PERKIN 2

Attractive and repulsive effects in the interactions between electron-rich and electron-deficient groups in *peri*-substituted naphthalenes

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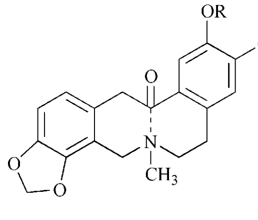
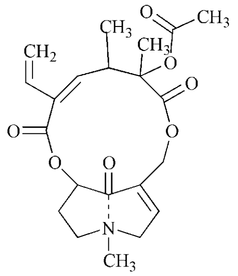
The 1,5 $Me_2N \cdots C(sp^2)$ separations in a series of *peri*-substituted naphthalene derivatives are sensitive to the through-space electron-attracting power of the carbon-containing functional group, while the corresponding $MeO \cdots C(sp^2)$ separations are relatively insensitive in accord with the different nucleophilicities of the two groups. These separations are a balance between a steric effect and a covalent interaction, and from a comparison of the $Me_2N \cdots C$ and $MeO \cdots C$ distances for a given functional group it is proposed that the $Me_2N \cdots C$ interaction has an attractive component if the $Me_2N \cdots C$ separation is less than ~($MeO \cdots C$ + 0.15) Å, the latter factor arising from the greater size of the bonded nitrogen atom.

Through-space interactions between functional groups are involved in a range of chemical and biochemical processes. Thus, van der Waals forces, hydrogen bonding, and dipole–dipole interactions all play important roles as attractive interactions in supramolecular processes such as crystal packing, host–guest chemistry and the mode of binding of a substrate to a biological receptor protein. The balance between attractive and repulsive forces determines the separation between a pair of interacting groups. Van der Waals radii were assigned originally from the closest measured intermolecular contacts between *like* atoms to provide estimates of the effective sizes of bonded atoms,[1,2] and have been modified subsequently by Nyburg to account for the asymmetric shapes of bonded atoms from the second and later rows of the Periodic Table.[3] However, to use these parameters for predicting the closest interaction distance between *unlike* atoms, by just adding the appropriate 'radii', is not likely to be very successful since there may be additional aspects to the interaction which are not present when either atom interacts with one of its own kind. Bent has made a wide survey of the types of compounds containing such interactions.[4] This is especially relevant for interactions between electron-rich and electron-poor atoms which may interact in a way akin to the early stage of a chemical reaction[5] as has been observed between tertiary amino groups and carbonyl groups.[6,7] Thus, Bürgi, Dunitz and Schefter pointed out that the interactions between a tertiary amino group and a carbonyl group in a series of alkaloids including molecules **1**–**3** showed a correlation between a decreasing $N \cdots C$ distance and an increasing C=O bond length, which parallels the process of the corresponding addition reaction.[7] Nevertheless, it is not necessarily straightforward to deduce whether there is an attractive component to an intramolecular interaction from the contact distance alone. Greater insight may be obtained in the future by analysis of the experimental charge density, determined from accurate low-temperature X-ray diffraction data, using Bader's 'Theory of Atoms in Molecules'[8] in which *bonding* interactions are characterised by saddle points in the total electron density.



1 R = CH_3
2 R,R = $-CH_2-$



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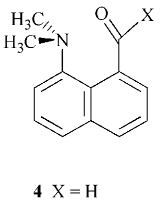
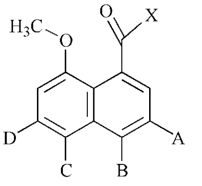
The *peri*-disubstituted naphthalene framework has played a prominent role in this area, most notably for investigating interactions between a dialkylamino or a methoxy group and a variety of electrophilic groups.[6,9,10] Since the original studies[6] of *peri* interactions of dimethylamino or methoxy groups with carbonyl-containing groups further data have become available, and selected geometric parameters for 16 compounds are given in Tables 1 and 3. In nearly all cases the carbonyl group is oriented so that one face of the group is presented to the *peri* substituent, and there are in-plane displacements of the two



4 X = H
5 X = Me
6 X = OH
7 X = OMe
8 X = NMe_2
9 X = NPr^i_2



10 X = H, A=D=H, B=OMe, C=OTs
11 X= H, A=B=D=H, C=OTs
12 X = Me, A=B=C=D=H
13 X = Me, A=D=H, B=OMe, C=OTs
14 X = OH, A=B=C=D=H
15 X = OH, A=B=D=H, C=OMe
16 X = OH, A=B=H, C=OMe, D=CO_2H
17 X = OMe, A=B=D=H, C=OMe
18 X = NMe_2, A=B=C=D=H
19 X = NPr^i_2, A=B=C=D=H

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(a) (b)

Fig. 1 Patterns of displacements in *peri*-substituted naphthalenes: (a) with nucleophilic group (N) and electrophilic group (E) displaced in the same direction, and (b) with these groups attracted towards each other.

functional groups in the same sense such that the dimethylamino or methoxy group is displaced towards the carbonyl-containing group which itself is displaced outward as shown in Fig. 1a. The orientations of the dimethylamino and alkoxy groups are such that a lone pair of electrons is directed towards the adjacent carbonyl group. This mode of displacement produces an angle of attack of the 'nucleophilic' nitrogen or oxygen atom on the carbonyl group of *ca.* 110°. These arrangements have been interpreted as attractive interactions involving overlap of lone pair electron density from the nitrogen or oxygen atom with the LUMO of the carbonyl group. Supportive of this are the small displacements (0.02–0.08 Å) of each carbonyl carbon atom from the plane of its bonded neighbours towards the *peri* substituent, which parallel the sort of distortion which would be expected as a nucleophile begins to add to a carbonyl group.

