A Crystallographic, AM1 and PM3 SCF-MO Investigation of Strong OH ··· π-Alkene and Alkyne Hydrogen Bonding Interactions

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A search of the Cambridge structural database reveals eleven alkenes and two alkynes in which particularly short OH ··· π-facial hydrogen bonding occurs, a feature largely unrecognised in the original reports of these structures. A wide structural diversity is found for these structures, and in two cases, the π-facial bonding may be associated with anomalous reported reactivity. Semi-empirical AM1 and PM3 SCF-MO calculations tend to overestimate the C ··· H distances in these structures, and very probably underestimate the energies of OH ··· π interaction.

Although spectroscopic evidence, mostly based on observed shifts in IR spectra, for π-facial interactions with hydroxy groups has long been available,[1] crystallographic evidence has been restricted to a small number of isolated reports of individual compounds.[2] A recent survey[3] based on the 1990 version of the Cambridge structural database[4] containing 82 129 structures suggests that the phenomenon may be more widespread than hitherto recognised. However, this reported survey of the literature did not extend to discussion of individual compounds or to whether any common structural features can be discerned. Since such weak interactions may represent important terms in molecular and chiral recognition,[5] it is important to identify the range of structural characteristics tolerated, and to assess whether standard theoretical procedures correctly reproduce these interactions.

At the molecular mechanics level of modelling, specific geometrical functions are often used in mechanics force fields to describe hydrogen bonding, and the unusual characteristics of π-facial interactions may fall outside the range of these functions. Recent advances[6] in using a distributed multipole analysis of the molecular charge distribution hold considerable promise for reproducing such non-classical hydrogen bonds, and it is therefore highly desirable to identify a number of specific examples for use in the calibration of various modelling methods. Semi-empirical SCF-MO based methods have not hitherto been evaluated for these types of interactions. Amongst these methods, the MNDO parametrisation performs poorly regarding both geometrical energetic predictions for hydrogen bonds involving oxygen or nitrogen.[6] The AM1 method represents a significant improvement in terms of the energetics of such interactions, although the predicted geometries tend towards bisected structures, whilst the most recent PM3 method appears to most consistently reproduce the dimensions of bonding to oxygen.[7] To provide a set of geometrical data against which to evaluate the characteristics of these methods, we performed a search of the 109 992 crystal structures in the current (March 1993) version of the Cambridge database in which we identified 13 compounds which exhibit particularly short OH ··· π-facial interactions. In the present paper we discuss these structures individually in order to establish if any common structural themes can be identified, and to clearly identify a set of compounds against which modelling techniques can be tested.

Computational Details

Theoretical calculations were carried out at the restricted Hartree–Fock level (*RHF*) using the AM1 or PM3 semi-empirical SCF-MO methods, as implemented in the MOPAC 93 program,[8] with the MMOK keyword enabled. Structures were optimised using the eigenvector following algorithm to a final gradient norm of < 0.1, a tolerance required to obtain reproducible distances for weak interactions. The search of the Cambridge structural database was performed using release 5.5 of the Quest software. Structures are identified in the text below using the Cambridge REFCODE. Structures for which the original authors have noted that the hydroxy hydrogens positions were refined are indicated in Table 1. All the *R* factors were acceptably small. Molecular diagrams were generated and inspected in true 3D stereo using a CAChe Scientific workstation. Computer readable files for Apple Macintosh and Microsoft Windows systems in Quicktime™ video animation format illustrating in colour the 3D properties of the structures in the Table are available for general access from the Gopher + server *gopher.ch.ic.ac.uk.* These files will reside in the Scientific_Publications/rzepa/Royal_Society_of_Chemistry/Perkin_Transactions_2/3056131 directory for a period of at least two years from the publication of this paper. A description of how to visualise such material, together with appropriate programs is available from the same source.

