MAGNETIC RESONANCE IN CHEMISTRY, VOL. 35, 351–356 (1997)

Experimental and Theoretical Study of the Ethoxy Group Conformational Effect on ^{13}C Chemical Shifts in *Ortho*-Substituted Phenetols

Dora G. de Kowalewski, Valdemar J. Kowalewski, Edith Botek and Rubén H. Contreras
Departamento de Física, FCEyN, Universidad de Buenos Aires, Buenos Aires, Argentina

Julio C. Facelli*
Center for High Performance Computing, University of Utah, Salt Lake City, Utah 84112, USA

The ^{13}C chemical shifts of nine 2-X-substituted phenetol derivatives were measured together with the ^{13}C chemical shifts of the corresponding X-monosubstituted benzenes. Using an additivity scheme, the ethoxy *cis*- and *trans-ortho*-SCSs (substituent chemical shifts) at C-6 and C-2, respectively, were determined to be shielding effects of 16.5 and 10.9 ppm, respectively, which are close to those determined previously in anisole derivatives. Optimized geometries at the Hartree–Fock level employing a D95 basis set for three different phenetol conformers were obtained and the corresponding chemical shifts of all ^{13}C nuclei were calculated using the same basis set and the CHF-GIAO approach. Results are discussed in terms of different interactions defining different conformations, particularly that between a polar bond and a proximate highly polarizable one.**

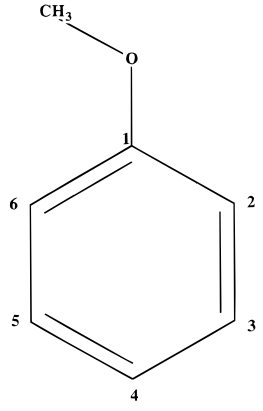
Magn. Reson. Chem. **35**, 351–356 (1997) No. of Figures: 1 No. of Tables: 6 No. of References: 39

KEY WORDS NMR; ^{13}C NMR; ^{13}C chemical shifts; conformational effects

Received 10 April 1996; accepted 6 July 1996

INTRODUCTION

It is known that the methoxy group *ortho*-SCS (substituent chemical shifts) on ^{13}C in benzene derivatives (**1**) depends strongly on the OMe conformation.[1–4] For a heavy atom planar conformation, a quantitative estimation of the difference between the *cis-ortho*- (C-6) and *trans-ortho*- (C-2) SCSs of 7.6 ppm was determined[5] using linear regression analysis in *ortho*-substituted anisoles and a difference of 7 ppm was measured by magic angle spinning solid-state NMR at 180 K in the parent compound.[4] This difference was rationalized as originating in an attractive interaction between the highly polarized O—CMe bond and the close aromatic π electronic system.[6–8] This rationalization was based on the following arguments:[9–11] when an attractive interaction between two moieties which are proximate in space takes place, a shielding effect on its heavy atoms is observed. This can be qualitatively explained by a decrease in the absolute value of the paramagnetic part of the magnetic shielding constant[9,10] due to the expansion of p orbitals. For a repulsive interaction between the two moieties, a deshielding effect is observed due to the contraction of these orbitals.[12–15]



1

The interaction commented upon above between a strong polar bond and a proximate bond which shows a high polarizability seems to be very important for defining conformations in methyl aryl ethers,[8] which, in turn, may be important in defining the biological activity of many compounds.[16] These considerations motivated us to undertake new studies intending to deepen the understanding of such interactions which could be dubbed 'polar bond–polarizable bond' (PB–PzB) interactions.

The aim of this work was to study how much this interaction in methoxybenzene derivatives is affected when the methyl group is replaced by an ethyl moiety. To this end, the ^{13}C NMR spectra of a series of nine *ortho*-substituted phenetols were studied and the orientational effect of the ethoxy group on the *ortho*-SCSs was determined using an additivity scheme for the aromatic ^{13}C SCSs.[17] This also required the measurement of the ^{13}C chemical shifts in the corresponding monosubstituted benzenes under similar experimental

* Author to whom correspondence should be addressed.

