Acta Crystallographica Section B
Structural Science
ISSN 0108-7681

Geometry and conformation of cyclopropane derivatives having σ-acceptor and σ-donor substituents: a theoretical and crystal structure database study

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Received 1 November 2011
Accepted 21 December 2011

The structures of cyclopropane rings which carry σ-acceptor or σ-donor substituents have been studied using density-functional theory (DFT), and mean bond lengths and conformational parameters retrieved from the Cambridge Structural Database. It is confirmed that σ-acceptor substituents, *e.g.* halogens, generate positive ring bond-length asymmetry in which there is lengthening of the distal bond (opposite to the point of substitution), and shortening of the two vicinal bonds. This is due to withdrawal of electron density from the cyclopropane $1e''$ orbitals, which are bonding for the distal bond and antibonding for the vicinal bonds. For σ-donor substituents such as SiH_3 or $Si(CH_3)_3$, the DFT and crystal structure data show negative ring bond-length asymmetry (distal bond shortened, vicinal bonds lengthened), owing to electron donation into the $4e'$ ring orbital, which are also bonding for the distal bond and antibonding for the vicinal bonds. The results also show that —OH substituents induce weak positive asymmetry, but that the effects of methyl or amino substituents are either non-existent or extremely small, certainly too small to measure using crystal structure information.

1. Introduction

Our interest in the cyclopropyl group arises from its common occurrence in active agrochemical and active pharmaceutical ingredients (AAIs and APIs). The AAIs include the pyrethroid insecticides, while the cyclopropyl group also occurs in a wide range of APIs including antibiotics, anticonvulsants, antidepressants and antiretrovirals. Cyclopropyl compounds are also being used in the development of prodrugs (Bender *et al.*, 2008), *i.e.* physiologically inactive compounds that are converted into active drugs by enzymatic action *in vivo*.

Building on an early database study of bond-length asymmetry in cyclopropanes (Allen, 1980), Cruz-Cabeza & Allen (2011) have recently described an extensive theoretical and database study of cyclopropane rings having π-acceptor substituents, for example >C═O, —C≡N, —COO*R*, —NO_2 *etc*. In these systems the $3e'$ orbitals of cyclopropane have the correct symmetry to interact with low lying unoccupied orbitals of the π-system, but only when the two orbital systems are parallel. This is always true for —C≡N, but only occurs for *e.g.* >C═O, —COO*R* when the C═O bond adopts (*a*) the *cis*- or (*b*) the *trans*-bisected conformation with respect to the ring, as illustrated in Fig. 1, thus enabling transfer of electron density from the $3e'$ orbital to the π-system. This weakens (lengthens) the ring C—C bonds for which the $3e'$ orbital has bonding character, *i.e.* the C1—C2 and C1—C3 bonds that are *vicinal* to the point of substitution, but strengthens (shortens) the *distal* C2—C3 bond, for which the $3e'$ orbital is anti-

bonding. Our recent paper (Cruz-Cabeza & Allen, 2011) presents crystallographic and computational data on the preferred conformations and ring bond-length variations exhibited in cyclopropyl–π-acceptor systems.

In the current paper we use information from the Cambridge Structural Database (CSD: Allen, 2002), together with DFT calculations, to study variations in C—C bond lengths in cyclopropane rings that carry σ-acceptor, σ-donor and π-donor substituents. Clark *et al.* (1984) provide a full discussion of the interactions of substituent and ring orbitals in these cases, and summarize the effect of these interactions on the ring bond lengths. For the common σ-acceptor substituents, *e.g.* halogens, withdrawal of electron density from the cyclopropane $1e''$ orbital, which is antibonding for the vicinal ring bonds but is bonding for the distal bond, generates bond-length asymmetry which is opposite in sense to that for the π-acceptor substituents discussed above, *i.e.* the vicinal C1—C2 and C1—C3 bonds will shorten and the distal C2—C3 bond will lengthen (Fig. 1). By contrast, σ- and π-donor substituents (*e.g.* SiX_3 species) will donate electron density into the $4e'$ LUMO of cyclopropane. This orbital is also antibonding for the vicinal ring bonds and bonding for the distal bond. However, electron donation into such an orbital will reverse the σ-acceptor effect just noted, lengthening the vicinal C1—C2 and C1—C3 bonds, while shortening the distal C2—C3 bond: *i.e.* yielding exactly the same asymmetry effect that is observed for π-donor substituents (Cruz-Cabeza & Allen, 2011).

