

# 1,6-Interactions between dimethylamino and aldehyde groups in two biphenyl derivatives

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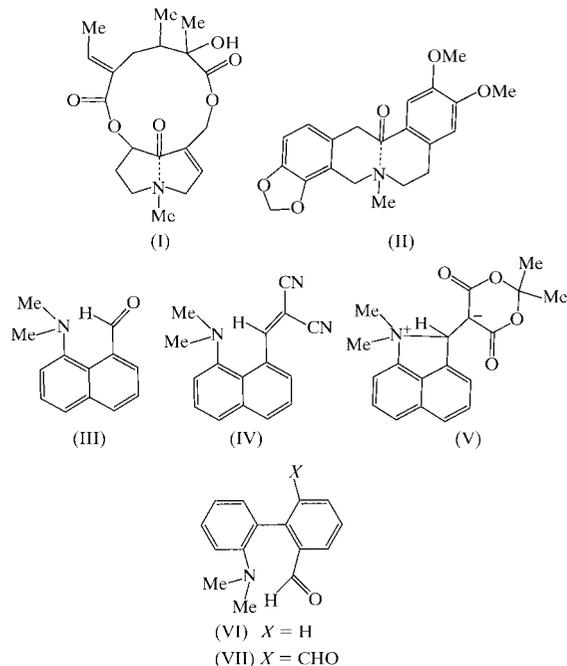
The title compounds, 2-(dimethylamino)biphenyl-2'-carboxaldehyde,  $C_{15}H_{15}NO$ , and 2-(dimethylamino)biphenyl-2',6'-dicarboxaldehyde,  $C_{16}H_{15}NO_2$ , show similar 1,6-interactions [ $N \cdots C=O$  2.929 (3) to 3.029 (3) Å] between the dimethylamino and aldehyde groups located in the *ortho* positions of the two rings, which lie at 58.1 (1)–62.4 (1)° to each other.

## Comment

Interactions between amino and carbonyl groups in natural products such as (I) and (II) have been interpreted as representing different stages in the progress of the corresponding chemical reaction (Bürgi *et al.*, 1973*a*). Decreasing  $N \cdots C$  distances are accompanied by increasing  $C=O$  bond lengths. 1,5- $N \cdots C$  interactions between dimethylamino groups and various carbonyl-containing functional groups have been observed in *peri*-naphthalene systems (Schweizer *et al.*, 1978; Clayden *et al.*, 1999; Hodgson *et al.*, 1999), though the shortest  $N \cdots C$  distance observed is only 2.489 (5) Å, for interaction with an aldehyde group in (III). Nevertheless, shorter 1,5-interactions are observed when the electrophilic group is an electron-deficient alkene, as in (IV) [ $N \cdots C$  2.413 (2) Å], and almost complete bond formation is observed in (V) [ $N-C$  1.651 (3) Å] (Bell & Wallis, 1999). The use of the  $N \cdots C$  distances in such systems as an indicator of the through-space electron-attracting powers of the electrophilic groups has been proposed (O'Leary *et al.*, 2001). In the naphthalene system, the *peri* groups are constrained to some degree by the bonding geometry of the ring system. We now report the structures of the biphenyls (VI) and (VII), which contain *ortho*-dimethylamino and *ortho*-aldehyde substituents on opposite rings such that they are capable of forming 1,6- $N \cdots C$  interactions, but are not compelled by the molecular framework to be near one another at all. The biphenyls were prepared by Suzuki and Stille coupling methodologies and their molecular structures were analysed by single-crystal X-ray diffraction at 150 K.

The results of the crystal structure determinations are shown in Fig. 1, and relevant molecular geometries are summarized in Table 1. Biphenyl (VII) contains two inde-