CCC 0749–1581/97/060351–06 $17.50

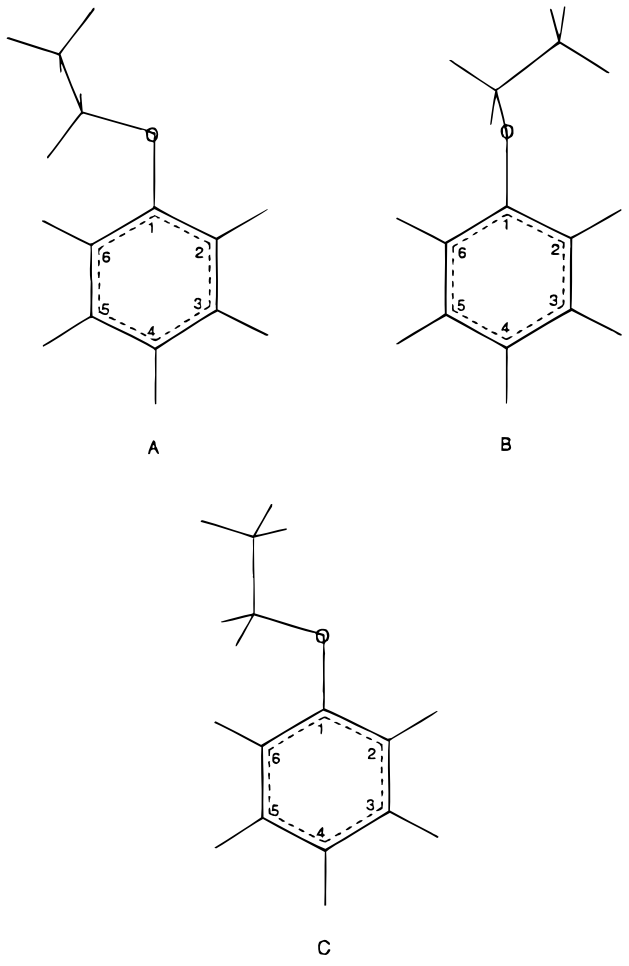


Figure 1. Phenetol conformers considered in this paper. The carbon numbering given here is used throughout the paper.

conditions. Quantum chemical calculations of the chemical shifts were performed for different conformations of phenetol to provide further insight into the experimental results.

EXPERIMENTAL

NMR measurements

Natural abundance, proton-decoupled ^{13}C NMR spectra were recorded using a Bruker AM 500 spectrometer in the FT mode, with acetonitrile-d_3 or dimethyl-d_6 sulfoxide as an internal lock, and with a digital resolution of 0.7 Hz per point. Standard 5 mm o.d. sample tubes were used. A relaxation delay between 0 and 1 s and a pulse width of 7 ms were used. The development of an adequate signal-to-noise ratio required between 128 and 504 scans.

All compounds studied were of commercial origin, none of them showing any impurity in their NMR spectra. Analytical-reagent grade solvents were used throughout without further purification. All samples were studied at 30 °C as 10% (w/w) acetonitrile-d_3–acetonitrile or dimethyl-d_6 sulfoxide–dimethyl sulfoxide (DMSO) solutions containing 5% (w/w) of hexamethyldisiloxane (HMDS) as internal reference. Chemical shifts were converted to the TMS scale as described in Ref. 18, i.e. adding 2.2 ppm for chemical shifts measured in acetonitrile solution and 2.0 ppm for chemical shifts measured in DMSO solution.

The assignments of the carbon resonances in the monosubstituted benzenes were made according to the values reported previously[19] and those in the 2-X-substituted phenetols were made following the additivity rule, using the SCSs determined in this paper from the X-monosubstituted benzenes. The uncertainties in the measured SCSs and the intrinsic deviations from additivity make the assignments of lines separated by less than 2 ppm tentative, but the interchange of these assignments does not affect the conclusions of this paper.

