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Cumulative Anomeric Effect: A Theoretical and X-ray Diffraction Study of Orthocarbonates

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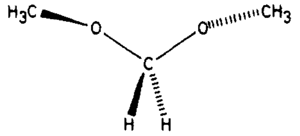
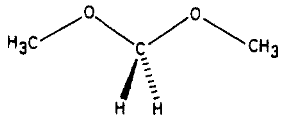
Abstract: The combined effect of six anomeric pair interactions at a single carbon atom has been examined by X-ray diffraction and molecular mechanics. MM2 calculations on $C(OR)_4$ (R = H, Me, Ph) indicate two closely spaced minima with S_4 and D_{2d} symmetry. An interesting low-energy pathway resembling a three-dimensional domino has been computed for the interconversion of the S_4 conformer to the D_{2d} form. Single-crystal X-ray structures determined for three $C(OAr)_4$ derivatives confirm that the energies of the two conformers do not differ significantly. Thus, the two crystallographically nonequivalent molecules in the unit cell of tetraphenoxymethane (**4**) as well as of tetrakis(3,5-dimethylphenoxy)methane (**5**) adopt conformations in which the central $C(OC)_4$ units have a near D_{2d} symmetry, while the corresponding fragment has a distorted S_4 symmetry in tetrakis(4-bromophenoxy)methane (**6**). The experimental C–O bond lengths and C–O–C and O–C–O angles are consistent with large anomeric interactions.

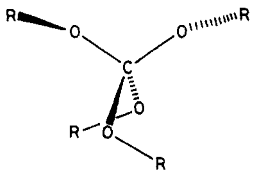
The importance of the anomeric effect in determining the structure, conformational energies, and reactivity in organic compounds is now widely appreciated.[1-7] While this stereoelectronic effect is quite a general phenomenon,[1,5-7] the anomeric effect at a saturated carbon attached to two oxygen atoms is particularly well documented.[1-4] Numerous crystal structures, especially those of carbohydrates,[3e,j,k] as well as empirical[4a] and quantum chemical calculations[1,4b,c,8] substantiate a well-defined conformational preference for R–O–C–O–R′ fragments. For example, in a simple model system, dimethoxymethane, the preferred conformation is the synclinal (+*sc*,+*sc* or –*sc*,–*sc*) geometry (**1a**), whereas the antiperiplanar (*ap*,*ap*) conformer (**1b**), also expected to be stable on purely torsional considerations, is higher in energy by 7.6 kcal/mol.[8] The C–O bond lengths as well as O–C–O bond angles also show a strong conformational dependence.[1,4a,8] The importance of lone-pair alignments in determining the reactivity of anomeric systems is borne out by the "antiperiplanar effect" in acetal and ortho ester hydrolysis.[1,2]



1a, C_2



1b, C_{2v}



2a, S_4

It is of considerable interest to study how these effects act in concert when more than two oxygen atoms are present at a single carbon. While bond length reductions due to multiple substitution by electronegative groups have been considered in detail,[6,9] systematic investigations on conformational preferences have not been carried out. Of particular interest are orthocarbonates, $C(OR)_4$, which contain the maximum possible number (six) of anomeric O–C–O pairs at a single carbon center.[10] These compounds may be expected to have conformational and structural features characteristic of multiple electronic interactions. In conformationally free orthocarbonates four R–O–C–O dihedral angles need to be specified to uniquely determine the conformation. Since there are three staggered orientations available for each O–R group, there are 81 torsionally ideal conformations, of which some are equivalent. However, unfavorable nonbonded contacts, dipole interactions, and anomeric interactions reduce the number of preferred conformations. In particular, if the consequence of anomeric interactions is extrapolated from relative energies of dimethoxymethane, only two distinct low-energy conformations need special consideration.[11] In one case, one R–O–C–O–R unit

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(1) Kirby, A. J. *The Anomeric Effect and Related Stereoelectronic Effects at Oxygen*; Springer-Verlag: Berlin, 1983.

(2) (a) Deslongchamps, P. *Stereoelectronic Effects in Organic Chemistry*; Pergamon: Oxford, 1983. (b) Szarek, W. A., Horton, D., Eds. *The Anomeric Effect: Origin and Consequences*; ACS Symposium Series 87; American Chemical Society: Washington, DC, 1979.

(3) For representative recent experimental studies, see: (a) Fuchs, B.; Ellencweig, A.; Tartakovsky, E.; Aped, P. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 287. (b) Anderson, J. E.; Heki, K.; Hirota, M.; Jorgensen, F. S. *J. Chem. Soc., Chem. Commun.* **1987**, 554. (c) Anet, F. A. L.; Kopelevich, M. *Ibid.* **1987**, 595. (d) Harcourt, M. P.; MoreO'Ferral, R. A. *Ibid.* **1987**, 823. (e) Cosse-Barbi, A; Dubois, J.-E. *J. Am. Chem. Soc.* **1987**, *109*, 1503. (f) Desilets, S.; St-Jacques M., *Ibid.* **1987**, *109*, 1641. (g) Praly, J.-P.; Lemieux, R. U. *Can. J. Chem.* **1987**, *65*, 213. (h) Penner, G. H.; Schaefer, T.; Sebastain, R.; Wolfe, S. *Ibid.* **1987**, *65*, 1845. (i) Chiang, C.-Y.; Butler, W.; Kuczkowski, R. *J. Chem. Soc., Chem. Commun.* **1988**, 465. (j) Cosse-Barbi, A.; Watson, D. G.; Dubois, J.-E. *Tetrahedron Lett.* **1989**, *30*, 163. (k) Dubois, J.-E.; Cosse-Barbi, A.; Watson, D. G. *Ibid.* **1989**, 30, 167.