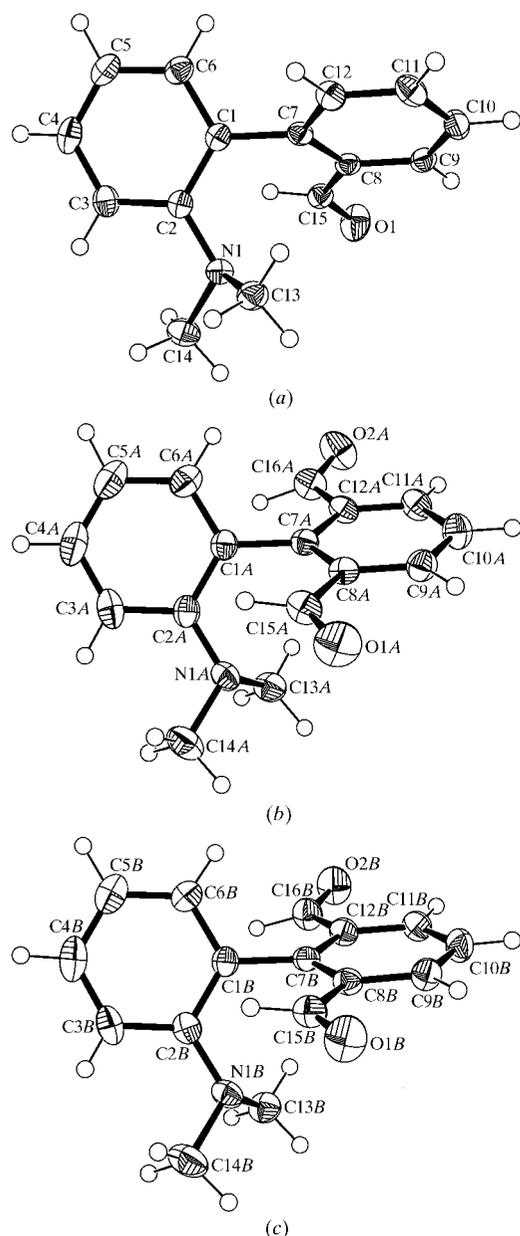
pendent molecules in the asymmetric unit. The three molecular conformations of (VI) and (VII) are very similar. The phenyl rings lie at 58.1 (1)–62.4 (1)° to each other such that there is a close  $N \cdots C$  contact between the amino N atom and a carbonyl C atom. The dimethylamino group adopts pyramidal geometry, with a  $N-CH_3$  bond making a torsion angle



of 13.2 (3)–15.0 (3)° to the C2–C3 bond of the phenyl ring and directed away from the second phenyl ring. The carbonyl group lies almost in its phenyl-ring plane, with the carbonyl bond directed away from the second phenyl ring. The  $N \cdots C$  contact distances, 2.929 (3)–3.029 (3) Å, are longer than in the related naphthalene, (III). The  $N \cdots C=O$  angles lie in the range 123.8 (2)–128.2 (2)°, and the theoretical directions of the amino N atom lone pairs lie *ca* 19–25° to the  $N \cdots C(=O)$  vectors. The dimethylamino N atom in (VI) is displaced out of the best plane through its phenyl ring by 0.042 (2) Å towards the carbonyl group, and the carbonyl C atom is displaced out of its phenyl-ring plane by 0.066 Å away from the dimethylamino group. In the two conformations of (VII), the out-of-plane displacements of the corresponding aldehyde C atoms are similar to those in (VI), with values of 0.071 and 0.064 Å, respectively, but the dimethylamino N atoms are not displaced significantly out of the planes of their phenyl groups. Indeed, the  $Me_2N-C$  bond lengths of 1.402 (3) and 1.410 (3) Å are slightly shorter than in (VI), 1.422 (2) Å. These two effects might be ascribable to the through-bond electron-attracting power of the second carbonyl group, though there are no other significant bond-length changes in the molecular skeletons. The second aldehyde group in (VII) has little effect on the molecular conformation, making only a van der Waals contact with atom H6 on the opposite phenyl ring, with  $C16 \cdots H6$  distances of 2.86 (2) and 2.99 (2) Å. There are no particularly short intermolecular interactions in the two crystal structures. In (VI), centrosymmetric  $C-H \cdots O$  interactions with graph-set  $R_2^2(10)$  are present [ $C9 \cdots O1^i$

3.4818 (15) Å and C—H...O<sup>i</sup> 164.8 (12)°; symmetry code: (i)  $1 - x, -y, -z$ ] and in (VII), chains form comprising C4<sub>A/B</sub>...O2<sup>ii</sup> distances of 3.253 (3) and 3.336 (3) Å, with C—H...O<sup>ii</sup> angles of 129 (2) and 159 (3)°, respectively [symmetry code: (ii)  $\frac{1}{2} + x, -y, z$  (for A) and  $-\frac{1}{2} + x, 1 - y, z$  (for B)].

