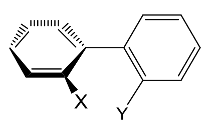
Interactions and Reactions in Some 2,2'-Disubstituted Biphenyls – An Open or Shut Case.

Jane O'Leary and John D. Wallis*

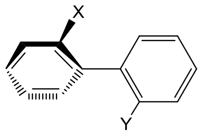
Received (in XXX, XXX) 1st January 2008, Accepted 1st January 2008
First published on the web 1st January 2008
DOI: 10.1039/b000000x

2-Dimethylaminobiphenyls bearing an electron deficient alkene in the 2' position show either Me_2N- - -C=C interactions (2.941-2.976 Å) or form a new N-C bond (1.586-1.604 Å) to give a zwitterion. The former provides a model for an intermolecular interaction, while the latter provides structural information on organic anionic systems uncoordinated by metal cations.

Substituted biphenyls have played an important role in organic chemistry, providing the first examples of resolvable enantiomers with axial chirality[1] and a range of ligands for use in metal catalysed reactions[2] including asymmetric synthesis.[3] Furthermore, biphenyls can be prepared by a range of well-established coupling procedures, and have been used as building blocks in supramolecular chemistry, e.g. in catenanes and crystalline biphenyl-peptide hybrids.[4] Here we report the use of the biphenyl skeleton for investigating by X-ray crystallography the interactions between an electrophilic functional group and a nucleophilic functional group located at the *ortho* positions of the two rings. The biphenyl system has the freedom to adjust the separation between the functional groups by rotation about the inter-ring bond or can allow the groups to completely avoid each other, as in conformers **1a** or **1b**. Thus, there is no strong coercion for the groups to be close together in contrast to the 1,5 interactions in the widely studied *peri*-naphthalene system.[5-7] Here we describe the solid state molecular structures of a series of 2-dimethylaminobiphenyls bearing different electron deficient alkenes in the 2' position, activated by one or more carbonyl, cyano or nitro groups **4**-**7**, which *all* show either an interaction or, indeed, a reaction between the groups.

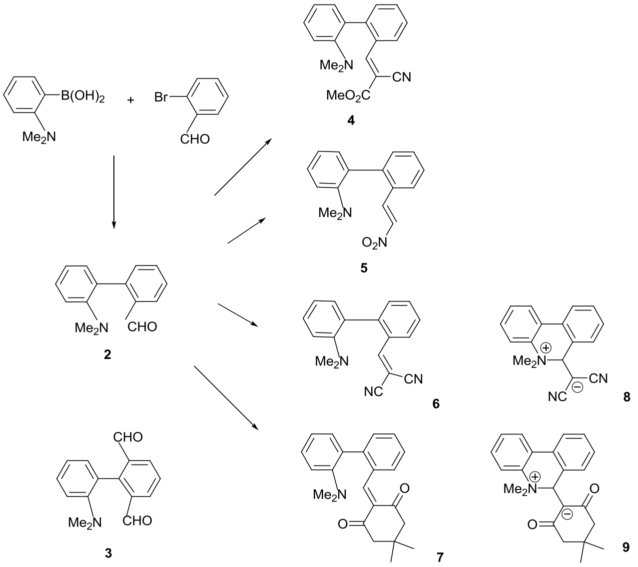


1a



1b

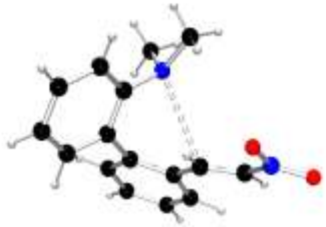
The materials were prepared by Knoevenagel condensations with the carbaldehyde **2** which was obtained by Suzuki coupling (Scheme 1). Crystals were grown by slow evaporation of solutions, and structural measurements made by X-ray diffraction at 120 K.[‡] Molecular structures are shown in Figure 1 with selected geometric details in Table 1 along with our data for the closely related aldehydes **2** and **3**.[8] It is immediately recognizable that the structures of the molecules fall into two groups, one (for **2**-**5**) with long Me_2N----sp^2C separations in the range 2.929(3) – 3.029(3) Å comparable to the 1,5 N---C=O interaction in methadone **10** (2.912(3) Å),[9] and the other (for **6** and **7**) in which, remarkably, there has been bond formation between the groups to give zwitterionic structures **8** and **9**. In no case do the functional groups in these cases choose to avoid an intramolecular interaction or reaction.