(4) For representative recent theoretical work see: (a) Norskov-Lauritsen, L.; Allinger, N. L. *J. Comput. Chem.* **1984**, *5*, 326. (b) Schleyer, P. v. R.; Jemmis, E. D.; Spitznagel, G. W. *J. Am. Chem. Soc.* **1985**, *107*, 6393. (c) Aped, P.; Apeloig, Y.; Ellencweig, A.; Fuchs, B.; Goldberg, I.; Karni, M.; Tartakovsky, E. *Ibid.* **1987**, *109*, 1486.

(5) Reed, A. E.; Schade, C.; Schleyer, P. v. R.; Kamath, P. V.; Chandrasekhar, J. *J. Chem. Soc., Chem. Commun.* **1988**, *67*. Apeloig, Y.; Stanger, A. *J. Organomet. Chem.* **1988**, *346*, 305.

(6) Reed, A. E.; Schleyer, P. v. R. *J. Am. Chem. Soc.* **1987**, *109*, 7362.

(7) Shiner, C. S.; Grauer, C. M.; Haltiwanger, R. C. *J. Am. Chem. Soc.* **1985**, *107*, 7167.

(8) Jeffrey, G. A.; Pople, J. A.; Binkley, J. S.; Vishveshwara, S. *J. Am. Chem. Soc.* **1978**, *100*, 373.

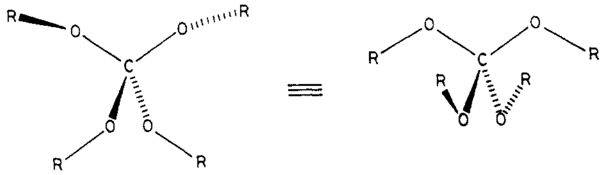
(9) (a) Patrick, C. R. *Adv. Fluorine Chem.* **1961**, *2*, 1. (b) Smart, B. E. *Molecular Structure and Energetics*; Liebman, J. F., Greenberg, A., Eds.; VCH: Deerfield Beach, FL, 1986; Vol. 3, p 141. (c) Lehn, J. M.; Wipff, G.; Bürgi, H. B. *Helv. Chim. Acta* **1974**, *57*, 493.

(10) For a few studies on the anomeric effect in orthoesters, see: (a) Banyard, S. H.; Dunitz, J. D. *Acta Crystallogr.* **1976**, *B32*, 318. (b) Lapasset, J.; Viani, R.; Bouab, O.; Lamaty, G.; Moreau, C. *Cryst. Struct. Commun.* **1980**, *9*, 1181. (c) Wroblewski, A. E.; Appelquist, J.; Takaya, A.; Honzatko, R.; Kim, S.-S.; Jacobsen, R. A.; Reitsma, B. H.; Yeung, E. S.; Verkade, J. G. *J. Am. Chem. Soc.* **1988**, *110*, 4144. Also see: Reference 3a.

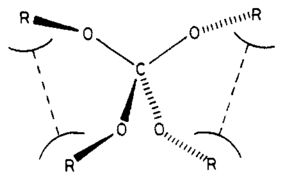
(11) (a) Mulhoff, F. C.; Geise, H. J.; van Schaick, E. J. M. *J. Mol. Struct.* **1973**, *20*, 393. (b) Ypenburg, J. W.; Gerding, H. *Recl. Trav. Chim. Pays-Bas* **1972**, *91*, 1245. (c) Lee, H.; Wilmhurst, J. K. *Spectrochim. Acta* **1967**, *23A*, 347.

0002-7863/90/1512-2937$02.50/0

has the (+*sc*,+*sc*) conformation while the other has the (−*sc*,−*sc*) orientation. This leads to the S_4 form (**2a**). Alternatively, two sets of R–O–C–O–R units adopt the (+*sc*,+*sc*) alignments. If the R–O–C–O dihedral angles are exactly 60°, the resulting conformation is a D_{2d} form (**2b**) or else it has D_2 symmetry (**2c**).



2b, D_{2d}



2c, D_2

Additional 1,5-nonbonded repulsions in the D_2 form may force the molecule to adopt perfect D_{2d} symmetry. Overall, the S_4 form contains two (+*sc*,+*sc*) anomeric pairs and four (+*sc*,*ap*) units. On the other hand, the D_{2d} conformer has four (+*sc*,+*sc*) fragments and two (*ap*,*ap*) units. By use of available ab initio relative energies of methanediol for these orientations and assuming additivity of anomeric interactions, D_{2d} was predicted to be 6 kcal/mol less stable than the S_4 conformer.[11a]

Available structural information on orthocarbonates is fragmentary. The only X-ray structure determination is that of the conformationally rigid spiroorthocarbonate (**3**).[12] Dielectric constant measurements seemed to indicate that $C(OPh)_4$ adopts an S_4 conformation in solution.[13] Electron diffraction studies on tetramethoxymethane in the gas phase also indicated predominance of the S_4 conformer.[11a] No appreciable amount of the alternative D_{2d} conformer was detected. However, variable-temperature Raman spectral data were interpreted in terms of a 90:10 mixture of S_4 and D_{2d} conformers, corresponding to an enthalpy difference of only 1 kcal/mol.[11b] An earlier interpretation of the spectra indicated the molecule to have a distorted S_4 symmetry. A recent ab initio study on $C(OH)_4$ also places the D_{2d} conformation only 2.4 kcal/mol above the S_4 conformation.[5]