The observed Me<sub>2</sub>N...C=O interactions are of similar lengths to the 1,5-Me<sub>2</sub>N/ketone carbonyl interactions in methadone of 2.911 and 2.912 Å (Bürgi *et al.*, 1973*b*; Bye, 1974), where the two groups are not forced to be near one another as they are in the *peri*-naphthalene series. However, when the <sup>13</sup>C NMR spectrum of (VI) was measured in DCl/D<sub>2</sub>O, the appearance of a new resonance at δ 90.2 indicated addition of the dimethylamino group to a protonated



**Figure 1**  
ORTEP (Johnson & Burnett, 1996) drawings of (a) compound (VI) and (b) and (c) the two molecules of compound (VII), with anisotropic displacement parameters drawn at the 50% probability level.

carbonyl group. There are no directly comparable biphenyl structures with 1,6-amino/carbonyl interactions in the Cambridge Structural Database (CSD; Allen & Kennard, 1993). The two molecules of 2,2'-bis(dimethylamino)biphenyl (Staab *et al.*, 1988) adopt conformations with the phenyl rings at 56.1 and 59.0° such that the pyramidal dimethylamino groups are on opposite sides of the molecule. 2-Methoxybiphenyl-2'-carboxylic acid (Krygowski *et al.*, 1989) adopts a conformation with the phenyl rings at 54.4 (1)° such that the methoxy O atom lies 3.023 (5) Å from the carboxyl C atom. The methoxy group lies close to the best plane of the phenyl ring, so that the unconjugated lone pair is not well aligned with the MeO...C=O vector. Studies in the naphthalene series have shown that 1,5-MeO...Csp<sup>2</sup> interaction distances are remarkably insensitive to the nature of the carbon-containing functional group. In general, biphenyls with one *ortho* substituent per phenyl ring tend to have their phenyl rings close to perpendicular. Exceptions occur when the substituents are small, as for fluoride or alkoxy, *e.g.* CSD refcode BAWPUK (Jones & Brown, 1982), DECFDP (Neronova, 1968), and NOZZOR and NOZZUX (Ferreira *et al.*, 1998), or can hydrogen bond, as in diols, *e.g.* JUPTOD (Sartori *et al.*, 1992), NUTSUQ (Byrne *et al.*, 1998), a hydroxy ether JAVHIX (Lin *et al.*, 1989) and the 2,2'-diamine DABIPH (Ottersen, 1977), where interplanar angles are *ca* 40–55°. The structures of (VI) and (VII) are likely to be more reasonable models for intermolecular interactions between dialkylamino groups and aldehydes than the structure of the related naphthalene derivative (III).

## Experimental

2-(*N,N*-Dimethylamino)biphenyl-2'-carboxaldehyde, (VI): sodium carbonate (6.42 g, 60.6 mmol) dissolved in degassed water (30 ml) was added to a mixture of 2-(*N,N*-dimethylamino)phenylboronic acid (1.80 g), Pd(PPh<sub>3</sub>)<sub>4</sub> (0.70 g, 0.61 mmol) and 2-bromobenzaldehyde (2.68 g, 14.5 mmol) in a mixture of dry ethanol (5 ml) and 1,2-dimethoxyethane (100 ml) and the mixture heated at reflux for 48 h. The cooled solution was diluted with diethyl ether (200 ml), extracted with 1 M NaOH (50 ml) and then 1 M HCl (4 × 150 ml). The acidic phase was made basic (pH 14) with 6 M NaOH and extracted with ether (3 × 150 ml). The dried (MgSO<sub>4</sub>) organic solution yielded the crude product which was purified by flash chromatography on silica, eluting first with chloroform followed by ethyl acetate to yield the product as a pale-yellow oil which solidified on standing (1.23 g, 85%), m.p. 348–351 K. <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ 9.57 (1H, s, CHO), 7.92 (1H, d, *J* = 7.7), 7.65 (1H, t, *J* = 7.6), 7.47–7.31 (*m*, 4H), 7.14 (1H, t, *J* = 7.4), 7.06 (1H, d, *J* = 7.2), 2.38 [6H, s, (CH<sub>3</sub>)<sub>2</sub>N]; <sup>13</sup>C NMR (CDCl<sub>3</sub>): δ 190.7 (C=O), 151.5, 142.7, 133.8, 133.1, 131.1 (×2), 130.0, 129.5, 127.5, 126.7, 123.0, 118.1, 42.2 [(CH<sub>3</sub>)<sub>2</sub>N]; ν<sub>max</sub>(cm<sup>-1</sup>) (KBr): 2832, 1689, 1594, 1492, 1450, 1247, 1193, 945, 770; HRMS (ES): found: 226.1229 (*M* + H)<sup>+</sup>; C<sub>15</sub>H<sub>15</sub>NO requires: 226.1232 (*M* + H)<sup>+</sup>.

