

# The rotation of the nitro and formyl groups relative to the aromatic ring in some *ortho*-nitroarylaldehydes

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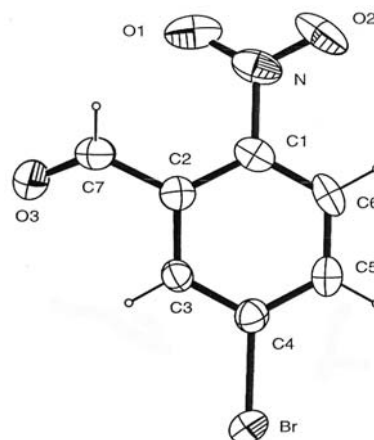
X-Ray crystallographic studies have shown that in *ortho*-nitroarylaldehydes the plane of an aryl nitro group is rotated relative to the aromatic ring to a greater extent than that of the adjacent formyl group.

**Keywords** steric hindrance, conformation, *o*-nitroaldehydes

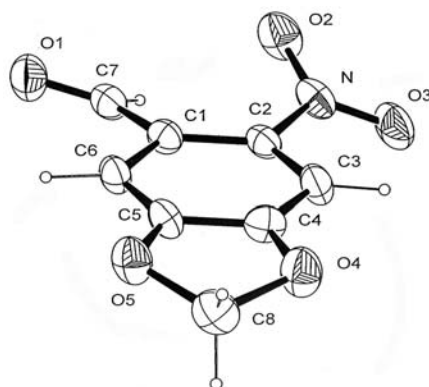
The steric interactions of a nitro group with an adjacent substituent on an aromatic ring may be relieved by its rotation out of the plane of the aromatic ring. There is a balance between the consequent loss of resonance energy and the relief of this steric compression.<sup>1</sup> This rotation has an impact on the chemistry of the *ortho* substituted aromatic nitro compounds in diminishing the rate of aromatic nucleophilic substitution of *para* bromo substituents<sup>2</sup> and the activation of aryl methyl groups by nitro groups in carbanion condensation reactions.<sup>3</sup> X-Ray crystallographic studies have shown<sup>4</sup> that one *ortho* substituent can produce a rotation between the plane of the nitro group and the aromatic ring of approximately 40° whilst two *ortho* substituents lead to a rotation of about 70°. The extent of this rotation of the plane of the nitro group may be diminished by an electron-donating *para* methoxy group.<sup>5</sup> When the nitro group is adjacent to a carbonyl group there is the possibility of interaction between the two dipoles which may affect the plane of rotation. In this paper, we compare by X-ray crystallography, the influence of substituents on the rotation of adjacent nitro and carbonyl groups in the solid state.

4-Bromo-2-formylnitrobenzene (5-bromo-2-nitrobenzaldehyde), prepared by the nitration of 3-bromobenzaldehyde,<sup>6</sup> gave suitable crystals for X-ray crystallography (see Fig. 1). The mutual interaction of the aldehyde and nitro groups led to their rotation relative to the plane of the aromatic ring to the extent of 32.6° and 25.8° respectively. The influence of a *para* oxygen substituent on the rotation of the formyl and nitro groups was then examined. Unfortunately 4,5-dimethoxy-2-nitrobenzaldehyde, prepared by nitrating veratraldehyde, crystallised from a number of different solvents as very fine needles that were unsuitable for X-ray crystallography. 4,5-Methylenedioxy-2-nitrobenzaldehyde, prepared by nitrating piperonal,<sup>7</sup> gave better crystals. Although the methylenedioxy group has a diminished electron-donating effect compared to the methoxy group,<sup>8</sup> the X-ray crystal structure of 4,5-methylenedioxy-2-nitrobenzaldehyde (Fig. 2) showed that the planes of rotation of the formyl and nitro groups were slightly diminished to 22.9° and 24.2°.

