Correlation between molecular dipole moment and centrosymmetry in some crystalline diphenyl ethers†

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The presence of a large molecular dipole moment in diphenyl ethers leads unequivocally to a centrosymmetric crystal structure.

Crystal engineering of non-centrosymmetric structures for second harmonic generation (SHG) in non-linear optic (NLO) applications has been a long investigated activity.[1] In this context, a key issue is whether or not a molecule with a high dipole moment prefers a centrosymmetric, and therefore SHG inactive, crystal structure. Generally, it is believed that as the dipolar characteristics of a molecule increase, so does the tendency for anti-parallel molecular arrangements, *i.e.*, centrosymmetry. On the other hand, Whitesell, Davis and co-workers (WD), in an influential 1991 paper based on a Cambridge Structural Database (CSD) study concluded, that "the high preference for organic molecules to crystallize in one of the centrosymmetric arrangements cannot be attributed to molecular dipole–dipole interactions". However, these authors also added that "this is not to say that local electrostatic interactions between molecules are unimportant".[2] The consensus view seems to be that while large/small molecular dipole moments may not correlate with the presence/absence of an inversion centre, local dipoles do influence molecular assembly.[3]

This matter is still relevant to non-centrosymmetric crystal engineering. The concept of the "vanishing dipole moment" was critical to the design of 3-methyl-4-nitropyridine *N*-oxide (POM) which is one of the most thoroughly investigated materials in NLO research.[4] The choice of octupolar molecules for SHG applications has been influenced, in part, by the notion that they have a better chance of crystallising in non-centrosymmetric space groups, than do dipolar molecules, because they have zero dipole moments.[5] WD arrived at their conclusions based on the fact that the distributions with respect to molecular dipole moments for randomly selected crystal structures in the non-centrosymmetric space groups $P1$ (28 structures) and $P2_1$ (174 structures), and in the centrosymmetric space group $P\bar{1}$ (161 structures), are practically identical. Considering the continuing importance of this matter and the fact that 15 years have elapsed since the WD paper, we decided to re-do their searches with a CSD that had increased threefold in size during the intervening period.[6]

To maintain consistency, our CSD searches (version 5.26, November 2004, 323 122 entries) employed, as far as possible, the protocols of WD. Accordingly, compounds with polyvalent halogen and pentavalent P or S were excluded, as were organometallics, polymers, salts, solvates and hydrogen bonded structures. As an additional screen we excluded molecules with a carbon content greater than C_{25}. A more lenient *R*-factor cutoff (0.075 instead of 0.05) was used for $P1$ because of the limited number of entries. We obtained 60, 1687 and 1081 hits in $P1$, $P\bar{1}$ and $P2_1$ respectively and from these we selected at random 60, 300 and 350 compounds for the dipole moment calculations. These values were obtained with the AM1 approximation with the single point option, that is with the molecular geometry used as found in the crystal without any further minimization.‡ The frequency distributions in the three space groups are shown in Fig. 1 along with the WD distributions. Details of all compounds are given in the supplementary information.†

One notes that there is practically no difference between the WD and the present histograms; the distributions are virtually the same for all three space groups. The median dipole moment fell slightly for $P1$ from 3.36 to 2.95 and for $P\bar{1}$ from 3.22 to 3.01. It rose a little for $P2_1$ (3.04 to 3.12). These differences are not statistically significant. Any correlation between molecular dipole moments and the presence/absence of an inversion centre in the crystal would appear to be very feeble when compared with other factors. One such factor arises from the nature of organic molecules themselves. A possible explanation for the almost identical distributions in the three space groups is that such a distribution of dipole moments would be seen in *any* random set of organic

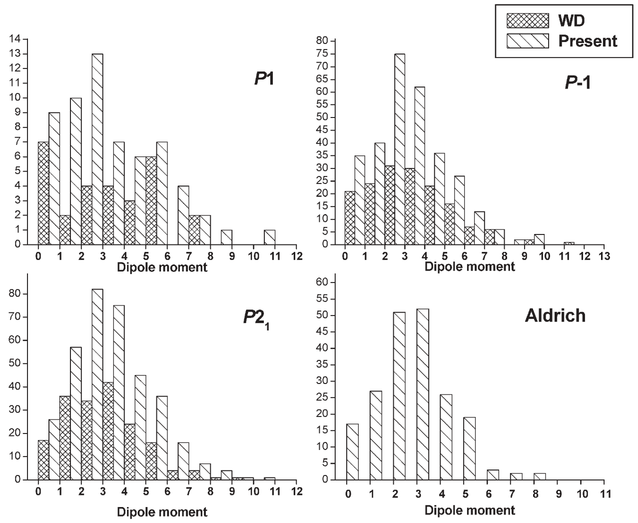

Fig. 1 Distribution of molecular dipole moments for randomly selected structures in space groups $P1$, $P\bar{1}$, $P2_1$ and in the Aldrich catalogue. WD refers to the Whitesell–Davis distributions (ref. 2).