2-(*N,N*-Dimethylamino)biphenyl-2',6'-dicarboxaldehyde, (VII): 2-trimethylstannyl-*N,N*-dimethylaniline (0.66 g, 2.35 mmol) and 2-bromoisophthalaldehyde (0.50 g, 2.35 mmol) were refluxed in dry tetrahydrofuran (THF) (25 ml) with Pd(PPh<sub>3</sub>)<sub>4</sub> (0.14 g, 0.12 mmol) and CuI (0.03 g, 0.17 mmol). After 24 h, the amounts of catalysts were doubled and the reaction refluxed for 48 h. The THF was removed on a rotary evaporator, ethyl acetate (50 ml) was added to the residue and the mixture was filtered through Celite. The filtrate was washed

with water (3 × 30 ml) and brine (30 ml), dried over Na<sub>2</sub>SO<sub>4</sub> and evaporated to yield a brown oil. Purification by flash chromatography (SiO<sub>2</sub>, 2:1 cyclohexane–diethyl ether) yielded (VII) as a yellow oil which solidified on standing (0.10 g, 17%), m.p. 371–374 K. <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ 9.75 (1H, s, CHO), 9.74 (1H, s, CHO), 8.24 (2H, d, J = 7.7), 7.62 (1H, t, J = 7.7), 7.45 (1H, m), 7.15 (3H, m), 2.45 [6H, s, (CH<sub>3</sub>)<sub>2</sub>N]; <sup>13</sup>C NMR (CDCl<sub>3</sub>): δ 191.2 (C=O), 152.4, 146.2, 133.9, 133.7, 132.6, 130.7, 128.0, 124.9, 122.3, 118.6, 42.5 [(CH<sub>3</sub>)<sub>2</sub>N]; ν<sub>max</sub>(cm<sup>-1</sup>) (KBr): 2859, 1681, 1491, 1456, 1386, 1234, 945, 922, 799, 770; HRMS (ES): found: 254.1178 (M + H)<sup>+</sup>; C<sub>16</sub>H<sub>15</sub>NO<sub>2</sub> requires: 254.1181 (M + H)<sup>+</sup>.

## Compound (VI)

### Crystal data

C <sub>15</sub> H <sub>15</sub> NO	$D_x = 1.233 \text{ Mg m}^{-3}$
$M_r = 225.28$	Mo $K\alpha$ radiation
Monoclinic, $P2_1/n$	Cell parameters from 2931 reflections
$a = 8.169 (2) \text{ \AA}$	$\theta = 2.9\text{--}27.5^\circ$
$b = 11.042 (3) \text{ \AA}$	$\mu = 0.08 \text{ mm}^{-1}$
$c = 13.745 (4) \text{ \AA}$	$T = 150 (2) \text{ K}$
$\beta = 101.89 (1)^\circ$	Block, yellow
$V = 1213.1 (6) \text{ \AA}^3$	$0.40 \times 0.40 \times 0.25 \text{ mm}$
$Z = 4$	

### Data collection

KappaCCD diffractometer	2211 reflections with $I > 2\sigma(I)$
$\varphi$ and $\omega$ scans	$R_{\text{int}} = 0.043$
Absorption correction: multi-scan (SORTAV; Blessing, 1995)	$\theta_{\text{max}} = 27.5^\circ$
$T_{\text{min}} = 0.906$ , $T_{\text{max}} = 0.983$	$h = -10 \rightarrow 10$
12 528 measured reflections	$k = -14 \rightarrow 14$
2783 independent reflections	$l = -15 \rightarrow 17$

