1, J = 15, 7 Hz) and 6:2 (d, 1, J = 15 Hz)] with that of its lower homologue described above. Analytical GC indicates two poorly resolved components in a 4:1 ratio for the third peak. These are tentatively identified as the isomeric 2-methyl-2,4-decadienes: IR 3020, 1655, 1620, 1080, 970, 940, 850 cm^{-1}; ^{1}H NMR δ 0.9 (m, 3), 1.2 (br s, 8), 1, 7 (br s, 6), 2.0 (m, 2), 5.5 (d of t, 1, J = 15, 7 Hz), 5.7 (d, 1, J = 11) and 5.9–6.3 (m, 1). These values are also very similar to those of the lower homologue described above.

Acknowledgment. We thank Dr. Steinar Børresen for preliminary work which paved the way for the present study.

Registry No. 1, 90047-74-8; 2, 90047-75-9; 3, 90047-76-0; 4, 90047-77-1; 6a, 90047-78-2; 6b, 60431-22-3; 6c, 90047-79-3; 7, 2806-55-5; 8a, 765-83-3; 8b, 5749-72-4; 8c, 7087-36-7; 9a, 1462-07-3; 9b, 4292-04-0; 9c, 17257-36-2; 10b, 42192-42-7; 10c, 59578-60-8; 10d, 90047-80-6; 11b, 53366-57-7; 11c, 89656-98-4; 12a, 90047-81-7; 12b, 90047-82-8; 12c, 90047-83-9; 12d, 90047-84-0; $CH_2{=}C{=}C(CH_3)_2$, 598-25-4.

Molecular Orbital Calculations and ^{13}C NMR Studies To Explain a Regiospecific Demethylation of 3-Alkyl-1,2-dimethoxybenzenes

Phillip W. Jardon,[1a] Euin H. Vickery,[1b] Leon F. Pahler, Naser Pourahmady, Gilbert J. Mains,* and Edmund J. Eisenbraun*

Department of Chemistry, Oklahoma State University, Stillwater, Oklahoma 74078

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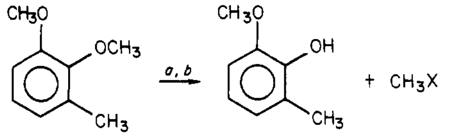
This study was performed to explain a regiospecific demethylation of 3-alkyl-1,2-dimethoxybenzenes. PRDDO–MO calculations show that the low-energy conformation of the carbon of a methoxy group having two ortho neighbors on a benzene ring is located out of the plane of the aromatic ring, whereas a methoxy group with only one ortho neighbor executes restricted rotation in the plane of the ring. The carbon portion of the methoxy group is turned away from the neighboring substituent. These calculations also show that the atomic charge on the oxygen atom in the former case exceeds that in the latter. The carbon of a methoxy group with two ortho neighbors yields ^{13}C NMR T_1 relaxation times longer than those with only one ortho neighbor, also suggesting that the methoxy group with two ortho neighbors is crowded out of the plane of the aromatic ring. ^{13}C NMR chemical shifts of these ortho-substituted methoxybenzenes did not correlate well with shifts predicted from published additive parameters; this again suggests an unusual methoxy group orientation and distribution of electrons. The forced rotation of a methoxy group out of the plane of the benzene ring diminishes the release of electrons from the methoxy group to the benzene ring. The resulting higher atomic charge on the oxygen and the orientation of the oxygen orbitals facilitate complexation with Lewis acids and methoxy group cleavage.

Our recent demonstration of the regiospecific cleavage of 3-alkyl-1,2-dimethoxybenzenes by boron tribromide and iodotrimethylsilane to 2-alkyl-6-methoxyphenols,[2a] along with earlier observations[2b–d] of similar effects, prompted a detailed analysis of the conformational orientation of the methoxy groups to elucidate the origin of this regiospecificity. Studies of Dreiding models suggested that the orientation of the p orbitals of the respective oxygen atoms is the source of this behavior and that providing or blocking access to them by Lewis acids during complexation and/or attack of nucleophiles on methoxy carbon is the key to the course of the reaction and the regiospecificity shown in Scheme I.

The Halgren–Lipscomb PRDDO program[3] was obtained and atomic charges for various nuclei at different dihedral angles and the total energy of each molecule were calculated. PRDDO is intermediate in complexity between CNDO/INDO and ab initio calculations, as it retains all three- and four-centered integrals. PRDDO is comparable in accuracy to the more sophisticated STO-3G calculations with respect to optimal geometries and requires computer costs only 2–3 times that of the less accurate CNDO/INDO computations.[3b,c]

Scheme I



3b

[a] Iodotrimethylsilane or boron tribromide. [b] H_2O.

Tables I–V of calculated atomic charges and dipole moments were developed. These are available as supplementary material and include information about the monomethoxybenzenes **1a–e** and **2a** (Table I) and the dimethoxybenzenes **3b** (Table II) and **3e** (Table III) as well as 4,5-dimethoxyindan (**4**) (Table IV). A summary of PRDDO electron densities and calculated dipole moments at minimum energy for **3b**, **3c**, **3d**, **3e**, and **4** is presented in Table V.

An appreciation of the relative magnitudes of the calculated rotational barrier energies for **1a**, **1b**, and **2a** can be gained from Figure 1. While the calculated barrier for **1a** is 1.50 kcal/mol, it must be remembered that these calculations are uncertain by at least this amount. Hence, this barrier should be regarded as merely low and the motion of the methoxy group as only slightly hindered at room temperature. On the other hand, the location of one methyl group ortho to methoxy, as in **1b**, effectively excludes the methoxy group from an angular region ±60° on either side of the methyl group. The addition of two ortho

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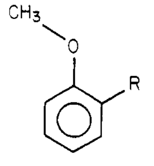
(1) (a) Jardon, P. W., MS Thesis, Oklahoma State University, 1982. (b) Vickery, E. H., Ph.D. Thesis, Oklahoma State University, 1979.