However, despite the expected difference in nucleophilicities between a dimethylamino and a methoxy group there is no clear systematic difference between the N···C=O and O···C=O distances for interactions with the same carbonyl-containing functional group. Thus, in the *peri*-dimethylamino methyl ketone **5** the N···C(=O) distance (2.557(3) Å)[6] is slightly shorter than the O···C(=O) distances in *peri*-methoxy methyl ketones **12** and **13** (2.606(9) and 2.579(3) Å)[6,11] but for the pairs of *N*,*N*-dimethyl- and *N*,*N*-diisopropylcarboxamides, **8**, **18** and **9**, **19**, the N···C(=O) distances (2.698(3) and 2.764(3) Å)[6,12] are distinctly longer than the O···C(=O) distances (2.597(5) and 2.623(2) Å). This latter result has been interpreted recently as indicating greater '*peri* bonding' between a methoxy and a carboxamide group than between a dimethylamino and a carboxamide group, and was used to explain the slower rate of racemisation of the *peri*-methoxy carboxamide **19** compared to the *peri*-dimethylamino carboxamide **9** which is effected by rotation about the aryl–carbonyl bonds.[12] We now examine more closely these interactions in the light of further results from *peri*-substituted electron-deficient alkenes.

If two *peri* groups were to react to form a bond then the two groups would be displaced *towards* each other as shown in Fig. 1b rather than in the same direction as shown in Fig. 1a. Indeed this trend has been found in our recent studies[9,10] on naphthalenes containing *peri* interactions between a dimethylamino group and an electron-deficient alkene. Structural data for these compounds along with some further data[13] from the Kirby group are summarised in Table 2. Along the series **25** to **20** there is a progressive decrease in the N···C=C separation culminating in the formation of a bond in **20** whose structure is better represented as the zwitterion **26** with a N–C bond length of 1.651 Å. Thus, the greatest degree of *peri* N···C interaction occurs when the alkene's terminal substituents are two lactone carbonyl groups both of which are coplanar with the alkene. The next largest degree of interaction is in **21** where the alkene substituents are both nitriles. We have now measured the structures of **27** and **28**, the *peri*-methoxy analogues of these two compounds, to investigate the degree of interaction of the electron-deficient alkenes with methoxy groups.

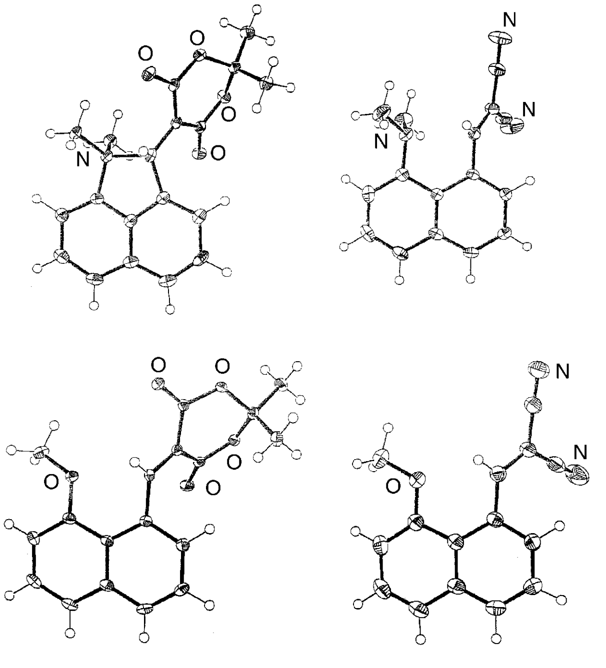
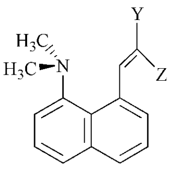
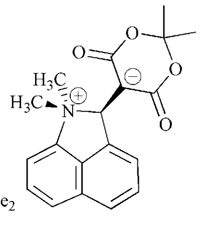


Fig. 2 Molecular structures of **20** (top left), **21** (top right), **27** (bottom left), **28** (bottom right), with anisotropic displacement parameters drawn at the 50% level.[38]



20 Y = Z = -(C(=O)O)$_2$CMe$_2$
21 Y = CN, Z = CN
22 Y = CN, Z = CO$_2$Et
23 Y = Z = COPh
24 Y = Br, Z = H
25 Y = Br, Z = H



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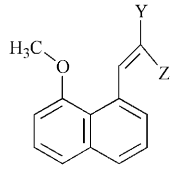
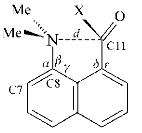