Results and Discussion

The distance defining significant hydrogen bonding interactions is to some extent arbitrary. Several recent reports[2] of π–OH bonding to an aromatic ring suggest the shortest contacts range between 2.2 and 2.5 Å for the approach of a hydrogen atom and the plane of the ring, compared with an estimate of the combined H and C van der Waals radii of ≈2.8 Å. Desiraju and co-workers[3] chose a criterion which resulted in a mean intermolecular H ··· C distance of 2.69 Å to alkynes and 2.77 Å to alkenes, values which are quite similar to the combined atomic van der Waals radii. There must remain some ambiguity about whether H ··· C distances of > 2.8 Å are predominantly dispersive or electrostatic in character. The very shortest of such interactions were not identified by Desiraju and co-workers.[3] In our own search, we had independently chosen to focus on both intra- and inter-molecular interactions significantly shorter (0.2–0.6 Å) than the van der Waals contact distances. We first defined our search of the Cambridge database as any intra- or inter-molecular contact of a specfied distance between an O–H proton and both carbon atoms of a C=C or C≡C bond. A value of ⩽ 2.5 Å produced five hits, with Cambridge 'REFCODE' of BETXAZ, BUTGOM, FIMNEU,

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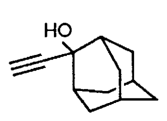
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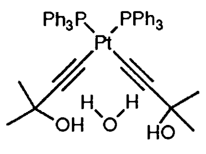
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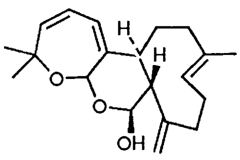
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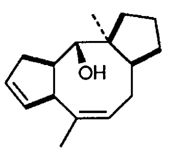
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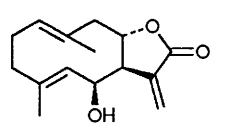
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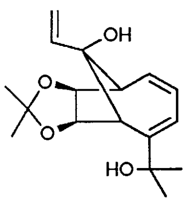
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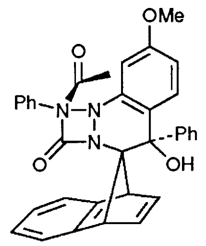
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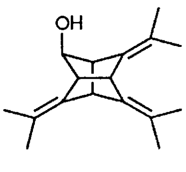
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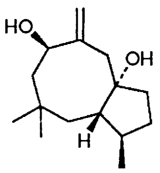
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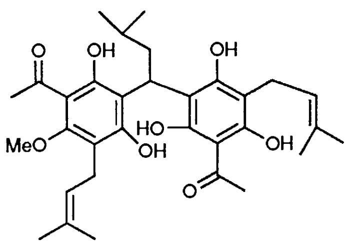
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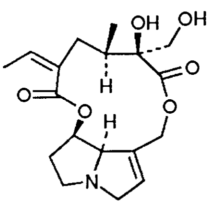
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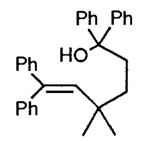
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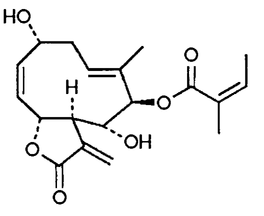

VIHGUO

QQQGTD01 and VIHGUO. Specifying that only one carbon atom need be within 2.4 Å of the hydrogen gave more hits (40), but a significant number of contacts are to enolic type alkenes and are not discussed here, as are two (BREFEL and FEJHOR) where the proton position was clearly mis-assigned in the original refinement.

Thirteen structures appear to exhibit OH···π-facial interactions significantly shorter than the van der Waals contact distances (Table 1, Fig. 1), of which four are intermolecular and the others intramolecular. The previous search of the 1990 database[4] using version 4 of the Quest software was restricted to searching only for intermolecular contacts. Only one of the OH···π interactions was correctly identified in the original papers reporting the structures (that for QQQGTD01). Another (BETXAZ) was misassigned to an intramolecular interaction (*vide infra*). This suggests that the phenomenon has not been clearly identified in the past, in part because the molecular structure and stereochemistry is frequently the principal reason for X-ray characterisation, rather than the detail of the intermolecular contacts.