MO calculations

Three different conformations of phenetol (see Fig. 1) were fully optimized using the Hartree–Fock *ab initio* approximation with the D95** basis set,[20] and the corresponding chemical shifts of all ^{13}C nuclei were calculated using the CHF-GIAO (Coupled Hartree–Fock Gauge Invariant Atomic Orbitals) method[21] with the same basis set as that employed in the geometry optimization. All calculations were performed using the Gaussian 94 package.[22] Transformation of the calculated chemical shieldings to the TMS scale was achieved by subtracting the estimated absolute chemical shielding of TMS, 191.8 ppm, which was obtained from the calculated shielding in methane, 198.8 ppm, using the CHF-GIOA-D95** ensemble, minus the 7 ppm reported as the difference between liquid TMS and gas-phase methane.[23]

RESULTS AND DISCUSSION

In Table 1 the experimental ^{13}C chemical shifts and SCS of the nine *ortho*-substituted phenetols studied in this work are displayed. The ethoxy-SCSs were obtained by subtracting from the chemical shifts in 2-X-phenetol the chemical shifts of the corresponding X-monosubstituted benzenes, which are shown in Table 2. In Table 3 the average ethoxy-SCSs are entered and compared with the methoxy-SCSs in 2-X-anisole derivatives taken from Ref. 5. Ethoxy- and methoxy-SCSs are notably similar in *ortho*-substituted phenetol and anisole derivatives even though the experimental data were measured in compounds with different sets of substituents and using different solvents.

The similar values of the SCSs for C-4 indicate that the resonance interaction between the oxygen π-type lone pair and the aromatic π-electronic system is essen-

Table 1. ^{13}C chemical shifts, δ(C-*i*), for *ortho*-substituted phenetols[a]

	δ(C-1)	δ(C-2)	δ(C-3)	δ(C-4)	δ(C-5)	δ(C-6)	δ(CH_2)	δ(CH_3)	δ(s.c.)
COOH[b]	158.9	119.5	133.7	122.7	136.0	114.6	67.1	15.0	166.8
	(28.1)	(−11.6)	(2.9)	(−7.0)	(1.6)	(−15.1)			
CN[b]	161.7	102.4	134.8	121.8	135.8	113.8	65.9	15.0	117.6
	(28.4)	(−10.8)	(1.5)	(−8.6)	(1.6)	(−16.6)			
CHO[b]	162.6	126.0	128.7	121.6	137.2	114.4	65.5	15.1	190.5
	(32.0)	(−11.8)	(−1.9)	(−8.6)	(1.6)	(−15.8)			
NCO[b]	154.1	124.7	124.5	122.2	127.7	113.2	66.0	15.0	132.2
	(28.2)	(−9.9)	(−1.4)	(−8.8)	(0.7)	(−17.6)			
$CONH_2$[c]	156.6	122.6	130.9	120.4	132.5	113.0	64.3	14.5	166.3
	(29.1)	(−11.7)	(3.4)	(−7.7)	(1.3)	(−15.2)			
NH_2[b]	147.4	138.9	115.6	122.2	118.5	113.1	64.9	15.5	—
	(31.8)	(−10.1)	(0.0)	(−8.0)	(0.2)	(−17.1)			
OH[b]	147.6	147.5	115.9	122.3	121.1	113.8	65.6	15.4	—
	(31.3)	(−10.5)	(−0.4)	(−8.4)	(0.2)	(−16.9)			
OCH_3[b]	149.7	150.3	114.4	121.8	121.9	113.2	65.1	15.4	56.4
	(34.8)	(−10.2)	(−0.5)	(−8.7)	(0.3)	(−17.3)			
CH_2OH[b]	157.4	131.3	128.9	121.4	129.3	112.4	64.7	15.3	60.6
	(29.8)	(−11.6)	(1.3)	(−7.7)	(1.6)	(−16.7)			

[a] Ethoxy substituent chemical shifts are given in parentheses, negative values corresponding to shielding effects. All values are in ppm. Chemical shifts were internally referenced to HMDS and converted to the TMS scale as described in Ref. 18. δ(s.c.) = side chain ^{13}C chemical shift.
[b] In acetonitrile.
[c] In DMSO.