2. Methodology

2.1. Data retrieval

All CSD searches were carried out using the program *ConQuest* (Bruno *et al.*, 2002) applied to CSD Version 5.32 (November 2010) a total of 541 748 entries. Structure visualization made use of *Mercury* (Bruno *et al.*, 2002; Macrae *et al.*, 2006, 2008) and data analysis was carried out using the new data analysis tools within *Mercury* (Sykes *et al.*, 2011). Searches for cyclopropane rings used the following secondary search criteria:

(i) single-crystal organic structures with full coordinate data available,

(ii) no residual errors after CSD evaluation,

(iii) no disorder,

(iv) no *catena* bonding and

(v) had $R \leq 0.075$ unless otherwise stated.

A total of 3094 CSD entries containing cyclopropane fit these criteria, an approximately 20-fold increase in data availability over the 146 entries ($R \leq 0.10$) that contributed to the earlier paper (Allen, 1980) which covered all types of ring substituents.

In this work we focus on the asymmetry effects of various specific substituents on the bond lengths in the cyclopropane ring. This means that we must avoid other electronically effective substituents on the same ring apart from the specific substituent under study. To do this we have made extensive use of the Boolean .NOT. operator available in *ConQuest* searches. Thus, we have searched for the specific substitution pattern discussed in subsequent sections, *e.g.* mono-, di-, tri- or hexa-halogenocyclopropanes, hydroxy- trimethylsilyl- or amino-cyclopropane *etc.*, but excluded the following types of substituents at all other points on the ring:

(i) any of the π-acceptor substituents identified in the earlier paper (Cruz-Cabeza & Allen, 2011), *i.e.* —C═O, phenyl, cyano, nitro, vinyl *etc.*;

(ii) any of the σ-acceptor or σ-donor substituents identified in this paper which are not the subject of the specific study, *i.e.* additional halogen substituents are not allowed when studying the asymmetry effects of hydroxy, trimethylsilyl or amino groups.

A result of these exclusions is that a major proportion of cyclopropane rings that survive the search process contains only the ring substituent of interest together with H or Csp^3 substituents.

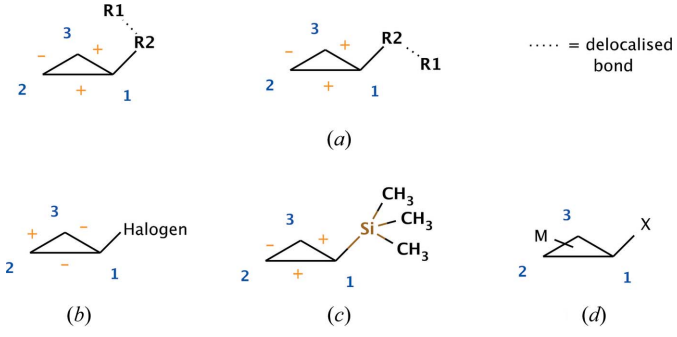

Figure 1
Ring bond-length asymmetry in cyclopropane due to (*a*) π-acceptor substituents in the *cis*-bisected (left) or *trans*-bisected (right) conformations [the R_1—R_2 bond may be double, delocalized double, triple or aromatic], (*b*) σ-acceptor substituents (*e.g.* halogen) and (*c*) σ-donor substituents (*e.g.* SiMe$_3$). The asymmetry (elongation or shortening) in each vicinal bond is one half of the absolute asymmetry (shortening or elongation) induced in the distal bond. Part (*d*) shows the nomenclature used in this paper: substituents are denoted as *X*, with the mid-point of the distal bond (*M*) being used in conformational calculations as noted in the text.

2.2. Geometrical analysis

There are three ways to determine a bond-length asymmetry parameter using the atomic numbering for cyclopropane shown in Fig. 1:

(i) By comparing the vicinal (d_{12}, d_{13}) and distal (d_{23}) bond lengths with the mean overall ring bond length determined from all cyclopropane rings which are unaffected by substituent effects.

(ii) By computing the parameters $\Delta(distal)$ as $d(distal) - D$ and $\Delta(vicinal) = D - \langle d(vicinal)\rangle$, where D is the mean of the three ring bond lengths in each individual ring, and $\langle d(vicinal)\rangle$ is the mean vicinal bond length $(d_{12} + d_{13})/2$. In this construct, $\Delta(distal)$ may be positive or negative corresponding to a lengthening or shortening of the distal bond and $\Delta(distal) = -2\Delta(vicinal)$. This method was used by Allen (1980) in an attempt to account for uncorrected librational effects in the CSD structures used.

Table 1
(*a*) This study.