27 Y = Z = -(C(=O)O)$_2$CMe$_2$
28 Y = Z = CN

The molecular structures of **27** and **28** are shown in Fig. 2, along with the structures of the corresponding dimethylamino compounds. Selected geometric data are given in Table 4. In **27** and **28** the MeO···C=C separations are *longer* than the corresponding Me_2N···C=C distances (**27**: 2.550(2) Å *cf.* **20**: 1.651(3) Å and **28**: 2.611(1) Å *cf.* **21**: 2.413(2) Å). The trend in the lengths of the N···C separations in **20** and **21** is mirrored in the O···C distances in **27** and **28**. However, in **27** and **28** the in-plane displacements of the two *peri* substituents are in the same sense, and there is no indication of the alkene substituent being attracted back towards the methoxy group. Nevertheless, both alkene groups show small pyramidalisations at the carbon attached to the naphthalene ring. The longer interatomic separations and the lack of inward displacement of both groups are consistent with an aryl methoxy group having a lower nucleophilicity than the aryl dimethylamino group, and so showing a reduced interaction with the electrophilic alkene.

Tables 1–4 contain geometric information on a wide range of 8-(dimethylamino)- and 8-methoxy-naphthalene derivatives which contain an sp^2 C atom in the 1-position and only hydrogen atoms *ortho* to these substituents. For the dimethylamino derivatives, the N···C distances decrease with *peri* group along the series: –CH=CHBr ~ –CONR$_2$, –CH=C(COPh)$_2$, –CO$_2$H ~ –CO$_2$R, –COCH$_3$, –CH=C(CN)CO$_2$CH$_3$, –CHO, –CH=C(CN)$_2$, –CH=C(C(=O)O)$_2$CMe$_2$ from 2.764 to 1.651 Å. This forms a relative order of through-space electron-accepting power of these groups. The decrease in the N···C distance is accompanied by a decrease in the outward bending of the alkenyl or carbonyl group, so that for the dicyanoethenyl

Table 1 Selected geometric data for 8-(dimethylamino)naphthalene-1-carbonyl derivatives

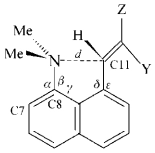


ΔC: deviation of C11 from plane of its three neighbours towards the *peri* substituent.

T1 and T2: torsion angles of N–Me bonds with the C7–C8 aryl bond.

	X	*d*/Å	α/°	β/°	γ/°	δ/°	ε/°	ΔC/Å	T1/°	T2/°
4[13]	H	2.489(5)	124.3(4)	116.0(3)	120.6(3)	122.2(4)	118.5(4)	0.061(4)	44.5(5)	−85.2(5)
5[6]	CH$_3$	2.557(3)	123.4(2)	116.6(2)	122.3(2)	123.2(2)	117.2(2)	0.088(3)	47.0(4)	−81.3(3)
6[6]	OH	2.606(5)	123.0(4)	117.4(3)	122.5(3)	123.9(3)	116.3(3)	0.061(5)	53.1(5)	−77.1(5)
7[6]	OCH$_3$	2.594(4)	123.6(3)	117.4(3)	122.4(3)	123.9(3)	116.3(3)	0.062(3)	48.2(5)	−80.1(4)
8[12]	NMe$_2$	2.698(3)	122.9(2)	117.0(2)	123.7(2)	124.8(2)	115.5(2)	0.055(3)	34.8(5)	−93.2(3)
9[12]	$\mathrm{NPr^i_2}$	2.764(3)	121.2(3)	118.4(2)	125.1(2)	125.4(2)	114.1(2)	0.051(3)	40.4(4)	−85.8(3)

Table 2 Selected geometric data for 8-(dimethylamino)naphthalene-1-alkenes



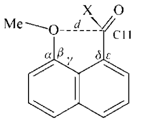
ΔC: deviation of C11 from plane of its three neighbours towards the *peri* substituent.

T1 and T2: torsion angles of N–Me bonds with the C7–C8 aryl bond.

	Y, Z	*d*/Å	α/°	β/°	γ/°	δ/°	ε/°	ΔC[a]/Å	T1/°	T2/°
20[9]	–(C(=O)O)$_2$CMe$_2$	1.651(3)	128.6(2)	108.8(2)	113.3(2)	109.9(2)	131.4(2)	0.362(2)	49.5(3)	−71.9(2)
21[9]	CN, CN	2.413(2)	124.3(2)	115.9(1)	120.4(1)	120.2(1)	120.3(1)	0.087(2)	49.7(2)	−81.4(2)
22[10]	CN, CO$_2$Et	2.531(2)	123.3(2)	116.8(1)	122.4(1)	121.6(1)	118.6(2)	0.041(2)	47.9(2)	−82.9(2)
23[9]	COPh, COPh	2.679(2)	122.3(2)	118.3(2)	123.5(2)	122.5(2)	117.6(2)	0.015(2)	26.0(2)	−105.0(2)
24[13]	Br, H	2.717(5)	122.0(4)	118.8(4)	124.0(4)	122.0(4)	117.8(4)	—	23.8(6)	−106.5(5)
24	Br, H	2.742(5)	122.0(4)	118.0(4)	125.1(4)	122.5(4)	118.1(4)	—	22.7(6)	−105.9(5)
24	Br, H	2.758(2)	123.2(1)	117.1(1)	127.0(1)	121.8(1)	116.6(1)	—	14.9(2)	−110.4(2)
25[13]	H, Br	2.749(5)	122.3(4)	118.5(3)	124.2(3)	123.3(3)	117.2(3)	—	26.6(5)	−103.6(4)

[a] Hydrogen atom positions for **24** and **25** were calculated, thus forcing ΔC to be zero.

