Articles

The Effect of a Para Substituent on the Conformational Preference of 2,2-Diphenyl-1,3-dioxanes: Evidence for the Anomeric Effect from X-ray Crystal Structure Analysis[1]

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The molecular structures of 2,2-di(para-substituted phenyl)-1,3-dioxanes were elucidated for the first time by X-ray crystallographic analysis, which revealed two important structural features: (1) These compounds have the chair conformation in which electron-withdrawing aryl groups [viz. *p*-nitro- or *p*-(trifluormethyl)phenyl] are always axial and electron-donating aryl groups (viz. *p*-methoxyphenyl) are always equatorial. (2) In these compounds as well as in symmetrically substituted 2,2-diphenyl-1,3-dioxane the axial C_2−aryl bond is longer than the equatorial C_2−aryl bond. The axial preference of the electron-withdrawing aryl group was also demonstrated in solution by ^{1}H and ^{13}C NMR spectroscopy. The anomeric carbon substituted with an electron-withdrawing aryl group resonates at an unusually high field, as does the aromatic carbon bearing the electron-withdrawing substituent. The observed ^{13}C NMR data clearly indicate enhanced electron density at these carbons due to the anomeric effect. Semiempirical molecular orbital calculations by the MOPAK PM3 method reproduced the bond lengthening for axial C_2−aryl, while the heat of formation derived from this calculation failed to support the axial preference of electron-withdrawing aryl groups. The X-ray crystallographic data on the conformational preference and bond lengths at the anomeric carbon, as well as the solution NMR spectroscopic data, clearly indicate the anomeric effect that is best rationalized in terms of stabilizing interaction between the lone-pair electrons on the ring oxygens and the antibonding orbital of the axial C_2−aryl bond.

Introduction

The tendency of electronegative substituents X at C_2 of tetrahydropyranes **1** to occupy an axial position is termed the anomeric effect.[2] Its origin may be found in destabilization of equatorial substituents due to unfavorable dipole−dipole (electrostatic) interactions.[3] An alternative view is stabilization due to favorable overlap between the orbital carrying a ring-oxygen lone-pair of electrons (n_O) and the antibonding orbital (σ^*) of the bond between C_2 and X.[4] It is not easy to find which of the interactions is sufficient to account for the observations, and this point has been a subject of extensive studies from experimental and theoretical viewpoints.[5−7] The best evidence for $n_O-\sigma^*$ delocalization is crystallographic data showing that species with O−C_2−X (axial) fragments have shorter C_2−O bonds and longer C_2−X bonds.[8,9] These changes in bond length cannot be rationalized on the basis of electrostatic effects, which suggests that delocalization alone sufficiently accounts for the observations.[2a,d]

During the course of our study on the use of chiral 1,3-diheterocyclic enones in asymmetric synthesis,[10] we found that π-facial selectivity in the conjugate addition of

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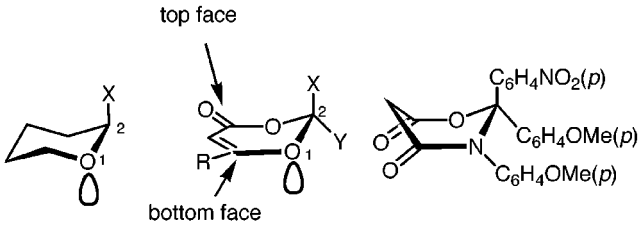
Scheme 1



1 **2** **3**

a: X = H or Me, Y = *tert*-Bu
b: X = Ph, Y = Me
c: X = CO_2Me, Y = Me or Ph

organometallic reagents to 1,3-dioxin-4-one derivatives is greatly affected by pseudoaxial substituents on the anomeric carbon. Thus, addition to **2a** (X = H[11,12] or Me[13]) occurs selectively from the more hindered top face, while addition to **2b** (X = Ph)[14] and **2c** (X = CO_2R)[15,16] proceeds selectively from the less hindered bottom face. While other explanations have been proposed for the top face attack,[12,13,17] we rationalized both selectivities by invoking two competing stereoelectronic effects.[14−16] Namely, the top face attack to **2a** is best rationalized by the Cieplack effect;[18] the lone-pair electrons of O_1 interact with the antibonding orbital ($\sigma_{‡*}$) of the incipient bond facilitating the top face attack. In **2b** and **2c**, the lone-pair electrons of O_1 interact strongly with the antibonding orbital of the pseudoaxial C_2−X bond and the Cieplack effect would become less effective, allowing the attack from the bottom face. We also found a characteristic boat conformation in the crystal structure of 2,2-diaryl-1,3-oxazine-4,6-diones **3** where the more electronegative aryl group occupies a pseudoaxial position (Scheme 1). We rationalized this conformational preference in terms of the stabilizing interaction between the lone-pair electrons on N_3 and/or O_1 and the σ* orbital of the pseudoaxial C_2−aryl bond.[19]