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† Electronic supplementary information (ESI) available: CSD refcodes, list of compounds selected from the Aldrich catalogue, synthesis, characterisation and crystallographic details of the 27 synthesized compounds, calculated dipole moments of all compounds. See http://www.rsc.org/suppdata/cc/b5/b502516h/

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compounds that arises from normal synthetic procedures.[7] To evaluate this possibility, we calculated the dipole moments of 200 randomly selected compounds from the Aldrich catalogue§ (details in supplementary information†). This histogram (Fig. 1) is very similar to those for the various space groups! So, these results are ambiguous. Rather than proving the absence of a correlation between dipole moments and crystal symmetry (as concluded by WD), they do not rule out the possibility that such a relationship exists, and (being weak) is completely swamped by a universal preference for dipole moments in the range 1.00–4.00 D that arises from the nature of organic synthetic procedures.

Other complicating factors that preclude a clear-cut answer to the question under consideration are that: (1) The three space groups selected for the CSD searches account only for 28% of the CSD and may not be representative; $P1$ is rare; $P2_1$ is populated by chiral molecules obtained from natural sources and the most common space group, $P2_1/c$, is not included. (2) A high dipole moment may be just one of many reasons why molecules adopt centrosymmetric packing. (3) Molecules selected randomly by WD and us do not have any particular connection with dipolar NLO activity; it may be more pertinent to focus on molecules that are closer to real NLO systems. (4) Centrosymmetric molecules, which by definition have zero dipole moments, nearly always adopt centrosymmetric crystal packing;[8] if additionally, molecules with high dipole moments tend to centrosymmetry, then centrosymmetric packing would be accessed by all types of molecules thereby masking any correlation of the type for which we are searching, using a CSD approach. In summary, we felt that while WD's CSD searches are reproducible today, their results do not necessarily allow one to conclude that "attempts to design molecular arrays based primarily on considerations of overall molecular dipole moments have, statistically speaking, a small chance of success".

We decided, at this stage, to address the question experimentally. Several workers have alluded to the fact that local dipole moments tend to direct a structure towards centrosymmetry[3] and our idea was to select a family of compounds, keeping in mind the difficulties stated above, and to experimentally determine the crystal structures of a large, statistically significant number. After some consideration, we selected the group of 4,4′-disubstituted diphenyl ethers, R–C_6H_4–O–C_6H_4–R′. The reasons for this choice were as follows: (1) There are already 18 such compounds in the CSD, and the crystal structures of another six have been reported recently.[9,10] (2) Preparation of other derivatives, with a wide range of electron donating and withdrawing R and R′ groups, is easy and the compounds crystallise well. (3) Electronically, the substituted diphenyl ethers are related to conjugated and aromatic compounds used for dipolar NLO applications. (4) Because of their bent geometry, a zero dipole moment is impossible even if R = R′. By varying R and R′, a wide range of dipole moments is accessible. (5) Polymorphism is supposedly unknown barring the unsubstituted and dipyridylamino compounds.[10,11] To obtain a statistically meaningful sampling, we prepared another 27 derivatives and determined their crystal structures. All in all, therefore, we secured a crystal structure database of 51 substituted diphenyl ethers. The dipole moments of these compounds ranged from 0.324 D (R = R′ = NHCOO*i*Pr) to 8.007 (R=NO_2, R′=NMe_2). Synthetic, spectroscopic and crystallographic details for the 27 synthesized molecules are given in the supplementary information,† as is a list of CSD refcodes for the 18 literature molecules and the six molecules studied earlier. In the context of the present study, it may be noted that there was no space group ambiguity or order/disorder issue related to the absence/presence of an inversion centre in any of the 27 newly determined and 24 literature crystal structures. As a matter of record, the range of *R*-factors for these crystal structures is between 0.0296 and 0.0885 (median 0.0469), ensuring overall accuracy.¶

The details of the space groups adopted by this database of compounds are given in Fig. 2. The populations for the non-centrosymmetric space groups are: $P2_1$ (2), Cc (2), $P2_12_12_1$ (5), $Pna2_1$ (5) and $Aba2$ (1). The populations for the centrosymmetric space groups are: $P\bar{1}$ (2), $P2_1/c$ and $P2_1/n$ (26), $P2_1/m$ (1), $C2/m$ (1), $Pbca$ (4). The preference for centrosymmetry (7 : 3) is not so pronounced as in the global population of crystal structures (9 : 2).[12] Molecules with low dipole moments, say less than 4.0 D, adopt either centrosymmetric or non-centrosymmetric space groups. However, if the dipole moment is greater than this, centrosymmetry is the only outcome: there are no exceptions.