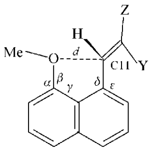
Table 3 Selected geometric data for 8-methoxynaphthalene-1-carbonyl derivatives



ΔC: deviation of C11 from plane of its three neighbours towards the *peri* substituent.

	X	*d*/Å	α/°	β/°	γ/°	δ/°	ε/°	ΔC/Å
10[11]	H	2.628(4)	123.4(2)	115.1(2)	122.5(2)	126.4(2)	114.9(2)	0.089(4)
11[11]	H	2.644(4)	123.5(3)	115.3(2)	123.9(3)	124.7(3)	115.8(3)	0.072(4)
12[6]	Me	2.606(9)	124.4(9)	115.9(8)	121.7(8)	125.5(8)	115.3(8)	0.044(10)
13[11]	Me	2.579(3)	124.0(2)	114.1(2)	122.0(2)	125.5(2)	115.3(2)	0.070(3)
14[6]	OH	2.559(4)	124.7(3)	113.2(3)	124.4(2)	123.4(3)	115.8(3)	0.022(5)
15[14]	OH	2.566(2)	124.7(2)	114.1(2)	123.3(2)	124.0(2)	115.0(2)	0.042(2)
16[15]	OH	2.526(3)	124.7(2)	114.1(2)	123.3(2)	122.1(2)	117.4(2)	0.036(2)
17[14]	OMe	2.588(3)	125.6(3)	114.3(2)	123.7(2)	124.2(2)	115.6(2)	0.037(2)
18[6]	NMe$_2$	2.597(5)	122.7(4)	114.4(4)	124.3(4)	124.0(3)	115.1(4)	0.039(4)
19[12]	$\mathrm{NPr^i_2}$	2.623(2)	124.2(2)	114.8(2)	123.4(2)	124.2(2)	116.0(2)	0.049(1)

Table 4 Selected geometric data for 8-methoxynaphthalene-1-alkenyl derivatives



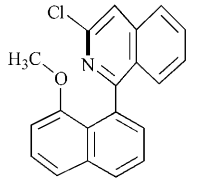
ΔC: deviation of C11 from plane of its three neighbours towards the *peri* substituent.

	Y, Z	*d*/Å	α/°	β/°	γ/°	δ/°	ε/°	ΔC/Å
27	–(C(=O)O)$_2$CMe$_2$	2.550(2)	123.6(2)	115.0(2)	122.9(2)	123.2(2)	117.3(2)	0.077(2)
28	CN, CN	2.611(1)	124.3(1)	114.9(1)	124.1(1)	123.5(1)	117.0(1)	0.029(1)

derivative **21** the *exo* angles where the alkene joins the aromatic ring are almost equal while for the carboxamide and bromoethenyl derivatives, **8**–**9** and **24**–**25**, the group is splayed out by 3–5.6°. In contrast, for the methoxy-substituted series there is much less variation in the O $\cdots$ C distances which only differ by 0.097 Å (2.526–2.623 Å), consistent with the much lower nucleophilicity of this group. In related work, Jones and Kirby have made the connection between structural chemistry and reactivity by relating the sensitivities of bond length changes in several series of acetals to their relative rates of hydrolysis.[16]

Of the carbonyl-containing functional groups in the *peri* derivatives discussed here, only the aldehyde group is sufficiently small to have the possibility of lying in, or close to, the naphthalene plane. Thus, it is indicative of the poorer nucleophilic character of the methoxy group that in the 8-methoxy-1-naphthaldehydes **10** and **11** the aldehyde groups lie at 30.8° and 38.5° to the naphthalene planes, and the methoxy oxygen atom is not directed at a face of the carbonyl group. Thus, these two compounds have been excluded from this survey of *peri* interactions with sp^2 carbon atoms. In comparison, the aldehyde group in 8-(dimethylamino)-1-naphthaldehyde **4** lies at 65.8° to the naphthalene plane and does show a short $Me_2N \cdots C{=}O$ contact.

It may not be realistic to look for clear trends among the O $\cdots$ C distances in these *peri*-methoxynaphthalene compounds, since the differences in these distances are of the same order as those produced by adoption of different packing arrangements or by different measurement temperatures. Thus, although the order of increasing O $\cdots$ C distances mirrors those of the N $\cdots$ C series more or less, the value for the dicyanoethenyl derivative **28** does appear to be out of step. To determine the trend with more confidence it would be necessary to measure a greater number of *peri*-methoxy compounds, including polymorphic forms where available, to average out the effects of crystal packing, and to make these measurements at very similar temperatures, ideally at *ca.* 100 K. It is interesting to consider compounds **29**[17] and **30**[18] which contain *peri* interactions between methoxy groups and aromatic rings. The O $\cdots$ C separations (**29**: 2.606(5) and 2.644(5) Å; **30**: 2.659(5) Å) do not lie far outside the range for the *peri*-methoxy compounds discussed above, further indicating the low sensitivity of the O $\cdots$ C separation to the electronic character of the carbon atom. The low variability in O $\cdots$ C separations indicates that these are controlled mainly by steric interactions.



