 (m, H_{6a}), 3.61−3.71 (m, **6**, H_{6e}), 3.84 (ddd, J = 1.4, 4.9, , 11.4 Hz, H_{6e}, **12**), 4.28 (dd, J = 2.5, 11.3 Hz, H_{4a}, **12**), 4.62 (q, J = 5.1 Hz, H_{2a}, **12**), 4.83 (q, J = 5.1 Hz, H_{2a}, **6**), 7.02−7.30 (m, Ar-H). ^{13}C NMR: δ 21.0 (Me, **6**), 21.6 (Me, **12**), 27.5 (C-5, **6**), 33.7 (C-5, **12**), 62.3 (C-6, **6**), 66.6 (C-6, **12**), 78.5 (C-4, **12**), 93.5 (C-2, **6**), 99.5 (C-2, **12**), 128.0, 142.8 (Ar, **12**), 127.1, 127.2, 127.5 (Ar, **6**). ^{2}H NMR (toluene, acetone-d_6 as reference): 46.5% total deuterium incorporation: δ 1.73 (D-5, 0.4% based on the total), 3.97 (D-6e, 0.6%), 4.79 (D-4a, 16.2%, **11**), 5.40 (D-4e, 26.85%, **10**), 7.50, 7.61 (Ar-D, 2.5%).

4-Phenyl-4-metallo-1,3-dioxane (18) for NMR Study.[31] The metallo derivative of 4-phenyl-1,3-dioxane was prepared by adding a THF-d_8 solution of 4-phenyl-1,3-dioxane to a solution of the Lochmann base cooled to −40 °C in a dry ice/acetonitrile bath. The base solution consisted of 1 equiv of *tert*-butoxide and 1 equiv of *n*-butyllithium (*n*-BuLi) in THF-d_8. To exclude air, all receptacles and syringes were flushed with argon (Ar). Half of the THF-d_8 was added via syringe to the Ar-filled testtube containing the *t*-BuOK (which was manipulated in a glovebag under Ar). After the solution was cooled to −40 °C, *n*-BuLi was added followed by the remainder of the THF-d_8. A deep red solution resulted when 4-phenyl-1,3-dioxane in THF-d_8 was added via syringe to the base solution. The red solution was transferred via cannula to an Ar-flushed NMR tube which was cooled to −40 °C and fitted with a septum and venting needle. The tube was kept in a Dewar flask and transported at −40 °C to a NMR probe which had been previously cooled to −40 °C. The ^{13}C spectrum was taken at −40, 0, and 22 °C. The spectrum taken at −40 °C is described in Table 1.

2-Phenyl-2-metallo-1,3-dioxane[31] **(17) for NMR Study.** The second carbanion studied by low temperature NMR, 2-phenyl-2-metallo-1,3-dioxane, was generated in a slightly different manner from that described for the 4-phenyl-4-metallo-1,3-dioxane. 2-Phenyl-1,3-dioxane crystals and *t*-BuOK were added to an Ar-flushed 10-mL round-bottomed flask. Then all the THF-d_8 was added at once, and after a septum was wired on, the flask was cooled to −78 °C under Ar. *n*-Butyllithium was then added dropwise, and the yellow solution instantly became bright orange. The orange (not red!) solution was transferred by cannula to an Ar-flushed NMR tube fitted with a septum and cooled to −78 °C. 2-Phenyl-2-metallo-1,3-dioxane is not stable at −40 °C. After being transported in a Dewar flask, the tube was transferred to the NMR probe which had been cooled to −78 °C. The solution had turned dark by this time and was difficult to lock on. The signals in the region of interest (>90 ppm) were weak and noisy even after 20 000 scans and did not improve with additional scanning. The poor quality of the NMR spectrum and a green color seen occasionally when preparing the sample suggest some radical is present. The best spectrum, described in Table 1, was obtained when the THF-d_8 was refluxed over Na/K alloy prior to use and the carbanion was generated immediately before acquiring NMR data. An attempt to rid the solution of radicals was made. A radical trap was desired whose own resulting radicals would readily dimerize. A possible candidate, 2-methyl-2-propanethiol (10%), was added via syringe to a THF-d_8 solution of *t*-BuOK. After being stirred at room temperature for 10 min, the solution was cooled to −78 °C under Ar. Then *n*-BuLi was added dropwise. The amount of Lochmann base had been increased 10% to account for reaction with the thiol. Finally, a solution of 2-phenyl-1,3-dioxane in THF-d_8 was added via syringe. After transferring the green/orange solution to a NMR tube and transporting it to a cooled NMR probe as described before, the ^{13}C spectrum was taken at −78 °C. Unfortunately the quality of the spectrum had not improved.

