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Alkyl Group Effect on the Conformational Isomerism of *trans*-2-Bromoalkoxycyclohexanes Analyzed by NMR Spectroscopy and Theoretical Calculations

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Ⓢ Supporting Information

ABSTRACT: Suitable $^3J_{H,H}$ coupling constants and theoretical calculations were used to define the conformational preferences of *trans*-2-bromoalkoxycyclohexanes (alkoxy = OMe, OEt, O^{i}Pr, and O^{t}Bu) for the isolated molecule and as a function of the medium. The diaxial conformer was preponderant, or at least similarly populated to the diequatorial form, for the *tert*-butoxy derivative only, while the diequatorial conformer was prevalent for the remaining alkoxy derivatives (except for the OMe derivative in CCl$_4$ solution). The conformational behavior of these compounds was analyzed on the basis of classical steric effects and attractive electron delocalizations, by means of natural bond orbital analysis.
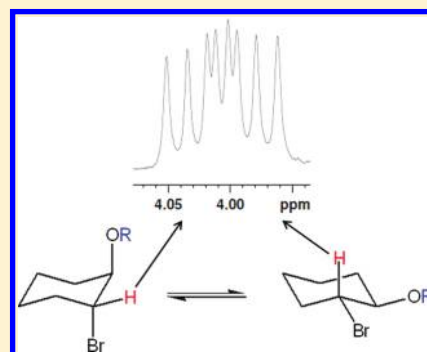
1. INTRODUCTION

The intramolecular hydrogen bond has been shown to play a determinant role in the conformational isomerism of *trans*-2-bromocyclohexanol, both in the vapor phase and in solution.[1−3] The diequatorial preference for *trans*-2-bromocyclohexanol with the hydroxyl group directed toward the bromine atom seems to be preferred to those in which the hydroxyl group is not directed toward the halogen due to intramolecular hydrogen bonding, in addition to the repulsive interaction between oxygen lone pairs and bromine (dipolar repulsion).[2] The replacement of the hydroxyl group in *trans*-2-bromocyclohexanol by a methoxy group increases the population of the diaxial conformer, possibly because the intramolecular hydrogen bonding as a stabilizing force of the diequatorial form disappears.[2]

Abraham et al.[4] have studied the conformational isomerism of *trans*-2-fluorocyclohexanol and its methyl ether, and they found that OH···F hydrogen bonding in the fluorohydrin governs its conformational isomerism, while the OMe···F attractive interaction does not occur. Therefore, the conformational isomerism of *trans*-2-bromoalkoxycyclohexanes may be ruled by classical steric and electrostatic effects, in addition to hyperconjugative interactions. However, conformer populations and their dependence with the size of the alkoxy groups have been systematically analyzed by nuclear magnetic resonance (by means of the well-known coupling constant approach[2]) and theoretical calculations (particularly using natural bond orbital (NBO) analysis[5]) only in a few cases.[6] Therefore, the study of the series methoxy, ethoxy,

isopropoxy, and *tert*-butoxy groups in *trans*-2-bromoalkoxycyclohexanes (Figure 1) is of interest.

Conformations of alkoxycyclohexanes have been carefully analyzed by Kleinpeter and Thielemann[7] (with references for the methoxycyclohexane therein), who found that steric effects, followed by hyperconjugation and transannular electrostatic interactions (for 1,4-dialkoxycyclohexanes), govern the preference for the equatorial (or diequatorial) conformation. Moreover, the increasing volume of the alkoxy substituent was found to destabilize the axial conformer. The data for the monosubstituted alkoxycyclohexanes can be used to evaluate the effect of bromine on the conformational isomerism of the titled compounds.