In this paper we have combined theoretical and experimental investigations on the conformations of orthocarbonates. Detailed molecular mechanics calculations[14] have been carried out on model systems. The various minima and the barriers separating them have been characterised. The question of additivity of anomeric interactions has been probed by comparing calculated conformational energies with those extrapolated from the MM2[15] relative energies of dimethoxymethane. Crystal structures of three tetrakis(aryloxy)methanes (**4**–**6**) have also been determined. These represent the first X-ray structural determination of conformationally flexible orthocarbonates.

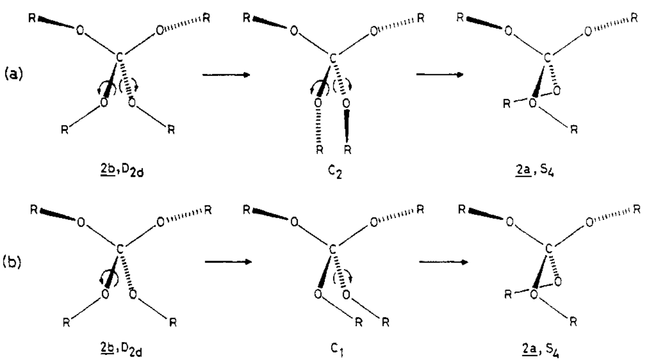


Figure 1. Least motion pathways for the interconversion of D_{2d} and S_4 conformers of orthocarbonates: (a) concerted rotation; (b) sequential rotation.

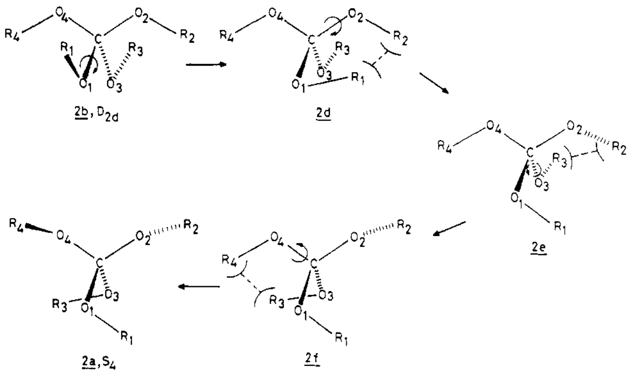


Figure 2. The three-dimensional domino pathway for the interconversion of D_{2d} and S_4 conformers of orthocarbonates.

Computational Results

Calculated Minima. For the three orthocarbonates studied, $C(OR)_4$ (R = H, Me, and Ph), MM2 calculations[15] predict two minima with S_4 and D_{2d} symmetry, in agreement with the earlier analysis. Geometry optimization from several initial coordinates consistently led to one of these two minima. In particular, D_2 geometries collapsed to more symmetric D_{2d} structures. While the S_4 conformer is more stable in each case, the D_{2d} form is found to be only slightly higher in energy. The calculated energy difference for $C(OH)_4$ (1.4 kcal/mol) compares favorably with the corresponding value computed at the 6-31G* level (2.4 kcal/mol).[5] In contrast, the value for $C(OMe)_4$ (1.2 kcal/mol) is much smaller than that estimated eariler (6 kcal/mol).[11a] The latter value was obtained from ab initio relative energies of methanediol assuming additivity of anomeric pair interactions. The discrepancy is significantly reduced if higher level (6-31G*) data are used.[8] The S_4 conformer of $C(OMe)_4$ would then be predicted to be more stable than the D_{2d} form by only 2.7 kcal/mol. The calculated relative energy (2.7 kcal/mol) for the phenyl derivative would again suggest that both S_4 and D_{2d} conformers of tetrakis(aryloxy)methanes should be experimentally accessible.

Interconversion of D_{2d} and S_4 Conformers. The process of converting D_{2d} to an S_4 conformation can be viewed as involving the rotation of two OR groups from an initial (+*sc*,+*sc*) orientation to a (−*sc*,−*sc*) orientation. The least motion pathway (Figure 1a) must go through a high-energy C_2 conformer calculated to be 17.8 kcal/mol above the D_{2d} conformer for $C(OMe)_4$. A concerted rotation of two dihedral angles will also be unfavorable entropically. A stepwise rotation is more likely (Figure 1b). MM2 calculations using a pair of sequential dihedral drives involving two OMe groups for tetramethoxymethane indicate a barrier of at least 8.5 kcal/mol for this pathway, which goes by a conformation in which one R–O–C–O–R unit has a (+sc,−*sc*) orientation (local C_s symmetry) while the other R–O–C–O–R unit has a favorable (+*sc*,+*sc*) orientation (local C_2 symmetry).

An alternative non-least-motion pathway for the D_{2d} to S_4 interconversion, involving the realignment of all four OR groups sequentially is conceivable (Figure 2). This is best visualized with

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(12) Meyer, H.; Nagorsen, G. *Angew. Chem., Intl. Ed. Engl.* **1979**, *18*, 551.