Table 2. ^{13}C chemical shifts for X-monosubstituted benzenes[a]

X	*ipso*	*ortho*	*meta*	*para*	Side-chain
COOH[b]	131.1	130.8	129.7	134.4	168.9
CN[b]	113.2	133.3	130.4	134.2	119.9
CHO[b]	137.8	130.6	130.2	135.7	193.8
NCO[b]	134.6	125.9	130.8	121.3	
$CONH_2$[c]	134.3	127.5	128.2	131.2	167.1
NH_2[b]	149.0	115.6	130.2	118.3	
OH[b]	158.0	116.3	130.7	120.9	
OCH_3[b]	161.2	115.3	131.0	122.0	55.8
CH_2OH[b]	142.9	127.6	129.1	127.8	64.7
OCH_2CH_3[b]	160.1	115.5	130.6	121.5	64.3, 15.3
OCH_2CH_3[c]	158.8	114.6	129.7	120.6	63.1, 14.9

[a] All values are in ppm. Chemical shifts were internally referenced to HMDS and converted to the TMS scale as described in Ref. 18. The corresponding SCSs were obtained by subtracting from these values the ^{13}C chemical shift in benzene, i.e. 129.6 ppm in acetonitrile and 128.3 ppm in DMSO.
[b] In acetonitrile.
[c] In DMSO.

Table 3. Average substituent chemical shift effects in substituted phenetols and anisoles[a]

Compound	Parameter	C-1	C-2	C-3	C-4	C-5	C-6
Phenetol	SCS	30.4	−10.9	0.5	−8.2	1.0	−16.5
	σ	2.1	0.7	1.5	0.6	0.4	0.9
Anisole[b]	SCS	28.9	−10.1	0.6	−8.5	−0.4	−17.7
	σ	4.0	1.1	1.3	0.6	1.3	1.1

[a] All values are in ppm. The σ values correspond to the standard deviations of the mean values calculated using the data in Table 1. Numbering according to Fig. 1.
[b] From Ref. 5.

tially the same for both substituents. This indicates that in all phenetol derivatives studied the preferential ethoxy group conformation is such that the methylene carbon is placed in the plane of the aromatic ring. The difference between the ethoxy-*cis*- and -*trans*-*ortho*-SCS (C-2 *vs.* C-6) shows an important side-chain conformational effect, which is just only slightly smaller than that of the methoxy group in *ortho*-substituted anisoles, 5.6 *vs.* 7.6 ppm.[5] However, this small difference is well within the dispersion of values in both series of compounds as estimated by the corresponding root-mean-square difference, σ. It is interesting that the *trans*-*ortho*- and *cis*-*ortho*-methoxy-SCSs in *o*-methoxyphenetol can also be obtained from data in Tables 1 and 2, and are −10.4 and −16.2 ppm, respectively. The corresponding SCSs for the ethoxy group are −10.2 and −17.3 ppm. The smaller shielding effect of the methoxy group for the *cis* orientation compared with that of the ethoxy group suggests that under the experimental conditions used in this work there is a slight destabilization of the planar methoxy group conformation. This is consistent with the results in several papers showing that in *o*-dimenthoxybenzene both methoxy groups are not simultaneously in a planar conformation.[24–26] Recently, such a trend was rationalized as originating in the PB–PzB destabilizing interactions between the adjacent methoxy groups.[8]

In Table 1, variations of the side-chain ethoxy-^{13}C chemical shifts are observed, being those corresponding to the $^{13}CH_3$ resonance smaller than those of the $^{13}CH_2$ resonance. They are too small to rationalize in a precise way, although it is observed that in general for electron-withdrawing substituents the methyl ^{13}C nucleus appears to be slightly more shielded than for

Table 4. Calculated ^{13}C chemical shift principal values of the *ortho* carbons in phenetol for the A conformer[a]

	δ_{11}	δ_{22}	δ_{33}
ortho-cis	205.1	121.5	9.3
ortho-trans	190.0	118.9	−6.1
Δ (*trans* − *cis*)[b]	−15.1 (−9, −12)	−2.6 (−2, −5)	−15.4 (−14, −13)

[a] All values in ppm referenced to TMS as described in the text.
[b] Values in parentheses correspond to the experimental and calculated values, respectively, in anisole, from Ref. 4.

electron-donating substituents, being the other way around for the methylene ^{13}C nucleus. This trend seems to indicate that the methylene carbon atom appears more deshielded when the ethoxy resonance interaction is enhanced owing to the electron acceptor group placed at its *ortho* position. This trend is similar to that described previously for the methyl ^{13}C chemical shift in methyl aryl ethers.[6]

If the ^{13}C chemical shifts for other side-chain groups shown in Table 1 are compared with those displayed in Table 2, also small differences are observed. With the exception of the OMe moiety, they appear more shielded in the former than in the latter. Most of them could be rationalized as originating in the resonance interaction between both side-chains.

