The conformation of some *ortho* substituted stilbenes

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The synthesis of some 2-cyano-4-nitrostilbenes is described and the influence of an *ortho*-cyano and a *ortho*-nitro group on the conformation of 2-cyano-4-nitro-, 2,4-dinitro-, 2,6-dinitro- and 2,4,6-trinitro-4'-methoxystilbene have been examined by X-ray crystallography.

Keywords: nitrostilbenes, conformation, X-ray crystallography

The wide range of biological properties, such as anti-fungal,[1] anti-leukaemic[2] and anti-oxidant[3] activity, which are shown by various stilbenes including resveratrol has stimulated interest in their chemistry. The interaction between the two rings has played an important part in the rationalisation of their biological activity. Consequently the influence of substituents on the planarity of the stilbene is of interest. Amongst several synthetic procedures, the condensation reaction 2,4-dinitrotoluenes with aromatic aldehydes has been shown to be a useful preparative method for stilbenes.[4-6] However, steric interactions between the methyl group and the *ortho* nitro groups on 2,4- and 2,6-dinitrotoluene not only contribute to the steric hindrance of the reaction but also, by rotatating the nitro group out of co-planarity with the aromatic ring, may reduce the activating effect and the resonance stabilisation of the anionic intermediate.[7] These steric interactions with *ortho* substituents may also affect the conformation of the resultant stilbene. In this context, a cyano group, whilst being an activating group for these condensations, places a smaller steric demand on the reaction and the conformation of the products. In this paper, we compare the consequences of the interaction between *ortho*-cyano and *ortho*-nitro groups and the alkene on the conformation of the stilbene. 2-Cyano-4-nitrotoluene has been shown[8] previously to undergo this condensation.

2-Cyano-4-nitrotoluene was easily prepared by the nitration of 2-cyanotoluene.[9] The condensation conditions that were used were refluxing pyridine containing a piperidine catalyst.[7] The aromatic aldehydes that were condensed with 2-cyano-4-nitrotoluene are given in Table 1. As expected the stilbenes possessed the *E*-geometry ($J_{7:8}$ c. 16Hz). However, 2-chlorobenzaldehyde gave a poor yield and it was not possible to isolate a clean product from 2,4-dichlorobenzaldehyde.

The comparative steric influence of the nitro and cyano groups was revelaled by the X-ray crystal structures of 2-cyano-4'-methoxy-4-nitrostilbene (Fig. 1), 2,4-dinitro-4'-methoxystilbene (Fig. 2), 2,6-dinitro-4'-methoxystilbene (Fig. 3)[9] and 4'-methoxy-2,4,6-trinitrostilbene (Fig.4). The steric interactions between the cyano or the nitro groups and C-7 have an increasing effect in twisting the C7:C8 alkene relative to the aromatic ring. The torsion angles, C2:C1:C7:C8 and C6:C1:C7:C8, which reveal this are set out in Table 2.

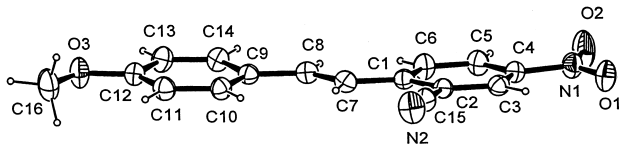

Fig. 1 X-Ray crystal structure of 2-cyano-4′-methoxy-4-nitrostilbene.

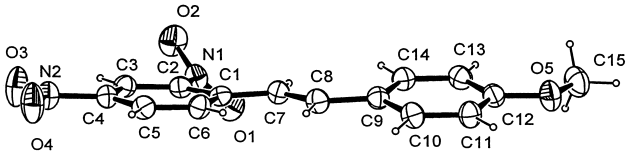

Fig. 2 X-Ray crystal structure of 2,4-dinitro-4′-methoxystilbene.

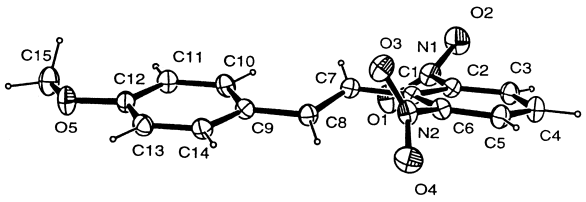

Fig. 3 X-Ray crystal structure of 2,6-dinitro-4′-methoxy-stilbene.