(13) Pigenet, C.; Jeminet, G.; Lumbroso, H. *C. R. Acad. Sci., Ser. C* **1969**, *269*, 1587; *Chem. Abstr.* **1970**, *72*, 89648z.

(14) Burkert, U.; Allinger, N. L. *Molecular Mechanics*; ACS Monograph Series 177; American Chemical Society: Washington, DC, 1982.

(15) Allinger, N. L.; *J. Am. Chem. Soc.* **1977**, *99*, 8127. The original version of the MM2 program [MM2(80)], available from the Quantum Chemistry Program Exchange, Indiana University, Bloomington, IN 47401, was used. The revised parameters for treating the anomeric effect[4a] were not included. As a result, the computed structrual features (especially C–O bond lengths) may be in error, but the computed energetics are not likely to be affected.[4a] This claim has been confirmed by a reviewer for $C(OMe)_4$ using the MM2(85) program.[4a] We thank the reviewer for this valuable input. As further suggested by the reviewer, we plan to carry out a molecular dynamics simulation of the three-dimensional domino process.

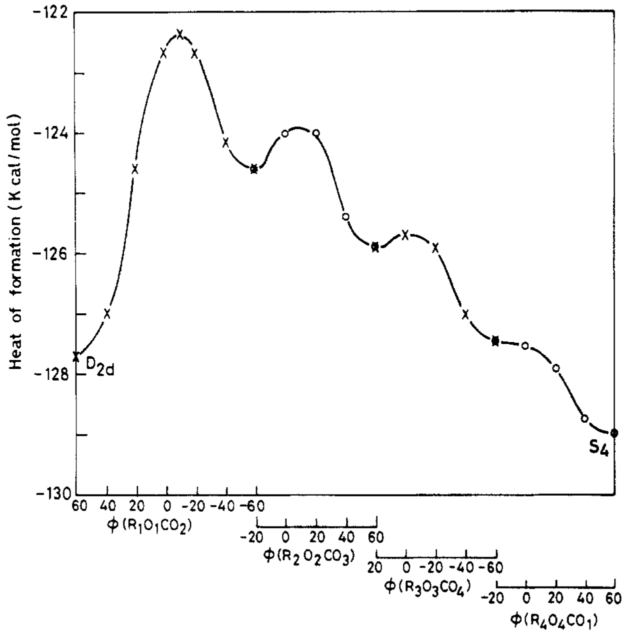

Figure 3. The calculated (MM2) potential energy profile for the three-dimensional domino pathway for the interconversion of D_{2d} and S_4 conformers of tetramethoxymethane.

models. Starting from the D_{2d} conformer, rotation of any one of the OR groups, say O_1R_1, in a clockwise direction (looking down the O–C bond) would bring the R_1 group in close proximity to the adjacent group R_2 (**2d**). This will result in an anticlockwise rotation of O_2R_2 bringing R_2 close to R_3 (**2e**). This sets O_3R_3 in a clockwise motion until at a certain point it sets O_4R_4 in a counterclockwise motion (**2f**). Thus, when all four OR groups have moved by a small amount, one obtains the S_4 conformer (**2a**). MM2 calculations on tetramethoxymethane confirm that the above process is indeed the preferred pathway for the D_{2d} to S_4 interconversion. The potential energy diagram computed for such a pathway is shown in Figure 3. Each segment shows the total energy as a function of a different dihedral angle. As the dihedral angle $R_1O_1CO_2$ is changed from its initial 60° value corresponding to the D_{2d} form, the energy reaches a maximum at the local eclipsed conformation (Figure 3). This structure is 5.4 kcal/mol above the D_{2d} form and is the highest energy conformer in the entire pathway. The energy drops as the O_1R_1 group again attains the staggered conformation. At this point the O_2R_2 group turns significantly away to minimize repulsions with the O_1R_1 group. The dihedral angle $R_2O_2CO_3$, which is −20°, increases to 0°, for which a small price of 0.7 kcal/mol is paid. The change in this dihedral angle from 0° to 60° is a downhill process. However, when it is near 60°, R_2 bumps into R_3 and starts a decrease in the $R_3O_3CO_4$ dihedral angle. The change in this dihedral from +20° to −60° costs even less, a mere 0.2 kcal/mol! The subsequent change in R_4O_4CO to reach the S_4 conformer requires no additional activation. This whole process may be visualized as a three-dimensional domino: after an initial "thrust" of one of the OMe groups in the required direction, additional rotations are generated sequentially by steric interactions. The potential energy profile is a smooth cascade after the first rotation; the energy required for the first dihedral drive corresponds to the overall activation energy for the entire process. Thus, only 5.4 kcal/mol is required for this D_{2d}–S_4 interconversion pathway compared to 8.5 and 17.8 kcal/mol computed for the alternatives considered above.

Attempts to freeze the conformational dynamics were made by studying the temperature dependence of the ^{1}H NMR spectrum of tetrakis(3,5-dimethylphenoxy)methane. No significant spectral changes were observed down to 210 K. This result is consistent with the calculated barrier (5.4 kcal/mol) for the S_4–D_{2d} conformational interconversion. However, it should be possible to observe such a process at lower temperatures[16] or with the use of different substituents. Alternative techniques, especially ultrasonic relaxation studies,[17] might enable the detection of conformational processes involving such relatively small barriers.