The axial preference of an alkoxycarbonyl group has been observed in tetrahydropyranes,[20] 1,3-dioxanes,[21,22] and 1,3-dithianes[23] from conformation analysis and has been rationalized by the anomeric effect. The influence of aryl groups on the conformation of anomeric compounds has been also studied. Köhler et al.[24] observed the axial preference of the 2-aryl group in 1,3-dithianes and attributed it to the anomeric effect. Some data concerning conformational preference[25] and X-ray crystal structures of 2-aryl-1,3-dioxanes[26,27] have been also reported. However, the electronic effects of the 2-aryl group on the conformational behaviors of 1,3-dioxanes have remained obscure, because the electronic character of the aryl group varies significantly with the substituent and its position on the aryl ring. In addition, it is not easy to estimate the purely electronic effect of the aryl group on the conformation because the conformation varies significantly with the steric interactions involving the aryl group, whose effective bulk varies with the positions (axial or equatorial) and with the torsion angle of the aryl ring.[28]

To prove our hypotheses on the origins of the π-facial selectivity in **2** and the conformational preference in **3** as well as to study the relative importance of the two origins of the anomeric effect, we carried out a more detailed study of the stereoelectronic effect of 2-aryl substituents in 1,3-dioxanes.

To study the purely electronic effects of the aryl group, we used a series of 2,2-di(para-substituted phenyl)-1,3-dioxane **4** as a probe. The two aryl substituents are sterically equivalent but electronically nonequivalent when an electron-withdrawing or -donating substituent is introduced to the para position. Moreover, even when the two aryl groups were electronically equivalent, we would be able to study the magnitude of the anomeric effect by comparing the lengths of the C_2-axial−aryl and the C_2-equatorial−aryl bonds via X-ray crystallographic analysis.

Thus, we analyzed the conformation and molecular structure of 2-(4-methoxyphenyl)-2-(4-nitrophenyl)-(**4a**), 2-(4-methoxyphenyl)-2-[(4-trifluoromethyl)phenyl]-(**4b**), and 2,2-diphenyl-1,3-dioxanes (**4d**) by X-ray crystallography (Scheme 2). The conformational preference of **4a**−**d** in solution was studied by ^{1}H and ^{13}C NMR spectroscopy. Finally, semiempirical molecular orbital calculations (MOPACK PM3 method) were done on the geometry and heat of formation for **4** where an electron-withdrawing aryl group occupies the axial position and

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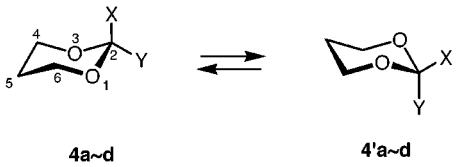
Scheme 2



4a~d **4'a~d**

a: X = $C_6H_4NO_2(p)$, Y = $C_6H_4OMe(p)$
b: X = $C_6H_4CF_3(p)$, Y = $C_6H_4OMe(p)$
c: X = C_6H_5, Y = $C_6H_4OMe(p)$
d: X = Y = C_6H_5

its conformational isomer **4′** where an electron-donating aryl group occupies the axial position, and the results were compared with the observed conformational preference and molecular structures in X-ray crystallography and NMR spectroscopy.