While no experimental information is available on the principal values of the ^{13}C chemical shift tensors in phenetol, their calculated values for the *ortho* carbons, given in Table 4, show similar trends to those observed in anisole.[4] The differential SCSs in the tensor components for the *ortho-cis* and *ortho-trans* carbons for anisole and phenetol are similar providing further evidence of the electronic equivalence of these substituents.

In Table 5 the relative energies of conformers **A**, **B** and **C** of phenetol are presented with their calculated isotropic chemical shifts for all ^{13}C nuclei. Conformers **A**, **B** and **C** are shown in Fig. 1 and some of their relevant structural data are displayed in Table 6. In spite of the similarity between the resonance interaction of the π-type oxygen lone pairs in phenetol and in anisole

Table 5. Relative energies and calculated ^{13}C chemical shifts for the A, B and C conformers of phenetol[a]

Parameter	A	B	C
Energy (kcal mol^{-1})[b]	0.00	0.91	10.50
δ(C-1)	152.7	152.7	153.4
δ(C-2)	112.0	118.9	113.6
δ(C-3)	128.7	126.7	126.8
δ(C-4)	112.0	117.2	113.3
δ(C-5)	127.1	126.7	126.8
δ(C-6)	101.0	117.2	102.2
δ(CH_2)	49.8	57.1	54.3
δ(CH_3)	6.6	7.8	11.0

[a] Calculated chemical shift are given in ppm referenced to TMS as explained in the text.
[b] Relative energies for the *ab initio* fully optimized geometries of all three conformers (see Fig. 1) calculated with the D95** basis set.

Table 6. Structural data for the A, B and C conformers of phenetol[a]

	A	B	C
Bond lengths (Å)			
C-1—C-2	1.3979	1.3903	1.4022
C-2—C-3	1.3825	1.3901	1.3812
C-3—C-4	1.3949	1.3898	1.3747
C-4—C-5	1.3842	1.3805	1.3828
C-5—C-6	1.3947	1.3893	1.3958
C-6—C-1	1.3909	1.3911	1.3914
C-1—O	1.3502	1.3630	1.3488
O—CH_2	1.4094	1.4172	1.4181
CH_2—CH_3	1.5239	1.5225	1.5231
Bond angles (°)			
C-6—C-1—O	125.16	119.40	128.08
C-2—C-1—O	115.37	120.51	113.20
C-1—O—CH_2	121.52	117.32	132.86
O—CH_2—CH_3	112.64	113.50	121.42
Dihedral angles(°)			
CH_3—CH_2—O—C-1	82.58	79.41	180.0
CH_2—O—C-1—C-2	180.0	−90.0	180.0

[a] Atom numbering according to Fig. 1.

derivatives noted above, the difference in energy between conformers **B** and **A** is lower than the corresponding value in anisole, where the differences between the 0° and the 90° conformations range between 11 and 1.5 kcal mol^{-1} (1 kcal = 4.184 kJ) depending of the type of calculation or measurement.[27,28] The latter value corresponds to a Hartree–Fock calculation using the D95** basis set with the fully relaxed geometry.

The results in Tables 1, 3 and 4 indicate that the PB–PzB interaction is similar in anisole and in phenetol, indicating that the lower relative energy between the 90° conformation and the in-plane conformation in phenetol compounds should originate in some other interaction. The longer O—CH_2 bond in **B** than in **A** suggests that this difference originates in the different ability of the O—CH_2 bond in phenetol and the O—CH_3 bond in anisole to hyperconjugate with the π aromatic system for the 90° conformation.