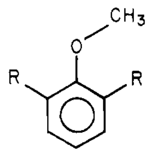
(2) (a) Vickery, E. H.; Pahler, L. F.; Eisenbraun, E. J. *J. Org. Chem.* **1979**, *44*, 4444. (b) Tietel, S.; Brossi, A. *Heterocycles* **1973**, *1*, 73. (c) Johnson, D. W.; Mander, L. N.; Master, T. J. *Aust. J. Chem.* **1981**, *34*, 1243. (d) Fujii, N.; Irie, H.; Yajima, H. *J. Chem. Soc., Perkin Trans. 1* **1978**, 2288.

(3) (a) We thank Drs. Halgren and Lipscomb for providing this program prior to its release to the QCPE program. Leading references about this program follow. (b) Halgren, T. A.; Lipscomb, W. N. *Proc. Nat. Acad. Sci. U.S.A.*, **1972**, *69*, 652. (c) Halgren, T. A.; Lipscomb, W. N. *J. Chem. Phys.* **1973**, *58*, 1569. (d) Eberhardt, M. K.; Chuchani, G. *J. Org. Chem.* **1972**, *37*, 3654. (e) Anderson, G. M.; Kollman, P. A.; Domelsmith, L. N.; Houk, K. N. *J. Am. Chem. Soc.* **1979**, *101*, 2344.

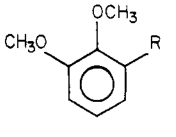
0022-3263/84/1949-2130$01.50/0



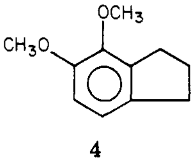
1a, R = H
b, R = CH_3
c, R = C_2H_5
d, R = i-C_3H_7
e, R = t-C_4H_9



2a, R = CH_3
b, R = C_2H_5
c, R = i-C_3H_7
d, R = t-C_4H_9



3a, R = H
b, R = CH_3
c, R = C_2H_5
d, R = i-C_3H_7
e, R = t-C_4H_9



4

methyl groups, as in **2a**, blocks the methoxy group from lying in the plane of the benzene ring and restricts it to regions perpendicular to either side of the ring.

Because the rigid rotation approximation becomes poorer as the conformational energy increases, the high-energy values in Figures 1, 4, and 5 are suspect. However, the resulting trends are correctly predicted.

Figures 2 and 3 show the variation of excess negative charge on the oxygen atom in **1a–e** and **2a** as the methoxy group is rotated out of the plane of the benzene ring. For all structures, the oxygen is more negatively charged when the angle of the methoxy group, with respect to the plane of the ring, is essentially 90°. A similar observation was made by Eberhardt and Chuchani[3d] for analogous molecules using CNDO/2 computations. Since this conformation is the preferred structure to **2a**, with the methoxy group restricted to near 90°, and is a conformation that is accessible to the methoxy groups in **1b–e**, wherein the methoxy executes a floppy rotation away from the alkyl group, it is safe to conclude that, on the average, the methoxy oxygen is more negative in **2a** than it is in **1a**, where rotation is comparatively unrestricted. Similarly, the electron density at the ortho and para positions varies according to the angle the methoxy group makes with the plane of the ring. As the oxygen atom becomes more negative, the electron density at the ortho and para ring positions is less in **2a** than in **1b–e**, which in turn are less than in **1a**.

The minimum energies of **3b**, **3e**, and **4** were determined at $\theta = 0°$ and $\phi = 60°$ (Tables II–IV) with θ and ϕ illustrated for **3b** in Figure 4. Calculations for **3c** and **3d** were carried out only for this minimum-energy position. A summary of the results is given in Table V. Anderson et al.[3e] have carried out ab initio STO-3G calculations and photoelectron studies on dimethoxybenzenes which show that *o*-dimethoxybenzene derivatives exist in predominantly nonplanar conformations in the gas phase.[3e] Their treatment of case **3a** (*o*-dimethoxybenzene) at five different values for θ and ϕ showed a preference for out-of-plane orientation.[3e] These authors also report X-ray crystal structure determinations which show that the central methoxy group of 1,2,3-trimethoxy systems is not coplanar with the aromatic ring.