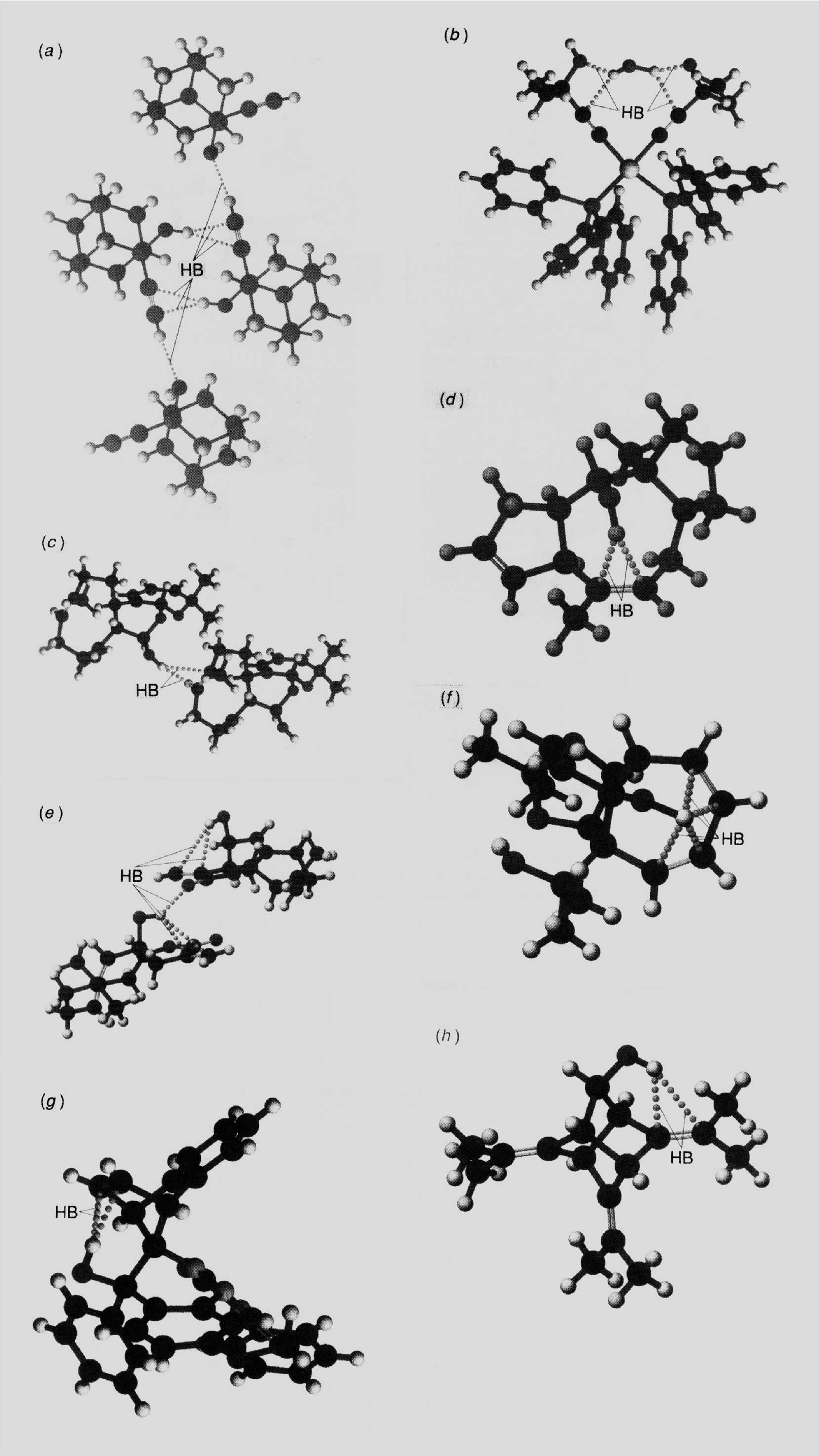
Two of the short intermolecular examples both involve alkynes. The structure of BETXAZ (Fig. 1) reveals a core dimeric π-C$\equiv$C···HO interaction (erroneously assigned to be intramolecular in the original report, Table 1), augmented by additional terminal C$\equiv$C–H···O interactions from two further molecular units.[9] This highly unusual structure is probably promoted by the hydrophobic and sterically constraining adamantyl group inhibiting more conventional O···HO interactions. We note in passing that similar simultaneous terminal C$\equiv$C···metal and π-C$\equiv$C···Na^+ ion interactions have also been reported.[10] Hanton and Hunter have also recently discussed other possible reasons for the promotion of non-classical hydrogen bonding interactions.[11] The phosphine–platinum complex DAXWOO reveals an unusual bifurcated interaction between water and an α-hydroxyalkyne in which the hydrogen bond appears to form to both the oxygen and one carbon of the alkyne. Given the presence of a heavy metal atom close to the refined proton position, this should be a good candidate for a more accurate structure determination to verify this interaction.