The larger dipole moments are found for molecules in which the two substituents, R and R′, are strongly electron donating and strongly electron withdrawing, respectively (NO_2, CN, Cl, Br, OH, OMe, Me). Examination of the crystal packing arrangements for these high dipole moment centrosymmetric structures (R, R′; NO_2, OH; NO_2, OMe; NO_2, I; NO_2, Cl; NO_2, Me; NO_2, NMe_2; NO_2, H; CN, Me; CN, OMe) is also instructive. Fig. 3 shows that there are four types of molecular association and that in each of these cases, molecules that are related by an inversion centre have important group dipoles (NO_2, CN) in close contact and in an anti-parallel orientation. These observations show that, for the diphenyl ethers, the presence of a high dipole moment leads unequivocally to centrosymmetric packing. Inasmuch as local dipole moments are important contributors to the molecular dipole moment in these compounds, our result confirms currently held ideas that local dipole moments are important. Indeed, such a result is only to be expected—long range electrostatic interactions are experienced by molecules earlier during crystallisation than short range van der Waals attractions. Accordingly, and given that crystallisation is a strongly kinetic phenomenon, there would be a good chance that supramolecular synthons with an anti-parallel

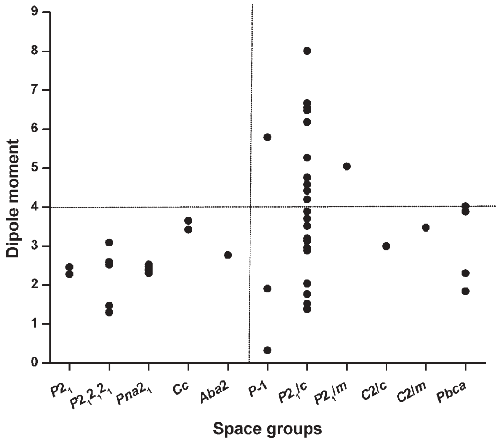

Fig. 2 Distribution with respect to molecular dipole moments of crystalline diphenyl ethers in non-centrosymmetric and centrosymmetric space groups.

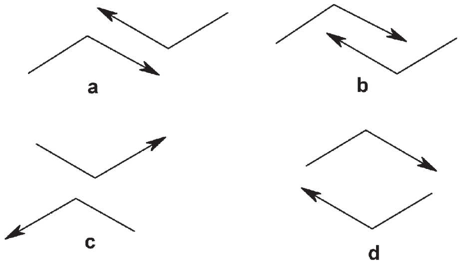

Fig. 3 Cartoon depiction of alignment of local dipoles arising from the electron withdrawing substituents in centrosymmetric diphenyl ethers. Four possibilities are indicated: (a) 4-(4-methoxyphenoxy)nitrobenzene; (b) 4-(4-methylphenoxy)benzonitrile; (c) 4-(4-nitrophenoxy)phenol and; (d) 4-amino-4′-cyanodiphenyl ether. Crystallization in space group $P2_1/c$ is especially common for such compounds.

geometry would be robust and well sustained in the final crystal packing.

This study shows that some matters relating to crystal packing may not be resolved easily with a purely statistical CSD type approach. Crystallisation is too complex an issue and many factors are in play in determining stable packing modes.[13] Accordingly, it would be simplistic to expect that questions of the type "will a high dipole moment lead to a centrosymmetric space group?" could be resolved one way or another with CSD searches. Secondly, general solutions to complex problems are often not available and the only working approach is to sacrifice generality for precision. In crystal engineering, this is done by selecting a subset of compounds rather than aiming for global correlations. In this particular case, the family selected is a good prototype for dipolar NLO materials and, in all probability, the correlation found here will apply to other polarizable systems. Finally, high throughput crystallography can and should be used in crystal engineering wherever possible because it can provide a route to the solution of otherwise difficult and subtle problems. We conclude that there is a strong tendency towards centrosymmetry for conjugated or aromatic molecules with large dipole moments.

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Notes and references

‡ The uncertainties in these values are estimated by comparison with values obtained with GAUSSIAN (B3LYP/6-31G(d,p). Typically, for 4-(4-methoxyphenoxy)-*N*,*N*-dimethylaniline, the dipole moment is 3.648 D with the AM1 approximation and 3.867 D with GAUSSIAN. Again, for 1-(trifluoroacetyl)imidazole, the dipole moment is 0.909 D (AM1) and 0.404 D (GAUSSIAN).

§ We selected the first and last non-metal atom containing compounds in 200 randomly selected pages from the Aldrich catalogue.

¶ CCDC 264996–265022. See http://www.rsc.org/suppdata/cc/b5/b502516h/ for crystallographic data in CIF or other electronic format.

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