organic compounds

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1-Chloro-3,6-dimethoxy-2,5-dimethylbenzene and 1-chloro-3,6-dimethoxy-2,4-dimethylbenzene

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The title compounds, 1-chloro-3,6-dimethoxy-2,5-dimethylbenzene, (IIIa), and 1-chloro-3,6-dimethoxy-2,4-dimethylbenzene, (IIIb), both C₁₀H₁₃ClO₂, were obtained from 2,5- and 2,6dimethyl-1,4-benzoquinone, respectively, and are intermediates in the synthesis of ammonium quinone derivatives. The isomers have different substituents around the methoxy groups and crystallize in different space groups. In both molecules, the methoxy groups each have different orientations with respect to the benzene ring. In both cases, one methoxy group lies in the plane of the ring and can participate in conjugation with the aromatic system, while the second is almost perpendicular to the plane of the aromatic ring. The C-O-C bond angles around these substituents are also different: 117.5 (4) and 118.2 (3) $^{\circ}$ in (IIIa) and (IIIb), respectively, when the methoxy groups lie in the plane of the ring, and 114.7 (3) and 113.6 (3) $^{\circ}$ in (IIIa) and (IIIb), respectively, when they are out of the plane of the ring.

Comment

We have been engaged in the synthesis of ammonium quinone derivatives as electron acceptors for charge-transfer studies, and had occasion to prepare the two chlorodimethoxydimethylbenzene isomers (IIIa) and (IIIb) as precursors to our targets. The chlorine substituents were introduced in order to prepare quinones with an electron-withdrawing group. These compounds were synthesized in a two-step sequence, namely treatment of a dimethylbenzoquinone with methanolic hydrogen chloride followed by O-methylation. For example, in the synthesis of (IIIa), 2,5-dimethyl-1,4-benzoquinone, (Ia), was treated with methanolic hydrogen chloride to give a quantitative yield of 2-chloro-4-methoxy-3,6-dimethylphenol, (IIa). This latter species was then methylated under phasetransfer conditions with dimethyl sulfate to give a 96% yield of the diether (IIIa). The synthesis of (IIIb) was similar, but gave lower yields along with more side products in each step of this

sequence, for reasons which are not clear. Starting with (III*a*) and (III*b*), we also synthesized unexpected dimers using amidomethylation reactions (Wiedenfeld *et al.*, 2004).



Isomers (III*a*) and (III*b*) have different substituents around the methoxy groups on the adjacent atoms of the ring and crystallize in different space groups (Figs. 1 and 2). In both molecules, the methoxy groups each have different orientations with respect to the benzene ring. In both cases, one lies in the plane of the ring and can participate in conjugation with the aromatic system [torsion angles C2-C3-O2-C9 =-179.4 (4)° in (III*a*) and C1-C6-O1-C7 = -179.9 (4)° in (III*b*)], and the second is almost perpendicular to the plane of the aromatic ring [torsion angles C1-C6-O1-C7 = 86.9 (5)° in (III*a*) and C2-C3-O2-C9 = 94.0 (4)° in (III*b*)].

Such different orientations of the methoxy groups about the benzene ring in (III*a*) and (III*b*) account for the distortion of the bond angles. Thus, we found an increase in the C3-O2-C9 angle to 117.5 (4)° in (III*a*) and in C6-O1-C7 to 118.2 (3)° in (III*b*) for the in-plane methoxy group. For the out-of-plane methoxy group, C6-O1-C7 and C3-O2-C9 are distinctly lower, at 114.7 (3)° in (III*a*) and 113.6 (3)° in (III*b*). We have previously found such effects in related compounds (Wiedenfeld *et al.*, 2003, 2004). Such geometry is usual for compounds containing OCH₃ groups with different orientations about aromatic rings (Gallagher *et al.*, 2001). Other bond lengths and angles in the title molecules have expected values (Allen *et al.*, 1987).

Analysis of the crystal packing of compounds (III*a*) and (III*b*) shows that there are very weak intermolecular contacts



Figure 1

A view of the molecule of (IIIa), with the atom-numbering scheme. Displacement ellipsoids are drawn at the 50% probability level and H atoms are shown as small spheres of arbitrary radii.