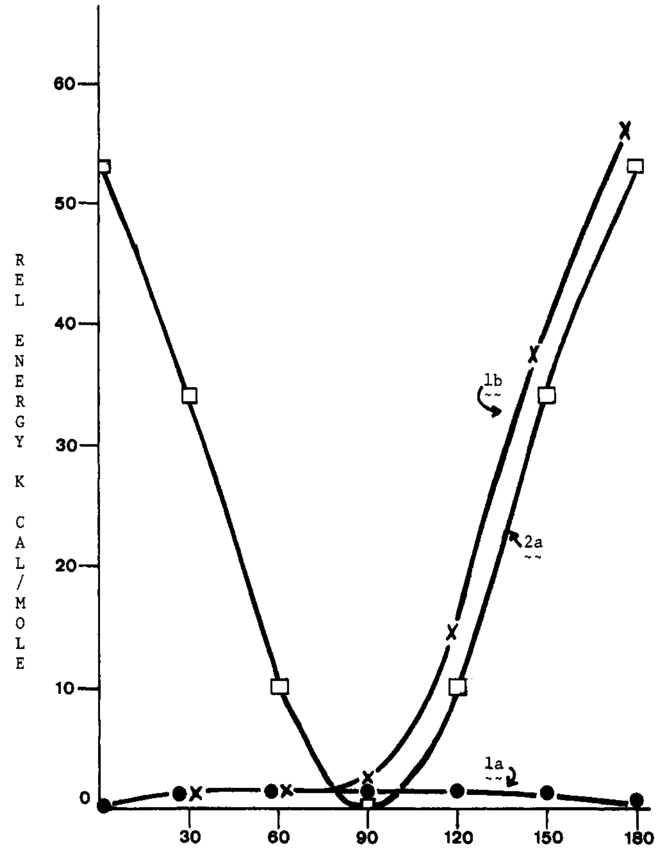


Figure 1. Rotational barrier for **1a**, **1b**, and **2a**.

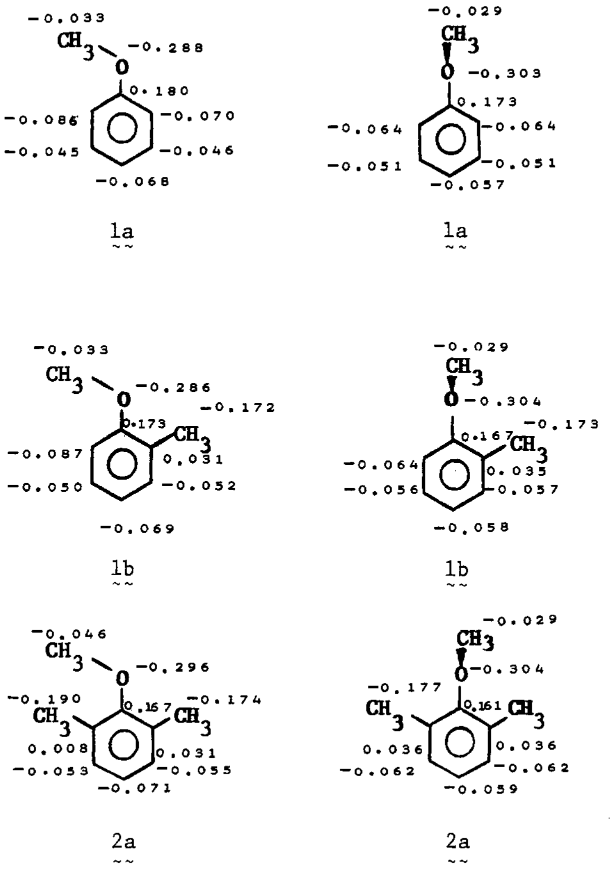


Figure 2. Atomic charges for positions $\phi = 0°$ and 90° for **1a**, **1b**, and **2a**.

Figure 4 shows how the energy of **3b** varies as θ is varied through all possible positions for various values of ϕ. No matter what the value of ϕ is, the minimum energy value of θ is 0° (exterior methoxy in the plane of the ring and rotated away from the other methoxy group). These calculations also suggest that the other methoxy group "prefers" to be out of the plane of the ring away from the methyl substituents. The energy of the system, including

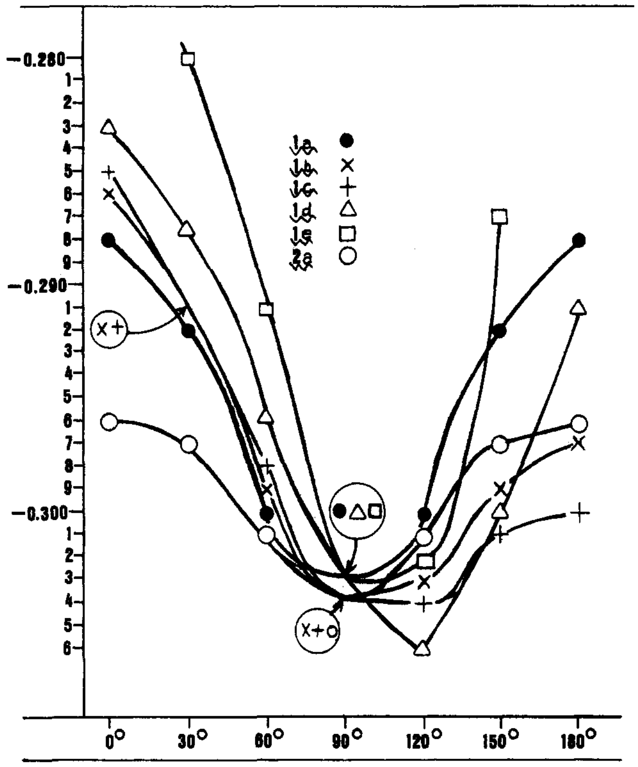


Figure 3. Atomic charge on methoxy oxygen.