2-Methoxy-4-methyl-1,3-dioxane (19) was prepared on a 0.2-mol scale as described in the literature.[29] The product was fractionally distilled; the first fraction (55−59 °C) had a 1:2.6 cis:trans ratio while the second fraction had a 10:1 cis:trans ratio (63−67 °C) and the third fraction had a 27:1 cis:trans ratio. The first fraction was used for the Grignard reaction to produce **7**. ^1H NMR: δ 1.19 (d, J = 6.3 Hz, 4-Me, trans), 1.28 (d, J = 6.1 Hz, 4-Me, cis), 1.43−1.56 (m, H_{5e}), 1.73 (ddd, J = 0.9, 1.7, 11.2, 13.2 Hz, H_{5a}), 3.34 (s, OMe, trans), 3.49 (s, OMe, cis), 3.68−3.98 (m, $H_{6a\&4a}$), 4.08−4.35 (m, H_{6e}), 5.15 (s, H_{2a}, cis), 5.37 (s, H_{2e}, trans). ^{13}C NMR: δ 21.2, 21.4 (4-Me's), 26.8, 31.8, 32.4 (C-5's), 52.6 (OMe), 58.3 (C-6, trans), 63.9 (C-4, trans), 64.6 (C-6, cis), 71.6 (C-4, cis), 108.9 (C-2, trans), 111.9 (C-2, cis).

2-Methoxy-4-phenyl-1,3-dioxane (20) was prepared from 1-phenyl-1,3-propanediol (1.08 g, 7.06 mmol), trimethyl orthoformate (0.75 g, 7.1 mmol), 20 mL of cyclohexane, and a catalytic amount of *p*-TSA in an analogous manner to **19** to yield a pale yellow oil (1.39 g, 102%) which was a 1:1.4 mixture of *cis* and *trans* isomers. ^1H NMR: d 1.615−1.79 (m, H_{5a}), 1.85−2.22 (m, H_{5a}), 3.39 (s, OMe, *trans*), 3.55 (s, OMe, *cis*), 3.81 (ddd, J = 1.6, 5.1, 11.1 Hz, H_{6e}), 3.98 (dt, J = 2.7, 12.0 Hz, H_{6a}), 4.19−4.40 (m, $H_{6e\&a}$), 4.82 (dd, J = 2.7, 11.4 Hz, H_{4a}), 5.17 (dd, J = 2.8, 11.6 Hz, H_{4a}), 5.35 (s, H_{2a}, cis), 5.54 (s, H_{2e}, trans), 7.25−7.38 (m, Ar-H). ^{13}C NMR: δ 32.4, 32.7 (C-5's), 52.6, 52.8 (OMe's), 58.8 (C-6, trans), 64.9 (C-4, trans), 69.6 (C-6, cis), 77.3 (C-4, cis), 109.3 (C-2, trans), 112.1 (C-2, cis), 125.7, 125.9, 126.6, 127.7, 127.8, 128.4, 141.3 (Ar-C).

Lochmann Base Treatment of Cyclohexylbenzene (21) with Inverse Deuterioethanol Quench. The procedure for the treatment of **3** was followed for cyclohexylbenzene (1.60 g, 10.0 mmol) with potassium *tert*-butoxide (1.24 g, 11.0 mmol), 20 mL of dry THF, *n*-BuLi (1.1 mL of 10 M in hexanes, 11 mmol), and 1 mL of EtOD in 4.5 mL of dry THF. A gold-colored liquid (1.79 g, 111%) was isolated. ^1H NMR: δ 1.11−1.64 (m, H_{axial}), 1.25 (s, new), 1.70−1.91 (m, $H_{equatorial}$), 1.83 (s, new), 2.415−2.56 (m, H α to Ar), 3.45−3.78 (m, new), 7.11−7.32 (m, Ar-H). ^{13}C NMR: δ 13.8, 14.1, 18.9 (new), 25.6 (new, C δ to Ar), 26.2 (C δ to Ar), 26.9 (C's γ to Ar), 31.2 (new, C γ to Ar), 34.5 (C's β to Ar), 34.9 (new, C's β to Ar), 44.6 (C α to Ar), 62.7, 67.9 (new), 125.7, 126.8, 127.1, 128.2, 148.0 (Ar-C), 125.6, 126.7, 128.1 (new, Ar-C). ^2H NMR (methylene chloride-d_2 reference): 19.8% total D incorporation: δ 1.48, 1.95, 2.15 (D-axial, D-equatorial, D-α, 2.2% of total), 4.0 (corresponds to new peak in ^1H NMR, 0.32%), 4.46 (unknown, 0.15%), 7.58 (Ar-D, 17.1%).