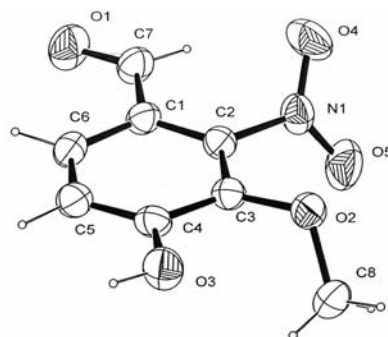
A difference between the rotation of the nitro group and the formyl group was observed in a comparison of the structures of 4-hydroxy-3-methoxy-2-nitrobenzaldehyde (2-nitrovanillin, Fig. 3), 4-acetoxy-3,5-dimethoxy-2-nitrobenzaldehyde (Fig. 4) and 5-bromo-2,3-dimethoxy-6-nitrobenzaldehyde (Fig. 5). These compounds were chosen to reflect the effect of substituents adjacent to and *para* to the nitro and formyl groups. 2-Nitrovanillin was obtained by nitrating 4-acetoxyvanillin and hydrolysing the acetate.<sup>9</sup> 4-Acetoxy-3,5-dimethoxy-2-nitrobenzaldehyde was obtained by nitrating the acetate of syringaldehyde.<sup>10</sup> The nitration of 3,4,5-trimethoxybenzaldehyde gave 3,4,5-trimethoxynitrobenzene as a consequence of *ipso* substitution of the formyl group. 5-Bromo-2,3-dimethoxy-6-nitrobenzaldehyde was prepared by brominating *o*-vanillin, methylating the phenol and



**Fig. 1** X-Ray crystal structure of 4-bromo-2-formylnitrobenzene; interplanar angles: nitro:aryl, 25.8°; formyl:aryl, 32.6°.

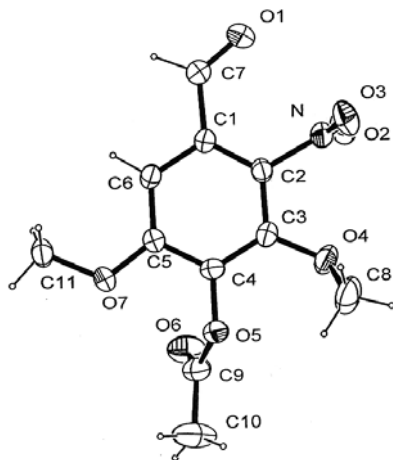


**Fig. 2** X-Ray crystal structure of 4,5-methylenedioxy-2-nitrobenzaldehyde; interplanar angles: nitro:aryl, 24.2°; formyl:aryl, 22.9°.

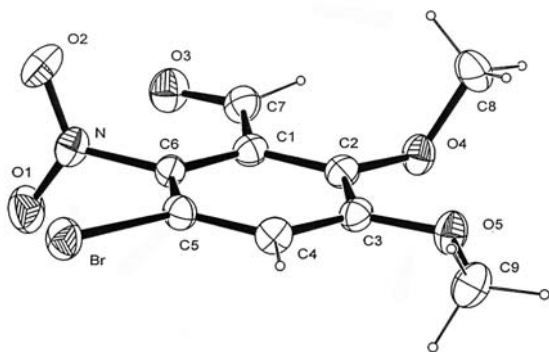


**Fig. 3** X-Ray crystal structure of 4-hydroxy-3-methoxy-2-nitrobenzaldehyde; interplanar angles: nitro:aryl, 61.8°; formyl:aryl, 1.7°.

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**Fig. 4** X-Ray crystal structure of 4-acetoxy-3,5-dimethoxy-2-nitrobenzaldehyde; interplanar angles: nitro:aryl, 89.3°; formyl:aryl, 4.7°.



**Fig. 5** X-Ray crystal structure of 5-bromo-2,3-dimethoxy-6-nitrobenzaldehyde; interplanar angles: nitro:aryl, 85.2°; formyl:aryl, 7.6°.

nitration.<sup>11</sup> In all cases, the plane of the nitro group was rotated significantly with respect to the aromatic ring (2-nitrovanillin, 61.8°, 4-acetoxy-3,5-dimethoxy-2-nitrobenzaldehyde, 89.3°, 5-bromo-2,3-dimethoxy-6-nitrobenzaldehyde, 85.2°) whilst the formyl group remained essentially co-planar with the aromatic ring (2-nitrovanillin, 1.7°, 4-acetoxy-3,5-dimethoxy-2-nitrobenzaldehyde, 4.7°, 5-bromo-2,3-dimethoxy-6-nitrobenzaldehyde, 7.6°).

Although these results were obtained in the crystalline state and may therefore be affected by crystal packing effects, they, nevertheless, show that the formyl group has far less of a tendency to rotate than the nitro group. This suggests that the electronic interactions between a formyl group and the aromatic ring may be stronger than those of a nitro group.

In the course of characterisation of 4-acetoxy-3,5-dimethoxy-2-nitrobenzaldehyde, the high-resolution mass spectrum was obtained by electrospray ionisation at room temperature. When this was carried out using methanol as a solvent, the molecular ion that was observed, was that of a methoxy hemi-acetal. The same effect was observed from the parent 4-acetoxy-3,4-dimethoxybenzaldehyde. The molecular ion of the aldehyde was observed using acetonitrile as the solvent. Since methanol is a common solvent for electrospray ionisation, this facile hemi-acetal formation from an aldehyde might be misleading.