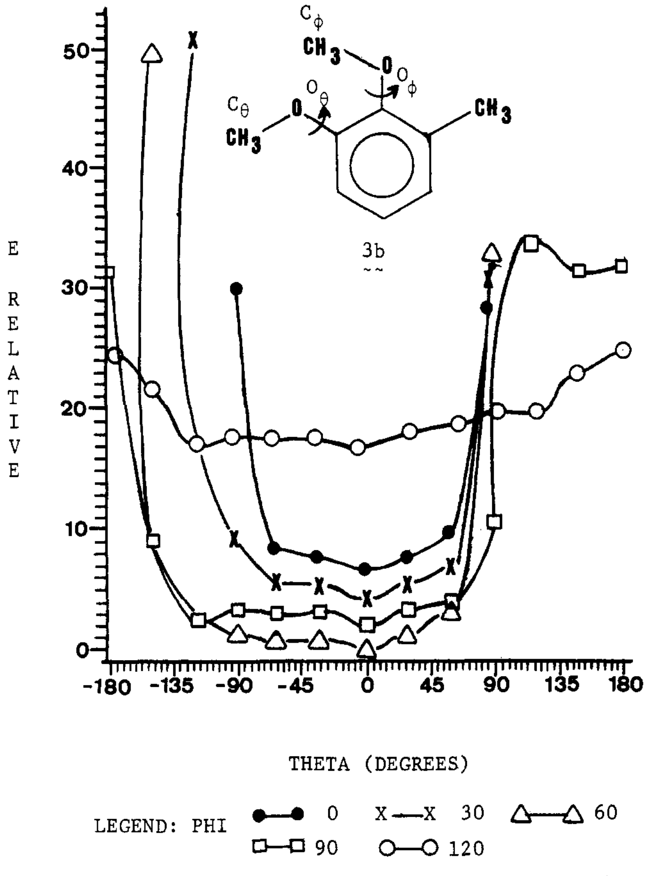


Figure 4. Relative energy as a function of θ for various values of ϕ for dimethoxytoluene (**3b**).

the methoxy substituents, rises rapidly as either methoxy group approaches an ortho substituent (θ = 180° and ϕ = 0° or 180°). In Figure 4, values for ϕ = 150° and ϕ = 180° are omitted because they become disproportionately large. Figure 5 shows the trend in a three-dimensional plot.

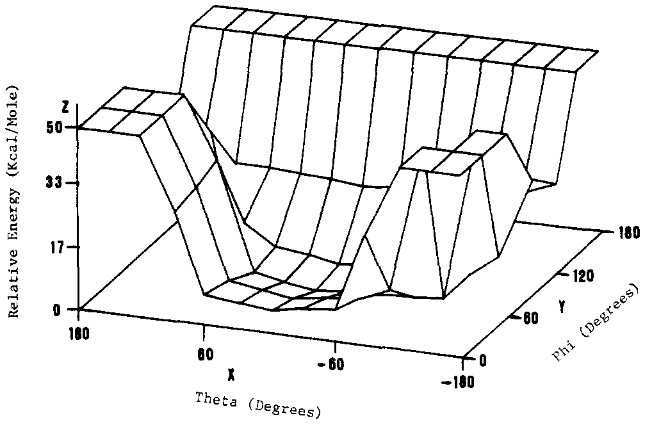


Figure 5. Relative energy as a function of θ and ϕ for 2,3-dimethoxytoluene (**3b**).

The conformational energy of **3b** and related compounds varies continuously upon change of θ and ϕ and not discontinuously as suggested in Figure 5. Additional grid points would result in a smoother plot but would not alter the concept. Inspection of Figure 5 suggests that the energetically most probable position of the θ (3-) methoxy group is in the plane of the ring, ±60°, and the correspondingly most probable orientation of the ϕ (2-) methoxy group is perpendicular to the benzene ring, ±30°. Thus, both methoxy groups may lie in the plane of the ring, but this conformation is less likely than having the ϕ methoxy group located above (or below) the plane of the ring.

When vicinal dimethoxybenzenes with a contiguous third substituent are considered, with the information gained from the monomethoxybenzenes, the oxygen atom on the methoxy group that is bent out of the plane (O_ϕ, ϕ = 90°) has a higher electron density than the one lying in the plane of the ring (O_θ, θ = 0°). This suggests an explanation for the regiospecific cleavage of this group. Lewis acids, as electrophilic reagents, interact with the oxygen atom bearing the higher electron density (O_ϕ) and are preferentially bound there. In addition, the orbitals of O_θ are "shielded" by the other methoxy group, whereas the orbitals of O_ϕ project above and away from the ring and are thus available for preferential attack.

We used ^{13}C NMR chemical shifts and T_1 relaxation times to substantiate these conclusions. The chemical shift data are presented in Table VI, and T_1 relaxation times in Figure 6. Methoxy groups with only one ortho neighbor do not show a significant shift from that of methoxybenzene (54.8 ppm).

Comparison of the ^{13}C chemical shifts of the ring carbons given in Table VI with those obtained from published tables of additive parameters[5b] shows that the ring positions ortho and para to the "crowded" methoxy group do not exhibit predicted ^{13}C chemical shifts. In every case, the expected shielding is diminished from what would be expected.

The methoxy groups flanked to two ortho substituents show a significant ^{13}C downfield shift, although an upfield shift is usually observed for crowded carbons.[4] This downfield shift increases as the substituents are increased in size. Dhami and Stothers have suggested that the ortho substituents interfere with the methoxy group so that the electron release by the methoxy oxygen is significantly reduced.[4] Steric deshielding effects between methyl groups occupying hindered positions have been described for 1,8-dimethylnaphthalene.[5a] These methyl groups are

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(4) Dhami, K. S.; Stothers, J. B. *Can. J. Chem.* **1966**, *44*, 2855.