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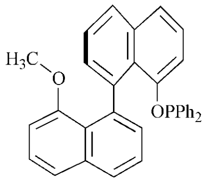

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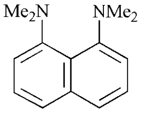
We propose that the $Me_2N \cdots sp^2C$ interactions have a significant attractive covalent component when the N $\cdots$ C distance is *shorter* than the corresponding O $\cdots$ C distance in accord with the greater nucleophilicity of a tertiary amine over an aryl methyl ether. However, when the $Me_2N \cdots sp^2C$ interaction is primarily steric in nature, the greater size of the nitrogen atom over the oxygen atom leads to the N $\cdots$ C distance between *peri* substituents being *longer* than the O $\cdots$ C separation. To develop this further, it would be helpful to have an estimate of the difference in effective sizes of the bonded nitrogen and oxygen atoms in these systems. Indeed, data from the Cambridge Structural Database[19] for *peri*-naphthalenes containing either two dimethylamino groups or two methoxy groups provide some useful information. The average N $\cdots$ N separation in 1,8-bis(dimethylamino) compounds of type **31**[20] is 2.81 Å, and the average O $\cdots$ O separation in 1,8-dimethoxy compounds of type **32**[21] is 2.50 Å. This corresponds to a difference in the effective sizes of bonded nitrogen and oxygen atoms of *ca.* 0.15 Å.[22] Thus, refining the original proposal, if a $Me_2N \cdots sp^2C$ interaction distance is less than the sum of the corresponding $MeO \cdots sp^2C$ interaction distance and the difference in size of the bonded nitrogen and oxygen atoms (~0.15 Å) the $Me_2N \cdots sp^2C$ interaction may have an attractive component. The larger this difference then the more attractive the $Me_2N \cdots sp^2C$ interaction. Thus, the interactions of a dimethylamino group with the electron-deficient alkenes in **20** and **21** have some covalent character ($d(MeO \cdots X) + 0.15 - d(Me_2N \cdots X) = 1.049$ and 0.348 Å), while the interactions of dimethylamino groups with carboxamides in **8** and **9** are dominated by steric effects ($d(MeO \cdots X) + 0.15 - d(Me_2N \cdots X) =$ 0.049 and 0.009 Å). This parallels chemical reactivity, with addition of amines to electron-deficient alkenes being much easier than addition of an amine to a carboxamide group. The interactions of dimethylamino groups with ketones and esters, for which $d(MeO \cdots X) + 0.15 - d(Me_2N \cdots X) = 0.185$ and 0.144 Å respectively, are interpreted as involving small attractive interactions which lead to the similarities in the $Me_2N \cdots C$ and $MeO \cdots C$ distances. The contractions in the N $\cdots$ C distances due to HOMO–LUMO overlaps are of the same order as the difference in the effective sizes of the nitrogen and oxygen atoms. This proposed interpretation is illustrated further by the naphtho-1-nitriles **33**[23] and **34**[24] which have a *peri*-dimethylamino or a *peri*-methoxy group respectively: the N $\cdots$ C distance in **33** is 2.704(6) Å and is greater than the O $\cdots$ C distance in **34** of 2.594(4) Å. The small value of 0.040 Å for the parameter [$d(MeO \cdots X) + 0.15 - d(Me_2N \cdots X)$] indicates that the *peri* dimethylamino–nitrile interaction is determined mainly by steric effects. Comparison with the series constructed earlier indicates that the (weak) through-space electron-attracting power of the nitrile group is similar to that of a carboxamide group.



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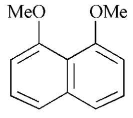

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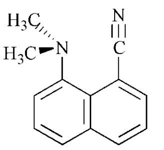

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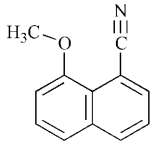

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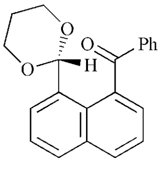
A further indication of the attractive nature of certain *peri* $Me_2N \cdots C$ interactions is the orientation of the dimethylamino group's lone pair towards the *peri* group. This is indicated by the torsion angles the two Me–N bonds make with the naphthalene ring (Tables 1 and 2). It is notable that as the N $\cdots$ C distance increases there is a greater tendency for the axis of the nitrogen atom's lone pair to move out of the naphthalene plane. In this way the lone pair can gain some conjugation with the π electrons of the aromatic system when there is little to gain by interaction with a *peri* substituent. Thus, for the ethenyl derivatives **23**–**25**, which have N $\cdots$ C distances in the range 2.679–2.758 Å, the lone pair axes make torsional angles of 38.5–47.8° with their naphthalene rings. Furthermore, a similar effect is observed for the *peri*-dimethylamino nitrile **33** in which the axis of the amino nitrogen's lone pair makes an angle of 43.5° to the aromatic plane, in line with the predicted minimal attractive interaction between this pair of functional groups.