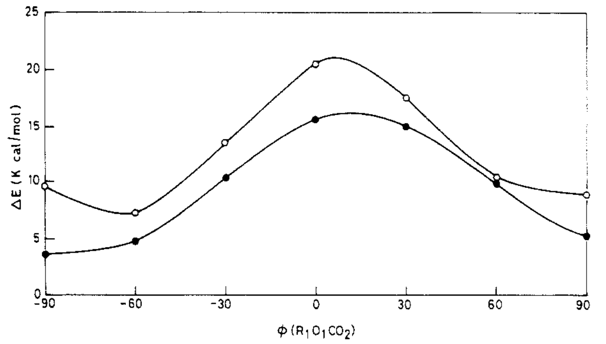

Figure 4. A typical cross section of the conformational potential energy surface of tetramethoxymethane calculated by the MM2 method (●) and by extrapolating from the energies of dimethoxymethane assuming additivity of pairwise anomeric interactions (○).

The three-dimensional domino process in $C(OR)_4$ molecules represents another intriguing example of correlated conformational dynamics. Iwamura and Mislow have ingeniously constructed several molecules in which torsional motions of two or more internal rotors are coupled.[18] However, unlike these latter systems, the correlated conformational process in orthocarbonates do not involve gearing of the rotors.

Additivity of Anomeric Interactions. Can the conformational energies of orthocarbonates be predicted from six pairwise additive anomeric interactions? This question was probed in detail by using MM2 data on the conformational surfaces of $C(OMe)_4$ and $CH_2(OMe)_2$.

An empirical potential function, given by (1) and (2), describing the anomeric and steric interactions of an R–O–C–O–R fragment

$$V(\phi) = \tfrac{1}{2}V_1(1 + \cos\phi) + \tfrac{1}{2}V_2(1 - \cos 2\phi) + \tfrac{1}{2}V_3(1 + \cos 3\phi) \quad (1)$$

$$V(\phi,\phi') = V_0 + V(\phi) + V(\phi') + A\exp(-Br_{15}^2) \quad (2)$$

was first obtained, which reproduces the MM2 surface of $CH_2(OMe)_2$. The form of the function is similar to that employed by Jorgensen and Ibrahim for representing the conformational energies of diethyl ether.[19] A nonlinear least-squares procedure was used to obtain a fit against 169 representative points on the conformational surface (V_0 = 2.93; V_1 = −0.77; V_2 = −2.05; V_3 = 1.93; A = 37.60; B = 0.24; SD = 0.1; B in Å^{-5}, all other values in kcal/mol). As in the earlier work,[19] the methyl–methyl distances (r_{15}) were determined from rigid rotation of the equilibrium geometry and differ somewhat from the values in the MM2 calculations. The conformational energies for $C(OMe)_4$ were then computed by assuming additivity of the six R–O–C–O–R interactions and using eq 2 for each pair. A typical cross section of the surface computed by the MM2 method and the additivity model is shown in Figure 4. The general trends in the MM2 energies are correctly reproduced by the simple model, although the latter values are consistently smaller. While the additivity approximation is reasonable, the true conformational surface is flatter.[20]

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(16) Processes involving a barrier of 6 kcal/mol begin to produce line broadening in ^{1}H NMR spectra (270 MHz) roughly below 150 K. For a typical example, see: Ernst, C. A.; Allred, A. L.; Ratner, M. A. *J. Organomet. Chem.* **1979**, *178*, 119.

(17) Walker, S. M. In *Internal Rotation in Molecules*; Orville-Thomas, W. J., Ed.; John Wiley: New York, 1974 and other chapters in this book.

(18) Iwamura, H.; Mislow, K. *Acc. Chem. Res.* **1988**, *21*, 175.

(19) Jorgensen, W. L.; Ibrahim, M. *J. Am. Chem. Soc.* **1981**, *103*, 3976.

(20) If anomeric interaction is present only when a p-type lone pair on oxygen is roughly parallel to an adjacent C–O σ* orbital, the additivity approximation is justified. However, stabilizing interactions are possible in orthocarbonates even when a lone pair is perpendicular to an adjacent C–O bond; in this orientation the lone pair can interact with the antisymmetric combination of the remaining two C–O σ* orbitals. Therefore the conformational surface is flatter than anticipated on simple additivity grounds.

Table I. Key Torsion Angles (in Degrees) of **4–6**

	4		**5**		
	a	**b**	**a**	**b**	**6**
C(11)-O(1)-C(1)-O(2)	-66.5 (2)	-64.0 (2)	-51.0 (5)	51.1 (5)	64 (4)
C(21)-O(2)-C(1)-O(1)	-51.6 (3)	-44.4 (3)	-60.4 (5)	51.1 (5)	87 (4)
C(31)-O(3)-C(1)-O(4)	-66.5 (2)	-64.0 (3)	-47.6 (5)	47.9 (5)	-52 (4)
C(41)-O(3)-C(1)-O(3)	-51.6 (3)	-44.4 (3)	-51.6 (5)	66.0 (5)	-95 (3)
C(11)-O(1)-C(1)-O(3)	171.5 (2)	173.6 (2)	-173.0 (5)	173.6 (5)	-50 (4)
C(21)-O(2)-C(1)-O(4)	-174.7 (2)	-166.9 (2)	-177.6 (5)	-169.1 (5)	-45 (4)
C(31)-O(3)-C(1)-O(1)	171.5 (2)	173.6 (2)	172.3 (5)	172.1 (5)	-170 (3)
C(41)-O(4)-C(1)-O(2)	171.5 (2)	-166.9 (2)	-177.0 (5)	-170.1 (5)	142 (3)