Figure 2

A view of the molecule of (IIIb), with the atom-numbering scheme. Displacement ellipsoids are drawn at the 50% probability level and H atoms are shown as small spheres of arbitrary radii.

 $[O1\cdots H7B(x, y-1, z) = 2.54 \text{ Å} \text{ in (III}a) \text{ and } O1\cdots H8B(1-x, \frac{1}{2}+y, 1-z) = 2.59 \text{ Å} \text{ in (III}b)], \text{ which can be}$ considered to be weak hydrogen bonds that link molecules in the crystals, with parameters $O1 \cdot \cdot \cdot C7 = 3.461$ (5) Å, C7-H7B = 0.96 Å and $C7 - H7B \cdot \cdot \cdot O1 = 161^{\circ}$ in (IIIa), and $O1 \cdots C8 = 3.524 (5) \text{ Å}, C8 - H8B = 0.96 \text{ Å} and O1 \cdots C8 - C8 - C8 = 0.96 \text{ Å}$ $H8B = 164^{\circ}$ in (IIIb).

In the crystal structure of (IIIb), the intermolecular distances Cl1···C5($-x, \frac{1}{2} + y, 1 - z$) [3.587 (5) Å] and $Cl1 \cdots C6(-x, \frac{1}{2} + y, 1 - z)$ [3.577 (5) Å] are slightly greater than the sum of the van der Waals radii (Rowland & Taylor, 1996) but shorter than in (IIIa), where the distance $Cl1 \cdots C4(x - \frac{1}{2}, \frac{1}{2} - y, z)$ is 3.613 (5) Å. Such weak intermolecular interactions could play a significant role in the stability of the crystal, especially in the case of (IIIb), which is more stable than (IIIa) under X-ray irradiation (see Experimental). The other intermolecular distances in both crystals are greater than the sums of the van der Waals radii of the atoms.

Experimental

For the preparation of 2-chloro-3,6-dimethyl-4-methoxyphenol, (IIa), 2,5-dimethyl-1,4-benzoquinone, (Ia) (1.36 g, 10 mmol), was added to an ice-cold solution of MeOH (70 ml) containing AcCl (7 ml, 0.1 mol) and stirred overnight at room temperature. The solution was then concentrated on a rotary evaporator and vacuum dried, giving 1.86 g (100%) of (IIa) as a pink crystalline solid, pure by NMR. ¹H NMR (DMSO-d₆, δ): 8.41 (s, 1H, OH), 6.72 (s, 1H, Ar-H), 3.71 (s, 3H, OCH₃), 2.19 (s, 3H, Ar-CH₃-3^{*}), 2.14 (s, 3H, Ar-CH₃-6^{*}); ¹³C NMR (DMSO-d₆, δ): 150.4 (Ar-C4), 144.4 (Ar-C1), 123.7 (Ar-C3), 122.5 (Ar-C2), 121.4 (Ar-C6), 111.8 (Ar-C5), 56.0 (OCH₃), 16.9 (Ar-CH₃-6), 12.9 (Ar-CH₃-3). 3-Chloro-2,6-dimethyl-4-methoxyphenol, (IIb), was prepared analogously to (IIa), starting from 2,6-dimethyl-1,4-benzoquinone, (Ib). ¹H NMR (CDCl₃, δ): 6.60 (s, 1H, Ar-H), 4.38 (br s, 1H, OH), 3.83 (s, 3H, OCH₃), 2.32 (s, 3H, Ar-CH₃-2^{*}), 2.24 (s, 3H, Ar- CH_3-6^*). For the preparation of compound (III*a*), a solution of KOH (1.98 g, 30 mmol, 3 equivalents at 85%) in H₂O (30 ml) was added to a solution of (IIa) (1.86 g, 10 mmol) and (n-Bu)₄NBr (0.97 g, 3 mmol, 0.3 equivalents) in CH_2Cl_2 (30 ml). To the vigorously stirred mixture was added Me₂SO₄ (2.85 ml, 30 mmol, 3 equivalents) in three portions over 6 h. After a further 3 h, 2 N aqueous NaOH (12 ml) was added and the mixture stirred overnight. Extractive work-up with CH₂Cl₂ gave an orange oil which, after chromatography on silica gel