2. EXPERIMENTAL SECTION

2.1. Syntheses. The *trans*-2-bromoalkoxycyclohexanes were prepared by the reaction of cyclohexene using *N,N*-dibromotoluenesulfonamide (TsNBr$_2$) as the bromine source, and the corresponding alcohol (ethanol, isopropyl alcohol, and *tert*-butyl alcohol), according to the procedure described in the literature.[8] Data for the methoxy derivative was already available in the literature.[2]
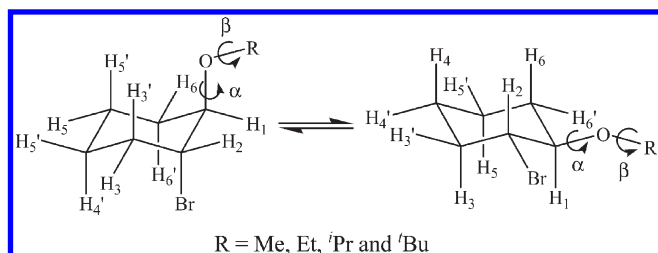
Figure 1. Conformational equilibrium of *trans*-2-bromoalkoxycyclohexanes.

TsNBr$_2$ (1.2 mmol) was added to a solution of cyclohexene (1.1 mmol) in 5 mL of the corresponding alcohol at room temperature. The TsNBr$_2$ color disappears immediately. After the complete reaction (ca. 10 min), about 200 mg of sodium thiosulfate was added and the reaction mixture was stirred for 20 min. Thus, the reaction mixture was taken up in ether, washed with brine, dried with sodium sulfate, and concentrated. The pure products were obtained by carrying out purification with flash chromatography on silica gel (230−400 mesh) using petroleum ether−EtOAc (5%) as eluent.

2.2. NMR Experiments. The solvents were commercially available and used without further purification. ^{1}H NMR spectra were recorded on a spectrometer equipped with 5 mm probe operating at 250.1 MHz or with a 5 mm *z*-gradient probe operating at 300.13 MHz for ^{1}H and 75.4 MHz for ^{13}C. Typical conditions for ^{1}H spectra were as follows: eight transients, spectral width 3600 Hz with 64 000 data points, giving an acquisition time of 9.08 s and zero filling up to 128 000. The spectra resolution is 0.1 Hz. The assignment for the methoxy derivative is already known,[2] while the assignments for the remaining compounds are given as follows, using ^{1}H−^{13}C gHSQC spectra to support assignments:

trans-2-Bromoethoxycyclohexane: (C$_6$D$_6$, 300.13 MHz), δ 1.15 (3H, t, 7.1, CH$_3$), 1.31 (3H, m, H$_4$, H$_5$, H$_6$), 1.61 (3H, m, H$_3$, H$_{4'}$, H$_{5'}$), 1.98 (1H, m, H$_{6'}$), 2.23 (1H, m, H$_{3'}$), 3.27 (2H, m, CH$_2$), 3.51 (1H, m, H$_1$), 3.94 (1H, ddd, 9.0, 8.0, 4.0, H$_2$).

trans-2-Bromoisopropoxycyclohexane: (C$_6$D$_6$, 250.13 MHz), δ 1.10 (3H, d, 6.1, CH$_3$), 1.14 (3H, d, 6.1, CH$_3$), 1.30 (3H, m, H$_4$, H$_5$, H$_6$), 1.70 (3H, m, H$_3$, H$_{4'}$, H$_{5'}$), 1.97 (1H, m, H$_{6'}$), 2.27 (1H, m, H$_{3'}$), 3.32 (1H, ddd, 8.3, 8.0, 3.9, H$_1$), 3.80 (1H, sep, 6.1, OCH), 3.93 (1H, ddd, 9.5, 8.0, 4.2, H$_2$).

trans-2-Bromo-*tert*-butoxycyclohexane: (C$_6$D$_6$, 300.13 MHz), δ 1.05 (9H, s, (CH$_3$)$_3$), 1.21 (3H, m, H$_4$, H$_5$, H$_6$), 1.54 (3H, m, H$_3$, H$_{4'}$, H$_{5'}$), 1.71 (1H, m, H$_{6'}$), 2.10 (1H, m, H$_{3'}$), 3.57 (1H, ddd, 6.3, 6.0, 3.9, H$_1$), 3.97 (1H, ddd, 8.1, 6.7, 3.8, H$_2$).