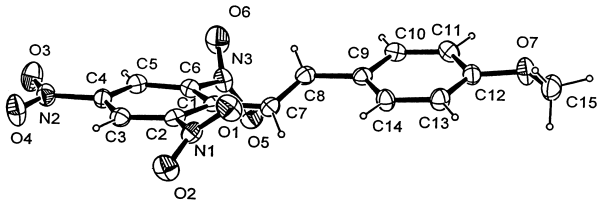

Fig. 4 X-Ray crystal structure of 4′-methoxy-2,4,6-trinitro-stilbene.

We examined the possibility that there might be a conjugative effect between the 4-nitro group and the alkene counteracting the twisting brought about by the steric interactions with the 2- and 6-substituents. However, the structure of 2,6-dinitro-

Table 1 Synthesis od 2-cyano-4-nitrostilbenes

Substrate	Product	% Yield[a]
2-Cyano-4-nitrotoluene		
Benzaldehyde	2-Cyano-4-nitrostilbene	60
Anisaldehyde	2-Cyano-4′-methoxy-4-nitrostilbene	53
Vanillin	2-Cyano-4′-hydroxy-3′-methoxy-4-nitrostilbene	60
2,3-Dimethoxybenzaldehyde	2-Cyano-2′,3′-dimethoxy-4-nitrostilbene	55
3,4,5-Trimethoxybenzaldehyde	2-Cyano-4′-nitro-3,4,5-trimethoxystilbene	60
2-Chlorobenzaldehyde	2′-Chloro-2-cyano-4-nitrostilbene	14

[a]Yield of recrystallised material.

* Correspondent.

Table 2 Selected torsion angles (°) in stilbenes

	C2:C1:C7:C8	C6:C1:C7:C8
2-Cyano-4′-methoxy-4-nitrostilbene[a]	179.66(17) 175.17(17)	0.2(3) –5.0(3)
2,4-Dinitro-4′-methoxystilbene[a]	–179.2(7) –169.22(19)	3.6(3) 14.2(3)
2,6-Dinitro-4′-methoxystilbene	150.99(15)	–30.29(23)
4′-Methoxy-2,4,6-trinitrostilbene	–147.38(17)	34.1(2)

[a]There were to independent molecules in the unit cell.

4'-methoxystilbene and 4'-methoxy-2,4,6-trinitrostilbene showed very similar alkene:aromatic ring torsion angles. The steric interactions between C-7 and the *ortho*-nitro groups are relieved by the aromatic ring. These are set out in Table 3. The juxtaposition of three substituents in 2,6-dinitro- and 2,4,6-trinitro-4'-methoxystilbene leads to a greater rotation of one of the nitro groups. Theoretical calculations of the extent of this twisting have been used in the rationalisation[10] of the facile nucleophilic displacement of one nitro group in the preparation of 2-aryl-4,6-dinitroindoles via 2,4,6-trinitrostilbenes.

In conclusion, we have shown that the smaller steric requirements of the 2-cyano group, when compared to the 2-nitro group, leads to a lower distortion of the stilbene from planarity. These effects of *ortho* substituents may modify the interactions between the rings. However, the nitro groups adjacent to the alkene are rotated significantly relative to the plane of the aromatic ring confirming theoretical calculations.[10]

Experimental

General experimental details: Extracts were dried over sodium sulfate. IR spectra were determined as nujol mulls. 1H NMR spectra were determined in d_6-dimethylsulfoxide at 300 MHz. Mass spectra were determined on a Fisons Autospec or a Bruker Daltonics Apex III electrospray mass spectrometer. 2-Cyano-4-nitrotoluene, prepared according to the literature method,[9] had m.p. 100°C, (lit.,[9] 105°C), ν_{max}/cm^{-1} 2234(CN), 1613(Ar), 1522(NO_2), 1353(NO_2); δ_H 2.65 (3H, s, Ar–Me), 7.55 (1H, d, *J*=8.5 Hz, 6-H), 8.35 (H, d, *J*=8.5Hz, 5-H), 8.50 (1H, s, 3-H).