Results and Discussion

X-ray Crystallographic Analysis. Compounds **4a**−**d** were prepared by condensation of diaryl ketones with 1,3-propanediol under an acid catalysis.[29] We analyzed the molecular structures of **4a** and **4b** by X-ray crystallography. For comparison purposes, the structure of symmetrical derivative **4d** was also analyzed by X-ray crystallography. Figure 1 contains molecular structures of **4a**, **4b**, and **4d**, and Table 1 contains selected bond distances at the anomeric carbon and ring oxygens and selected bond angles. As expected, the 4-nitrophenyl group that is much more electron-withdrawing than the 4-methoxyphenyl group occupied an axial position in **4a**. This conformation is not incidentally caused by crystal packing, because compound **4b** also took the conformation having the electron-withdrawing 4-(trifluoromethyl)-phenyl group at the axial position. In the crystal of **4a**, the axial C_2−nitrophenyl bond (1.544 Å) is much longer than the equatorial C_2−methoxyphenyl bond (1.526 Å), which is close to the accepted average value for the Csp^3−Csp^2 bond (1.504 Å).[30] Bond lengths for O_1−C_2 (1.405 Å) and O_3−C_2 (1.413 Å) are shorter than those for O_1−C_6 (1.440 Å) and O_3−C_4 (1.444 Å) as has been generally observed in 1,3-dioxanes.[9a,26,27] The bond lengths at the anomeric carbon for **4b** are comparable to those for **4a**; the axial C_2−aryl bond (1.539 Å) is longer than the equatorial C_2−aryl bond (1.520 Å). It is of interest to note that these characteristic features in the bond length at the anomeric carbon are essentially retained in the molecular structure of 2,2-diphenyl derivative **4d**; the axial C_2−phenyl bond (1.540 Å) is longer than the equatorial C_2−phenyl bond (1.521 Å).

X-ray crystal structure analyses of 2-monoaryl-1,3-dioxanes with equatorial and axial aryl groups have been reported.[26,27] The bond length at the anomeric carbon and ring oxygens and selected bond angles for equatorial 4-chlorophenyl (**5**), axial 4-chlorophenyl (**6**), and axial 4-(trifluoromethyl)phenyl derivatives (**7**) are given in Table 1, respectively. The axial C_2−aryl bond in **6** and **7** (1.532 Å) is longer than the equatorial C_2−aryl bond (1.50 Å) in **5**. Nader et al.[27b] suggested the anomeric effect as one of the reasons for the axial bond lengthening in **7** (Chart 1).

The data for bond lengths of **4** are almost comparable to those for **5**−**7**. However, the bonds at the anomeric carbon of **4** are slightly longer than those of **5**−**7** as seen from Table 1. This difference in bond lengths at the anomeric carbon arises from a steric reason; a repulsive interaction due to the steric congestion for the tertiary anomeric carbon in **4** results in the longer bonds compared to the 2-monoaryl analogues **5**−**7**. This rationalization is well evidenced by the remarkable bond lengthening in the sterically much congested **3** where all of the bonds at the anomeric carbon are markedly lengthened (axial C_2−aryl, 1.524; equatorial C_2−aryl, 1.527; O_1−C_2, 1.524; N_3−C_2, 1.465 Å).[19]

The observed conformations for **4a** and **4b** and the remarkable bond lengthening at the axial C_2−aryl in **4a**,**b**,**d** strongly suggest an anomeric effect that is best rationalized in terms of the n_O−σ^* stabilizing interactions.

^{1}H and ^{13}C NMR Spectroscopic Analyses. To study the conformational behaviors of **4** in solution, we examined ^{1}H and ^{13}C NMR spectroscopy. Figure 2 contains selected data obtained at 25 °C in $CDCl_3$. The signals for C_5 methylene protons are greatly affected by the introduction of para substituents on the phenyl ring; the signals for diphenyl derivative **4d** and 2-(4-methoxyphenyl)-2-phenyl derivative **4c** appeared as quintets at 1.77 and 1.81 ppm (each 2H), respectively, indicating a fast exchange of two conformers **4** and **4′**, while that for **4a** and **4b** appeared as well-separated multiplets (**4a**, 1.70 and 1.95 ppm; **4b**, 1.75 and 1.88 ppm). The observed nonequivalence of the two protons at C_5 strongly suggests that **4a** and **4b** are conformationally fixed to a great extent in solution due to the anomeric effect. This assumption is strongly supported by ^{13}C NMR data. The chemical shifts of anomeric carbons in **4a** (100.19 ppm) and **4b** (100.50 ppm) appeared at higher fields than in diphenyl derivative **4c** (101.03 ppm) by 0.84 and 0.53 ppm, respectively. In addition, the nitrated carbon (147.32 ppm) and trifluoromethylated carbon (129.83 ppm) also appeared at higher fields by 0.98 and 1.01 ppm than those for nitrobenzene **8** (148.30 ppm) and α,α,α-trifluorotoluene **9** (130.84 ppm), respectively. In good contrast, the chemical shift of methoxylated carbons for **4a**−**c** (159.25−159.68 ppm) is almost the same as that for anisole itself (159.74 ppm). Though compounds **8**−**11** are not ideal models for **4**, the observed high-field shifts for the anomeric carbon and the para carbon of the axial aryl group strongly indicates enhanced electron density by the stabilizing interaction between the lone-pair electrons of O_1 and O_3 and antibonding orbital of the axial C_2−aryl bond. Köhler et al.[24] found that in conformationally locked 2-phenyl-1,3-dithiane derivatives the para carbon of the axial phenyl diastereoisomer appears at higher field than that of the equatorial phenyl diastereoisomer, and they interpreted this observation in terms of the n_O−σ^* stabilizing interaction.