2.3. Theoretical Calculations. Stable conformers were identified by locating the energy minima in the two-dimensional (for methoxy and *tert*-butoxy derivatives) and three-dimensional (for ethoxy and isopropoxy derivatives) potential energy surfaces, built by means of semiempirical AM1 calculations. Each minimum was subsequently optimized at the B3LYP/aug-cc-pVDZ level, as well as the NBO calculations.[4] The coupling constant calculations were carried out at the B3LYP method and EPR-III (for C and H) and aug-cc-pVDZ (for O and Br) basis sets. All calculations were performed using the Gaussian 03 package of programs.[9]

3. RESULTS AND DISCUSSION

For *trans*-2-bromocyclohexanol, the diequatorial preference in nonpolar solution and for the isolated molecule has been
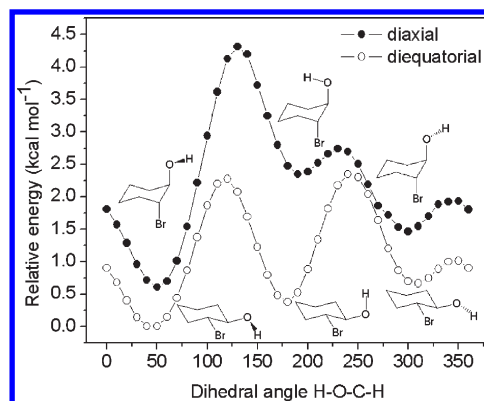

Figure 2. Potential energy surfaces for *trans*-2-bromocyclohexanol, obtained at the B3LYP/6-31g(d,p) level and using the implicit, Onsager model to account for the solvation effect of acetonitrile. The conformer structures are positioned close to the respective minimum.

attributed to intramolecular hydrogen bonding OH···Br.[1,3] This interpretation was reanalyzed according to the results of new theoretical calculations, as follows.

Thus, the predominance of the diequatorial form with the hydroxyl hydrogen directed toward the bromine atom instead of the other two diequatorial possibilities could also be explained by their dipolar interaction, involving the oxygen lone pairs and bromine. In order to attest that intramolecular hydrogen bonding is really operating in *trans*-2-bromocyclohexanol, the energetic profile of the rotation around the OH bond was computationally evaluated using the Onsager implicit model to account for the effect of acetonitrile. Since specific interactions between solute and solvent molecules do not take place in this case, implicit solvation models can describe with a good precision the behavior of molecules in solution. In this highly polar solvent, repulsive, intramolecular electrostatic interactions are expected to be reduced significantly, but even under this condition, the diequatorial conformer with OH directed toward Br is the most stable one, while the remaining diequatorial forms become, in general, more stable than the diaxial conformers (Figure 2). However, when the hydroxyl group in *trans*-2-halocyclohexanol is replaced by alkoxy groups, the conformational behavior is expected to change, both due to the nonexistence of intramolecular hydrogen bonds and due to the difference in substituent sizes, as discussed below.

The *trans*-2-bromoalkoxycyclohexanes have torsional angles (α and β in Figure 1) which may give rise to a series of rotamers to each of the chairlike diaxial and diequatorial conformers. In order to find out all possible minima for these compounds, two- and three-dimensional potential energy surfaces (PES) were built using the semiempirical AM1 method (see the Supporting Information); each minimum was then optimized at the DFT/B3LYP/aug-cc-pVDZ level, as shown in Figure 3. The calculation results indicate that, among the several rotamers obtained, the diequatorial form is prevalent for the OMe, OEt, and O^{i}Pr derivatives in the isolated state; for the O^{t}Bu derivative, in which only one rotamer was found for each diaxial and diequatorial form, the diaxial conformation is preferred (Table 1).