Table II. Key Bond Angles (in Degrees) of **4–6**

	O–C–O (*sc*,*sc*)				O–C–O (*ap*,*ap*)		
	1	2	3	4	5	6	av
4a	113.5 (2)	114.0 (2)	113.5 (2)[a]	114.0 (2)[a]	102.0 (2)	100.4 (2)	109.6 (1)
4b	113.7 (2)	113.6 (2)	113.7 (2)[a]	116.2 (2)[a]	101.0 (2)	101.4 (2)	109.6 (1)
5a	113.6 (4)	113.0 (4)	114.9 (4)	114.5 (5)	102.2 (4)	99.3 (4)	109.6 (2)
5b	110.8 (5)	116.4 (5)	115.2 (6)	116.3 (5)	100.9 (5)	102.7 (5)	110.4 (2)
6	116 (3)	110 (3)	111 (3)	114 (3)	111 (3)	93 (3)	109 (1)

[a] Values are related by 2-fold axis.

Experimental Results

Single-crystal X-ray structures of three orthocarbonates, tetraphenoxymethane (**4**), tetrakis(3,5-dimethylphenoxy)methane (**5**), and tetrakis(4-bromophenoxy)methane (**6**), were solved by direct methods.[21] The refinements could be carried out to desirable precision for **4** and **5** (*R* index of 0.042 and 0.063, respectively). However, due to rapid deterioration of crystals during data collection for the bromo derivative, **6**, the corresponding *R* index was much higher (0.118).

Structures **4** and **5** have two independent molecules in the asymmetric part of the unit cell. These are denoted by **4a**,**4b** and **5a**,**5b**, respectively. It is interesting that all four molecules, **4a–5b**, have a near-D_{2d} symmetry about the central $C(OC)_4$ unit[22] (Figures 5 and 6). Two sets of C–O–C–O units have torsion angles corresponding approximately to the (+*sc*,+*sc*) conformation, while two others resemble the (*ap*,*ap*) alignment. Thus, the C–O–C–O dihedral angles involving C(11)–O(1)–C(1)–O(2)–C(21) and C(31)–O(3)–C(1)–O(4)–C(41) units are close to 60°, whereas the corresponding angles involving C(11)–O(1)–C(1)–O(3)–C(31) and C(21)–O(2)–C(1)–O(4)–C(41) fragments are approximately 180° (Table I). In contrast, the structure of **6** corresponds to a distorted S_4 symmetry about its central $C(OC)_4$ unit on the basis of its C–O–C–O dihedral angles (Table I). However, the deviations from ideal torsional angles are considerably higher in **6** than in the case of the D_{2d} forms **4a–5b**. In **6**, the torsion angles for the C(11)–O(1)–C(1)–O(2)–C(21) unit correspond to a (+*sc*,+*sc*) arrangement, while those of the C(31)–O(3)–C(1)–O(4)–C(41) fragment correspond to a (–*sc*,–*sc*) alignment. These dihedral angles are rather similar to those observed in tetrakis(thiophenoxy)methane[23] and tetrakis(thiomethoxy)methane.[24] These results confirm that the energy difference between S_4 and D_{2d} conformers in orthocarbonates is indeed small and of the order of crystal-packing energies. Thus, both forms are experimentally accessible in the solid state. The flatness of the potential energy surface is further borne out by

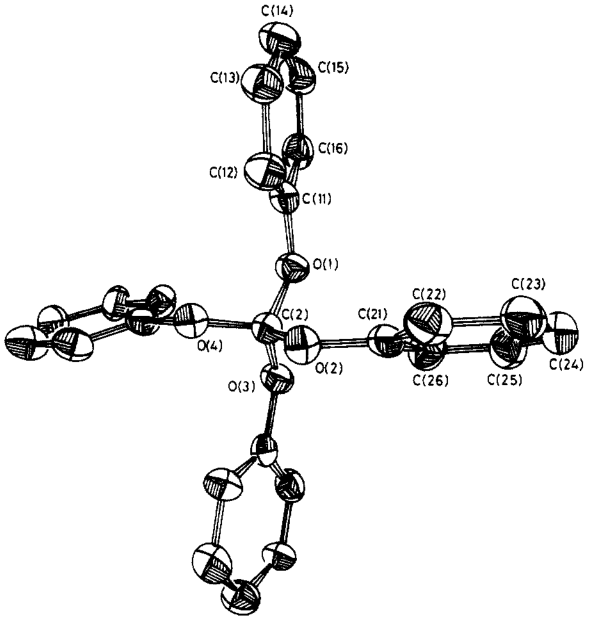

Figure 5. ORTEP drawing of the crystallographically determined structure of **4b**.