Computational Analysis

The conformational preference of **4a**,**b** over **4′a**,**b** is now clear from the above X-ray crystallographic and NMR spectroscopic studies. Thus, we finally examined semiempirical molecular orbital calculations on the conformational preference and molecular structure of 2,2-diaryl-1,3-dioxanes **4a**−**d**.

Geometries for **4a**−**d** and their conformational isomers **4′a**−**c** were calculated by MOPAK PM3 on a Tektronix

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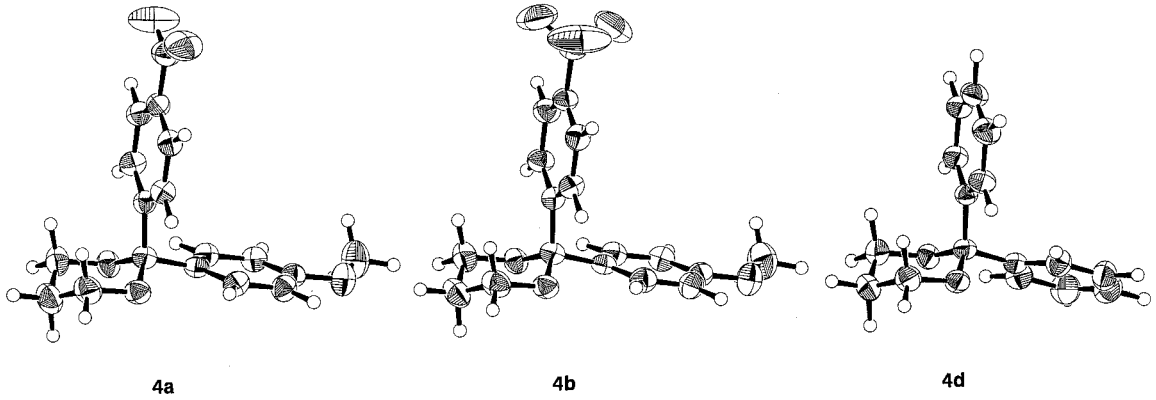
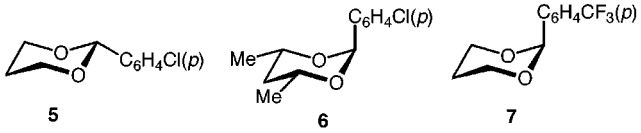


Figure 1. Molecular structures for **4a**, **4b**, and **4d** from X-ray crystallographic analysis.

Table 1. Selected Bond Lengths and Angles for 1,3-Dioxanes 4−7 Observed in X-ray Crystallography