Table VI. Carbon-13 NMR Chemical Shifts of Methoxybenzenes[a]

substituent	methoxy carbon 1	methoxy carbon 2	aromatic carbons C-1		C-2		C-3		C-4		C-5		C-6	
2-H	54.8		159.3	−0.6[b]	113.6	−0.5[b]	129.1	−0.4[b]	120.3	−0.5[b]	129.1	−0.4[b]	113.6	−0.5[b]
2-CH_3	54.9		157.5	−3.2	126.4[c]	3.0	130.4	0.1	120.1	−0.7	126.5[c]	−1.1	109.6	−4.5
2-C_2H_5	55.0		157.1	−2.4	132.4	2.7	128.7	−0.4	120.3	−0.5	126.6	−0.3	109.9	−4.2
2-(*i*-C_3H_7)	55.0		156.5	−0.9	136.7	2.4	126.3[c]	−0.7	120.4	−0.5	125.7	−1.4	110.1	−4.1
2-(*t*-C_4H_9)	54.8		158.3	1.5	138.0	1.5	126.7	0.3	120.1	−0.6	126.3	−0.3	111.4	−2.6
2,6-$(CH_3)_2$	59.3		156.7	−4.8	130.5	7.1	128.5	1.1	123.5	2.7	128.5	1.1	130.5	7.1
2,6-$(C_2H_5)_2$	60.7		155.9	−3.2	136.6	6.9	126.7	0.2	123.9	3.1	126.7	0.2	136.6	6.9
2,6-(*i*-$C_3H_7)_2$	61.9		154.4	−0.5	141.4	7.0	123.8	−0.8	124.3	3.3	123.8	−0.8	141.4	7.0
2,6-(*t*-$C_4H_9)_2$	64.1		159.3	5.6	143.4	7.0	126.3	2.8	122.8	2.2	126.3	2.8	143.4	7.0
2-CH_3, 4-OCH_3	55.3[c]	55.5[c]	153.1	0.1	127.4	3.0	116.7	0.8	151.7	−0.5	110.4	0.8	110.5	−4.6
2-OCH_3	55.2	55.2	148.5	3.0	148.5	3.0	110.9	−4.2	120.3	−1.5	120.3	−1.5	110.9	−4.2
2-OCH_3, 3-CH_3	54.9	59.2	146.8	1.3	152.0	5.7	131.1	6.7	122.1	−0.5	123.0	1.2	109.5	−2.7
2-OCH_3, 3-*i*-C_3H_7	55.1	60.2	152.1	6.7	145.9	2.9	141.9	6.6	117.8	−1.5	123.5	1.8	109.3	−3.4
d	56.0	59.7	150.3	7.5	145.0	3.9	136.5	6.3	137.5	0.6	118.6	1.2	110.7	−1.7
2,3-$(OCH_3)_2$	55.7	60.4	153.1	6.6	137.8	6.7	153.1	6.6	105.0	−2.4	123.2	0.4	105.0	−2.4

[a] In ppm from Me_4Si as 1.8 M in $CDCl_3$. [b] Values in this column represent the numberical difference between the observed chemical shifts and those calculated from published substituent parameters, e.g., first entry 159.9 (calcd) − 0.6 = 159.3 (obsd). [c] Values may be exchanged. [d] 4,5-Dimethoxyindan; for purposes of this table, 4 is numbered as a substituted methoxybenzene.

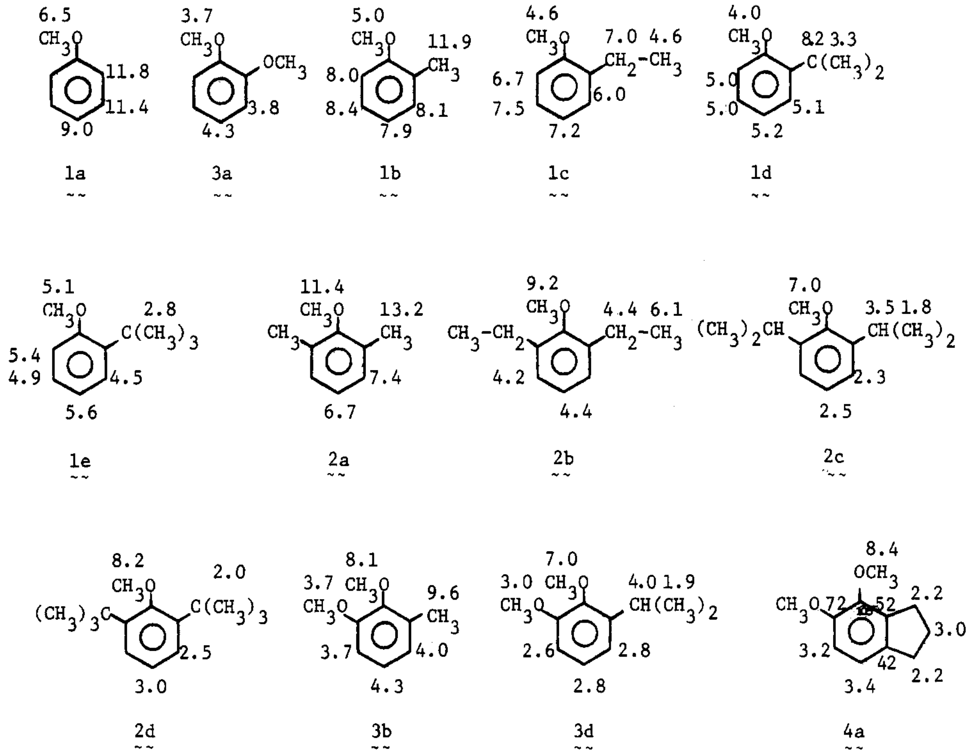

Figure 6. T_1 values (s) as an average of three consistent (±10%) runs.

deshielded by 6.6 ppm relative to that of methylnaphthalene.[5a] Another explanation for the deshielding of a "hindered" methoxy carbon (two bulky neighbors) is that the methoxy group is rotated out of the plane of the aromatic ring and the C_{ar}–O bond loses its resonance-stabilized double-bond character and thus experiences less shielding.[6]

The downfield chemical shift experienced by the carbon of a methoxy group with two ortho neighbors increases with the bulk of the substituent alkyl groups. This shows that an ε steric factor may also be involved. The shifts for the alkyl carbons are greater in the 2,6-dialkyl-substituted methoxybenzenes than with the 2-alkyl cases.[5a] Thus, a mutual deshielding is evident.