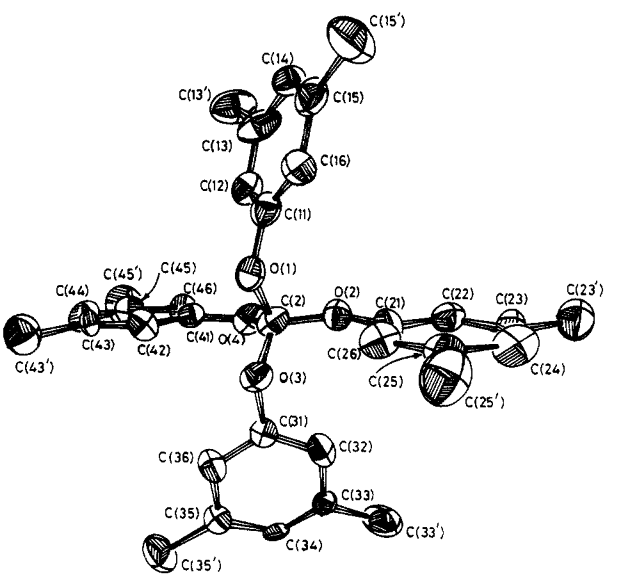

Figure 6. ORTEP drawing of the crystallographically determined structure of **5b**.

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(21) (a) SHELX86: Sheldrick, G. M. *Program for crystal structure solution*, University of Gottingen, 1986. (b) SHELX76: Sheldrick, G. M. *Program for crystal structure determination and refinement*, University of Cambridge, 1976. (c) SFLS: Shiono, R. *A block diagonal least squares program for the IBM 1130 computer*, University of Pittsburgh, 1960. (d) MULTAN80: *A system of computer programs for the automatic solution of crystal structures from X-ray diffraction data*, University of York, U.K., and University of Louvain, Belgium.

(22) The orientations of the phenyl rings are mainly responsible for the loss of ideal D_{2d} and S_4 symmetry in **4–6**.

(23) Kato, v. K. *Acta Crystallogr.* **1972**, *B28*, 606.

(24) Perdok, W. G.; Terpstra, P. *Recl. Trav. Chim. Pays-Bas* **1943**, *62*, 687; **1946**, *65*, 493.

Table III. Key Bond Lengths (in Angstroms) of **4–6**

	inner C–O				outer C–O				average	
	1	2	3	4	5	6	7	8	I(C–O)	O(C–O)
4a	1.391 (3)	1.396 (3)	1.391 (3)[a]	1.396 (3)[a]	1.412 (2)	1.415 (3)	1.412 (2)[a]	1.415 (2)[a]	1.395 (2)	1.414 (1)
4b	1.389 (3)	1.391 (3)	1.389 (3)[a]	1.391 (3)[a]	1.407 (3)	1.407 (3)	1.407 (3)[a]	1.407 (3)[a]	1.390 (2)	1.407 (2)
5a	1.364 (6)	1.394 (8)	1.417 (6)	1.392 (8)	1.420 (8)	1.374 (8)	1.412 (8)	1.453 (8)	1.392 (4)	1.415 (4)
5b	1.424 (8)	1.407 (9)	1.378 (8)	1.395 (8)	1.427 (8)	1.430 (8)	1.416 (8)	1.358 (8)	1.401 (4)	1.408 (4)
6	1.33 (5)	1.33 (4)	1.39 (4)	1.29 (5)	1.49 (5)	1.35 (4)	1.68 (6)	1.70 (6)	1.35 (2)	1.56 (2)

[a] Values are related by 2-fold axis.

Table IV. Details of Data Collection and Refinement

	4	**5**	**6**
crystal size, mm	0.2 × 0.15 × 0.15	0.22 × 0.13 × 0.1	0.3 × 0.2 × 0.1
range of measd reflcns	$0 \le h \le 14$, $-21 \le k \le 21$, $-16 \le l \le 16$	$0 \le h \le 9$, $0 \le k \le 18$, $0 \le l \le 43$	$0 \le h \le 11$, $-12 \le k \le 12$, $-13 \le l \le 13$
scan type	$\omega-2\theta$	ω	$\omega-2\theta$
2θ range, deg	2.0–50.0	2.0–46.0	2.0–46.0
no. of measd reflcns	5200	4500	3600
no. of obsd reflcns	2270	2664	1506
obsvn criterion	$I \ge 2.5\sigma(I)$	$I \ge 2.5\sigma(I)$	$I \ge 4\sigma(I)$
R_{int}	0.021	0.027	0.073
weighting	unit	σ	σ
(shift/esd)max	<0.1	<0.1	<0.5
no. of variables	350	666	153
$R(F)$	0.042	0.063	0.118
$R_w(F)$		0.065	0.137

the fact that two molecules in the same crystal have two slightly different sets of torsional angles for **4** and **5**.

The central O–C–O bond angles in **4a–5b** show an interesting pattern: four of these (average 114°) are significantly greater than the ideal tetrahedral value while the remaining two (average 104°) are smaller (Table II). The larger values involve atoms having the (*sc*,*sc*) conformation. On the other hand, the smaller angles correspond to the (*ap*,*ap*) units. Identical trends in bond angles are found in the (*sc*,*sc*) and (*ap*,*ap*) conformers of dimethoxymethane also.[4a,25] These angle deformations have been attributed to nonbonded interactions.[4a,26] The transferability of these effects from dimethoxymethane to tetrakis(aryloxy)methane is indeed remarkable. The geometry about the central carbon in orthocarbonates seems to be determined by a simple sum of six independent anomeric pair interactions.