Conspicuous differences are also observed for the calculated ethoxy group ^{13}C chemical shifts in conformers **A**, **B** and **C**. Such differences can be ascribed to the expansion and contraction of p-type orbitals of the respective carbon atoms owing to attractive or repulsive

interactions, respectively, between the side-chain and the substrate.[9–11] Therefore, a detailed comparison between the changes in the chemical shifts in the different conformers and their respective energies may yield an insight into interactions defining the preferential conformation. For instance, in conformer **A**, the CH_2—CH_3 bond is almost perpendicular to the ring plane, i.e. this C—C bond is almost parallel to the aromatic π-orbitals. The large deshielding effect on the methyl ^{13}C shielding constant on going from the **A** to the **C** conformation, 4.4 ppm, suggests that the configuration for the CH_2—CH_3 bond in **A** originates in a stabilizing interaction between this bond and the π aromatic system.

The *ortho–para* equivalence[29] for the substituent effect on the magnetic shielding constant can be observed by comparing in Table 5 δ(C-4) with δ(C-2) in **A** and δ(C-4) with δ(C-6) in **B**. In **A**, C-6 is more shielded than C-2 by 11.0 ppm. This difference should be compared with the experimental value in Table 1, i.e. 5.6 ppm, indicating that the present theoretical calculations overestimate the shielding effect originated in the PB–PzB interaction between the O—CH_2 bond and the C-1—C-2 aromatic bond. One of the possible reasons for this overestimation could be the existence of low-lying torsional states which are populated at room temperature in the liquid phase when a high dielectric constant solvent is used. In such torsional states the PB–PzB interaction could be weaker than in the isolated molecule. On going from the **A** to the **B** conformation, this interaction is relaxed and the difference between δ(C-6) and δ(C-2) comes to 1.7 ppm. This last difference originates in the non-symmetrical configuration of the CH_2—CH_3 bond in **B**, which yields a small deshielding effect on C-2. On the other hand, for the conformation **C** the difference between δ(C-6) and δ(C-2) amounts to 11.4 ppm. This last result suggests that in conformations **A** and **C** there is a similar PB–PzB interaction between the O—CH_2 bond and the C-1—C-6 aromatic bond.

The inhibition of the PB–PzB interaction in **B** affects also the methylene ^{13}C chemical shift. In fact, in **B** it is deshielded in 7.3 ppm with respect to **A**. This value parallels the well known deshielding effect in an out-of-plane methoxy group conformation in anisole derivatives.[6,7,30] On the other hand, for this change in conformation the methyl ^{13}C shielding constant is reduced by only 1.2 ppm, suggesting that the asymmetric configuration of the CH_2—CH_3 bond in **B** originates in an attractive interaction between the methyl moiety and the aromatic π electronic system.

In **B**, the C-4 carbon is more shielded (9.5 ppm) than C-3 and C-5. This result can be rationalized as showing that for the 90° conformation there is still a strong resonance interaction between the oxygen lone pairs and the aromatic π electronic system. This observation parallels those reported in crowded anisoles[30,31] and those found from a theoretical point of view in 2-methoxypyridine.[6]

In the preferential conformer, **A**, the C-1—C-2 bond is slightly shorter than the C-1—C-6 bond. This result resembles that reported in anisole by Konschin[32] and suggests that the PPB–PzB interaction yields a slight shortening of the highly polarizable bond. In other words, not only should both moieties, OCH_3 and OCH_2CH_3, prefer a conformation *cis* to the *ortho* aromatic bond with a larger mobile bond order,[8,33,34] but also this conformation renders a further fixation of that mobile bond order.

The slightly shorter C-1—O bond in **C** than in **A** suggests that the resonance interaction between the π-type oxygen lone pair and the electronic π aromatic system is stronger in the former than in the latter. This result is in agreement with the slightly larger chemical shifts for C-4 in **C** than in **A**.