For the neat liquid, conformer populations obtained by means of infrared band intensities have shown congruent behavior to theoretical results for the isolated state.[10] Nevertheless, the conformational dependence with solvents has not been evaluated yet for the series of *trans*-2-bromoalkoxycyclohexanes, particularly using the coupling constant approach, in which the conformer
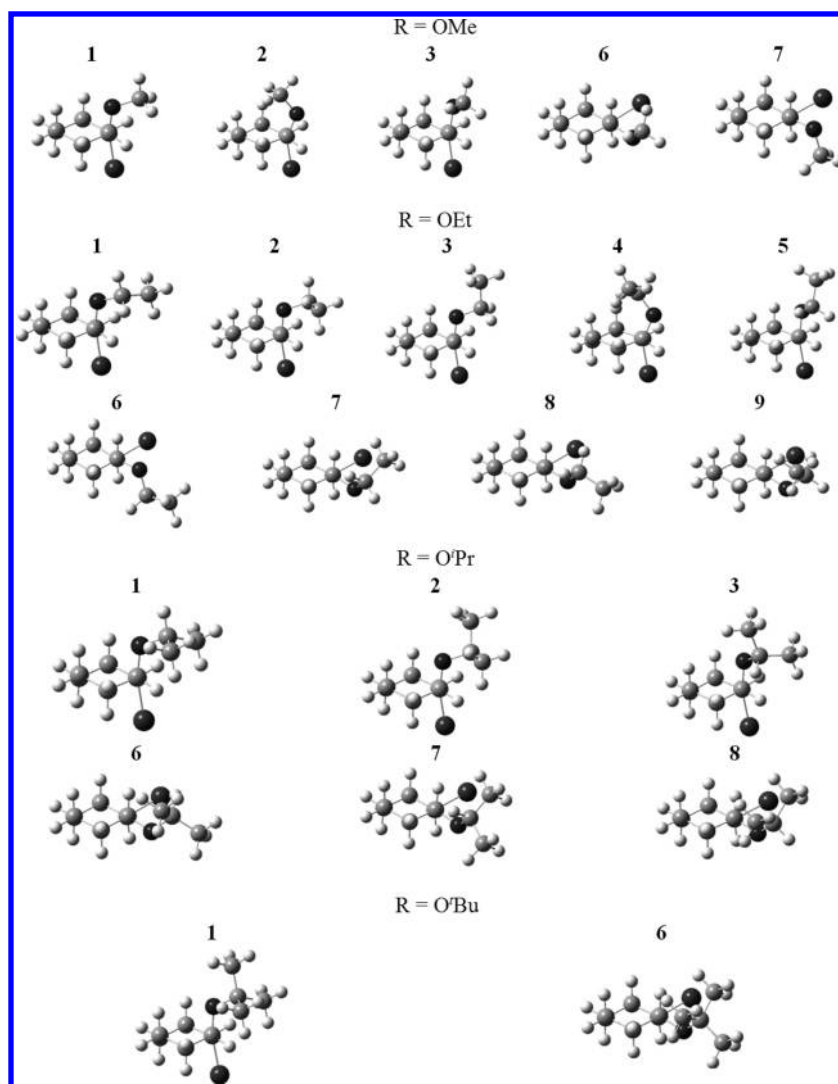
Figure 3. Stable conformers for *trans*-2-bromoalkoxycyclohexanes.