General procedure for preparing the 2-cyano-4-nitrostilbenes: 2-Cyano-4-nitrotoluene (1.6 g) and the aldehyde (105 g) were dissolved in pyridine (18 cm^3) and piperidine (2 cm^3) was added. The reaction was heated under reflux for 1 h. The solution was cooled and poured into dill. hydrochloric acid. The product was filtered and recrystallised from glacial acetic acid. Some products required purification using charcoal. The results are given in Table 1.

The following compounds were obtained:

2-Cyano-4-nitrostilbene: M.p. 146–148° (lit.,[8] 146°C), (Found: M$^+$ 250.074, $C_{15}H_{10}N_2O_2$ requires M$^+$ 250.074), ν_{max}/cm^{-1} 2225 (CN), 1631 (C=C), 1603 (Ar), 1513 (NO2), 1340 (NO2); δ_H 7.35 (1H, d, *J*=16.2 Hz, 8-H), 7.40 (1H,t, *J*=7.4 Hz, 4'-H), 7.45 (2H,t, *J*=7.4 Hz, 3'-and 5'-H), 7.65 (2H, d, *J*=7.4 Hz, 2'- and 6'-H), 7.75 (1H, d, *J*=16.2 Hz, 7-H), 8.30 (1H, d, *J*=8.5 Hz, 2-H), 8.50 (1H, d, *J*=8.5 Hz, 3-H), 8.70 (1H, s, 5-H).

2-Cyano-3′-hydroxy-4-nitrostilbene: M.p. 210°C, (Found: M$^+$ 266.069, $C_{15}H_{10}N_2O_3$ requires M$^+$ 266.069), ν_{max}/cm^{-1} 3393 (br)(OH), 2225 (CN), 1626 (C=C), 1601 (Ar), 1519 (NO_2), 1346 (NO_2); δ_H 6.85 (1H, d, *J*=7.9 Hz, 4'-H), 7.10 (1H, s, 2'-H), 7.15 (2H, d, *J*=7.9 Hz, 6'-H), 7.30 (1H,t, *J*=7.9 Hz, 3'-H), 7.40 (1H, d, *J*=16.2 Hz, 8-H), 7.75 (1H, d, *J*=16.2 Hz, 7-H), 8.35 (1H, d, *J*=8.9 Hz, 6-H), 8.52 (1H, d, *J*=8.9 Hz, 5-H), 8.77 (1H, d, 3-H), 9.72 (1H, s, OH).

2-Cyano-4'-methoxy-4-nitrostilbene: M.p. 200°C, (Found: M$^+$ 280.085, $C_{16}H_{12}N_2O_3$ requires M$^+$ 280.085), ν_{max}/cm^{-1} 2229 (CN), 1629 (C=C), 1596 (Ar), 1515 (NO_2), 1340 (NO_2); δ_H 3.80 (3H, s, OMe), 7.00 (2H, d, *J*=8.0 Hz, 3'- and 4'-H), 7.25 (1H, d, *J*=16.1 Hz, 8-H), 7.60 (2H, d, *J*=8.0 Hz, 2'- and 6'-H), 7.75 (1H, d, *J*=16.2 Hz, 7-H), 8.25 (1H, d, *J*=8.9 Hz, 6-H), 8.45 (1H, d, *J*=8.9 Hz, 5-H), 8.65 (1H, s, 3-H).

2-Cyano-4'-hydroxy-3'-methoxy-4-nitrostilbene: M.p. 199–200°C, (Found: M$^+$ 296.078, $C_{16}H_{12}N_2O_4$ requires M$^+$ 296.079), ν_{max}/cm^{-1} 3392(br)(OH), 2227 (CN), 1632 (C=C), 1596 (Ar), 1515 (NO_2), 1347 (NO_2); δ_H 3.85 (3H, s, OMe), 6.89 (1H, d, *J*=8.0 Hz, 3'-H), 7.15 (1H, d, *J*=8.0 Hz, 2'-H), 7.20 (1H, d, *J*=16.1 Hz, 8-H), 7.25 (1H, s, 6'-H), 7.70 (1H, d, *J*=16.2 Hz, 7-H), 8.20 (1H, d, *J*=8.5 Hz, 6-H), 8.42 (1H, d, *J*=8.9 Hz, 5-H), 8.70 (1H, s, 3-H), 9.65 (1H, s, OH).