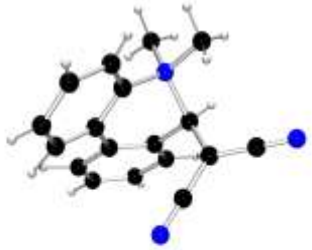
Scheme 1.

The uncyclised biphenyls **2**-**5** adopt similar conformations. The pyramidal dimethylamino group is oriented with N-Me bonds at *ca.* 112° and 19° to the neighbouring phenyl ring, and the carbonyl or alkene bond lies at 6.2-14.6° to its phenyl ring. There is only a small variation (0.1 Å) in the separation of N and sp^2 C atoms, the largest difference occurs for the two crystallographically independent molecules of **3**. Thus, any trend there might be in these distances is small and hidden by the influences which crystal packing effects have on these separations. This is in contrast to analogues in the *peri*-naphthalene series, for which the corresponding separations are much more sensitive and range from 2.489(5) Å for the aldehyde **11**, to 2.531(2) Å for the cyanoester **12**, to 2.6417(16) Å for the nitroalkene **13**, but where the groups have been *forced* into close contacts. In the biphenyl series **2**-**5** there is no significant pattern to the

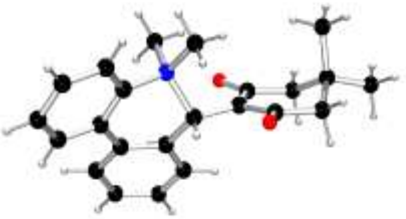
4: N···C: 2.941 Å



5: N···C: 2.943 & 2.976 Å



8: N-C: 1.604 & 1.586 Å



9: N-C: 1.586 Å

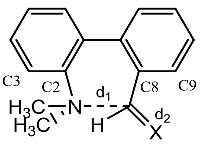
Figure 1. Molecular structures of **4**, **5**, **8** and **9** showing either interactions (**4** and **5**) or bond formation (**8** and **9**) between the functional groups. One of two crystallographically independent molecules is shown for **5** and **8**.

displacements (0 – 0.09 Å) of the two groups from their respective phenyl planes, though there are no examples of both the groups being displaced towards each other. Furthermore, the sp^2 C atoms involved in the interactions are not significantly pyramidalised, in contrast to the naphthalene series. The carbonyl and alkene bond lengths are typical for the groups involved. Thus, the ring between the phenyl groups is either open or closed, there is no range of interactions as in the *peri*-naphthlenes.

The constant occurrence of short contacts in the series of biphenyls **2**-**5** suggests that there is an attractive interaction between the two groups. The interactions in these four biphenyl systems are much more akin to intermolecular interactions between the pairs of functional groups than to incipient bonding interactions which are only observed if the groups are forced to be close to one another. Methadone **10**, with a long 1,5 Me$_2$N- - - C=O interaction between groups disposed along a chain, falls also into this class of unforced interactions.

The formation of a new bond in zwitterionic structures **8** and **9** closes a ring which adopts a twisted half chair conformation similar to that of 9,10-dihydrophenanthrene.[10] The angle between the planes of the two benzene rings in **8** and **9** is reduced to 23.75(6)-27.70(9)° from 58.1(1)-62.4(1)° for the uncyclised cases **2**-**5**. The new N-C bonds (1.5857(14)-1.604(3) Å) are considerably longer than the two N-CH$_3$ bonds (1.499(2)-1.513(2) Å). In each case, the anionic portion of the molecule is so aligned that π electron density can be donated into the new bond's σ* orbital so weakening the bond, however delocalisation of the negative charge into the neighbouring nitrile and carbonyl groups is considerably stronger, as indicated by the far more substantial shortening of the bonds from the anionic centre to the carbonyl and nitrile groups (1.402(3)-1.4215(16) Å) than to the sp^3 C atom at the end of the new C-N bond (1.487(3)-1.5038(15) Å. Compared to the open chain forms **2**-**5**, the N-Me bonds in **8** and **9** are lengthened by *ca.* 0.04 Å to 1.4999(15)-1.508(3) Å, comparable to the

Table 1. Selected Molecular Geometry for **2**-**5**,**8** and **9**.