Bond lengths for cyclopropane rings having only one or two halogen substituents on the same C atom: (i) from DFT calculations, and (ii) from crystal structures in the CSD. The CSD results are averages of the form $d(\sigma,n)$, where σ is the e.s.d. of the sample, and n the number of contributors to the sample. *d*1, *d*2 are the vicinal bonds, *d*3 is the distal bond, *D* is the overall average ring bond length and the asymmetry parameters δ, Δ (defined in §2.2 of the text) are for a single halogen substituent in each case. All bond lengths are in Å.

	DFT results					CSD results				
C-substituent	*d*1,*d*2	*d*3	δ	*D*	Δ	*d*1,*d*2	*d*3	δ	*D*	Δ
F,H	1.485	1.514	+0.015	1.495	+0.019	–	–	–	–	–
Cl,H	1.490	1.507	+0.009	1.496	+0.011	–	–	–	–	–
Br,H	1.489	1.507	+0.009	1.495	+0.012	–	–	–	–	–
F,F	1.470	1.540	+0.018	1.493	+0.024	1.468(12,26)	1.540(12,13)	+0.018	1.492	+0.024
Cl,Cl	1.487	1.514	+0.007	1.496	+0.009	1.499(8,132)	1.531(11,66)	+0.008	1.510	+0.011
Br,Br	1.489	1.512	+0.006	1.497	+0.008	1.503(10,44)	1.524(13,22)	+0.005	1.510	+0.007

(*b*) Literature data for mono- and difluoro-cyclopropane from previous computational studies (MP2, DFT) and from microwave (MW) experimental data.

C-substituent	*d*1,*d*2	*d*3	δ	*D*	Δ
Monofluoro-cp					
MP2/6-31G*[a]	1.488	1.518	+0.015	1.498	+0.020
B3LYP/6-31+G*[b]	1.493	1.526	+0.017	1.504	+0.022
Difluoro-cp					
MP2/6-31G*[a]	1.472	1.545	+0.018	1.496	+0.025
B3LYP/6-31+G*[b]	1.477	1.553		1.502	
MW[c]	1.464	1.553	+0.020	1.494	+0.030

References: (*a*) Wiberg & Marquez (1998); (*b*) Rademacher (2006); (*c*) Perretta & Laurie (1975).

(iii) By averaging the two vicinal bonds as above: $\langle d(vicinal)\rangle = (d_{12} + d_{13})/2$ and then computing the quantity $2\delta = d(distal) - \langle d(vicinal)\rangle$. Again, δ will be positive or negative for lengthened or shortened distal bonds. Method (iii) also accounts, to some extent, for uncorrected librational effects in CSD structures. Simple arithmetic shows that $\delta = 3\Delta(distal)/4$ or $3\Delta(vicinal)/2$ [method (ii)].

The asymmetry parameters are calculated for an individual substituent (*X*), and are derived as far as possible from structures that have *X* as the only electronically effective substituent, *i.e.* other substituents have no effect on ring geometry (*i.e.* H or Csp^3). However, in this paper we need to study systems in which cyclopropane is multiply substituted, either at the same or different C atoms, and we also need to invoke the additivity principle of Allen (1980), which states that the observed ring bond-length asymmetry can be approximated by summing the asymmetry effects of its individual substituents. This is most easily effected by using the asymmetry parameters $\Delta(distal)$ and $\Delta(vicinal)$ [where $\Delta(distal) = 2\Delta(vicinal)$] that arise from method (ii) above. Further, as a useful shortcut, we use the single symbol $\Delta = \Delta(distal)$ throughout this paper to quantify ring asymmetry calculated using method (ii).

2.3. Ab *initio* calculations

Starting molecular geometries were generated from molecular sketches using the *ChemBio3D* software (CambridgeSoft Inc., 2009). Molecular models were then geometry optimized using *GAUSSIAN*03 (Frisch *et al.*, 2004) at the B3PW91/aug-cc-pVTZ level of theory. The level of theory was chosen because of a recent highly detailed theoretical and experimental study (Jalkanen *et al.*, 2008) concluding that the B3PW91 hybrid functional with the aug-cc-pVTZ basis set reproduced geometrical and vibrational data with high precision for cyano-cyclopropane derivatives.