CONCLUSION

The *cis-ortho* and *trans-ortho* ^{13}C SCSs of the ethoxy group in *ortho*-substituted phenetols presented in this work are similar to those reported previously for the methoxy group in *ortho*-substituted anisoles.[4,5] In addition, the close agreement between the ethoxy and methoxy *para*-SCS indicates that the resonance interaction between the π-type oxygen lone pair and the aromatic π electronic system of the benzene ring is similar in phenetol and in anisole derivatives. This result also indicates that the PB–PzB interaction between the polarized O—CMe bond with the *cis*-π aromatic bond is similar in both types of compounds. For this reason, it can be expected that for unhindered phenetol derivatives, the ethoxy group preferential conformation is *cis* to the adjacent C—C bond with a larger mobile bond order, unless there is more than one PB–PzB interaction involving the π electronic system and they correspond to a destabilizing interaction like in *p*-dimethoxybenzene.[8,26] These results indicate that in fused aromatic systems, e.g. naphthalene, where the mobile bond order is different for the different C—C bonds,[35] either a methoxy or an ethoxy group attached to ring position 2 should prefer an orientation *cis* to the ring position 1. An effect of this type has recently been observed also for the vinyloxy group,[36] in the solid-state spectrum of 2-methoxydibenzofuran[37] and in results reported a few years ago by Joseph-Nathan *et al.*[38] for several fused aromatic compounds with methoxy substituents, that can be rationalized along the same lines. The preferential orientation of any of these groups towards the adjacent aromatic bond with the larger mobile bond order originates mainly in the PB–PzB interaction, which is similar to that described a few years ago by Bond and Schleyer[39] in methyl vinyl ether and related compounds.

As a final remark, it should be noted that in fused aromatic compounds either of these two substituents, methoxy and ethoxy groups, can be used as adequate probes to assess the degree of fixation of the π mobile bond order if they are attached to an unhindered ring position: it is only necessary to determine the difference between both *ortho*-^{13}C-SCSs.

Acknowledgements

The Argentinian authors gratefully acknowledge economic support from CONICET (LANAIS-NMR-500) and UBACYT. E. B. acknowledges a fellowship from SECYT-UNNE. Computer time for this project was provided by the Center for High Performance Computing of the University of Utah.