T1,T2 = Torsion angles of N-Me bonds with the C3-C2 aryl bond.
T3 = Torsion angle of C=X bond with the C8-C9 aryl bond

2,3 X =O; **4-7**, X= C

	d$_1$/Å	d$_2$/Å	T1/°	T2/°	T3/°
2	2.989(2)	1.209(1)	116.5(1)	-14.9(2)	6.2(2)
3	2.929(3)	1.193(3)	118.9(3)	-13.3(3)	10.3(4)
	3.029(3)	1.199(3)	116.0(3)	-15.1(3)	7.7(4)
4	2.9414(16)	1.3495(18)	111.96(14)	19.04(18)	15.6(2)
5	2.943(4)	1.332(4)	103.3(3)	-25.4(4)	13.6(5)
	2.976(4)	1.320(4)	106.1(3)	-23.9(4)	14.8(4)
8	1.604(3)	1.493(3)	-103.9(2)	16.4(2)	-101.1(2)
	1.586(3)	1.487(3)	103.5(2)	-16.6(2)	96.7(2)
9	1.5857(14)	1.5038(15)	100.79(12)	-17.82(15)	21.36(16)

difference in the N-Me bond lengths for the $-NMe_3^+$ and pyramidal $–NMe_2$ groups in cation **15**.[11] Furthermore, the bond from the N atom to the phenyl ring is lengthened by *ca*. 0.07 Å, and the zwitterions have a slightly shorter bond between benzene rings (by *ca*. 0.016 Å).

In zwitterion **9** the anionic group, an enolate of a cyclic β-diketone, takes a pseudo-equatorial position with respect to the newly formed ring and is oriented at 54.61(5)° to the best plane through the whole ring system, but in the two independent molecules of zwitterion **8** the negatively charged dicyanomethide groups take pseudoaxial positions and are oriented at 69.37(12) and 75.0(2)° to the best plane through each ring system. The molecules of zwitterion **9** are linked in chains along the *a* axis by hydrogen bonding between the carbonyl oxygens and an intervening water molecule (O----H-O: 1.941(19) & 1.870(19) Å). The pseudoequatorial conformation of the cyclic enolate may gain some stabilization from intramolecular through-space electrostatic interactions between the enolate and the tetra-substituted ammonium group.

In the enolate portion of zwitterion **9** the negative charge is delocalized into both carbonyl bonds which are lengthened to 1.2544(14) and 1.2577(14) Å, while the intervening C-C bonds show some double bond character with lengths of 1.4215(16) and 1.4274(15) Å. In the dicyanomethide anions of zwitterion **8** the negative charge is delocalized into the cyano groups leading to lengthened nitrile bonds (1.161(3)-1.167(3) Å) compared to the neutral dinitrile **14** (1.142(2) Å at 150 K),[7b] and shortened C-C bonds to the nitrile groups (1.402(3)-1.405(3) Å, cf. **14**: 1.433(2)-1.437(2) Å). Similar effects are seen in the room temperature structures of zwitterions **16**[12] and **17**[13] containing the unconjugated $C(CN)_2^-$ ion (C-C: 1.39(2)-1.424(6) Å; C≡N: 1.15(1)-1.155(5) Å), and salts containing $HC(CN)_2^-$ coordinated through nitrogen to lithium or sodium cations (C-C: 1.372-1.412 Å, C≡N: 1.140-1.168 Å).[14] The cyano N atoms of zwitterion **8** are involved in short intermolecular contacts to hydrogen, in two cases to a hydrogen next to the positively charged nitrogen atom (N---H: 2.37-2.39 Å), and two other cases to phenyl hydrogens (N---H: 2.46-2.53 Å).

