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Angular group-induced bond alternation (AGIBA). Part 5—Conformation dependence and additivity of the effect: structural studies of 3,5-dimethoxybenzaldehyde derivatives and related systems

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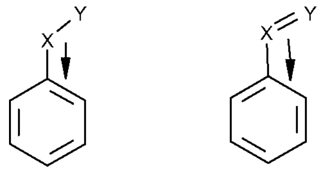
ABSTRACT: X-ray structure analysis of 3,4,5-trimethoxybenzadehyde and 3,5-dimethoxy-4-(1-bromoethoxy)benzaldehyde gave their molecular geometries which showed a vague AGIBA effect. To clarify the situation, *ab initio* optimizations at the MP2/6–31G** level of theory of 12 conformers of 1,3,5-trimethoxy-, 1,3-dimethoxy-5-formyl-, 1,3-diformyl-5-methoxy- and 1,3,5-triformylbenzene derivatives were carried out. The results support the occurrence of additive AGIBA effects, even if some weak interactions are possible between the methoxy and formyl groups. Copyright © 2001 John Wiley & Sons, Ltd.

KEYWORDS: AGIBA effect; *ab initio* calculations; methoxy substituent; formyl substituent; additivity of substituent effect

INTRODUCTION

Angular group-induced bond alternation is a well-documented structural effect[1–5] which reveals itself as illustrated in Scheme 1.



Scheme 1

The effect has also been observed experimentally for —X—Y substituents in other ring systems with equal bond lengths such as boraxine[6] and borazine,[7] which are not considered as aromatic.[8–11] Recently, an interplay between the through-resonance effect of interactions between methoxy and imino groups in the *para*-position and the typical AGIBA effect on the geometry of the ring in 3,4-dimethoxybenzaldehyde derivatives has been studied.[12] It has also been shown that monosubstituted species exhibit an approximately three times weaker structural effect than trisubstituted species, provided that all groups are of the same kind and act in line.[13]

The AGIBA effect is composed of at least two sub-effects.[1–5,13] One may be related to the Mills–Nixon effect,[14] which is associated with the rehybridization at the junction carbon atom.[15–17] Another is considered to be a through-space π-electron effect which is clearly present in cases of angular groups of the —X=Y type.

The purpose of this paper is to present a systematic study of interactions between two different substituents, an electron-donating group, methoxy, and an electron accepting group, formyl, and to show the interplay of the AGIBA effects from these two different kinds of substituents as well as their mutual interference due to the conformational changes.

EXPERIMENTAL

Calculation of the optimized geometry were carried out at the *ab initio* MP2/6–31G** level of theory employing the Gaussian 94 program.[18]

For the synthesis of 3,5-dimethoxy-4-(1-bromoethoxy)benzaldehyde, a mixture of 3,5-dimethoxy-4-hydroxybenzaldehyde (2.28 g, 12.5 mmol), 1,2-dibromoethane (5.6 g, 2.5 ml, 30 mmol) and K_2CO_3 (4.3 g, 30 mmol) in DMF was heated at 80 °C for 1 h. After cooling, the reaction was quenched with 10% HCl and

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Table 1. X-ray and crystal data