## Experimental

**General experimental details:** <sup>1</sup>H NMR spectra were determined at 300 MHz for solutions in deuteriochloroform. IR spectra were

determined as nujol mulls. Mass spectra were determined on a Bruker Daltonics Apex III electrospray mass spectrometer. The following *ortho*-nitrobenzaldehydes were prepared by literature methods. 4-Bromo-2-formylnitrobenzene had m.p. 71°C (lit.,<sup>6</sup> 69.1–70.8°C); 4,5-methylenedioxy-2-nitrobenzaldehyde had m.p. 97°C (lit.,<sup>7</sup> 98.5°C); 4-hydroxy-3-methoxy-2-nitrobenzaldehyde had m.p. 136°C (lit.,<sup>9</sup> 137°C); 5-bromo-2,3-dimethoxy-6-nitrobenzaldehyde had m.p. 141°C (lit.,<sup>11</sup> 141°C).

**Nitration of 3,4,5-trimethoxybenzaldehyde:** A nitrating mixture of conc. nitric acid (6 cm<sup>3</sup>) and conc. sulfuric acid (12 cm<sup>3</sup>) was prepared and cooled in an ice-bath. 3,4,5-Trimethoxybenzaldehyde (2 g) was added in portions over a period of 10 min and the mixture was left at room temperature for 45 min. It was poured into ice-water and the product was filtered and recrystallised from aqueous methanol to give 3,4,5-trimethoxynitrobenzene (0.7 g) as needles, m.p. 98°C (lit.,<sup>12</sup> 99°C),  $\nu_{\max}/\text{cm}^{-1}$  1619, 1523, 1497, 1338;  $\delta_{\text{H}}$  3.95 (9H, 3 × OMe), 7.50 (2H, s, ArH).

**Nitration of 4-acetoxy-3,5-dimethoxybenzaldehyde:** A nitrating mixture comprising conc. nitric acid (8 cm<sup>3</sup>), glacial acetic acid (5 cm<sup>3</sup>) and acetic anhydride (5 cm<sup>3</sup>) was carefully prepared with ice-cooling behind a screen.

**CAUTION:** Mixtures of fuming nitric acid and acetic anhydride are known to be dangerously unstable and can detonate.<sup>13–15</sup> Although in the present case the acid used is not fuming, caution is advised.

4-Acetoxy-3,5-dimethoxybenzaldehyde<sup>10</sup> (1.5 g) in glacial acetic acid (10 cm<sup>3</sup>) was added and the mixture was left in ice for 1 h. It was poured onto ice to give 4-acetoxy-3,5-dimethoxy-2-nitrobenzaldehyde (1.2 g) which crystallised from aqueous methanol as needles, m.p. 112°C,  $\nu_{\max}/\text{cm}^{-1}$  1777, 1701, 1584, 1531, 1336;  $\delta_{\text{H}}$  2.39 (3H, s, OAc), 3.95 (6H, s, 2 × OMe), 7.26 (1H, s, ArH), 9.93 (1H, s, CHO); HRMS Found (in MeOH) M<sup>+</sup> 324.0682 C<sub>12</sub>H<sub>15</sub>NO<sub>8</sub>Na requires 324.0689; Found (in MeCN) M<sup>+</sup> 292.0419 C<sub>11</sub>H<sub>11</sub>NO<sub>7</sub>Na requires 292.0428. We thank Dr. Ali Al-Sada for these measurements.

### X-Ray crystal data and structure determinations

Data were collected using a Kappa CCD diffractometer. No absorption corrections were applied. Structures were solved by direct methods and refined using SHELXL-97. The drawings used ORTEP-3 for Windows. The CCDC Numbers given below contain the supplementary crystallographic data for this paper. The data can be obtained free of charge from the Cambridge Crystallographic Centre via [www.ccdc.cam.ac.uk/data\\_request.cif](http://www.ccdc.cam.ac.uk/data_request.cif).