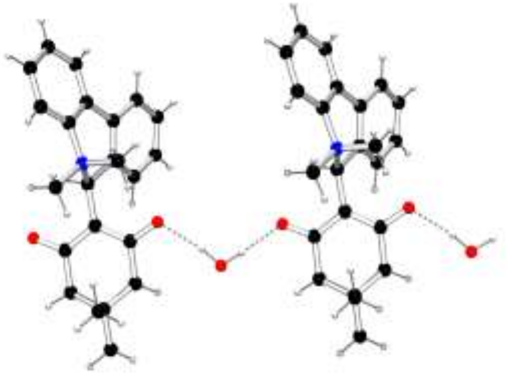
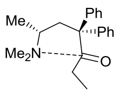
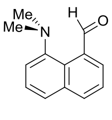


Figure 2: Bridging water molecules linking enolate groups in the crystal structure of zwitterion **9**.

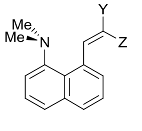
In the *peri*-naphthalene series, ring-closed zwitterions are only formed for **18**, a close analogue of enolate **9**, and for **19** where nitro and benzoyl groups can stabilize the negative charge, while the dinitrile **14** remains uncyclised but shows the shortest separation between a dimethylamino and a sp^2 C atom (2.413(2) Å).[6c,7b] In $CDCl_3$ solution NMR spectra show that the zwitterion **9** retains its structure, judging by the downfield shift of the N-methyl groups (δ_H: 3.36, δ_C: 51.1 ppm) which are similar to those of zwitterions **18** (δ_H: 3.37 and δ_C: 51.7 ppm) and **19** (δ_H: 3.33 and δ_C: 51.7ppm), but distinctly different from open chain compounds **2-5** (δ_H: 2.38-2.45 and δ_C: 42.2-42.6 ppm). The methine group adjacent to the positively charged nitrogen in **9** shows signals at δ_H: 6.47 and δ_C: 75.1 ppm and the carbanionic centre is at δ_C: 101.0 ppm.



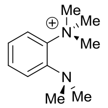
10



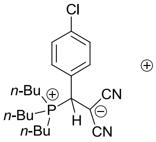
11



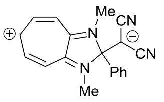
12 **Y = CO_2Et; Z = CN**
13 **Y = NO_2; Z = H**
14 **Y = Z =CN**



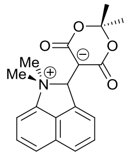
15



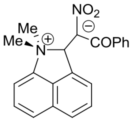
16



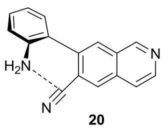
17



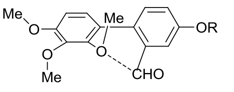
18



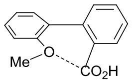
19



20



21 R = benzyl
22 R = methyl



23

In contrast, NMR measurements indicate that the zwitterionic dinitrile **8** exists in its open form **6** in $CDCl_3$ solution. However, in d_6-DMSO it exist as an equilibrium between its open and closed zwitterion forms **6** and **8**. Thus, the observed chemical shifts of the N-methyl groups (δ_H: 2.92 δ_C: 46.3 ppm) are intermediate between those of zwitterions **9**, **18** and **19** (δ_H: 3.36-3.60, δ_C: 51.1-53.1 ppm) and the open form **6** in $CDCl_3$ (δ_H: 2.45 δ_C: 42.3 ppm). The two carbon atoms most affected by formation and opening of the ring show broad peaks at δ_C: 118 (*C*H(C(CN)$_2$) and δ_C: 43 (-*C*(CN)$_2$) ppm. The former lies between the shifts for corresponding carbons in the open chain form **6** (162.2 ppm) and zwitterion **9** **(**75.1 ppm), and the latter between the neutral carbon (79.4 ppm) in **6** and the negatively charged carbon (21.3 ppm) in the zwitterionic dinitrile **17**. Similarly, the nitrile carbon shifts (120.6 ppm) lie between those from **6** and **17** (112.9/114.4 and 124.9 ppm). The solution behaviour suggests that zwitterion **9** is the more stable, and this parallels the solid state structures in the naphthalene series where the dinitrile takes an open chain structure but the bislactone adopts the cyclic zwitterion structure **18**.