Only two short intermolecular examples to alkenes were found (RTRSIN and BIWDEQ), the latter to a *trans* double bond present in a nine-membered ring. No monosubstituted alkene examples were found, in accord that such alkenes are normally regarded as being less basic than more heavily substituted systems. Surprisingly, four alkenes bearing conjugated substituents were identified, CUSCIC and VIHGUO to a carbonyl group, SEDBIM to one coplanar phenyl group and FIMNEU as a diene. It appears that conjugation does not reduce the basicity of the π-bond sufficiently to inhibit such bonding. In the first three examples, the hydrogen bonding is localised largely to the alkene, but remarkably in FIMNEU the OH group has an equal attraction to both double bonds. In CUSCIC and POITDL, an additional intermolecular OH···O hydrogen bond is present at one or both π-bonding centres (Fig. 1).

A number of the structures show an essentially symmetric interaction with the π-system (< 0.25 Å difference between the two C···H distances, *cf.* BETXAZ, BUTGOM, FIMNEU, POITDL, QQQGTD01 and VIHGUO) whilst in the remaining structures, the asymmetry is closer to 0.4 Å (Table 1). In all the intramolecular examples except SEDBIM, the proximity of the OH and alkene is enforced structurally, although the O–H bond is potentially free to rotate away from the double bond and hence to form intermolecular OH···O interactions.

In two instances, it is noted in the original structural report that unexpected reactivity was observed. For example, BUTGOM was observed to cyclise on standing to an ether, and for SEDBIM intramolecular photochemical H-transfer occurs in the solid state (Table 1). In neither case was an explanation suggested, but the association of unexpectedly high reactivity and π-facial hydrogen bonding may provide one such explanation. Clearly, other instances of anomalous reactivity may come to light if the phenomenon is more widely recognised.

Theoretical Calculations.—The semi-empirical calculations reveal that in general these methods tend to overestimate the length of the π-C···HO interactions, with broadly similar behaviour between the AM1 and PM3 methods. For the intermolecular interaction in BETXAZ, we calculated both the dimeric unit, and the extended tetramer which also includes an additional terminal C$\equiv$C–H···O interaction. In the dimer, the H···C distance is ≈0.3 Å too long at both the AM1 and PM3 levels, although the asymmetry in the π-interaction is reproduced well (Table 1). In the calculated tetramer, the additional polarisation induced by the terminal C–H···O interaction [$r_{CH\cdots O}$ 2.26, $r_{CH\cdots O}$ 1.83 (PM3), $r_{CH\cdots O}$ 2.26 Å