The interactions of dimethylamino or methoxy groups with carbonyl or alkenyl groups lead to small pyramidalisations of the sp^2 C atoms (0.01–0.09 Å) involved in the short contact, such that the carbon atom appears drawn towards the nitrogen or oxygen atom. This feature has been interpreted as indicating an attractive interaction since it represents a small deviation along the reaction path for the addition reaction. However, this feature is not always diagnostic for an attractive interaction. Thus, a survey of all aryl alkyl ketones in the CSD shows a mean pyramidality at the carbonyl carbon of 0.014 Å. Indeed, in a more detailed study Cieplak[5] has pointed out that the molecular environment can induce a small pyramidality at carbonyl carbon. Two specific examples from the *peri*-naphthalenes are the benzoyl derivatives **35**[25] and **36**,[26] in which each carbonyl carbon is slightly pyramidalised (by 0.029 and 0.042 Å) towards an incipient hydrogen atom belonging to the other *peri* substituent, but this may simply be a way for each benzoyl group to increase its distance from the *peri* substituent. In summary, it is misleading to interpret some of the small pyramidalities at the carbonyl or alkenyl carbon atom in compounds **4**–**28** as indicators of attractive interactions. A comparison of $Me_2N\cdots C$ and $MeO\cdots C$ separations provides a better criterion.



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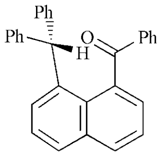

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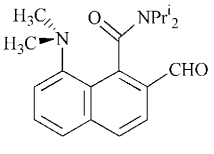
In view of these proposals the slower rate of racemisation of the *N*,*N*-diisopropyl 8-methoxy-1-naphthamide **19** over the corresponding 8-(dimethylamino)-1-naphthamide **9** needs consideration. An even larger effect is seen in the rates of racemisations of compounds **37** and **38** which have an additional 2-substituent. The differences in rates correspond to differences in the free energy of activation of *ca.* 5.8 kJ mol^{-1} for **9** and **19** and of at least 10 kJ mol^{-1} for **37** and **38**. These results were ascribed to 'stronger *peri* bonding' in the methoxy derivatives on account of the $MeO\cdots C{=}O$ contacts being shorter than the $Me_2N\cdots C{=}O$ contacts, yet 'stronger *peri* bonding' would not be expected for interaction of the amide with the less nucleophilic group. We propose that the shorter $O\cdots C$ contacts are simply a reflection of the smaller size of the methoxy oxygen atom, and that the reason for the difference in racemisation rates must be sought elsewhere. The transition states for these racemisations must have the carboxamide group coplanar with the naphthalene ring, but this will involve significant steric pressure from the *peri* substituent. A *peri* methoxy group is limited in the amount to which it can splay away from the carboxamide group by the steric interaction of the methyl group with the *ortho* hydrogen atom. This effect is not so severe for the dimethylamino group since neither methyl group lies in the aromatic plane, and the bonding geometry at nitrogen could distort somewhat from pyramidal towards a planar arrangement in the transition state for racemisation. A further point to consider is that in the transition state a *peri* methoxy group may rotate out of the aromatic plane to avoid repulsion from the *ortho* hydrogen atom. This requires loss of conjugation with the aromatic system and has no counterpart in the racemisations of the dimethylamino systems where in the ground state the nitrogen atom's only lone pair lies close to the aromatic plane, not perpendicular to it. Thus, loss of conjugation between the methoxy group and the naphthalene ring would contribute to the greater activation energy for the racemisation process. The most stable conformation of anisole in a molecular beam has been determined experimentally[27] to be that with the methoxy group coplanar with the benzene ring, and this is supported by numerous observations from the solid state.[28] Furthermore, no other energy minimum was detected corresponding to any other orientation of the methoxy group.[27] The energy difference between conformations of anisole in which the methoxy group lies coplanar with, or perpendicular to, the aromatic ring has been calculated to be 5.8 and 10 kJ mol^{-1} for the isolated molecule.[29,30] Measurements from the liquid phase have given values of 6.3 and 25.2 kJ mol^{-1}.[31,32]



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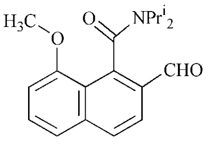

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It is notable that in the *peri*-dimethoxynaphthalene derivatives, *i.e.* molecules containing fragment **32**, the methoxy groups have in-plane displacements of *ca.* 2.5° towards one another. Thus, there cannot be a strong repulsive interaction between them at this rather short distance, which the van der Waals radius would have predicted. The stronger influences are the steric interaction of the *O*-methyl group with the *ortho* hydrogen atom (typical $H\cdots CH_3$ distance ~ 2.42 Å), and the retention of conjugation with the naphthalene which acts to reduce slightly the electron density at oxygen. Thus, in the many *peri*-methoxy derivatives discussed above the conjugation of the methoxy group with the aromatic system is the root of the constraint which displaces the methoxy group towards the other *peri* substituent. In contrast, in 1-(dimethylamino)naphthalenes, the nitrogen atom has something to gain by not having its lone pair lying in the plane of the naphthalene ring.