A search of the CSD[15] shows that 2,2'-disubstituted biphenyls tend to have their two phenyl rings near to perpendicular unless the substituents are small, as for fluoride and alkoxy, or there is hydrogen bonding between them e.g. for a phenol with either a phenolate or an ether, in which cases interplanar angles are *ca*. 33-55°. There are very few biaryl structures showing 1,6 electrophile/nucleophile contacts; the phenylisoquinoline **20**[16] shows a $\mathrm{Me_2N}$---C≡N contact of 3.070(5) Å, and there are MeO---C=O contacts in aldehydes **21**-**22** (2.7516(13) -2.9499(14) Å)[17] and in the carboxylic acid **23** (3.023(5) Å).[18] No short intramolecular O---C contacts were observed in biphenyl-2,2'-dicarboxylic acid.[19] Gandour and others have exploited the biarylethyne skeleton to probe interactions between functional groups.[20]

These results show that the structures of 2,2'-disubstituted biphenyls can provide insight into intermolecular interactions between a particular pair of functional groups, at least in cases where the groups do not react. The concept of a molecular torsion balance has been introduced by Wilcox,[21] and utilised by others,[22] as a way of quantifying molecular interactions in solution, and the biphenyl system may offer another scaffold for such studies. However, the very low energy barrier (*ca* 2 kcal[23]) in rotating one aryl ring by *ca* 80° through the conformation with the rings mutually perpendicular, contrasts with the much higher energy barrier in the systems of Wilcox (> 18 kcal $\mathrm{mol^{-1}}$).

In the two cases where there has been a reaction between the substituents, they provide stable materials for probing the detailed structures of organic anions. The ease of synthesis and the common crystallinity of biphenyls is an advantage to the extension of this approach to other pairs of functional groups, as well as to the preparation of a much larger series of materials to search for trends in the separations or bond lengths between the two groups.

We thank the EPSRC for a studentship, the EPSRC National Crystallography Service, Southampton University, for datasets and the EPSRC Mass Spectrometry Service, Swansea University, for data. We thank the UK Chemical Database Service[24] for access to the CSD.

Notes and references

[a] *School of Science and Technology, Nottingham Trent University, Clifton Lane, Nottingham NG11 8NS. Fax: +44 115 848 8077; Tel: +44 115 848 8053; Email: john.wallis@ntu.ac.uk*

† Electronic Supplementary Information (ESI) available: [details of any supplementary information available should be included here]. See DOI: 10.1039/b000000x/

‡ *Crystal data* for **4**: $C_{19}H_{18}N_2O_2$, M_r = 306.4, monoclinic, a =8.2446(2), b = 17.2928(4), c = 11.6833(2) Å, β = 107.1770(13)°, V = 1591.42 $Å^3$, Z = 4, space group = $P2_1/a$, $F(000)$ = 648, ρ_c = 1.28 g cm^{-3}, MoK_α (λ = 0.71073 Å), μ = 0.08 mm^{-1}, T = 120 K, 2θ range = 5.82-54.92°, 15927 measured reflections, 3568 unique reflections, $R_{int.}$ = 0.049, 2837 with $F_o > 4\sigma(F_o)$, 280 parameters, GOF on F^2 = 1.03, R_1 = 0.043, wR_2 = 0.107, residual electron density max./min. = 0.28 / -0.22 e $Å^{-3}$.

Crystal data for **5**: $C_{16}H_{16}N_2O_2$, M_r = 268.31, triclinic, a = 8.8510(2), b = 9.8816(3), c = 18.2164(7) Å, α = 92.1632(14) β = 96.4141(15), γ = 116.416(2)°, V = 1411.10 $Å^3$, Z = 4, space group = $P\bar{1}$, $F(000)$ = 568, ρ_c = 1.26 g cm^{-3}, MoK_α (λ = 0.71073 Å), μ = 0.08 mm^{-1}, T = 120 K, 2θ range = 5.96-54.90°, 19681 measured reflections, 6275 unique reflections, R_{int} = 0.07, 3632 with $F_o > 4\sigma(F_o)$, 489 parameters, GOF on F^2 = 1.03, R_1 = 0.076, wR_2 = 0.202, residual electron density max./min. = 0.41 / -0.38 e $Å^{-3}$.