Table 1. Relative Energies (E_{rel} in kcal mol^{-1}, and Conformer Percentages in Parentheses) for Conformers 1–9 at the Isolated State (B3LYP/aug-cc-pVDZ), Dipole Moments (μ, in D), and Geometric Parameters (Dihedral Angles, in deg)

OR	parameter	diaxial					diequatorial			
		1	2	3	4	5	6	7	8	9
OMe	E_{rel}	0.5 (24)	6.6 (0)	0.7 (18)			2.5 (1)	0 (57)		
	μ	1.7	2.9	2.2			3.2	3.3		
	$\alpha_{H-C-O-C}$	32.8	208.3	315.8			171.8	324.7		
OEt	E_{rel}	2.0 (2)	1.7 (3)	0.5 (21)	9.2 (0)	0.7 (15)	2.6 (1)	1.6 (3)	0 (50)	1.3 (6)
	μ	2.0	1.9	1.9	3.0	2.3	3.3	3.1	3.1	2.7
	$\alpha_{H-C-O-C}$	1.2	25.5	31.7	195.0	318.1	173.6	327.4	329.6	359.4
	$\beta_{C-O-C-C}$	76.1	276.5	181.8	260.0	173.3	182.6	86.0	178.0	282.5
O^{i}Pr	E_{rel}	3.1 (0)	0.5 (21)	0.9 (10)			0 (48)	0.5 (21)	3.7 (0)	
	μ	2.3	2.0	2.3			2.6	3.1	2.9	
	$\alpha_{H-C-O-C}$	4.2	27.9	331.1			0.8	326.4	338.3	
	$\beta_{C-O-C-H}$	179.2	37.7	322.7			42.7	323.4	181.7	
O^{t}Bu^a	E_{rel}	0 (79)					0.8 (21)			
	μ	2.3					2.8			
	$\alpha_{H-C-O-C}$	4.4					339.8			

^{a} Although two minima for each of the diaxial and diequatorial conformers of *trans*-2-bromo-*tert*-butoxycyclohexane have been identified in PES, only the exceedingly more stable forms converged to stable structures at the B3LYP/aug-cc-pVDZ level using the available means.

Table 2. Experimental Coupling Constants (Hz) for the *trans*-2-Bromoalkoxycyclohexanes

solvent	ε	$^3J_{\text{H-1,H-2}}$	$^3J_{\text{H-1,H-6}}$	$^3J_{\text{H-1,H-6'}}$	$^3J_{\text{H-2,H-3}}$	$^3J_{\text{H-2,H-3'}}$	n_{aa}	$\Delta G^\circ_{\text{aa−ee}}$
				OMe[a]				
CCl$_4$	2.2	7.04	–	–	7.76	–	0.57	−0.17
pyridine-d_5	12.4	8.07	–	–	9.96	–	0.34	0.39
acetone-d_6	20.7	8.14	–	–	10.02	–	0.33	0.42
CD$_3$CN	37.5	8.60	–	–	10.60	–	0.28	0.56
DMSO	46.7	8.42	–	–	10.26	–	0.31	0.47
neat liquid	5.7	7.48			9.18		0.42	0.19
				OEt				
C$_6$D$_6$	2.3	8.0	8.0	3.9	9.0	4.0	0.44	0.14
CDCl$_3$	4.8	8.4	8.4	4.4	9.9	4.1	0.35	0.37
CD$_2$Cl$_2$	8.9	8.5	8.6	4.5	10.3	4.3	0.31	0.47
acetone-d_6	20.7	8.2	8.6	4.1	9.9	4.2	0.35	0.37
CD$_3$CN	37.5	8.6	8.6	4.3	10.6	4.3	0.28	0.56
DMSO	46.7	8.6	8.6	4.6	10.1	4.3	0.33	0.42
				O^{i}Pr				
C$_6$D$_6$	2.3	8.0	8.3	3.9	9.5	4.2	0.39	0.26
CDCl$_3$	4.8	8.4	9.1	4.5	10.2	4.1	0.32	0.45
CD$_2$Cl$_2$	8.9	8.4	9.1	4.4	10.2	4.3	0.32	0.45
acetone-d_6	20.7	8.3	8.7	4.3	10.2	4.3	0.32	0.45
CD$_3$CN	37.5	8.6	9.1	4.2	10.7	4.3	0.27	0.59
DMSO	46.7	8.6	9.1	4.2	10.6	4.3	0.28	0.56
				O^{t}Bu				
C$_6$D$_6$	2.3	6.3	6.0	3.4	6.3	3.9	0.72	−0.56
CDCl$_3$	4.8	7.8	7.7	4.0	7.1	3.8	0.64	−0.34
CD$_2$Cl$_2$	8.9	6.7	6.7	3.9	8.1	3.8	0.54	−0.09
acetone-d_6	20.7	6.7	6.7	3.7	7.2	4.0	0.63	−0.32
CD$_3$CN	37.5	7.4	7.4	3.8	8.7	3.8	0.48	0.05
DMSO	46.7	7.3	7.3	3.8	8.6	3.9	0.49	0.02