**4-bromo-2-formylnitrobenzene** (5-bromo-2-nitrobenzaldehyde), C<sub>7</sub>H<sub>4</sub>BrNO<sub>3</sub>; M<sub>r</sub> 230.02, monoclinic, space group P2<sub>1</sub>/c (No 14),  $a = 7.4931(4)$ ,  $b = 3.8750(2)$ ,  $c = 26.9313(15)$  Å,  $\alpha = \beta = \gamma = 90^\circ$ ,  $V = 95.952(3)$  Å<sup>3</sup>,  $Z = 4$ ,  $D_{\text{calc}} = 1.96$  g cm<sup>-3</sup>,  $\mu = 5.25$  mm<sup>-1</sup>, F(OO0) 448. Crystal size 0.4 × 0.2 × 0.2 mm. A total of 3650 reflections were collected for 3.87 <  $\theta$  < 25.00° and  $-8 \leq h \leq 8$ ,  $-4 \leq k \leq 4$ ,  $-29 \leq l \leq 32$ . There were 1359 independent reflections and 1197 reflections with  $I > 2\sigma(I)$  were used in the refinement. The final R indices were [ $I > 2\sigma(I)$ ] R<sup>1</sup> 0.033, wR<sup>2</sup> 0.069 and (all data) R<sup>1</sup> 0.040, wR<sup>2</sup> 0.071. The largest difference peak and hole were 0.60 eÅ<sup>-3</sup> and  $-0.58$  eÅ<sup>-3</sup>. CCDC No. 267843.

**4,5-methylenedioxy-2-nitrobenzaldehyde**, C<sub>8</sub>H<sub>5</sub>NO<sub>5</sub>; M<sub>r</sub> 195.13, orthorhombic, space group Pna2<sub>1</sub> (No 33),  $a = 14.017(2)$ ,  $b = 3.7688(6)$ ,  $c = 14.6047(16)$  Å,  $\alpha = \beta = \gamma = 90^\circ$ ,  $V = 771.5(2)$  Å<sup>3</sup>,  $Z = 4$ ,  $D_{\text{calc}} = 1.68$  g cm<sup>-3</sup>,  $\mu = 0.14$  mm<sup>-1</sup>, F(OO0) 408. Crystal size 0.1 × 0.1 × 0.1 mm. A total of 3351 reflections were collected for 4.03 <  $\theta$  < 26.13° and  $-15 \leq h \leq 17$ ,  $-4 \leq k \leq 4$ ,  $-17 \leq l \leq 18$ . There were 1430 independent reflections and 1002 reflections with  $I > 2\sigma(I)$  were used in the refinement. The final R indices were [ $I > 2\sigma(I)$ ] R<sup>1</sup> 0.050, wR<sup>2</sup> 0.103 and (all data) R<sup>1</sup> 0.082, wR<sup>2</sup> 0.119. The largest difference peak and hole were 0.25 eÅ<sup>-3</sup> and  $-0.23$  eÅ<sup>-3</sup>. CCDC No. 267844.

**4-hydroxy-3-methoxy-2-nitrobenzaldehyde**, C<sub>8</sub>H<sub>7</sub>NO<sub>5</sub>; M<sub>r</sub> 197.15, orthorhombic, space group P2<sub>1</sub>2<sub>1</sub>2<sub>1</sub> (No 19),  $a = 3.8388(2)$ ,  $b = 14.4247(5)$ ,  $c = 15.2432(8)$  Å,  $\alpha = \beta = \gamma = 90^\circ$ ,  $V = 844.07(7)$  Å<sup>3</sup>,  $Z = 4$ ,  $D_{\text{calc}} = 1.55$  g cm<sup>-3</sup>,  $\mu = 0.13$  mm<sup>-1</sup>, F(OO0) 408. Crystal size 0.2 × 0.2 × 0.1 mm. A total of 10960 reflections were collected for 3.89 <  $\theta$  < 26.00° and  $-4 \leq h \leq 4$ ,  $-17 \leq k \leq 17$ ,  $-18 \leq l \leq 18$ . There were 1662 independent reflections and 1429 reflections with  $I > 2\sigma(I)$  were used in the refinement. The final R indices were [ $I > 2\sigma(I)$ ] R<sup>1</sup> 0.036, wR<sup>2</sup> 0.091 and (all data) R<sup>1</sup> 0.044, wR<sup>2</sup> 0.096. The largest difference peak and hole were 0.19 eÅ<sup>-3</sup> and  $-0.19$  eÅ<sup>-3</sup>. CCDC No. 267849.