Parameter	**1**	**2**
Empirical formula	$C_{10}H_{12}O_4$	$C_{11}H_{13}O_4Br$
Formula weight	196.20	289.12
Temperature	293(2) K	293(2)K
Wavelength	0.71073 Å	0.71073 Å
Crystal system	Monoclinic	Monoclinic
Space group	$P2(1)/c$	$P2(1)/n$
Unit cell dimensions	$a = 30.293(6)$ Å	$a = 20.826(4)$ Å
	$b = 4.5940(10)$Å	$b = 4.2270(10)$ Å
	$c = 14.083(3)$ Å	$c = 27.522(6)$ Å
	$\beta = 103.41(3)°$	$\beta = 100.31(3)°$
Volume	1906.4(7) $Å^3$	2383.7(9) $Å^3$
Z	8	8
Calculated density	1.367 mg m^{-3}	1.611 mg m^{-3}
Absorption coefficient	0.106 mm^{-1}	3.445 mm^{-1}
$F(000)$	832	1168
Crystal size	0.35 × 0.2 × 0.1 mm	0.3 × 0.2 × 0.2 mm
Theta range for data collection	2.07 –23.43°	3.29 –28.38°
Index ranges	$0 \leq h \leq 28$	$-27 \leq h \leq 27$
	$-5 \leq k \leq 0$	$-5 \leq k \leq 3$
	$-15 \leq l \leq 15$	$-35 \leq l \leq 36$
Reflections collected/unique	2590/2552 [R(int) = 0.0180]	13111/5509[R(int) = 0.0768]
Refinement method	Full-matrix least-squares on F^2	
Data/restraints/parameters	2515/0/284	5509/0/322
Goodness-of-fit on	1.031	1.078
F^2		
Final R indices	$R1 = 0.0594$,	$R1 = 0.0738$,
[I > 2 σ (I)]	$wR2 = 0.1496$	$wR2 = 0.1818$
F^2		
Final R indices	$R1 = 0.0594$,	$R1 = 0.0738$,
[I > 2 σ (I)]	$wR2 = 0.1496$	$wR2 = 0.1818$
R indices (all data)	$R1 = 0.1313$,	$R1 = 0.1455$,
	$wR2 = 0.2747$	$wR2 = 0.2116$
Extinction coefficient	0.011(2)	0.0006(6)
Largest diff. peak and hole	0.196 and −0.258 e $Å^{-3}$	0.547 and −0.753 e $Å^{-3}$

extracted with chloroform. The combined extracts were washed with water and dried over $MgSO_4$. After evaporation of the solvent, the residue was chromatographed (hexane–diethyl ether, 5:2) to give a colourless solid (2.3 g, 65%), m.p. 73–75 °C (colourless needles from ethanol). ^1H NMR, δ (ppm) 3.60 (t, 2H, $J = 6.94$ Hz), 3.91 (s, 6H), 4.34 (t, 2H, $J = 6.94$ Hz), 7.11 (s, 2H), 9.85 (s, 1H); ^{13}C NMR, δ (ppm) 29.4 (CH_2), 56.1 (CH_3), 76.9 (CH_2), 106.5 (CH), 132.1 (C), 141.7 (C), 153.6 (C), 190.8 (CH); IR (KBr) (cm^{-1}), 2843, 2736, 1683, 1132, 745.

Melting-points were determined on a Köffler apparatus of the Boetius type. The ^1H and ^{13}C NMR spectra were recorded on a Bruker AC 200F spectrometer using $CDCl_3$ solution with TMS as internal standard (chemical shifts δ in ppm). The IR spectra were recorded on a Nicolet Magna 550 FTIR spectrometer as KBr pellets. The reaction products were isolated by column chromatography performed on 70–230-mesh silica gel (Merck). Thin-layer chromatograms were developed on aluminium TLC sheets precoated with silica gel F_{254}. The spots were visualized with 50% sulphuric acid after heating. All the solvents were dried and freshly distilled prior to use.

3,4,5-Trimethoxybenzadehyde (Aldrich) was recrystallised from ethanol.

X-ray measurements. X-ray measurements of monocrystalline 3,4,5-trimethoxybenzaldehyde (**1**) were carried out on a KM-4 KUMA diffractometer with graphite monochromated Mo Kα radiation. The intensities were collected at room temperature using the $\omega - 2\theta$ scan technique. The intensity of control reflections varied by less than 3% and a linear correction factor was applied to account for this effect. The measurement of crystalline 3,5-dimethoxy-4-(1-bromoethoxy)benzaldehyde (**2**) was performed on a Kuma KM4CCD κ-axis diffractometer with graphite-monochromated Mo Kα radiation. The crystal was positioned 65 mm from the KM4CCD camera and 760 frames were measured at 0.60° intervals with a counting time of 40 s. Data reduction and analysis were carried out with the Kuma Diffraction programs.