In summary we propose that the character of nucleophile–electrophile interactions in *peri*-substituted napthalenes can be deduced by observing the relative sizes of the contact distances between the electrophile and two groups of differing nucleophilicity, and this approach should be transferable to other systems. Further details of the interactions can be approached experimentally by examining the topography of the total electron density measured by X-ray diffraction measurements. Recently, Akiba *et al.* have published the structure of a 1,8-dimethoxyanthracene which carries a carbocation group ($(MeO)_2C^+$–) in the 9-position.[33] This group lies perpendicular to the anthracene system and has a *peri* interaction to each side with a methoxy group, leading to a five-coordinate carbon atom. Not surprisingly, the $MeO\cdots C^+$ separations of 2.43(1) and 2.45(1) Å are *ca.* 0.1 Å shorter than any of the $MeO\cdots C$ contacts in Tables 3 and 4.

Experimental

NMR spectra were measured on a JEOL GX 270 machine at 270 MHz for ^{1}H and 67.8 MHz for ^{13}C spectra using deuterated chloroform as solvent and tetramethylsilane (TMS) as standard, and measured in ppm downfield from TMS unless otherwise stated. Coupling constants (*J*) are given in Hz. IR spectra were recorded on an ATI Mattson Genesis Series FTIR instrument as Nujol mulls or liquid films. Mass spectra were recorded at the EPSRC Mass Spectrometry Centre, University of Wales, Swansea. Flash chromatography was performed on 40–63 silica gel (Merck). UV spectra were obtained on a PU 8740 UV–Vis scanning spectrophotometer using methanol as a solvent unless otherwise stated. Capillary melting points were taken on a Gallenkamp melting point apparatus and are uncorrected.

8-Methoxy-1-naphthaldehyde

8-Hydroxy-1-naphthaldehyde (3.02 g, 17.6 mmol) was dissolved in methanol (40 ml) and powdered potassium hydroxide (2.24 g, 40 mmol) and methyl iodide (10 g, 22.8 ml, 70.4 mmol) were added to the stirred mixture and left overnight at RT. The resulting solution was evaporated under reduced pressure, the residue extracted with chloroform and subjected to flash chromatography on silica, eluting with chloroform. This yielded the desired ether (2.38 g, 73%) as cream crystals, mp 71 °C. ν_{max}/cm^{-1}: 1729, 1263, 818, 768; λ_{max}/nm: 217, 237, 249, 312, 323; δ_H: 11.08 (1H, s, O=C-*H*), 7.98 (1H, dd, *J* = 8.2, 1.4 Hz, Ar-H_1), 7.94 (1H, dd, *J* = 7.3, 1.4 Hz, Ar-H_1), 7.55–7.40 (3H, m, Ar-H_3), 6.97 (1H, dd, *J* = 7.4, 1.4 Hz, Ar-H_1), 3.99 (3H, s, O-CH_3); δ_C: 195.51 (*C*=O), 156.10, 135.21, 134.93, 133.03, 127.15, 126.42, 125.64, 123.24, 121.42, 106.70 (Ar-C_{10}), 55.60 (O-*C*H$_3$).

5-(8′-Methoxy-1′-naphthylmethylidene)-2,2-dimethyl-1,3-dioxane-4,6-dione 27

8-Methoxy-1-naphthaldehyde (200 mg, 1.1 mmol) was dissolved in DMSO (3 ml) and Meldrum's acid (500 mg, 3.5 mmol) was added. The stirred mixture was left for 48 h. Distilled water (20 ml) was added and the resulting mixture was extracted with chloroform (5 × 30 ml). The organic extracts were washed with water (6 × 20 ml) and the organic layer dried (MgSO$_4$). The solvent was removed under reduced pressure and the residue subjected to flash chromatography on silica eluting with 1 : 1 ether–hexane. This yielded **27** (90 mg, 26.2%) as yellow crystals, mp 139 °C. ν_{max}/cm^{-1}: 1733, 1608, 1270, 1267, 1228, 1189, 1187, 1069, 929, 772; λ_{max}/nm: 225, 233; δ_H: 9.41 (1H, s, *H*-C=C), 7.91 (1H, dd, *J* = 7.6, 1.9 Hz, Ar-*H*), 7.40–7.51 (4H, m, Ar-H_4), 6.91 (1H, dd, *J* = 7.3, 1.5 Hz, 7′-H), 3.93 (3H, s, O-CH_3), 1.85 (6H, s, C–CH_3); δ_C: 164.4 (H-*C*=C), 163.1 and 159.7 (C=O), 155.9, 135.2, 130.9, 129.4, 127.2, 126.6, 125.3, 123.3, 121.4 (Ar-C_9), 113.1 (HC=*C*), 106.5 (Ar-C_1), 104.6 (*C*(CH$_3$)$_2$), 56.2 (O-*C*H$_3$), 29.7 (C-(*C*H$_3$)$_2$); HRMS (EI): Found: 312.0994, $C_{18}H_{16}O_5$ requires: 312.0998.