compd	substituent		bond length (Å)						bond angle (deg)			
no.	X	Y	C_2-X	C_2-Y	O_1-C_2	O_3-C_2	O_1-C_6	O_3-C_4	$O_1-C_2-O_3$	$C_2-O_3-C_4$	$C_2-O_1-C_6$	ref
4a	$C_6H_4NO_2(p)$	$C_6H_4OMe(p)$	1.544(3)	1.526(3)	1.405(3)	1.413(3)	1.440(3)	1.444(3)	112.0(2)	112.5(2)	113.1(2)	
4b	$C_6H_4CF_3(p)$	$C_6H_4OMe(p)$	1.539(4)	1.520(4)	1.412(3)	1.539(4)	1.440(4)	1.442(4)	111.4(2)	113.0(2)	113.2(2)	
4d	C_6H_5	C_6H_5	1.540(2)	1.521(3)	1.418(2)	1.413(2)	1.443(3)	1.436(3)	111.6(2)	114.0(2)	113.7(2)	
5	H	$C_6H_4Cl(p)$		1.50	1.41	1.40	1.42	1.45	111	111	111	26a
6	$C_6H_4Cl(p)$	H	1.532		1.408	1.412	1.450	1.442	112.5	113.7	113.5	27c
7	$C_6H_4CF_3(p)$	H	1.532		1.409	1.412	1.452	1.447	112.3	113.9	113.7	27a

Chart 1



CAChe work system using EF (eigenvector-following) method. The heat of formation and selected bond distances and angles for **4a**−**d** are listed in Table 2. The axial C_2−aryl bonds are somewhat longer compared to the equatorial C_2−aryl bonds, and increased electronegativity of the axial aryl group results in the increased bond length of the axial C_2−aryl. The calculated bond lengths of axial C_2−aryl and equatorial C_2−aryl for **4a**,**b**,**4d** are relatively close to those observed in their crystal structures listed in Table 1. In **4′a** and **4′b** where the electron-donating *p*-methoxyphenyl group occupies an axial position and the electron-withdrawing aryl group occupies an equatorial position, the axial C_2−aryl bonds are shortened and equatorial C_2−aryl bonds are lengthened compared to those in **4a** and **4b**, respectively. However, the bond lengths for O_1-C_2 (1.428−1.429 Å) are longer and those for O_1-C_6 (1.415−1.417 Å) are shorter compared to the data obtained by the crystallographic analysis. In addition, calculated heat of formation indicated **4a** and **4b** are less stable by 0.78 and 0.57 kcal/mol than **4′a** and **4′b**, respectively. Thus, it became apparent that this semiempirical calculation is not sufficient to account for the conformational preference of 2,2-diaryl-1,3-dioxanes, while this method clearly indicates that increased electronegativity of axial C_2−aryl results in increased bond lengthening of the axial C_2−aryl.

Conclusion

We analyzed the conformation and molecular structure of a series 2,2-diaryl-1,3-dioxanes by X-ray crystallography and ^1H and ^{13}C NMR spectroscopy, and the result was compared with the data obtained by semiempirical molecular orbital calculations. The X-ray crystallographic analysis of **4a** and **4b** provided excellent evidence for the anomeric effect of the aryl group; the more electron-withdrawing aryl group always occupies an axial position and the axial C_2−aryl bond is remarkably lengthened. It should be emphasized that the anomeric effect was also observed in the 2,2-diphenyl derivative as revealed by the comparable bond lengthening of the axial C_2−phenyl bond with those of the analogues with a strong electron-withdrawing aryl group. The nonequivalence of the two protons at C_5 in **4a** and **4b** is attributable to the conformational fixation by the anomeric effect caused by the electron-withdrawing aryl group. The high-field shifts of the anomeric carbons and nitrated and trifluoromethylated carbons of **4a** and **4b** in their ^{13}C NMR spectra clearly show enhanced electron density at these carbons. Though calculations by the MOPAK PM3 method could not reproduce these experimental results except for the bond lengthening for axial C_2−aryl, the crystallographic and NMR spectroscopic data clearly show $n_O-\sigma^*$ stabilizing interaction in 2-aryl-1,3-dioxanes. Thus, we conclude that the delocalization is more substantiative than the electrostatic explanation for the anomeric effect. Moreover, the result well supports our hypothesis concerning operation of the anomeric effect in **2b**, **2c**, and related compounds including 1,3-oxazine-4,6-dione **3**.

Experimental Section

General Methods. All melting points were recorded on a Yanagimoto micro-hot stage and are uncorrected. IR spectra were measured on a JASCO A-102 spectrophotometer. ^1H and ^{13}C NMR spectra were measured at 25 °C on a Varian Gemini 2000 spectrometer with tetramethylsilane as an internal standard. The ^{13}C NMR spectra were measured using 0.5 M sample solutions. High-resolution mass spectra were recorded on a JEOL JMS-DX-303 or JMS-AX-500 spectrometer. Wakogel (C-200) silica gel and Merck aluminum oxide 90 (neutral, activity stage I) were used in the column chromatographies.