Corrections for Lorentz and polarization effects were

Table 2. Selected bond lengths (Å) and angles (°) for **1** and **2**

	1		**2**	
Parameter	**A**	**B**	**A**	**B**
C(11)—C(61)	1.341(7)	1.354(8)	1.379(8)	1.391(9)
C(11)—C(21))	1.369(7)	1.373(8)	1.388(9)	1.405(9)
C(11)—C(71)	1.450(8)	1.442(7)	1.471(10)	1.482(9)
C(21)—C(31)	1.366(7)	1.353(6)	1.385(9)	1.389(9)
C(31)—O(21)	1.344(6)	1.337(6)	1.362(7)	1.373(7)
C(31)—C(41)	1.366(7)	1.369(7)	1.383(8)	1.402(8)
C(41)—O(31)	1.353(5)	1.358(5)	1.364(7)	1.375(7)
C(41)—C(51)	1.364(7)	1.367(7)	1.411(8)	1.414(9)
C(51)—O(41)	1.333(6)	1.352(6)	1.376(7)	1.346(7)
C(51)—C(61)	1.351(7)	1.379(9)	1.391(9)	1.382(8)
C(61)—C(11)—C(21)	121.6(5)	121.6(5)	120.8(6)	121.9(5)
C(61)—C(11)—C(71)	119.3(6)	120.3(6)	121.2(7)	121.4(6)
C(21)—C(11)—C(71)	119.1(6)	118.1(6)	118.0(6)	116.6(6)
O(21)—C(31)—C(21)	124.7(5)	125.8(5)	124.0(6)	123.9(6)
O(21)—C(31)—C(41)	115.1(4)	115.1(4)	115.7(6)	115.7(5)
C(21)—C(31)—C(41)	120.2(5)	120.1(5)	120.3(6)	120.4(6)
O(31)—C(41)—C(51)	119.7(4)	118.7(5)	119.1(5)	118.4(5)
O(31)—C(41)—C(31)	119.6(4)	120.6(4)	121.5(6)	120.2(5)
C(51)—C(41)—C(31)	120.6(4)	120.7(4)	119.3(5)	121.2(5)
O(41)—C(51)—C(41)	116.3(4)	115.8(4)	114.4(5)	114.4(5)
O(41)—C(51)—C(61)	124.7(5)	124.0(5)	124.8(8)	127.6(6)
C(41)—C(51)—C(61)	119.0(5)	120.2(5)	120.2(6)	118.0(6)

made, but no absorption correction was applied. The structure was solved by direct methods[19] and refined using SHELXL.[20] The refinement was based on $F2$ for all reflections except those with very negative $F2$. The weighted R factor, wR and all goodness-of-fit S values are based on $F2$. The non-hydrogen atoms were refined anisotropically, whereas the hydrogen atoms were placed in the calculated positions, and their thermal parameters were refined isotropically. The atomic scattering factors were taken from the *International Tables*.[21] Details of the X-ray measurements and crystal data for both compounds are given in Table 1, and their ORTEP scheme and labelling of atoms are shown in Fig. 1. Table 2 presents selected geometric parameters of the compounds. Crystallographic data for the structures **1** and **2** have been deposited with the Cambridge Crystallographic data centre as supplementary publication No. CCDC 144198 (**1**) and CCDC 144199 (**2**).

RESULTS AND DISCUSSION

3,4,5-Trimethoxybenzadehyde (**1**) and 3,5-dimethoxy-4-(1-bromoethoxy)benzaldehyde (**2**) represent molecules in which the two dimethoxy groups act in the opposite sense of the AGIBA effect. Thus the effect of the formyl group

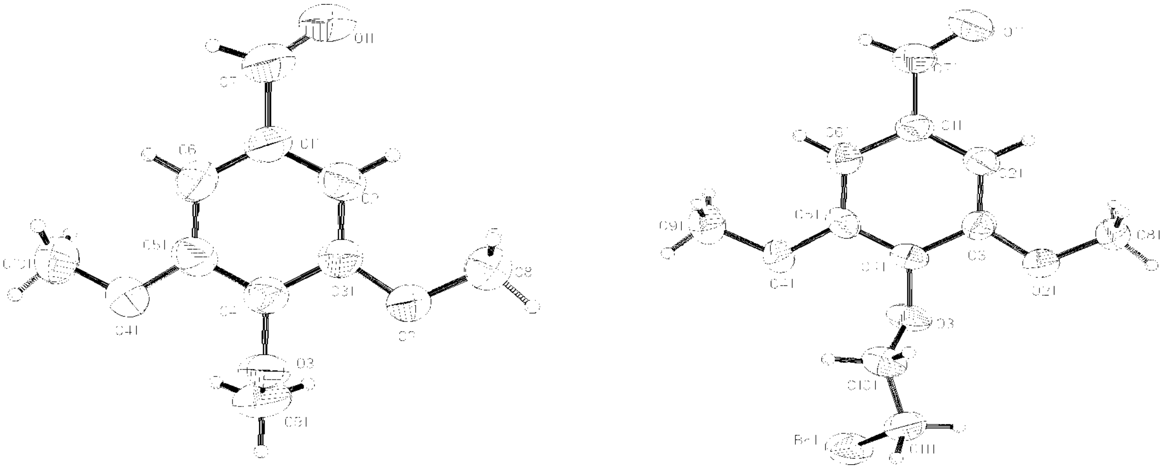
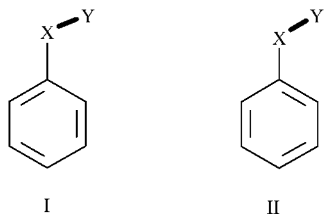