Further evidence for the presence of cumulative anomeric effect in orthocarbonates is provided by the "inner" (C_{alkyl}–*O*) and "outer" (C_{aryl}–O) C–O bond lengths. In agreement with the earlier electron diffraction study on tetramethoxymethane,[11a] the inner C–O bonds are consistently shorter in all the structures determined in this study (Table III). This result is all the more remarkable in the tetrakis(aryloxy)methanes because the outer bonds involve sp^2 carbon atoms. The average inner and outer C–O bond lengths obtained from 212 crystal structures of anisoles surveyed through the Cambridge Crystallography Database are 1.415 (16) and 1.371 (15) Å, respectively.[27] The trend is reversed in the tetrakis(aryloxy)methanes. The shortening of the inner bonds is a combination of the electronegativity effect due to multiple oxygen substitution[9c] and the anomeric effect. The lengthening of the outer bonds clearly indicates that the π lone pair on each of the oxygen atoms is used for negative hyperconjugation with adjacent C–O σ^* orbitals rather than for conjugation with the phenyl ring. Consistent with these interpretations, the outer C–S bonds are significantly shorter than the inner ones in tetrakis(thiophenoxy)methane[23] and tetrakis(thiomethoxy)methane.[24] The anomeric effect involving two sulfur atoms has been established to be negligible,[4b] and hence, conjugation with the phenyl ring is the dominant electronic effect in this molecule.

Conclusions

While the anomeric effect is generally associated with strong conformational preferences, the cumulative anomeric effect due to four oxygen substituents at a single saturated carbon leads to a relatively flat conformational energy surface. Both S_4 and D_{2d} structures for orthocarbonates are computed to be energetically accessible minima with a small energy difference. X-ray diffraction studies on three tetrakis(aryloxy)methanes provide confirmation: tetraphenoxymethane and tetrakis(3,5-dimethylphenoxy)methane adopt approximately D_{2d} geometries while a distorted S_4 structure is found for tetrakis(4-bromophenoxy)methane. The presence of multiple anomeric interactions is evident in the observed bond lengths and angles.

The conformational energies of orthocarbonates may be predicted reasonably well by a sum of six pairwise anomeric interactions. The additivity hypothesis is supported by the experimental O–C–O bond angles, which follow the same conformational dependence as found in simple model systems.

A novel correlated torsional motion, best visualized as a three-dimensional domino, is suggested to be involved in the interconversion of D_{2d} and S_4 minima of orthocarbonates.

Experimental Section

Compounds **4–6** were prepared according to literature procedures.[28] Three-dimensional intensity data were collected on an Enraf Nonius CAD-4 diffractometer with graphite-monochromated Mo Kα (0.7107 Å) radiation. Control reflections monitored at 1-h intervals showed only statistical fluctuations in the intensity for **4** and **5**, while **6** showed a decrease in intensity as the crystal was found to be unstable to X-rays. Four crystals were needed to complete the data collection. Routine intensity data reduction was applied for all three crystals. The data for **6** were averaged to a common scale. The structures were solved by direct methods.[21] Non-hydrogens were refined anisotropically and hydrogens isotropically in the case of **4**. In **5**, hydrogens were included only for structure factor calculation and not refined because of parameter limitations in both SHELX76 and *SFLS* programs.[21] In **6**, the hydrogens were not included. The refinements converged at *R* values of 0.042, 0.063, and 0.118 for compounds **4**, **5**, and **6**, respectively.

Crystal data. **4**: $C_{25}H_{20}O_4$; MW 384.4; mp 99–100 °C; monoclinic; space group $I2/c$; a = 14.816 (1), b = 19.505 (1), c = 13.308 (1) Å; β = 90.36 (2)°; V = 3851.5 Å^3; D_{measd} = 1.32, D_{calcd} = 1.330 g cm^{-3}; Z = 8; $F(000)$ = 1616. **5**: $C_{33}H_{36}O_4$; MW 496.6; mp 156–157 °C; orthorhombic; space group $Pbn2_1$; a = 8.314 (7), b = 16.929 (3), c = 39.797 (4) Å; V = 5601.3 Å^3; D_{measd} = 1.18, D_{calcd} = 1.178 g cm^{-3}; Z = 8; $F(000)$ = 2128. **6**: $C_{25}H_{16}O_4Br_4$; MW 700.0; mp 139–140 °C; space group $P\bar{1}$; a = 10.221 (1), b = 11.100 (1), c = 11.944 (2) Å; α = 71.87 (2), β = 103.93 (2), γ = 101.37 (2)°; V = 1239.9 Å^3; D_{measd} = 1.87, D_{calcd} = 1.874 g cm^{-3}; Z = 2; $F(000)$ = 676. Other details are given in Table IV.

Supplementary Material Available: Twelve tables listing final fractional atomic coordinates, isotropic temperature factors, bond lengths, and bond angles involving non-hydrogen atoms of **4a**, **4b**, **5a**, **5b**, and **6** (9 pages). Ordering information is given on any current masthead page.

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(25) Astrup, E. E. *Acta Chem. Scand.* **1973**, *27*, 3271.

(26) Gorenstein, D. G.; Findlay, J. B.; Luxon, B. A.; Kar, D. *J. Am. Chem. Soc.* **1977**, *99*, 3473. Gorenstein, D. G.; Kar, D. *Ibid.* **1977**, *99*, 672.

(27) Nyburg, S. C.; Faerman, C. H. *J. Mol. Struct.* **1986**, *140*, 347.

(28) Narasimhamurthy, N.; Samuelson, A. G. *Tetrahedron Lett.* **1986**, *27*, 991.