REFERENCES

1. P. W. Jardon, E. H. Vickery, L. F. Pahler, N. Pourahmady, G. J. Mains and E. J. Eisenbraun, *J. Org. Chem.* **49**, 2130 (1984).
2. S. R. Salman, *Spectrochim. Acta, Part A* **39**, 1073 (1983); S. R. Salman and F. S. Kamounah, *Magn. Reson. Chem.* **25**, 966 (1987).
3. G. H. Penner and R. E. Wasylishen, *Can. J. Chem.* **67**, 525 (1989).
4. J. C. Facelli, A. M. Orendt, Y. J. Jiang, R. J. Pugmire and D. M. Grant, *J. Phys. Chem.* **100**, 8268 (1996).
5. R. R. Biekofsky, A. B. Pomilio, R. H. Contreras, D. G. de Kowalewski and J. C. Facelli, *Magn. Reson. Chem.* **27**, 158 (1989).
6. R. H. Contreras, R. R. Biekofsky, D. G. de Kowalewski, A. M. Orendt and J. C. Facelli, *J. Phys. Chem.* **97**, 91 (1993).
7. A. L. Esteban, M. P. Galache, E. Diez, R. R. Biekofsky and R. H. Contreras, *Magn. Reson. Chem.* **32**, 199 (1994).
8. R. R. Biekofsky, A. B. Pomilio, R. A. Aristegui and R. H. Contreras, *J. Mol. Struct.* **344**, 143 (1995).
9. S. Li and D. B. Chesnut, *Magn. Reson. Chem.* **23**, 625 (1985).
10. S. Li and D. B. Chesnut, *Magn. Reson. Chem.* **24**, 93 (1986).
11. J. C. Facelli, R. H. Contreras and M. F. Tufró, *J. Mol. Struct. THEOCHEM* **281**, 61 (1993).
12. G. W. Gribble, D. J. Keavy, E. R. Olson, I. D. Rae, A. Staffa, T. E. Herr, M. B. Ferraro and R. H. Contreras, *Magn. Reson. Chem.* **29**, 422 (1991).
13. D. W. Boykin, R. L. Hertzler, J. K. Delphon and E. J. Eisenbraun, *J. Org. Chem.* **54**, 1418 (1989); D. W. Boykin, B. Dewprashad and E. J. Eisenbraun, *J. Org. Chem.* **55**, 425 (1990).
14. A. Soderquist, J. C. Facelli, W. J. Horton and D. M. Grant, *J. Am. Chem. Soc.* **117**, 8441 (1995).
15. M. S. Solum, J. C. Facelli, J. Michl and D. M. Grant, *J. Am. Chem. Soc.* **108**, 6464 (1986).
16. J. J. Knittel and A. Makriyannis, *J. Med. Chem.* **24**, 906 (1981).
17. P. C. Lauterbur, *J. Am. Chem. Soc.* **83**, 1946 (1961).
18. D. G. de Kowalewski, C. de los Santos and E. Marceca, *Magn. Reson. Chem.* **28**, 1 (1990).
19. K. Fujieda, K. Takahashi and T. Stone, *Bull. Chem. Soc. Jpn.* **58**, 1587 (1985); G. Levy and G. L. Nelson, RMN de C-13, Belaaterra, Spain (1976).
20. T. H. Dunning and P. J. Hay, in *Methods in Electronic Structure Theory*, edited by H. F. Schaefer, III, p. 1. Plenum Press, New York (1977).
21. R. Ditchfield, *Mol. Phys.* **27**, 789 (1974).
22. M. J. Frisch, G. W. Trucks, H. B. Schlegel, P. M. W. Gill, B. G. Johnson, M. A. Robb, J. R. Cheeseman, T. A. Keith, G. A. Petersson, J. A. Montgomery, K. Raghavachari, M. A. Al-Laham, V. G. Zakrzewski, J. V. Ortiz, J. B. Foresman, J. Cioslowski, B. B. Stefanov, A. Nanayakkara, M. Challacombe, C. Y. Peng, P. Y. Ayala, W. Chen, M. W. Wong, J. L. Andres, E. S. Replogle, R. Gomperts, R. L. Martin, D. J. Fox, J. S. Binkley, D. J. Defrees, J. Baker, J. P. Stewart, M. Head-Gordon, C. Gonzalez and J. A. Pople, *Gaussian 94* (*Revision A.1*). Gaussian, Pittsburgh, PA (1995).
23. A. K. Jameson and C. J. Jameson, *Chem. Phys. Lett.* **134**, 461 (1981).
24. G. M. Anderson, III, P. A. Kollman, L. N. Domelsmith and K. N. Houk, *J. Am. Chem. Soc.* **101**, 2344 (1979).
25. O. Exner and V. Jehlicka, *Collect. Czec. Chem. Commun.* **48**, 1030 (1983).
26. J. C. Facelli, *J. Mol. Struct. THEOCHEM* **276**, 307 (1992).
27. M. A. Vincent and I. H. Hillier, *Chem. Phys. Lett.* **140**, 35 (1990); D. C. Spellmeyer, P. D. J. Grootenhuis, M. D. Miller, L. F. Kuyper and P. A. Kollman, *J. Phys. Chem.* **94**, 4483 (1990).
28. T. Schaefer and R. Sebastian, *Can. J. Chem.* **67**, 1148 (1989).
29. A. M. Orendt, R. R. Biekofsky, A. B. Pomilio, R. H. Contreras and J. C. Facelli, *J. Phys. Chem.* **95**, 6179 (1991).
30. I. I. Schuster, *J. Org. Chem.* **50**, 1656 (1985).
31. I. I. Schuster, M. Parvez and A. J. Freyer, *J. Org. Chem.* **53**, 5819 (1988).
32. M. Konschin, *J. Mol. Struct.* **105**, 213 (1983).
33. D. A. Forsyth, V. M. Osterman and J. R. DeMember, *J. Am. Chem. Soc.* **107**, 818 (1985).
34. W. J. Chazin and L. D. Colebrook, *Can. J. Chem.* **64**, 2220 (1986).
35. M. H. Sherwood, J. C. Facelli, D. W. Alderman and D. M. Grant, *J. Am. Chem. Soc.* **113**, 750 (1991).
36. A. V. Afonin, A. V. Vashchenko and R. H. Contreras, to be published.
37. W. Wang, C. G. Phung, D. W. Alderman, R. J. Pugmire and D. M. Grant, *J. Am. Chem. Soc.* **117**, 11984 (1995).
38. P. Joseph-Nathan, C. García-Martínez and M. S. Morales-Ríos, *Magn. Reson. Chem.* **28**, 311 (1990).
39. D. Bond and P. von R. Schleyer, *J. Org. Chem.* **55**, 1003 (1990).