(a)
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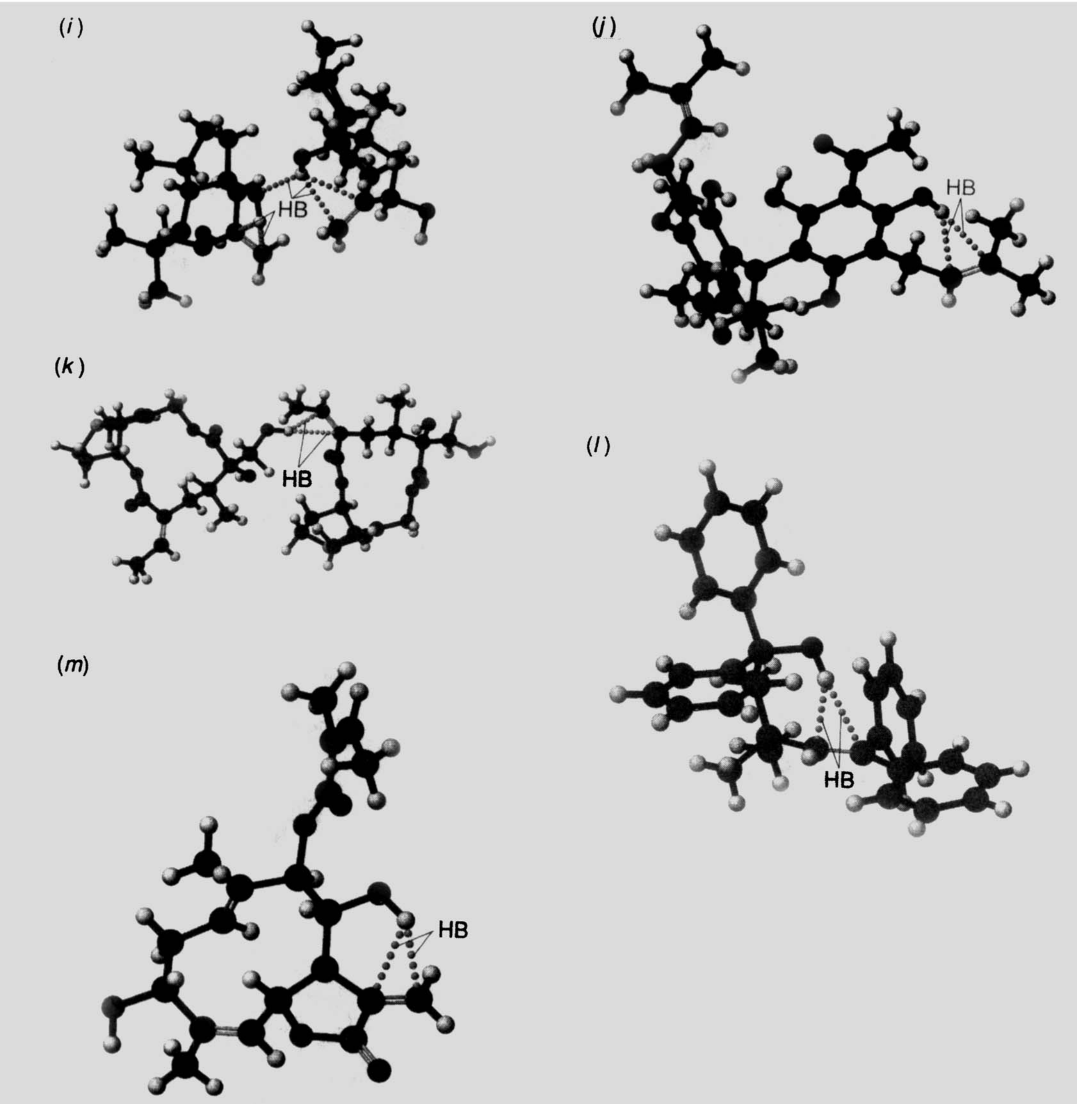

Fig. 1 3D structures for (*a*) BETXAZ, (*b*) DAXWOO, (*c*) BIWDEQ, (*d*) BUTGOM, (*e*) CUSCIC, (*f*) FIMNEU, (*g*) KALHAG, (*h*) KUMYOG, (*i*) POITDL, (*j*) QQQGTD01, (*k*) RTRSIN, (*l*) SEDBIM, (*m*) VIHGUO. Hydrogen bonds are shown with dotted lines (HB). These diagrams can be inspected in colour using the electronic publishing mechanism referred to in the text.