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using 25:1 hexanes-EtOAc as eluant, afforded 1.92 g (96%) of pure product as a colourless oil that crystallized slowly. After recrystallization from 10% EtOAc in hexane, the melting point was 321-322 K. ¹H NMR (CDCl₃, *δ*): 6.56 (*s*, 1H, Ar-H), 3.79 (*s*, 3H, OCH₃-6*), 3.76 (s, 3H, OCH₃-3*), 2.29 (s, 3H, Ar-CH₃-2*), 2.24 (s, 3H, Ar-CH₃-5*); ¹³C NMR (CDCl₃, δ): 153.9 (Ar-C3), 148.0 (Ar-C6), 129.2 (Ar-C5), 128.9 (Ar-C1), 123.6 (Ar-C2), 110.8 (Ar-C4), 60.1 (OCH₃-6), 55.9 (OCH₃-3), 16.4 (Ar-CH₃-5), 12.8 (Ar-CH₃-2). For the preparation of compound (IIIb), O-methylation of (IIb) was analogous to that for (IIa). After recrystallization from 10% EtOAc in hexane, the melting point was 323–324 K. ¹H NMR (CDCl₃, δ): 6.61 (s, 1H, Ar-H), 3.85 (s, 3H, OCH₃-6), 3.66 (s, 3H, OCH₃-3), 2.33 (s, 3H, Ar-CH₃-2), 2.28 (s, 3H, Ar-CH₃-4); ¹³C NMR (CDCl₃, δ): 151.3 (Ar-C6), 150.9 (Ar-C3), 130.8 (Ar-C2), 129.3 (Ar-C4), 120.4 (Ar-C1), 111.3 (Ar-C5), 60.2 (OCH₃-3), 56.3 (OCH₃-6), 16.3 (Ar-CH₃-4), 13.6 (Ar-CH₃-2). For X-ray analysis, crystals of both compounds were grown from 10% ethyl acetate in hexanes by slow evaporation at room temperature. X-ray investigations revealed that the crystals of these compounds exhibit different behaviour under an X-ray beam. Thus, the structure of compound (IIIa) was investigated several times, but the crystals decomposed during the experiments, while crystals of (IIIb) did not decay. For (IIIa), the crystal was coated with a two-component epoxy glue, which successfully protected the crystal and prevented further decay.

Compound (IIIa)

Crystal data	
$C_{10}H_{13}ClO_2$	Mo $K\alpha$ radiation
$M_r = 200.65$	Cell parameters from 24
Orthorhombic, Pna2 ₁	reflections
a = 14.490(3) Å	$\theta = 11-12^{\circ}$
b = 4.1470 (8) Å	$\mu = 0.34 \text{ mm}^{-1}$
c = 16.848 (3) Å	T = 295 (2) K
V = 1012.4 (3) Å ³	Prism, colorless
Z = 4	$0.50 \times 0.40 \times 0.30 \text{ mm}$
$D_x = 1.316 \text{ Mg m}^{-3}$	
Data collection	
Enraf–Nonius CAD-4	$\theta_{\rm max} = 30.0^{\circ}$
diffractometer	$h = -20 \rightarrow 20$
$\theta/2\theta$ scans	$k = -5 \rightarrow 0$
2961 measured reflections	$l = 0 \rightarrow 23$
1507 independent reflections	3 standard reflections
1010 reflections with $I > 2\sigma(I)$	every 97 reflections
$R_{\rm int} = 0.098$	intensity decay: 3%

Refinement

Refinement on F^2	$w = 1/[\sigma^2(F_o^2) + (0.09P)^2]$
$R[F^2 > 2\sigma(F^2)] = 0.063$	where $P = (F_o^2 + 2F_c^2)/3$
$wR(F^2) = 0.163$	$(\Delta/\sigma)_{\rm max} < 0.001$
S = 1.03	$\Delta \rho_{\rm max} = 0.60 \ {\rm e} \ {\rm \AA}^{-3}$
1507 reflections	$\Delta \rho_{\rm min} = -0.47 \text{ e } \text{\AA}^{-3}$
122 parameters	Absolute structure: Flack (1983),
H-atom parameters constrained	with 20 Friedel pairs
	Flack parameter $= 0.18$ (14)

Table 1

Selected geometric parameters (Å, °) for (IIIa).