2-Cyano-2',3'-dimethoxy-4-nitrostilbene: M.p. 196–198°C, (Found: M$^+$+Na 333.085 $C_{17}H_{14}N_2O_4$ requires M$^+$ 333.085), ν_{max}/cm^{-1} 2226 (CN), 1632 (C=C), 1603 (Ar), 1520 (NO_2), 1347 (NO_2); δ_H 3.85 and 3.90 (each 3H, s, OMe), 7.20 (1H,t, *J*=7.2 Hz, 5'-H), 7.22 (1H, d, *J*=7.2 Hz, 4'-H), 7.40 (1H, d, *J*=7.2 Hz, 6'-H), 7.62 (1H, d, *J*=16.3 Hz, 8-H), 7.90 (1H, d, *J*=16.3 Hz, 7-H), 8.35 (1H, d, *J*=8.5 Hz, 6-H), 8.55 (1H, d, *J*=8.9 Hz, 5-H), 8.80 (1H, s, 3-H).

2-Cyano-4-nitro-3',4',5'-trimethoxystilbene: M.p. 159°C, (Found: M$^+$ 340.106 $C_{18}H_{16}N_2O_5$ requires M$^+$ 340.106), ν_{max}/cm^{-1} 2227 (CN), 1629 (C=C), 1603 (Ar), 1522 (NO_2), 1351 (NO_2); δ_H 3.65 (3H, s, OMe), 3.80 (6H, s, 2×OMe), 7.00 (2H, s, 2' and 6'-H), 7.35 (1H, d, *J*=16.3 Hz, 8-H), 7.70 (1H, d, *J*=16.3 Hz, 7-H), 8.20 (1H, d, *J*=8.5 Hz, 6-H), 8.50 (1H, d, *J*=8.9 Hz, 5-H), 8.65 (1H, s, 3-H).

2-Chloro-2-cyano-4-nitrostilbene: M.p. 189–194°C, (Found: M$^+$ 284.036 $C_{15}H_0C_1N_2O_4$ requires M$^+$ 284.035), ν_{max}/cm^{-1} 2228 (CN), 1604 (C=C), 1604 (Ar), 1518 (NO_2), 1352 (NO_2); δ_H 7.50 (2H,m, 5; and 6'-H), 7.60 (1H, d, *J*=16.2 Hz, 8-H), 7.65 (1H,t, *J*=7.2 Hz, 4'-H), 8.00 (1H, d, *J*=16.2 Hz, 7-H), 8.05 (1H, d, *J*=7.2 Hz, 3'-H), 8.40 (1H, d, *J*=8.9 Hz, 6-H), 8.55 (1H, d, *J*=8.9 Hz, 5-H), 8.85 (1H, s, 3-H).

X-Ray crystallographic data and structure determinations:

(a) 2-Cyano-4'-methoxy-4-nitrostilbene, $C_{16}H_{12}N_2O_3$, M_r 280.28, monoclinic, space group $P2_1/c$ (No.14), *a*=12.7728(3), *b*=16.2804(4), *c*=14.1254(3)Å, α=γ=90°, β=111.557(1)°, V=2731.67(11)Å^3, *Z*=8, $D_{calc.}$=1.36g cm^{-3}, μ=0.10mm^{-1}, *F*(000)=1168. Data were collected using a crystal of size .0.30 × 0.25 × 0.20 mm^3 on a KappaCCD diffractometer. A total of 34392 reflections were collected for 3.89<θ<25.01° and –15≤*h*≤15, –19≤*k*≤19, –16≤*l*≤16. There were 4802 independent reflections and 3334 reflections with $I>2\sigma(I)$ were used in the refinement. No absorption correction was applied. The structure was solved by direct methods and refined using SHELXL-97. The drawings used ORTEP-3 for Windows. The final R indices were [$I>2\sigma(I)$] R_1=0.047, wR_2=0.108 and (all data) R_1=0.079, wR_2=0.124. The goodness-of-fit on F^2 was 1.023 and the largest difference peak and hole was .016 and –0.23 e.Å^{-3}. There were two independent molecules in the unit cell.