Table 1 Short O–H ··· C=C or C≡C contacts from a Quest search of the Cambridge Structural Database

REFCODE	$r(\mathrm{OH}\cdots\mathrm{C})_{\mathrm{exp}}$	*R*-factor	ΔH_f(PM3)[AM1]	$r_{\mathrm{OH}\cdots\mathrm{C}}$(PM3)[AM1]
BETXAZ	2.25, 2.35[a]	0.050	−36.4 [−47.4][n]	2.51, 2.60 [2.56, 2.69]
			−81.3 [−97.0][o]	2.51, 2.53 [2.44, 2.81]
DAXWOO	2.28, 2.89, 2.30, 2.72[b]	0.052		
BIWDEQ	2.35, 2.66[c]	0.060	−179.5 [−197.9]	3.51, 2.70 [3.31, 2.61]
BUTGOM	2.12, 2.31[d]	0.036	−40.5 [−43.5]	2.34, 2.41 [2.35, 2.41]
CUSCIC	2.40, 2.87; 2.42, 2.85[e]	0.038	−204.0 [−200.6]	2.62, 3.09; 2.81, 3.23 [2.65, 3.20, 2.83, 3.24]
FIMNEU	2.42, 2.21, 2.22, 2.42[f]	0.050	−123.7 [−125.3]	2.56, 2.44; 2.39, 2.44 [2.52, 2.42, 2.39, 2.45]
KALHAG	2.17, 2.64[g]	0.053	50.6 [124.6]	2.29, 2.61 [2.31, 2.85]
KUMYOG	2.27, 2.64[h]	0.049	−1.1 [21.5]	2.35, 2.73 [2.32, 2.70]
POITDL	2.37, 2.55; 2.43, 2.53[i]	0.050	−206.9 [−206.5]	2.74, 2.70; 2.59, 2.63
QQQGTD01	2.22, 2.44[j]	0.060	−325.9 [−312.9]	2.95, 3.24 [2.43, 2.73]
RTRSIN	2.31, 2.76[k]	0.06	−462.4 [−450.5]	2.68, 3.44 [3.50, 4.04]
SEDBIM	2.11, 2.57[l]	0.054	64.2 [66.3]	2.38, 3.07 [2.36, 3.18]
VIHGUO	2.29, 2.21[m]	0.042	−208.5 [−210.3]	2.48, 2.61 [2.52, 2.55]

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(AM1)] has only a slight effect on the calculated π–C≡C $\cdots$ HO distances (Table 1), with the asymmetry being increased with AM1, and decreased with PM3. The other intermolecular examples (BIWDEQ and RTRSIN) do not show significantly different behaviour from the remaining intramolecular examples. Several of the intramolecular systems (FIMNEU, KALHAG, KUMYOG) reveal a quite close correspondence between calculated and observed structures. The energy of the π-interaction orientation in FIMNEU is calculated to be 1.3 kcal mol^{-1} lower at both the AM1 and PM3 levels than the rotamer involving no π-facial interaction, a value which appears on the low side, and commensurate with the over-estimated bond lengths. The corresponding dimerisation energies for the triple bonded system BETXAZ are 3.2/2.8 kcal mol^{-1} (PM3/AM1) or 1.6/1.4 for the monomer. These values are lower than the energies of O $\cdots$ HO interactions obtained using the AM1 or PM3 methods, which tend to be in the range of 3–5 kcal mol^{-1}, suggesting that π-hydrogen bonds will only form when other structural factors favour them.

Conclusions

Whilst HO $\cdots$ π-alkene hydrogen bonding with $r_{H \cdots C}$ < 2.4 Å remains a relatively rare phenomenon, we note that a wide structural diversity appears to be tolerated. Several of these interactions may directly reflect the reactivity, and we also anticipate that such bonding will also play a significant role in chiral recognition and other intermolecular phenomena.[12] These systems should serve a valuable role in evaluating the reliability of both present modelling methodology such as PM3 and future methodology based on *e.g.* a distributed multipole analysis of the charge distribution. Furthermore, the prospects of specifically designing molecules in which such interactions are enhanced based on the systems identified here appear promising.

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