Cl1-C1	1.738 (3)	O2-C3	1.385 (5)
O1-C6	1.362 (5)	O2-C9	1.417 (6)
O1-C7	1.418 (5)		
C6-O1-C7	114.7 (3)	C3-O2-C9	117.5 (4)
C9-O2-C3-C2	-179.4(4)	C7-O1-C6-C1	86.9 (5)

Compound (IIIb)

Crystal data

 $\begin{array}{l} C_{10}H_{13}ClO_2\\ M_r = 200.65\\ Monoclinic, P2_1\\ a = 6.0740 \ (12) \ {\rm \AA}\\ b = 9.1250 \ (18) \ {\rm \AA}\\ c = 9.4450 \ (19) \ {\rm \AA}\\ \beta = 103.11 \ (3)^{\circ}\\ V = 509.85 \ (18) \ {\rm \AA}^3\\ Z = 2 \end{array}$

Data collection

Enraf–Nonius CAD-4 diffractometer $\theta/2\theta$ scans 1688 measured reflections 1559 independent reflections 999 reflections with $I > 2\sigma(I)$ $R_{\rm int} = 0.056$

Refinement

Refinement on F^2 $R[F^2 > 2\sigma(F^2)] = 0.051$ $wR(F^2) = 0.155$ S = 1.071559 reflections 122 parameters H-atom parameters constrained $D_x = 1.307 \text{ Mg m}^{-3}$ Mo $K\alpha$ radiation Cell parameters from 24 reflections $\theta = 11-12^{\circ}$ $\mu = 0.34 \text{ mm}^{-1}$ T = 295 (2) K Prism, colorless $0.45 \times 0.35 \times 0.25 \text{ mm}$

 $\begin{array}{l} \theta_{\max} = 30.0^{\circ} \\ h = 0 \rightarrow 8 \\ k = 0 \rightarrow 12 \\ l = -13 \rightarrow 12 \\ 3 \text{ standard reflections} \\ \text{every 97 reflections} \\ \text{intensity decay: 3\%} \end{array}$

$$\begin{split} w &= 1/[\sigma^2(F_o^2) + (0.09P)^2 \\ &+ 0.04P] \\ \text{where } P &= (F_o^2 + 2F_c^2)/3 \\ (\Delta/\sigma)_{\text{max}} &< 0.001 \\ \Delta\rho_{\text{max}} &= 0.31 \text{ e } \text{Å}^{-3} \\ \Delta\rho_{\text{min}} &= -0.20 \text{ e } \text{Å}^{-3} \\ \text{Absolute structure: Flack (1983),} \\ \text{with 11 Friedel pairs} \\ \text{Flack parameter} &= 0.02 (13) \end{split}$$

All H atoms were placed in geometrically calculated positions and refined using a riding model, with C–H distances of 0.93 Å for aromatic and 0.96 Å for CH₃ groups, and with $U_{iso}(H) = 1.2U_{eq}(C)$.

For both compounds, data collection: *CAD-4 Software* (Enraf-Nonius, 1989); cell refinement: *CAD-4 Software*; data reduction: *SHELXTL-Plus* (Sheldrick, 1994); program(s) used to solve structure: *SHELXS*97 (Sheldrick, 1990); program(s) used to refine structure.

Table 2 Selected competition percompeters $(Å, \circ)$

Selected geometric parameters (Å, °) for (IIIb).

Cl1-C1 O1-C6 O1-C7	1.735 (4) 1.358 (4) 1.421 (5)	O2-C3 O2-C9	1.378 (4) 1.426 (5)
C6-O1-C7	118.2 (3)	C3-O2-C9	113.6 (3)
C9-O2-C3-C2	94.0 (4)	C7-O1-C6-C1	-179.9 (4)

ture: *SHELXL*97 (Sheldrick, 1997); molecular graphics: *SHELXTL-Plus*; software used to prepare material for publication: *SHELXL*97.

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: GG1216). Services for accessing these data are described at the back of the journal.

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