[a] Data obtained from the literature.[2]

Table 3. Calculated Coupling Constants (Hz) for *trans*-2-Bromoalkoxycyclohexanes

conformer	$^3J_{\text{H-1,H-2}}$	$^3J_{\text{H-2,H-3}}$	$^3J_{\text{H-2,H-3'}}$	$^3J_{\text{H-1,H-6}}$	$^3J_{\text{H-1,H-6'}}$
			OMe		
1	3.6	3.5	4.5	3.6	4.1
2	3.0	3.5	4.4	2.4	6.5
3	3.9	3.5	4.4	3.6	3.3
6	11.3	12.7	5.7	12.6	5.1
7	10.3	13.3	6.0	11.3	5.6
			OEt		
1	3.9	3.6	4.3	3.8	3.7
2	3.7	3.5	4.4	3.6	4.1
3	3.6	3.6	4.4	3.6	4.1
4	2.8	3.3	4.7	2.3	6.9
5	3.9	3.5	4.4	3.6	3.3
6	11.4	12.7	5.7	12.6	5.0
7	10.3	13.3	5.9	11.3	5.6
8	10.4	13.3	6.0	11.4	5.6
9	10.2	13.5	5.8	11.7	5.9
			O^{i}Pr		
1	3.9	3.6	4.3	3.8	3.9
2	3.7	3.5	4.5	3.6	4.2
3	3.9	3.6	4.3	3.7	3.4
6	10.2	13.4	5.8	11.8	5.8
7	10.3	13.3	5.9	11.2	5.6
8	10.2	13.5	5.7	11.1	5.6
			O^{t}Bu		
1	3.9	3.6	4.3	3.8	3.9
6	10.2	13.4	5.6	11.1	5.4

molar fractions can be obtained by the relationships below. In addition, the NMR method avoids possible problems related to molar absorptivities of the infrared methodology.[11,12]

$$J_{\text{obs}} = n_{\text{aa}}J_{\text{aa}} + n_{\text{ee}}J_{\text{ee}} \qquad (1)$$

$$n_{\text{aa}} + n_{\text{ee}} = 1 \qquad (2)$$

where J_{obs} is coupling constant observed at a given condition (an average of J_{aa} and J_{ee}), J_{aa} and J_{ee} are the intrinsic coupling constants for the diaxial and diequatorial conformers, respectively, and n_{aa} and n_{ee} are the corresponding molar fractions, respectively.

Signals referred both to H-1 and H-2 are free from signal superposition in the NMR spectra of *trans*-2-bromoalkoxycyclohexanes. The H-2 signal (the less shielded one, according to irradiation experiments) shows a coupling constant ($^3J_{\text{H-2,H-3}}$) more dependent on solvent variation than the H-1 signal, and therefore, $^3J_{\text{H-2,H-3}}$ was chosen as the coupling constant to perform the conformational analysis. H-2 exhibits a ddd coupling pattern, due to couplings with H-1, H-3, and H-3', as depicted in Table 2. $^3J_{\text{H-2,H-3}}$ values are general large (>9 Hz) for the OMe (except in CCl$_4$ solution), OEt, and O^{i}Pr derivatives, indicating that H-1 and H-3 are preponderantly antiperiplanar and, consequently, that the diequatorial conformation is preferred in all solutions. In fact, conformer populations could be obtained by using the experimental coupling constants and the calculated ones for all energy minima (Table 3) through eqs 1 and 2; the calculated