3. Halogen substituents

3.1. Rings carrying one or two halogen substituents on the same ring-C atom

DFT results are given in Table 1 for cyclopropane rings which have only mono-halo or *gem*-dihalo substitution at a single ring-C atom, and the comparative CSD results in Table 1 include those rings having these substituent patterns as the only electronically effective substituents as described in §2.1. Within these requirements, the CSD contains no 'pure' monohalides but the DFT results for C_3H_5X species (X = halogen) confirm bond-length asymmetry: the distal C—C bond is elongated (positive values of δ and Δ) as expected for σ-acceptor substituents (Clark *et al.*, 1984), with *X*-induced elongation in the order F > Cl $\simeq$ Br. This trend is reinforced by the DFT results for the *gem*-dihalides, where the cumulative effect of two halogens doubles the actual asymmetry *via* the additivity principle. There are 13, 66 and 22 examples of cyclopropane rings in crystal structures that have *gem*-dihalo substitution, F_2, Cl_2 and Br_2, within the caveats above. Here, the mean bond lengths derived from the CSD yield asymmetry parameters for a single halogen substituent that are in excellent agreement with the DFT results for both C_3H_5X and $C_3H_4X_2$ species. Indeed, *gem*-difluoro substitution generates very significant asymmetry in the ring bond lengths, more than double that generated by either Cl or Br, for which asymmetry parameters are relatively small and almost equal.

There has been considerable interest in bond-length asymmetry in both mono- and *gem*-difluorocyclopropane over many years, and the earlier activity is summarized by Allen (1980). Some relevant computational and experimental data are collected in Table 1(*b*). The key experimental microwave study of the difluoro compound by Perretta & Laurie (1975) gave δ = +0.020 Å and Δ = + 0.030 Å, very similar to the overall asymmetry derived from the crystal structure results in Table 1(*a*). The two most recent computational studies using MP2/6-31G* (Wiberg & Marquez, 1998) and B3LYP/6–31+G*

Table 2
DFT (B3PW91/aug-cc-pVTZ) and crystallographic results for cyclopropane (cp) and some *cis*-trihalo- and hexahalocyclopropanes.

All distances are in Å and all angles are in degrees. Crystal structure values have their e.s.d.s in parentheses and for angles the second number in parentheses is the number of independent values contributing to the mean value.

	DFT results			Crystal structure data					
Compound	*d*1, *d*2, *d*3 and *D*	θ(CC*X*)	*d*(*X*−*X*)	*d*1	*d*2	*d*3	*D*	Mean θ(CC*X*)	*d*(*X*−*X*)
cp[a]	1.500	118.0	–	1.499 (1)	1.499 (1)	1.500 (1)	1.499	118.0 (5,6)	–
Trichloro (FITSIK[b])†	1.505	121.4	3.322	1.489 (6)	1.492 (5)	1.492 (5)	1.491	120.8 (3,3)	3.267
Tribromo (FITSUW[c])	1.501	122.6	3.552	1.455 (18)	1.470 (20)	1.470 (20)	1.465	122.2 (8,3)	3.503
Hexachloro (HCCYPR01[d])‡	1.532	118.9	3.219	1.525 (6)	1.527 (6)	1.527 (6)	1.526	118.9 (4,12)	3.204
Hexabromo (FITTAD[c])	1.525	119.7	3.422	1.543 (22)	1.549 (21)	1.541 (25)	1.544	119.5 (14,12)	3.417

References: (*a*) Nijveldt & Vos (1988); (*b*) Schrumpf & Jones (1987*a*); (*c*) Schrumpf & Jones (1987*b*); (*d*) Schrumpf & Jones (1987*c*). † Librationally corrected X-ray bond lengths are given as *d*1 = 1.501, *d*2 = 1.506, *d*3 = 1.506 Å. ‡ Librationally corrected X-ray bond lengths are given as *d*1 = 1.537, *d*2 = 1.538, *d*3 = 1.538 Å.

(Rademacher, 2006) levels of theory provide geometrical data (Table 1*b*) which is in close agreement with our current DFT analysis in Table 1(*a*).