Crystal data for **8**: $C_{18}H_{15}N_3$, M_r = 273.33, monoclinic, a = 11.4599(4), b = 8.2053(3), c = 14.7752(7) Å, β = 92.1424(13)°, V = 1388.37 $Å^3$, Z = 4, space group = $P2_1$, $F(000)$ = 576, ρ_c = 1.31 g cm^{-3}, MoK_α (λ = 0.71073 Å), μ = 0.08 mm^{-1}, T = 120 K, 2θ range = 6.10-54.92°, 10941 measured reflections, 5657 unique reflections (including Friedel pairs), $R_{int.}$ = 0.052, 4750 with $F_o > 4\sigma(F_o)$, 495 parameters, GOF on F^2 = 0.99, R_1 = 0.046, wR_2 = 0.106, residual electron density max./min. = 0.20 / -0.25 e $Å^{-3}$, racemate in $P2_1$ with two crystallographicially independent *R*- and *S*- enantiomers, Flack parameter = 0.2(19).

Crystal data for **9**: $C_{23}H_{25}NO_2 .H_2O$, M_r = 347.45, triclinic, a = 9.3343(2), b = 10.2514(2), c = 11.3449(2) Å, α = 114.4419(8), β = 91.7559(8), γ = 105.0489(8)°, V =942.56 $Å^3$, Z = 2, space group = $P\bar{1}$, $F(000)$ = 392, $\rho_{calc.}$ = 1.29 g cm^{-3}, MoK_α (λ = 0.71073 Å), μ = 0.08 mm^{-1}, T = 120 K, 2θ range = 5.82-54.96°, 14933 measured reflections, 4243 unique reflections, R_{int} = 0.041, 3328 with $F_o > 4\sigma(F_o)$, 352 parameters, GOF on F^2 = 1.05, R_1 = 0.042, wR_2 = 0.104, residual electron density max./min. = 0.21 / -0.26 e$Å^{-3}$.

---

1. H. Christie, J.H. Kenner, *J. Chem. Soc.*, **1922**, *121*, 614-620; K. Mislow, *Angew. Chem.*, **1958**, *70*, 683-689; E.L. Eliel, S. Wien, Stereochemistry of Organic Compounds, John Wiley, New York, 1994, Ch 14.
2. D.W. Old, J.P. Wolfe, S.L. Buchwald, *J. Amer. Chem. Soc*., **1998**, *120*, 9722-9723; S.D. Walker, T.E. Barder, J.R. Martinelli, S.L. Buchwald, *Angew. Chem. Int. Ed. Eng*., **2004**, *43*, 1871-1876.
3. F. Leroux, H. Mettler, *Synlett*, **2006**, 766-770; S. Jeulin, S.B. De Paule, V. Ratovelomanana-Vidal, J.P. Genet, N. Champion, P. Dellis, *PNAS*, **2004**, *101*, 5799-5804; T. Morimoto, K.Yoshikawa, M. Murata, N.Yamamoto, K. Achiwa, *Chem. Pharm. Bull.*, **2004**, *52*, 1445-1450; H. Tsuruta, T. Imamoto, *SynLett*., **2001**, 999-1002; W. Tang, X. Zhang, *Chem. Rev*., **2003**, *103*, 3029-3069.
4. M. Asakawa, P.R. Ashton, S.E. Boyd, C.L. Brown, S. Menzer, D. Pasini, J.F. Stoddart, M.S. Tolley, A.J.P. White, D.J. Williams, P.G. Wyatt, *Chem. Eur. J*., **1997**, *3*, 463-481; B. Herradon, A. Montero, E. Mann, M.A. Maestro, *CrystEngComm*., **2004**, *6*, 512-521.
5. W.B. Schweizer, G. Procter, M. Kaftory, J.D. Dunitz, *Helv. Chim. Acta*, **1978**, *61*, 2783-2808.
6. (a) P.C. Bell, J. D. Wallis, *J. Chem. Soc. Chem. Commun.,* **1999**, 257-258; (b) P.C. Bell, J. O'Leary, J.D. Wallis, W.B. Schweizer, *J. Chem. Soc. Perkin Trans* 2, **2001**, 133-139; (c) J. O'Leary, W. Skranc, X. Formosa, J.D. Wallis, *Org. Biomol. Chem*., **2005** , 3, 3273-3283; (d) J. O'Leary, J.D. Wallis, *Chem. Eur. J*., **2006**, 7724-7732.
7. (a) K.A. Lyssenko, S.M. Aldoshin, M.Y. Antipin, *Mendeleev Comm*., **2004**, 98-100; (b) C.S. Frampton, H. Straver, J. D. Wallis, S. C. Coles, "Charge Density Characterisation of a Weak Through-Space Interaction in a Peri-Naphthalene" Gordon Conference, South Hadley, MA, USA, **2004**.
8. J. O'Leary, J.D. Wallis, M.L. Wood, *Acta Crystallogr.* **2001**, *C57*, 851-852.
9. H.B. Bürgi, J.D. Dunitz, E. Schefter, *Cryst. Struct. Commun.*, **1973**, *2*, 667-672; E. Bye, *Acta Chem. Scand*., **1974**, *B28*, 5-12.
10. R. Cosmo, T.W. Hambley, S. Sternhell, *J. Org. Chem.*, **1987**, *52*, 3119-3123.
11. H. Bock, N. Nagel, *Z. Naturforsch. B, Chem. Sci.*, **1998**, *53*, 792-804.
12. G. Ferguson, C.A. Fyfe, W.C. Marsh, *Can. J. Chem*., **1973**, *51*, 2794-2798.
13. W.F. Richter, K. Hartke, W. Massa, G. Munninghoff, *Chem. Ber*., **1989**, *122*, 1133-1137.
14. W. Hiller, S. Frey, J. Strahle, G. Boche, W. Zarges, K. Harms, W. Marsch, R. Wollert, K. Dehnicke, *Chem. Ber.*, **1992**, *125*, 87-92.