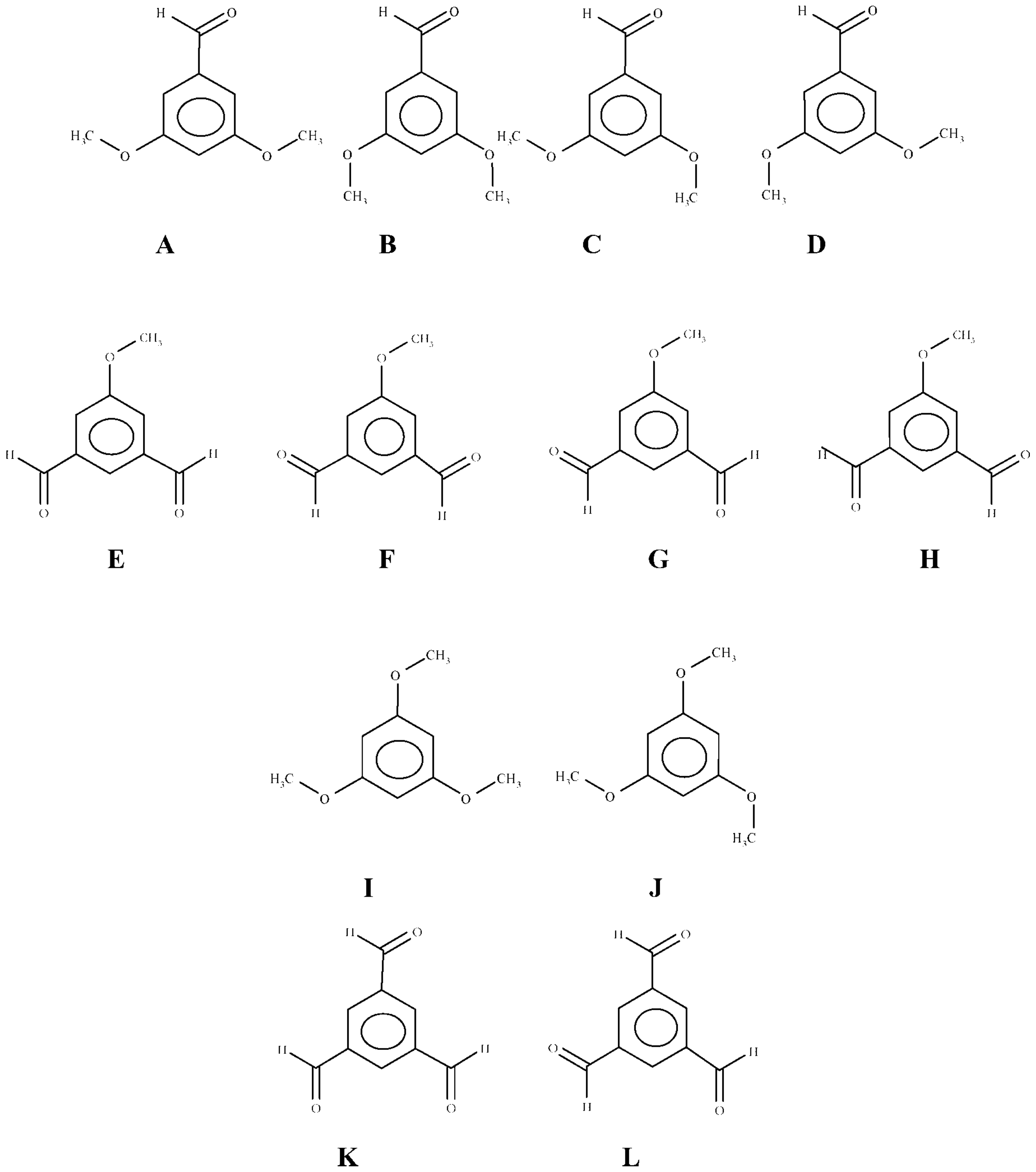
Figure 1. Structures of compounds **1** and **2**. Thermal ellipsoids are drawn at the 50% probability level