1,1-Dicyano-2-(8′-methoxy-1′-naphthyl)ethene 28

8-Methoxy-1-naphthaldehyde (200 mg, 1.1 mmol) was dissolved in DMSO (3 ml) and malononitrile (250 mg, 3.8 mmol) was added. The stirred mixture was left for 48 h. Distilled water (20 ml) was added and the resulting mixture was extracted with chloroform (5 × 30 ml). The organic extracts were washed with water (6 × 20 ml) and the organic layer dried (MgSO$_4$). The solvent was removed under reduced pressure and the residue subjected to flash chromatography on silica (eluting with 1 : 1 ether–hexane). This yielded **28** (50 mg, 19%) as yellow crystals, mp 128–127 °C. ν_{max}/cm^{-1}: 2226, 1580, 1241, 1072, 902, 768, 722; λ_{max}/nm: 222, 226; δ_H: 9.05 (1H, s, *H*-C=C), 7.99 (1H, d, *J* = 8.2 Hz, Ar-H_1), 7.70 (1H, d, *J* = 7.1 Hz, Ar-H_1), 7.49–7.57 (3H, m, Ar-H_3), 6.98 (1H, dd, *J* = 3.0, 2.9 Hz, 7′-*H*), 3.99 (3H, s, O-CH_3); δ_C: 166.5 (H-*C*=C), 155.7, 135.3, 133.1, 128.3, 127.6, 127.2, 125.6, 122.6, 121.6 (Ar-C_9), 113.8 (*C*≡N), 112.3 (*C*≡N), 107.4 (Ar-C_1), 83.0 (*C*(CN)$_2$), 56.1 (O-*C*H$_3$); HRMS (EI): Found: 234.0793, $C_{15}H_{10}N_2O$ requires: 234.0793.

X-Ray crystallography for 27 †

Crystal data: $C_{18}H_{16}O_5$, $M_r = 312.3$, monoclinic, $a = 10.291(2)$, $b = 11.607(3)$, $c = 12.988(3)$ Å, $\beta = 105.421(4)°$, $V = 1495.5(6)$ Å^3, $Z = 4$, *Cc*, $D_c = 1.39$ g cm^{-3}, μ (CuKα) = 0.842 mm^{-1}, 1317 unique reflections with $F > 4\sigma(F)$, $R = 0.026$, $wR = 0.078$. The data were measured at 103 K. The structure was solved with SIR97[34] and refined with SHELXL-93.[35] Hydrogen atom positions were located in difference Fourier maps and refined with individual isotropic displacement parameters.

X-Ray crystallography for 28 †

Crystal data: $C_{15}H_{10}N_2O$, $M_r = 234.25$, monoclinic, $a = 6.5046(3)$, $b = 17.5411(7)$, $c = 10.3306(3)$ Å, $\beta = 99.499(2)°$, $V = 1162.54(8)$ Å^3, $Z = 4$, $P2_1/c$, $D_c = 1.34$ g cm^{-3}, μ (MoKα) = 0.086 mm^{-1}, 2046 unique reflections with $I > 2\sigma(I)$, $R = 0.044$, $wR = 0.113$. The data set was collected at the EPSRC National Service at 150 K, solved with SHELXS-86[36] and refined as for **27**. Hydrogen atoms were located in difference Fourier maps and included in the refinement with their own isotropic displacement parameters.

Acknowledgements

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20 Data for Me$_2$N···NMe$_2$: refcodes: DIGZIC, DMANAP10, HOMFAQ, HOMFEU, NUPJIR, RISBAW, VIZNOH.
21 Data for MeO···OMe: refcodes: JIPNOL, KEPKUL, REHGAM, RIBKOC, RISBAW, RISBEA.
22 The value of 0.15 Å for the difference in the effective radii of the nitrogen and oxygen atoms is intended only as a 'reasonable estimate' based on the nearest possible comparison data. There is no perfect comparison compound for determining the N···N separation in a naphthalene derivative which has two *peri* dimethylamino groups oriented so that the lone pairs are facing each other. The nearest to this situation is in the structure of the 2,7-dimethoxy derivative,[19] in which the N···N distance is 2.756 Å, *ca.* 0.05 Å shorter than in the derivatives without *ortho* substituents. However, each dimethylamino group will experience some steric repulsion from an *ortho* methoxy group which acts to decrease the N···N separation. In the structures of the bis(dimethylamino)-naphthalenes which are used to estimate an effective radius for nitrogen, each functional group is oriented with one methyl group roughly in the aromatic plane and directed to the *ortho* position. The two remaining methyl groups are directed to opposite sides of the aromatic plane, so that the two lone pair axes lie on average at 54° to the aromatic plane. The fact that the lone pairs are not directed at each other would be expected to reduce the repulsion between the

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† CCDC reference number 188/282. See http://www.rsc.org/suppdata/p2/b0/b008226k/ for crystallographic files in .cif format.

nitrogen atoms, however each in-plane methyl group will experience a larger steric repulsion from the *ortho* proton than if it had adopted a conformation with the lone pair lying in the molecular plane which would be expected to decrease the N···N separation. Thus, half of this N···N separation distance may not be a bad estimate! The estimation of typical O···O separations is not fraught with such problems since the methoxy groups lie in the aromatic plane. However, it is notable that for naphthalene-1,8-diols the average O···O separations are longer (by *ca.* 0.08 Å) than in the dimethoxy cases, due to the reduced *ortho* repulsions. Thus, it is important to recognise that the values for the effective radii of the nitrogen and oxygen atoms are specific for the particular functional group and its environment and not necessarily for wider application. Estimates of the van der Waals radii for nitrogen and oxygen rarely differ by more than 0.1 Å.

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