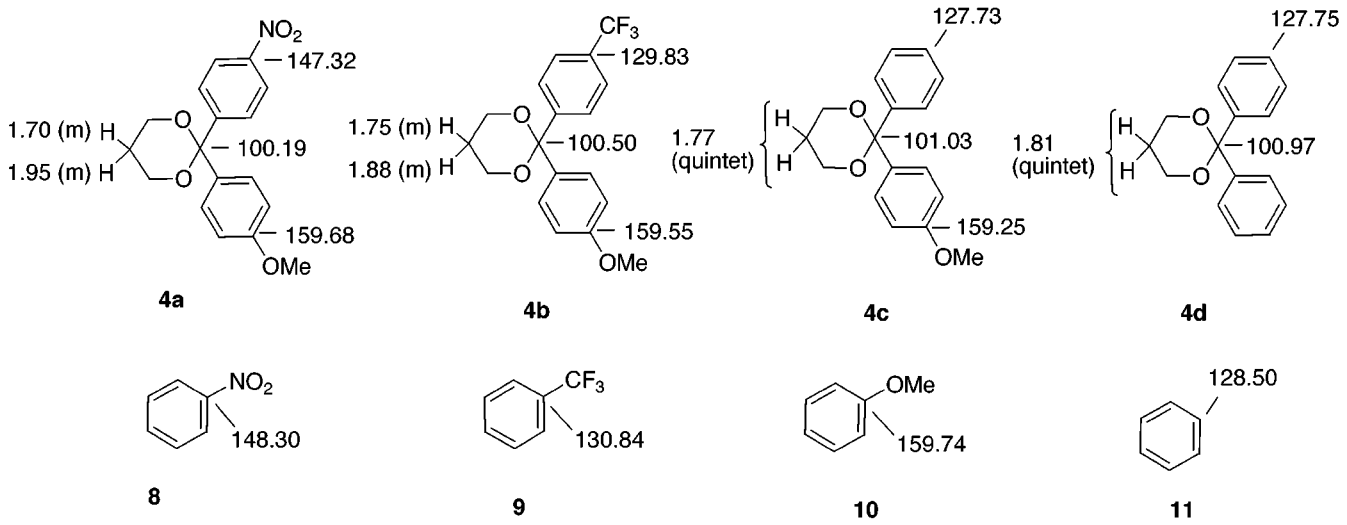


Figure 2. Selected ^{1}H and ^{13}C NMR data (ppm, $CDCl_3$, 25 °C) for **4a**−**d**.

Table 2. Heat of Formation and Selected Geometry Parameters for 4 and 4′ Calculated by PM3 Method

compd	substituent		heat of formation	bond length (Å)				bond angle (°)		
no.	X	Y	(kcal/mol)	C_2−X	C_2−Y	O_1−C_2, O_3−C_2	O_1−C_6, O_3−C_4	O_1−C_2−O_3	C_2−O_3−C_4	C_2−O_1−C_6
4a	$C_6H_4NO_2$(*p*)	C_6H_4OMe(*p*)	−70.12	1.534	1.525	1.428	1.416	105.8	114.6	115.5
4b	$C_6H_4CF_3$(*p*)	C_6H_4OMe(*p*)	−219.78	1.533	1.526	1.428	1.415	106.0	115.2	115.2
4d	C_6H_5	C_6H_5	−23.53	1.530	1.528	1.429	1.415	105.5	115.0	115.1
4′a	C_6H_4OMe(*p*)	$C_6H_4NO_2$(*p*)	−70.90	1.529	1.529	1.428	1.417	105.1	113.9	115.3
4′b	C_6H_4OMe(*p*)	$C_6H_4CF_3$(*p*)	−220.35	1.528	1.529	1.429	1.415	106.0	115.0	115.0

The ratios of solvent mixtures for chromatography are shown as volume/volume.