For the mono-ortho-substituted methoxybenzenes, the values calculated through use of additivity of the substituent effects[5b] agree well with the experimental data, especially for C-4 and C-5 (see Table VI). At C-6, the shifts are consistently at higher field than predicted. This effect can be explained by assuming that the carbon of the methoxy group is in the plane of the ring away from the alkyl group, and the consequent crowding at the C-6 position causes shielding at this position.

For C-1 of mono-ortho-substituted methoxybenzenes, no consistent deviation is observed and the shifts agree well with values predicted by considering that the position has an ortho neighbor. The predicted shielding for C-2 is consistently large for this series. Since the methoxy group spends most of its time in the vicinity of C-6, the amount of shielding at C-2 decreases. In methoxybenzene, para-

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(5) (a) Buchanan, G. W.; Montaudo, G; Finocchiaro, P. *Can. J. Chem.* 1974, *52*, 767. (b) Wehrli, F. W.; Wirthlin, T. "Interpretation of Carbon-13 NMR Spectra"; Heyden & Sons, Ltd.: London, 1980; pp 129–275.

(6) Levy, G. C.; Licther, R. L.; Nelson, G. L. "Carbon-13 Nuclear Magnetic Resonance Spectroscopy"; Wiley: New York, 1980; pp 211–246.

substituted methoxybenzenes, and meta-substituted methoxybenzenes, the methoxy group causes nearly equal shielding at both ortho positions and consequently, good results are obtained by assuming additivity of substituent parameters.[4]

For the 2,6-di-ortho-substituted methoxybenzenes, the ^{13}C chemical shifts calculated by assuming additivity of parameters do not agree well with the experimentally obtained values. The aromatic carbons ortho and para to the crowded methoxy group show less shielding than predicted. The deviations range from 1.2 to 2.8 ppm for the para position and from 1.3 to 7.5 ppm for the ortho positions. This effect has been attributed to steric inhibition of resonance.[4] Since less shielding for C-2, C-4, and C-6 is observed in the ^{13}C NMR data (Table VI) than is expected from use of additivity parameters, the decrease can be attributed to rotation of the methoxy group out of the plane of the benzene ring. Thus, the usual ortho, para shielding increment observed when a methoxy group is attached to a benzene ring is diminished.

In the 3-alkyl-substituted 1,2-dimethoxybenzenes, the C-6 position is shifted to higher field than predicted. The methoxy group with only one ortho neighbor is forced to lie in the plane of the ring away from the other methoxy group. This places the carbon of the 1-methoxy group in close proximity to C-6, which, in turn, causes C-6 to be shielded like the C-6 position of 2-alkyl-1-methoxybenzenes. The shielding of the C-1 (carbon bearing the hindered methoxy group) is greater than predicted. This is probably caused by through-space factors like those causing the C-2 signal to be shifted in the 2-alkyl-1-methoxybenzenes.[4]

Additional evidence that a hindered methoxy group is rotated out of the plane of the ring came from T_1 measurements (Figure 6). The major mechanism of relaxation for carbons bonded to protons is through the ^{13}C–H dipole–dipole mechanism. In such cases, an increase in the rate of reorientation of ^{13}C nuclei will result in less efficient relaxation and therefore longer T_1 values. Hence, T_1 values can be used as a measure of the relative rotation rates of these nuclei in solution.

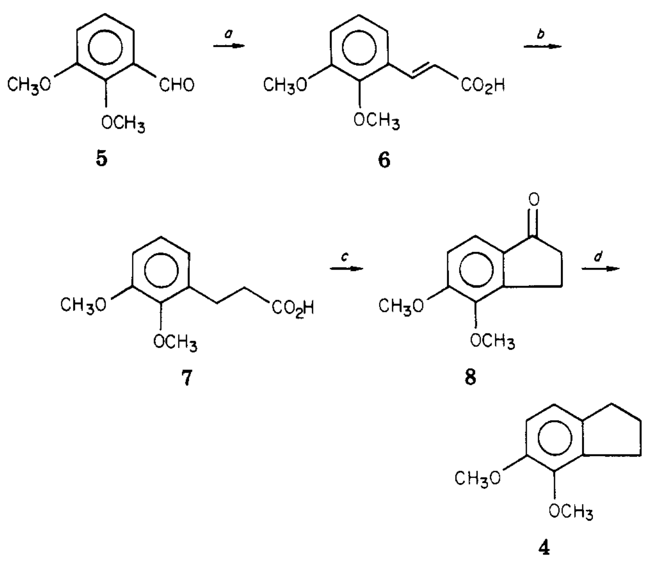
As shown in Figure 6, carbons of methoxy groups that have two ortho neighbors show a larger T_1 value (≥ 6.6 s in every case) than those with only one ortho neighbor (≤ 5.1 s in every case). The methoxy group of the latter lies in the plane of the ring away from the ortho substituent (see the PRDDO calculations in Tables II–IV). In this conformation, rotation around the $O-CH_3$ bond is coupled weakly to the adjacent ring hydrogen.[7] Alternatively, rotation around the $O-CH_3$ bond in the former case is unhindered because the methoxy group is away from the plane of the benzene ring, and thus longer T_1 values result. The methoxy group of methoxybenzene is relatively free to rotate around the $O-C_{ar}$ bond so that rotation around the $O-CH_3$ bond is not substantially coupled to the ortho hydrogen and thus a relatively long T_1 is observed.