Scheme 2. XY represents either OMe or CHO groups

should dominate. However, this group exerts a rather weak AGIBA effect[13] and hence only in the case of **1** is the effect observable: the canonical structure II weights (Scheme 2) are 44.38 and 46.32 for the two independent molecules in the elementary units, respectively.

A different situation is found for **2**, which exists in the crystal lattice as two independent molecules. One of them follows the AGIBA effect with a weight of 42.41% whereas the other has a weight of 51.30% and does not follow the rule of the AGIBA effects. This difference may be explained as a result of intermolecular interactions which cause greater bond angles at carbon atoms substituted by methoxy groups (Table 2) and hence may mask a weak AGIBA effect. Additionally, owing to the



Scheme 3

Table 3. HOSE values of the weighting factors and those from the additivity rule

Molecule/ conformer	Lower value of the weight from the HOSE model	From the additivity rule
A	48.30	47.56
B	48.32	47.56
C	42.40	42.80
D	38.81	37.92
E	45.19	45.18
F	45.46	45.18
G	49.14	49.94
H	41.27	40.30
I	45.22	45.18
J	36.14	35.54
K	47.45	47.56
L	42.68	42.68

poor precision of measurements, the results cannot be considered as strongly conclusive. In order to understand better the AGIBA effect in systems in which two different substituents may act in-line or in oppositely senses, we carried out theoretical studies as described below.

All conformers of 1,3,5-substituted benzene derivatives with CHO and MeO substituents shown in Scheme 3 were subjected to *ab initio* geometry optimization, allowing the estimation of the Kekulé structure weights (Scheme 2) by use of the HOSE model.[22] Application of the HOSE model is advantageous since the calculated weights of the canonical structures take into account the whole ring geometry, whereas individual differences in bond lengths would be misleading for the cases when the different groups, MeO and CHO, acted in opposite direction with no significant local changes in geometry.

Since the MeO and CHO groups act within the frame of the AGIBA effect in opposite directions, the weights of canonical structures, say **I**, for anisole and benzaldehyde, are one below 50% and the other above 50%, namely 45.18% and 52.44%, respectively. Assuming additivity of the AGIBA effect, which has been documented by us earlier,[13] we accepted the convention in this paper that the changes in weights associated with a particular group in this study are −4.82% for the MeO group and +2.44% for the CHO group. If these groups are oriented in-line in a given conformer, the increments are of opposite sign; if they are opposite in direction, their increments are of the same sign. Then the sum of the increments from each group is subtracted from 50%, giving a final value of the canonical weight resulting from the additivity rule. Scheme 3 shows the conformers of 1,3,5-trimethoxy-, 1,3-dimethoxy-5-formyl-, 1,3-diformyl-5-methoxy- and 1,3,5-triformylbenzene derivatives considered in this study.

Table 3 presents the weights of a canonical structure lower than 50% calculated by use of the HOSE model directly from the geometry and the value resulting from the additivity rule.

The imbalance between the two Kekule structures I and II in the molecules and their conformers **A**–**L** presented in Table 2 is significant. It is expressed as only one weight; evidently the other is a supplement to 100%. As is known from our earlier work,[13] the methoxy group acts more strongly than the formyl group. Even in the case where MeO acts against two CHO groups acting in-line, case **G**, the MeO group dominates, even over the expectation resulting from the additivity rule.

It is worth mentioning that in the case of homo-trisubstituted species, such as cases **I, J, K** and **L**, the deviations from the additivity rule are much smaller (mean deviation = 0.19) than in other cases (0.60). This effect may result from a slight mesomeric interaction between the electron-donating MeO group and the electron-accepting CHO group. It is well known that in the *meta*-position such an effect is rather small but it does still exist, accounting for about one-third of that in the *para*-position.[23]

CONCLUSIONS

This work provides support for a strong conformation dependence and the additive nature of the AGIBA effect which functions even in cases where some weak mesomeric interactions able to perturb the effect exist.

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