values of J used to determine the conformational isomerism were those for the most stable rotamer of each diaxial and diequatorial conformation. As supposed, the diequatorial conformer prevails in all media (except in CCl$_4$ for the OMe derivative) for the OMe, OEt, and O^{i}Pr derivatives, and the conformer population presents similar behavior on going from nonpolar to highly polar solvents (with the most polar conformation increasing in population with the solvent polarity). Also, it was found that *trans*-2-bromo-*tert*-butoxycyclohexane is preferentially diaxial in nonpolar/moderately polar solutions, but the conformer population roughly inverts in acetonitrile and dimethyl sulfoxide solutions, indicating that diaxial and diequatorial conformers are equally populated when electrostatic interactions are absent.

The conformational preferences of the *trans*-2-bromoalkoxycyclohexanes can be evaluated on the basis of NBO analysis,[5] which provides information about the electron delocalization energies stabilizing chemical structures. For all compounds, the diaxial conformer is more stabilized by hyperconjugative interactions than the diequatorial form (Table 4), and the main contributor for this is the antiperiplanar $\sigma_{\text{C−H3}} \rightarrow \sigma^*_{\text{C−Br}}$ hyperconjugation, in addition to the $\sigma_{\text{C−H6}} \rightarrow \sigma^*_{\text{C−O}}$ interaction. This suggests that, although the larger stability of the diaxial conformer is due to hyperconjugative interactions, the diequatorial form is preferred for OMe, OEt, and O^{i}Pr; i.e., the classical concept of steric hindrance in axially substituted cyclohexanes governs the prevalence of the

Table 4. Energies for Selected Antiperiplanar Hyperconjugative Interactions and Total Energy of Hyperconjugation (kcal mol^{-1}) for the Most Stable Diaxial and Diequatorial Conformers

interaction	OMe		OEt		O^{i}Pr		O^{t}Bu	
	aa	ee	aa	ee	aa	ee	aa	ee
C−H$_{3'}$ → C−Br*	7.60	−	7.61	−	7.56	−	7.67	−
C−Br → C−H$_{3'}$*	2.24	−	2.24	−	2.24	−	2.26	−
C−Br → C−O*	4.19	−	4.16	−	4.21	−	4.33	−
C−O → C−Br*	2.83	−	2.85	−	2.95	−	3.13	−
C−H$_{6'}$ → C−O*	5.19	−	5.20	−	5.33	−	5.56	−
C−O → C−H$_{6'}$*	1.23	−	1.22	−	1.21	−	1.18	−
C$_3$−C$_4$ → C−Br*	−	4.30	−	4.34	−	4.46	−	4.21
C−Br → C$_3$−C$_4$*	−	2.91	−	2.93	−	2.91	−	3.03
C$_1$−C$_6$ → C−Br*	−	4.67	−	4.71	−	4.86	−	5.11
C−Br → C$_1$−C$_6$*	−	2.83	−	2.80	−	2.63	−	2.44
C$_2$−C$_3$ → C−O*	−	2.69	−	2.75	−	2.92	−	2.87
C−O → C$_2$−C$_3$*	−	1.66	−	1.64	−	1.51	−	1.55
C$_5$−C$_6$ → C−O*	−	3.00	−	2.98	−	2.92	−	3.00
C−O → C$_5$−C$_6$*	−	1.33	−	1.35	−	1.50	−	1.41
total hyperconjugation	435.59	432.19	482.72	479.22	527.01	524.64	580.44	578.62