General Procedure for the Synthesis of 2,2-Diaryl-1,3-dioxanes (4a−d). Compounds **4a**−**d** were prepared by the reported procedure.[29] A solution of diaryl ketone (1.0 mmol), 1,3-propanediol (3.0 mmol), and a catalytic amount of *p*-toluenesulfonic acid (30 mg) in benzene (60−75 mL) was refluxed with a Dean−Stark trap for removal of water. After 10−30 h, saturated $NaHCO_3$ solution was added, and the mixture was extracted with ether. The organic layer was washed with brine and dried over anhydrous $MgSO_4$. The solvent was removed in vacuo, and the residue was purified by alumina column chromatography.

2-(4-Methoxyphenyl)-2-(4-nitrophenyl)-1,3-dioxane (4a). Following the general procedure, 4-methoxy-4′-nitrobenzophenone (257 mg, 1.0 mmol)[30] was condensed with 1,3-propanediol (228 mg, 3.0 mmol). Purification of the crude product by alumina column chromatography (hexane−chloroform, 3:1) gave **4a** (222 mg, 71%) as a solid. Recrystallization from ether afforded pure **4a** as yellowish prisms: mp 161−163 °C; ^{1}H NMR ($CDCl_3$) δ 1.65−1.74 (1H, m), 1.88−1.99 (1H, m), 3.77 (3H, s), 3.95−4.11 (4H, m), 6.85−6.90 (2H, m), 7.38−7.43 (2H, m), 7.65−7.70 (2H, m), 8.11−8.17 (2H, m); ^{13}C NMR ($CDCl_3$) δ 25.30, 55.18, 61.60, 100.19, 114.27, 123.65, 126.99, 127.98, 132.67, 147.32, 150.76, 159.68; IR ($CHCl_3$): 1610, 1520, 1530 cm^{-1}; HRMS calcd for $C_{17}H_{17}NO_5$ 315.1107, found 315.1110. Anal. Calcd for $C_{17}H_{17}NO_5$: C, 64.75; H, 5.43; N, 4.44. Found: C, 64.85; H, 5.64; N, 4.45.

2-(4-Methoxyphenyl)-2-[4-(trifluoromethyl)phenyl]-1,3-dioxane (4b). 4-Methoxy-4′-(trifluoromethyl)benzophenone was prepared as follows. 4-(Methoxyphenyl)magnesium bromide (9.0 mmol, 1.2 M ether solution, 7.5 mL) was added dropwise to a solution of 4-(trifluoromethyl)benzaldehyde (894 mg, 5.14 mmol) in THF (10 mL) at 0 °C. The mixture was stirred at room temperature for 12 h. A solution of 5% HCl was added, and the mixture was extracted with ether. The organic layer was washed with brine, dried over anhydrous $MgSO_4$, and evaporated in vacuo to afford crude α-(4-methoxyphenyl)(4-trifluoromethyl)benzyl alcohol[32] as a solid. A solution of 8 M Jones reagent (1.0 mL, 8.0 mmol) was added to the solution of the benzyl alcohol in acetone (40 mL) at room temperature. After being stirred for 2 h, 2-propanol (5 mL) was added to the mixture. The whole was extracted with dichloromethane. The organic layer was washed with saturated $NaHCO_3$ solution, dried over anhydrous $MgSO_4$, and evaporated. Recrystallization of the residue from a mixture of hexane and dichloromethane afforded the 4,4′-disubstituted benzophenone (814 mg, 57%, two steps) as prisms, mp 123−124 °C (lit.[33] mp 123−124 °C). Following the general procedure, 4-methoxy-4′-(trifluoromethyl)benzophenone (266 mg, 0.95 mmol) was condensed with 1,3-propanediol (228 mg, 3.0 mL). Purification of the crude product by alumina column chromatography (hexane/chloroform 3:1) gave **4b** (210 mg, 65%) as a solid. Recrystallization from ether afforded colorless prisms: mp 118−119 °C; ^{1}H NMR ($CDCl_3$) δ 1.72−1.79 (1H, m), 1.82−1.90 (1H, m), 3.78 (3H, s), 3.95−4.11 (4H, m), 6.85−6.91 (2H, m), 7.39−7.45 (2H, m), 7.56−7.66 (4H, m). ^{13}C NMR ($CDCl_3$) δ 25.44, 55.19, 61.61, 100.50, 114.11, 124.27 (q, J = 271.0 Hz), 125.48 (q, J = 3.4 Hz), 126.72, 127.96, 129.83 (q, J = 31.9 Hz), 133.67, 147.33, 159.55; IR ($CHCl_3$)1605, 1505, 1320 cm^{-1}; HRMS calcd for $C_{18}H_{17}F_3O_3$ 338.1130, found 338.1150. Anal. Calcd for $C_{18}H_{17}F_3O_3$: C, 63.90; H, 5.06. Found: C, 64.15; H, 5.24.