Based on the information derived from the PRDDO calculations and ^{13}C NMR data, it is possible to predict the selectivity and even specificity of methoxy group cleavage with Friedel–Crafts reagents. We anticipate that these observations will be of utility in natural product work and medicinal chemistry.

Experimental Section

^{13}C NMR. the ^{13}C NMR spectra were recorded at 25.2 MHz and 24 490 G in the FT mode on a Varian XL-100-15 instrument interfaced with a TT-100 Nicolet computer. Chemical shifts are given in parts per million downfield from Me_4Si. Concentrations are 1.8 M in $CDCl_3$.

Scheme II



^{a} Malonic acid, piperidine in pyridine, Δ. ^{b} H_2, Pd/C, ethyl acetate, Δ. ^{c} PPA, Δ. ^{d} H_2, Pd/C, acetic acid, Δ.

T_1 values were obtained with the following parameters: pulse sequence, T_1 IR_3; τ values, 0.1, 1.0, 2.5, 4.0, 7.0, 14.0, 30.0, 70.0, and 170.0 s; delay (D_5), 216.0 s; acquisition time, 1.360 s; spectra, 8000. The samples were degassed after argon was bubbled through them by repeated freezing (−78 °C) and thawing under vacuum.

Several compounds needed for this study were commercially available: **1a**, **1b**, **3a**, phenols **1c–1e**, and **3d**. The phenols corresponding to **2a**, **2b**, **2c**, and **2d** were kindly supplied by the Ethyl Corp.[8] Of these ethers, all except **2d** were readily prepared by methylation using a procedure involving 12 h of Vibromixer agitation at room temperature of a mixture of 0.1 mol of phenol, 0.15 mol of NaOH, 0.25 mol of dimethyl sulfate, 500 mL of H_2O, 500 mL of CH_2Cl_2, and 0.55 mol of *N*-benzyltrimethylammonium hydroxide.[9] The isolation procedure included washing with Claisen's alkali[10] to remove unreacted phenol.

2,6-Di-*tert*-butyl-1-methoxybenzene (2d). The above procedure was unsatisfactory for preparation of **2d**. Instead, the procedure of Kornblum and Seltzer was used.[11] 2,6-Di-*tert*-butylphenol was first recrystallized from aqueous ethanol, and a dried 20-g (0.10-mol) sample was dissolved in 50 mL of *tert*-butyl alcohol. To this solution was added 100 mL of a 0.10 M solution of potassium *tert*-butoxide in *tert*-butyl alcohol. Diglyme (50 mL distilled from CaH_2) and 25 mL of methyl iodide were added to the solution, and the reaction mixture was stirred for 12 h at room temperature.

The reaction product mixture was added to water, extracted with ether, washed twice with water, dried ($MgSO_4$), and concentrated to 17 g of yellow liquid. The product was Soxhlet extracted[12] through a column of basic alumina and distilled (Kugelrohr apparatus) to give colorless **2d**.

2,3-Dimethoxytoluene (3b). A 50-g sample of 2,3-dimethoxybenzaldehyde (**5**) (50 g, 0.30 mol), potassium hydroxide (33 g, 0.59 mol), hydrazine (50 mL, 1.6 mols), and 430 mL of diethylene glycol (DEG) were added to a stainless steel Wolff-Kishner flask.[13] The reaction mixture was heated at 90–100 °C for 1.5 h and the product distilled into a Dean-Stark trap as the reaction proceeded. The product was separated from DEG, dissolved in ether, washed

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[7] Makriyannis, A.; Knittel, J. J. *Tetrahedron Lett.* **1979**, 2753.

[8] We thank Drs. R. L. Shubkin and J. B. Hinkamp, Ethyl Corp., Ferndale, MI, for these samples.

[9] McKillop, A.; Fiaud, F. C.; Hug, R. P. *Tetrahedron* **1974**, *30*, 1379.

[10] Fieser, L. F.; Fieser, M. "Reagents for Organic Synthesis"; Wiley: New York, 1968; Vol. I, p 153.

[11] Kornblum, M.; Seltzer, R. *J. Am. Chem. Soc.* **1961**, *83*, 3668.

[12] Browne, C. E.; Buchanan, W. L.; Eisenbraum, E. J. *Chem. Ind.* (*London*), **1977**, 35.

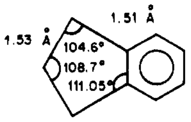
[13] Eisenbraun, E. J.; Hall, H. *Chem. Ind.* (*London*) **1970**, 1535.

with 10% hydrochloric acid, dried (Na_2CO_3), concentrated, and distilled (Kugelrohr apparatus) to give 36 g (81%) of colorless **3b**.