### Refinement

Refinement on $F^2$	$w = 1/[\sigma^2(F_o^2) + (0.0776P)^2 + 0.0677P]$
$R[F^2 > 2\sigma(F^2)] = 0.051$	where $P = (F_o^2 + 2F_c^2)/3$
$wR(F^2) = 0.126$	$(\Delta/\sigma)_{\text{max}} = 0.008$
$S = 1.08$	$\Delta\rho_{\text{max}} = 0.23 \text{ e \AA}^{-3}$
2783 reflections	$\Delta\rho_{\text{min}} = -0.38 \text{ e \AA}^{-3}$
214 parameters	
All H-atom parameters refined	

## Compound (VII)

### Crystal data

C <sub>16</sub> H <sub>15</sub> NO <sub>2</sub>	Mo $K\alpha$ radiation
$M_r = 253.29$	Cell parameters from 4682 reflections
Orthorhombic, $Pca2_1$	$\theta = 2.9\text{--}27.5^\circ$
$a = 14.161 (3) \text{ \AA}$	$\mu = 0.08 \text{ mm}^{-1}$
$b = 27.913 (6) \text{ \AA}$	$T = 150 (2) \text{ K}$
$c = 6.7018 (13) \text{ \AA}$	Block, yellow
$V = 2648.9 (9) \text{ \AA}^3$	$0.25 \times 0.20 \times 0.08 \text{ mm}$
$Z = 8$	
$D_x = 1.270 \text{ Mg m}^{-3}$	

### Data collection

KappaCCD diffractometer	2378 reflections with $I > 2\sigma(I)$
$\varphi$ and $\omega$ scans	$R_{\text{int}} = 0.052$
Absorption correction: multi-scan (SORTAV; Blessing, 1995)	$\theta_{\text{max}} = 27.5^\circ$
$T_{\text{min}} = 0.873$ , $T_{\text{max}} = 0.994$	$h = -13 \rightarrow 18$
14 314 measured reflections	$k = -28 \rightarrow 36$
3238 independent reflections	$l = -8 \rightarrow 8$

### Refinement

Refinement on $F^2$	All H-atom parameters refined
$R[F^2 > 2\sigma(F^2)] = 0.044$	$w = 1/[\sigma^2(F_o^2) + (0.0635P)^2]$
$wR(F^2) = 0.100$	where $P = (F_o^2 + 2F_c^2)/3$
$S = 0.97$	$(\Delta/\sigma)_{\text{max}} = 0.005$
3238 reflections	$\Delta\rho_{\text{max}} = 0.18 \text{ e \AA}^{-3}$
463 parameters	$\Delta\rho_{\text{min}} = -0.23 \text{ e \AA}^{-3}$

**Table 1**

Selected molecular geometry (Å, °) for (VI) and (VII).

	(VI)	(VIIA)	(VIIB)
N1...C15	2.9891 (16)	2.929 (3)	3.029 (3)
N1...C15—O1	126.48 (9)	123.8 (2)	128.1 (2)
Inter-ring angle	58.94 (6)	58.1 (1)	62.4 (1)
N1—C2	1.4220 (15)	1.402 (3)	1.410 (3)
Σ bond angles at N1	341.8 (3)	342.5 (2)	341.3 (2)
C14—N1—C2—C3	14.89 (16)	-13.3 (3)	15.0 (3)
O1—C15—C8—C9	6.16 (19)	-10.3 (4)	-7.7 (4)

All H atoms were located in difference Fourier maps and refined with individual isotropic displacement parameters. The C—H bond lengths are 0.947 (16)–1.033 (15) Å in (VI) and 0.92 (3)–1.08 (2) Å in (VII). For compound (VII), reflection data include 1362 merged Friedel pairs (as the absolute structure was not determined).

For both compounds, data collection: *DENZO* (Otwinowski & Minor, 1997) and *COLLECT* (Hooft, 1998); cell refinement: *DENZO* and *COLLECT*; data reduction: *DENZO* and *COLLECT*; program(s) used to solve structure: *SHELXS97* (Sheldrick, 1990); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *ORTEPIII* (Johnson & Burnett, 1996).

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: GG1051). Services for accessing these data are described at the back of the journal.

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