15. Cambridge Structural Database, F.H Allen, *Acta Crystallogr.*, **2002**, *B58*, 380-388 & 407-422.
16. A. Chiaroni, H. Doucerain, C. Riche, *Acta Crystallogr*., **1976**, *B32*, 1920-1922.
17. V. Mamane, P. Hannen, A. Furtsner, *Chem. Eur. J*., **2004**, *10*, 4556-4575.
18. T. M. Krygowski, R. Anulewicz, T. Daniluk, T. Drapala, *Struct. Chem*., **1990**, *1*, 371-378.
19. F.R. Fronczek, S.T. Davis, L.M.B. Gehrig, R.D. Gandour, *Acta Crystallogr*., **1987**, *C43*, 1615-16 18; F.R. Fronczek, Cambridge Structural Database, Private Communication, **2004**.
20. E.T. Huang, K.L. Evans, F.R. Fronczek, R. D. Gandour, *Acta Crystallogr.*, **1992**, *C48*, 763-765; P. Prince, K.L. Evans, V.M. Rosas-Garcia, R.D. Gandour, F.R. Fronczek, *Tetrahedron Lett*., **1992**, *33*, 6432-6434; M. Pilkington, J.D. Wallis, G.T. Smith, J.A.K. Howard, *J. Chem. Soc. Perkin Trans 2*., **1996**, 1849-1854.
21. E. Kim, S. Paliwal, C.S. Wilcox, *J. Amer. Chem. Soc*., **1998**, *120*, 11192-11193; S. Paliwal, S. Geib, C.S. Wilcox, *J. Amer. Chem. Soc*., **1994**, *116*, 4497-4498.
22. W. B. Motherwell, J. Moïse, A. E. Aliev, M. Nič, S. J. Coles, P. N. Horton, M. B. Hursthouse, G. Chessari, C. A. Hunter, J. G. Vinter, *Angew. Chem., Int. Ed. Eng*., **2007**, 7823-7826; F.R. Fischer, W. B. Schweizer, F. Diederich, *Angew. Chem., Int. Ed. Eng*., **2007**, *46*, 8270-8273; S.L. Cockcroft, C.A. Hunter, *Chem. Commun.*, **2006**, 3806-3808.
23. M.P. Johansson, J. Olsen, *J. Chem. Theory Comp.*, **2008**, DOI: 21/ct800182e.
24 The United Kingdom Chemical Database Service, D.A. Fletcher, R.F. McMeeking, D.J. Parkin, *Chem. Inf. Comput. Sci*., **1996**, *36*, 746-749.