2-(4-Methoxyphenyl)-2-phenyl-1,3-dioxane (4c). Following the general procedure, 4-methoxybenzophenone (424 mg, 2.0 mmol) was condensed with 1,3-propanediol (456 mg, 6.0 mmol). Purification of the crude product by alumina column chromatography (hexane/chloroform 5:1) gave **4c** (95 mg, 18%) and 4-methoxybenzophenone (316 mg, 69%). Recrystallization of **4c** from ether afforded colorless prisms: mp 53−54 °C (lit.[34] mp 52−53 °C); ^{1}H NMR ($CDCl_3$) δ 1.77 (2H, quintet), 3.74 (3H, s), 4.01 (4H, t), 6.82−6.87 (2H, m), 7.19−7.53 (7H, m); ^{13}C NMR ($CDCl_3$) δ 25.54, 55.16, 61.55, 101.03, 113.80, 126.53, 127.73, 127.91, 128.48, 134.82, 142.75 159.25.

2,2-Diphenyl-1,3-dioxane (4d). Following the general procedure, benzophenone (911 mg, 5.0 mmol) was condensed

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Table 3. Crystallographic Data for Compounds 4a,b,d

compound	**4a**	**4b**	**4d**
chemical formula	$C_{17}H_{17}NO_5$	$C_{18}H_{17}F_3O_3$	$C_{16}H_{16}O_2$
a, Å	26.157(1)	26.871(1)	8.238(2)
b, Å	7.947(2)	8.017(2)	13.239(2)
c, Å	7.380(1)	7.471(2)	6.249(2)
β, °	93.15(1)	90.81(1)	111.67(2)
V, Å^3	1531.7(7)	1609.2(8)	635.9(2)
Z	4	4	2
space group	$P2_1/a$	$P2_1/a$	$P2_1$
R^a	0.055	0.067	0.039
R_w	0.105	0.123	0.069

[a] $R = \Sigma||F_o| - |Fc||/\Sigma|F_o|$, $R_w = [\Sigma w(|F_o| - |Fc|)^2/\Sigma wF_o^2]^{1/2}$.

with 1,3-propanediol (1.14 g, 15.0 mmol). Purification of the crude product by alumina column chromatography (hexane/dichloromethane 3:1) gave **4d** (795 mg, 62%). Recrystallization from ether afforded colorless prisms: mp 113−115 °C (lit.[29] mp 111.5−112.5 °C); ^{1}H NMR ($CDCl_3$) δ 1.81 (2H, quintet), 4.05 (4H, t), 7.21−7.55 (10H, m); ^{13}C NMR ($CDCl_3$) δ 25.48, 61.54, 100.97, 126.49, 127.75, 128.48, 142.48.

X-ray Crystallographic Analyses of 4a, 4b, and 4c. Diffraction data collections were made on a Rigaku AFC-5R for **4a** and **4b** and a Rigaku AFC-7R for **4d** with Cu Kα radiation (λ = 1.541 78 Å) at room temperature. Lorentz, polarization, empirical absorption, and secondary extinction corrections were applied to all data. Crystal data and selected parameters for all three compounds are shown in Table 3. The number of measured and observed ($I > \sigma(I)$) reflections are 2691 and 2073 for **4a**, 2811 and 2157 for **4b**, and 1326 and 1263 for **4d**, respectively.

The structure was solved by direct method with SHELX-86[35] and expanded with DIRDIF 92.[36] Positions and anisotropic displacement parameters were refined for all non-hydrogen atoms by the full-matrix least-squares technique. Hydrogen atoms were placed at the calculated positions with an isotropic parameter equal to 1.2 times that of the attached atom and were fixed but included in the refinement. All calculations were carried out using teXsan software package of Molecular Structure Corp.[37] All of the X-ray analytical data are deposited as Supporting Information.

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Supporting Information Available: X-ray crystallography data for compounds **4a**,**b**. This material is available free of charge via the Internet at http://pubs.acs.org.

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