(b) 2,4-Dinitro-4'-methoxystilbene, $C_{15}H_{12}N_2O_5$, M_r 300.27, monoclinic, space group $P2_1/c$ (No.14), *a*=13.0098(4), *b*=15.7766(7), *c*=14.7814(6)Å, α=γ=90°, β=115.698(4)°, V=2733.8(2)Å^3, *Z*=8, $D_{calc.}$=1.46g cm^{-3}, μ=0.11mm^{-1}, *F*(000)=1248. Data were collected using a crystal of size .0.3 × 0.2 × 0.2 mm^3 on a KappaCCD diffractometer. A total of 15252 reflections were collected for 3.71<θ<25.02° and –15≤*h*≤15, –15≤*k*≤18, –17≤*l*≤17. There were 4738 independent reflections and 3758 reflections with $I>2\sigma(I)$ were used in the refinement. No absorption correction was applied. The structure was solved by direct methods and refined using SHELXL-97. The drawings used ORTEP-3 for Windows. The final R indices were [$I>2\sigma(I)$] R_1=0.052, wR_2=0.130 and (all data) R_1=0.069, wR_2=0.143.

Table 3 Rotation of the planes (°) of the nitro groups relative to the aromatic ring

	2-Nitro	4-Nitro	6-Nitro
2-Cyano-4'-methoxy-4-Nitrostilbene[a]		5.21(0.16) 2.79(0.14)	
2,4-Dinitro-4'-methoxystilbene[a]	44.70(0.47) 40.16(0.13)	2.53(0.18) 7.98)0.22	
2,6-Dinitro-4'-methoxystilbene	41.70(0.07)		62.41(0.07)
4'-Methoxy-2,4,6-trinitrostilbene	40.78(0.09)	4.18(0.19)	57.73(0.08)

[a]There were two independent molecules in the unit cell

The goodness-of-fit on F^2 was 1.065 and the largest difference peak and hole was 0.67 and –0.26 e.Å^{-3}. There were two independent molecules in the unit cell.

(c) 4'-methoxy-2,4,6-trinitrostilbene, $C_{15}H_{11}N_3O_7$, M_r 345.27, monoclinic, space group $P2_1/c$ (No.14), a=12.3993(4), b=8.7750(2), c=13.9439(5)Å, $\alpha=\gamma=90°$, β=103.405(2)°, V=1475.72(8)Å^3, Z=4, $D_{calc.}$=1.455g cm^{-3}, μ=0.13mm^{-1}, F(000)=712. Data were collected using a crystal of size .0.3×0.3×0.3 mm^3 on a KappaCCD diffractometer. A total of 18899 reflections were collected for $3.77<\theta<25.04°$ and $-14\leq h\leq 14$, $-150\leq k\leq 10$, $-16\leq l\leq 16$**.** There were 2603 independent reflections and 2057 reflections with $I>2\sigma(I)$ were used in the refinement. No absorption correction was applied. The structure was solved by direct methods and refined using SHELXL-97. The drawings used ORTEP-3 for Windows. The final R indices were [$I>2\sigma(I)$] R_1=0.037, wR_2=0.092 and (all data) R_1=0.054, wR_2=0.102. The goodness-of-fit on F^2 was 1.031 and the largest difference peak and hole was 0.19 and –0.21 eÅ^{-3}. The crystallographic data for 2,6-dinitro-4'-methoxystilbene have been published previously.[7] the crystallographic data have been deposited with the Cambridge Crystallographic Data Centre as nos. CCDC 249904 (2-cyano-4'-methoxy-4-nitrostilbene), 249905 (2,4-dinitro-4'-methoxystilbene) and 250705 (4'-methoxy-2,4,6-trinitrostilbene).

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