4,5-Dimethoxyindan (4). 4,5-Dimethoxyindan (**4**) was prepared from 2,3-dimethoxybenzaldehyde (**5**) via the sequence in Scheme II. As shown, the condensation of 8.6 g (0.52 mol) of **5** with 69 g (0.42 mol) of malonic acid in 166 mL of refluxing pyridine containing 4% of piperidine catalyst gave 108 g (98%) of 2,3-dimethoxycinnamic acid (**6**), mp 178–180 °C (lit.[14] 179–180 °C). Acid **6** (103 g, 0.5 mol) was hydrogenated (5% Pd/C in ethyl acetate) at 40 psi and 40 °C to give 82 g (80%) of 2,3-dimethoxyhydrocinnamic acid (**7**). Recrystallization from hexane–toluene gave colorless crystals, mp 65–66 °C (lit.[14] 69–70 °C). Cyclization of 50 g of **7** in PPA[15] at 60 °C gave 29 g (60%) of 4,5-dimethoxy-1-indanone (**8**), mp 73–74 °C (lit.[15] 74–75 °C). A 13.9-g sample of ketone **8** was hydrogenolyzed in the presence of 1 g of 5% Pd/C in 75 mL of acetic acid at 55 °C and 55 psi to give 10.9 g (84%) of distilled **4**, bp 113–114 °C (3.2 mm).[7,16]

MO Calculations. MO calculations were carried out on a PRDDO program supplied by Halgren[3] using an IBM-360 computer. The convergence criteria were set at 10^{-4} root-mean-square change in the density matrix.

The calculations were carried out by using the following distances and angles; C_{ar}–C_{ar} = 1.40 Å, C_{ar}–H = 1.084 Å, C_{ali}–C_{ali} = 1.54 Å, C_{ar}–O = 1.36 Å, O–CH_3 = 1.43 Å, C_{ali}–H = 1.101 Å; sp^3 carbon angles, 109.5°; benzene ring angles, 120°; ether angles, 120°.[17] The zero values for θ and ϕ, as shown in Figure 4, for **3b** are in the plane of the aromatic ring. Rotations around the O–Ar bond are clockwise as viewed from the center of the aromatic ring. All bond rotations in this paper conform to these operations. The other dimensions used for the five-membered ring of indan were as shown.



In the case where R = C_2H_5, the methyl carbon of the alkyl group was placed in the plane of the ring away from the methoxy group. In the case where R = i-C_3H_7, the hydrogen on the branched carbon was placed in the plane of the ring toward the methoxy group so that the methyls in the alkyl group were at the maximum distance from the methoxy group. One of the methyl carbons of the t-C_4H_9 group was placed in the plane of the ring away from the methoxy group because this position proved to be of lower energy than that having the methyl carbon in the plane of the ring toward the methoxy group.

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Registry No. **1a**, 100-66-3; **1b**, 578-58-5; **1c**, 14804-32-1; **1d**, 2944-47-0; **1e**, 2944-48-1; **2a**, 1004-66-6; **2b**, 2944-51-6; **2c**, 2944-52-7; **2d**, 1516-95-6; **3b**, 4463-33-6; **3d**, 71720-27-9; **3e**, 82895-30-5; **4**, 51932-57-1.

Supplementary Material Available: Tables I–V listing PRDDO energies, atomic charges, and dipole moments for compounds **1a**, **1b**, **1c**, **1d**, **1e**, **2a**, **3b**, **3d**, **3e**, and **4** (8 pages). Ordering information is given on any current masthead page.

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[14] Perkin, W. H., Jr.; Robinson, R. *J. Chem. Soc.* **1914**, *105*, 2376.

[15] Koo, J. *J. Am. Chem. Soc.* **1953**, *75*, 1981.

[16] The ^1H and ^{13}C NMR and mass spectra of the compounds cited in this paper were consistent with the cited structures.

[17] Goodwin, T. H.; Drzybylska, M.; Robertson, J. M. *Acta Crystallogr.* **1950**, *3*, 279.

[18] Korp, J. D.; Thummel, R. P.; Bernal, I. *Tetrahedron* **1977**, *33*, 3069.

Experimental Evidence for an Electron-Transfer Mechanism in the Reaction between 2-Phenyl-3-(phenylimino)-3*H*-indole and Grignard Reagents: Application of the Marcus Theory

Lennart Eberson*

Division of Organic Chemistry, Chemical Center, University of Lund, S-220 07 Lund, Sweden

Lucedio Greci*

Istituto Chimico, Facoltà di Ingegneria, Università Bologna, Viale Risorgimento 2, I-401 36 Bologna, Italy

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2-Phenyl-3-(phenylimino)-3*H*-indole reacts with 5-hexenylmagnesium bromide to give products of 1,2- and 1,4-addition and reduction. For both addition modes, the products are mixtures of 5-hexenyl- and cyclopentylmethyl-substituted derivatives. Since the 5-hexenyl radical undergoes cyclization to the cyclopentylmethyl radical, the reaction is interpreted on the basis of an electron-transfer mechanism. This is also supported by estimates of electron-transfer rate constants according to the Marcus theory.

Previously, one of us[1] studied the reaction between 2-phenyl-3-(arylimino)-3*H*-indole and organolithium reagents. On the basis of the composition of the reaction products (of 1,2- and 1,4-addition and reduction), the reaction mechanism was suggested to involve competition between nucleophilic attack and nonbonded electron transfer (the term "nonbonded" is to be preferred over "outer-sphere" in connection with organic electron-transfer processes).[2,3] 2-Phenyl-3-(phenylimino)-3*H*-indole has now been found to react with Grignard reagents under conditions slightly different from those used for reaction with RLi,[1] which gives another possibility to probe the reaction

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[1] Berti, C.; Greci, L.; Marchetti, L. *J. Chem. Soc., Perkin Trans 2* **1977**, 1032.

[2] Littler, J. S. *Spec. Publ. Chem. Soc.* **1970**, *no. 24*, 383.

[3] Eberson, L. *Adv. Phys. Org. Chem.* **1982**, *18*, 79.