diequatorial conformer in OMe, OEt, and O^{i}Pr. It is worth mentioning that this steric effect is different from *syn*-1,3-diaxial repulsion between hydrogens and the alkyl group in alkylcyclohexanes, or even from alternative explanations for this effect,[13] since the R group in the diaxial alkoxy derivatives can avoid interaction with *syn*-1,3-diaxial hydrogens, opposite to, e.g., a ^{t}Bu group in *tert*-butylcyclohexane. Actually, the O^{t}Bu group in the diequatorial conformation presents a methyl group somewhat directed toward the Br substituent, while such an interaction may be relieved for the remaining derivatives by rotating the β torsional angle; for instance, the most stable diequatorial conformer for the O^{i}Pr derivative exhibits the methynic hydrogen directed to Br instead of any methyl groups (Figure 3). Therefore, the diequatorial conformer of the O^{t}Bu derivative is less stabilized due to steric effects than for the remaining derivatives.

Nevertheless, such repulsion is larger for the diaxial conformer, in all compounds. This can be quantitatively achieved by partitioning the full energy of each conformer into hyperconjugation and classical, Lewis-type energies; the hyperconjugative contribution can be obtained by ΔE_{hyp} (total hyperconjugation from Table 4 for diaxial minus for diequatorial conformer), while the full energy difference ΔE_{full} is given in Table 1 (E_{rel}, accounted only for the most stable form of each diaxial and diequatorial conformation). Consequently, $\Delta E_{Lewis\ (aa−ee)}$ is given by

$$\Delta E_{Lewis(aa−ee)} = \Delta E_{full(aa−ee)} + \Delta E_{hyp(aa−ee)} \qquad (3)$$

where E_{hyp} is considered to be a negative value, since it is an attractive interaction. This gives that electrostatic and especially steric effects predominate in the diaxial conformation over the diequatorial one by ca. 3.9, 4.0, 2.9, and 1.0 kcal mol^{-1} for OMe, OEt, O^{i}Pr, and O^{t}Bu derivatives, respectively. It is clear that hyperconjugation in the diaxial conformer of O^{t}Bu predominates over steric hindrance in this conformation.

For the O^{t}Bu derivative in nonpolar solvents, where dipolar interactions O/Br operate in the diequatorial form, the diaxial conformer is more stable, in agreement with the hyperconjugative

trend; in polar solvents, where electrostatic interactions are expected not to be experienced importantly in the diequatorial conformer, the conformational equilibrium is not shifted, indicating that the attractive forces operating in the diaxial conformer (hyperconjugation) plus the repulsive, steric effects in the diequatorial conformer seem to be of similar magnitude to the steric hindrance in the diaxial form.

While experimental $\Delta G°_{aa−ee}$ values for monoalkoxycyclohexanes were found to be 0.84, 1.09, 1.09, and 1.60 kcal mol^{-1} for OMe-, OEt-, O^{i}Pr-, and O^{t}Bu-cyclohexanes, respectively,[7] the corresponding values for the brominated ethers in polar (DMSO) solution (absent of intramolecular dipolar interactions) are 0.47, 0.42, 0.56, and 0.02 kcal mol^{-1}. On the basis of our results and those available in the literature,[7] introduction of a bromine atom in alkoxycyclohexane is preferred to give the diaxial conformation rather than the diequatorial one, especially for the O^{t}Bu derivative, because the bromine effect increases ΔE_{hyp} in the diaxial conformation in comparison to monoalkoxycyclohexanes, in which hyperconjugative interactions favor the axial conformation by only about 1 kcal mol^{-1}, and because of the appearance of a Br/OR repulsion in the diequatorial conformation.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information. Potential energy surfaces obtained at the AM1 level for *trans*-2-bromomethoxycyclohexane, *trans*-2-bromoethoxycyclohexane, *trans*-2-bromoisopropoxycyclohexane, and *trans*-2-bromo-*tert*-butoxycyclohexane; Cartesian coordinates (standard orientation) for their conformers. This material is available free of charge via the Internet at http://pubs.acs.org.

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