**4-acetoxy-3,5-dimethoxy-2-nitrobenzaldehyde**, C<sub>11</sub>H<sub>11</sub>NO<sub>7</sub>; M<sub>r</sub> 269.21, monoclinic, space group P2<sub>1</sub>/c (No 14),  $a = 11.7974(12)$ ,

$b = 9.6022(6)$ ,  $c = 11.0234(12)$  Å,  $\alpha = \gamma = 90^\circ$ ,  $\beta = 101.882(3)^\circ$ ,  $V = 1222.0(2)$  Å<sup>3</sup>,  $Z = 4$ ,  $D_{\text{calc}} = 1.46$  g cm<sup>-3</sup>,  $\mu = 0.13$  mm<sup>-1</sup>, F(OOO) 560. Crystal size  $0.40 \times 0.25 \times 0.01$  mm. A total of 5799 reflections were collected for  $3.53 < h < 26.03^\circ$  and  $-14 \leq h \leq 13$ ,  $-11 \leq k \leq 8$ ,  $-13 \leq l \leq 9$ . There were 2375 independent reflections and 1764 reflections with  $I > 2\sigma(I)$  were used in the refinement. The final R indices were  $[I > 2\sigma(I)]$  R<sup>1</sup> 0.049, wR<sup>2</sup> 0.110 and (all data) R<sup>1</sup> 0.075, wR<sup>2</sup> 0.122. The largest difference peak and hole were 0.35 eÅ<sup>3</sup> and  $-0.27$  eÅ<sup>3</sup>. CCDC No. 267850.

*5-bromo-2,3-dimethoxy-6-nitrobenzaldehyde*, C<sub>9</sub>H<sub>8</sub>BrNO<sub>5</sub>;  $M_r$  290.07, monoclinic, space group P2<sub>1</sub>/c (No 14),  $a = 13.0649(7)$ ,  $b = 10.0560(5)$ ,  $c = 8.0993(4)$  Å,  $\alpha = \gamma = 90^\circ$ ,  $\beta = 100.158(3)^\circ$ ,  $V = 1047.41(9)$  Å<sup>3</sup>,  $Z = 4$ ,  $D_{\text{calc}} = 1.84$  g cm<sup>-3</sup>,  $\mu = 3.13$  mm<sup>-1</sup>, F(OOO) 576. Crystal size  $0.25 \times 0.08 \times 0.05$  mm. A total of 14371 reflections were collected for  $3.42 < h < 26.03^\circ$  and  $-16 \leq h \leq 16$ ,  $-12 \leq k \leq 12$ ,  $-10 \leq l \leq 9$ . There were 2087 independent reflections and 1675 reflections with  $I > 2\sigma(I)$  were used in the refinement. The final R indices were  $[I > 2\sigma(I)]$  R<sup>1</sup> 0.030, wR<sup>2</sup> 0.059 and (all data) R<sup>1</sup> 0.043, wR<sup>2</sup> 0.063. The largest difference peak and hole were 0.32 eÅ<sup>3</sup> and  $-0.32$  eÅ<sup>3</sup>. CCDC No. 276702.

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## References

- 1 B.M. Wepster in *Progress in stereochemistry* W. Klyne and P.B.D. de la Mare (eds), Butterworths, London, 1958, p.99.
- 2 W.C. Spitzer and G.W. Wheland, *J. Am. Chem. Soc.*, 1940, **62**, 2995.
- 3 J.R. Hanson, P.B. Hitchcock and H. Saberi, *J. Chem. Res.*, 2004, 667.
- 4 J.H. Bryden, *Acta Crystallogr.*, 1972, **B28**, 1395.
- 5 J.R. Hanson and P.B. Hitchcock, *J. Chem. Res.*, 2004, 670.
- 6 G. Vob and H. Gerlach, *Chem. Ber.*, 1989, **122**, 1199.
- 7 J.B. Ekeley and M.S. Klemme, *J. Am. Chem. Soc.*, 1928, **50**, 2711.
- 8 V.K. Daukas, G.V. Purvaneckas, E.B. Udrenalte, V.L. Gineityte and A.V. Barauskaite, *Heterocycles*, 1981, **15**, 1395.
- 9 R. Pschorr and C. Sumuleanu, *Ber.*, 1899, **32**, 3405.
- 10 K. Freudenberg and H.H. Huber, *Chem. Ber.*, 1952, **85**, 1181.
- 11 W. Davies, *J. Chem. Soc.*, 1923, **122**, 1575.
- 12 V.J. Harding, *J. Chem. Soc.*, 1911, **99**, 1585.
- 13 *Bretherick's Handbook of reactive chemical hazards*, 6th edn. P.G. Urban (ed.), Vol.1, 1568, Butterworth Heinemann, Oxford, 1999.
- 14 T.A. Brown and J.A.C. Watt, *Chem. Brit.*, 1967, **3**, 504.
- 15 G.A. Olah, *Chem. Brit.*, August 1996, **32**, 21.