Lochmann Base Treatment of 4-Methyl-1,3-dioxane (1). The procedure for the treatment of **3** was followed in part for 4-methyl-1,3-dioxane (1.02 g, 10.0 mmol) with potassium *tert*-butoxide (1.12 g, 10.0 mmol), 20 mL of dry THF, and *n*-BuLi (6.25 mL of 1.6 M solution in hexanes, 10.0 mmol). Changes to the procedure followed for **3** included the reaction time at −78 °C (1 h), the quench method (direct) and the workup (distillation and preparative GC). Ethanol-*d* (0.59 mL, 0.47 g, 10 mmol) in approximately the same volume of dry THF was added quickly. After being stirred at −78 °C for ca. 0.5 h, the mixture was warmed to room temperature and poured into 25 mL of brine and 50 mL of ether. The ether layer was isolated and dried over Mg_2SO_4. After filtration, the ether and the majority of the THF were removed by fractional distillation. Residual THF and byproduct, *tert*-butyl alcohol, were removed by preparative gas chromatography: Carbowax 20M on Chromosorb P packed column at 100 °C, injector at 255 °C, and the detector at 250 °C. The broad peak with the longest retention time was collected. ^1H NMR: δ 1.25 (d, 3H, 4-Me), 1.45−1.55 (m, 1H, H_{5e}), 1.7−1.8 (m, 1H, H_{5a}), 3.7 (m, 2H, $H_{6a\&4a}$), 4.16 (m, 1H, H_{6e}), 4.71 (d, J = 6.5 Hz, H_{2a}, 1 H), 5.03 (d, J = 6.5 Hz, H_{2e}, 0.60 H), in good agreement with the reported[32] spectrum. (The expected triplet for H_{2a} in the deuterated product appeared to lie under the downfield signal of the 4.71 ppm doublet.) ^{13}C NMR: δ 21.6 (4-Me), 33.6 (C-5), 66.6 (C-6), 72.7 (C-4), 93.4 (t, C-2), 93.7 (s, C-2). ^2H NMR ($CDCl_3$ reference): 35.6% total incorporation: δ 4.035 (D_{6e}, 4.4%), 4.99 (D_{2e}, 31.2%). Extension of the base treatment to 2 h gave as much as 58% D incorporation at C(2).

1-Phenyl-1,3-propanediol (22). This compound was prepared per a literature procedure.[33] The white, opaque oil (1.81 g, 71%) was distilled at 111.5−137 °C under 0.035 mmHg of pressure. ^1H NMR: δ 2.00 (m, 2 H, $-CH_2-$), 2.80 (broad s, 3 H, −OH), 3.84 (dt, 2 H, J = 1.8, 5.4 Hz, $-CH_2OH$), 4.94 (ddd, 1 H, J = 1.4, 8.1 Hz, Ar-CH-O), 7.21−7.37 (m, Ar-H). [lit.[34] ^1H NMR: δ 1.80 (q, 2 H), 3.70 (t, 2 H), 4.85 (t, 1 H), 7.35 (m, 5 H).] ^{13}C NMR: δ 40.4 ($-CH_2-$), 61.4 ($-CH_2$-OH), 74.2 (Ar-CH-OH), 125.6, 127.6, 128.5, 144.3 (Ar-C).

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(31) Per ref 6, it is uncertain whether the counterions are Li or K or both. However, the similarity in the upfield shifts of the ortho and para protons in **16** (vs **15**) and **18** (vs **5**) suggests that the counterion, at least in **18**, is K. (The upfield shifts in the Li salt corresponding to **16** are 17.5 ppm for H_{ortho} and 28.6 ppm for H_{para}.)

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