3.2. Rings carrying halogen substituents on different ring C atoms

Crystal structures have been reported for *cis*-1,2,3-trichlorocyclopropane (Schrumpf & Jones, 1987*a*: CSD refcode FITSIK) and *cis*-1,2,3-tribromocyclopropane (Schrumpf & Jones, 1987*b*: FITSUW), as well as the hexachloro (Schrumpf & Jones, 1987*c*: HCCYPR01) and hexabromo (Schrumpf & Jones, 1987*b*: FITTAD) derivatives of cyclopropane. Geometrical data from DFT calculations and from the original X-ray studies for these compounds are collected in Table 2. In the case of symmetrical substitution of cyclopropane by three or six identical halogen atoms, we would expect the additivity rule (Allen, 1980) to operate, and for there to be zero asymmetry in the ring C—C bond lengths, which should also be close to their values in unsubstituted rings. Table 2 shows generally good agreement between the computed and experimental C—C bond lengths, with the exception of tribromocyclopropane and hexabromocyclopropane (FITSUW and FITTAD, discussed below). However, while the mean bond length in trichlorocyclopropane (FITSIK) is acceptably close to the value for the parent ring, the values for the hexahalo species are significantly longer. Schrumpf & Jones (1987*b*) point out that in the trihalo species, the C—C—halogen valence angles [θ(CC*X*) in Table 2] expand to >120°, while angles involving the small H substituents close up slightly. The CSD shows that θ(CC*X*) for smaller ring substituents, *e.g.* H, N, O, C, normally fall into the range from 117.0 to 119.0°. The small valence angle distortions engendered by the larger halogen substituents increase the halogen–halogen separation and reduce non-bonded repulsions. However, such distortions are of no energetic benefit in the hexahalo species where multiple eclipsed halogen–halogen repulsions cannot be avoided, so that the θ(CC*X*) values return to the 'undistorted' range, but the ring C—C bond lengths all increase by 0.02–0.03 Å as a result of the non-bonded repulsions. This is a typical elongation for Cl—Csp^3—Csp^3—Cl cyclic single bonds for which the C—Cl bonds are eclipsed or nearly so. For this analysis we selected torsion angles in the range −20° to +20° as representing eclipsed or near-eclipsed chlorines. There are 183 such bonds in CSD structures with $R \leq 0.05$, and the mean C—C bond length is 1.571 (16) Å, which may be compared to a bond length of 1.542 (11) Å for C2—Csp^3—Csp^3—C2 bonds (Allen *et al.*, 1987).

We also note that both DFT and early gas-phase experimental studies have also been carried out for *cis*-1,2,3-trifluorocyclopropane (denoted CpF_3) and hexfluorocyclopropane (denoted CpF_6). The microwave structure of CpF_3 has all C—C bonds at 1.507 (1) Å (Gillies, 1976), while in the electron diffraction study of CpF_6 all C—C are 1.505 (3) Å (Chiang & Bernett, 1971). No C—C—F angles are given in either study. A recent DFT study (Rademacher, 2006) of CpF_3 has all the C—C ring bonds at 1.513 Å, while in CpF_6 they are all 1.527 Å. Whilst no C—C—F valence angles are given in the DFT study, the overall lengthening of the C—C bonds in the hexafluoro compound mirrors similar lengthenings in the corresponding hexachloro and hexabromo compounds for the reasons already discussed.

In Table 2 the clear outlier from the foregoing discussion is the X-ray structure of tribromocyclopropane (FITSUW). Here the ring bond lengths are all very short by comparison with the parent ring and with the other compounds in Table 2, although valence angle values are expanded to an average value in excess of 122° to minimize Br···Br repulsions. Schrumpf & Jones (1987*b*) present an interpretation of their crystal structure, based partly on an assumption that the trihalo substitution will generally shorten all three ring bond lengths – an assumption which appears to contradict the available evidence presented above. Crystal structure data for FITTAD (Schrumpf & Jones, 1987*b*) also disagree with the DFT calculations: despite the near-equality of the equilibrium bond lengths in this crystal structure, they are significantly longer than those from DFT. We note, however, that the halogeno-cyclopropane structures presented by Schrumpf & Jones (1987*a*,*b*,*c*) were all performed some 25 years ago using data collected at room temperature and, in the case of the bromo compounds (FITSUW and FITTAD), rather difficult specimens subject to significant absorption effects. As a result, the precision of bond lengths is poor, of the order of 0.020 Å in both cases, and modern, low-temperature crystallographic re-

Table 3
Cyclopropane ring bond lengths and asymmetry parameters δ and Δ (see text) in Å for a variety of substituents.

Mean values from the CSD have σ(sample) in parentheses. The DFT level of theory used is B3PW91/aug-cc-pVTZ.

Substituent (X)	N(obs)	d_{12},d_{13}	d_{23}	δ	D	Δ	d(C—X)
CH_3							
X-ray [*gem*-$(CH_3)_2$]	101	1.511 (11)	1.515 (12)	+0.002	1.512	+0.003	1.511 (11)
DFT (mono-CH_3)		1.500 (–)	1.503 (–)	+0.002	1.501	+0.002	1.505 (–)
Si(R)$_3$							
X-ray ($SiMe_3$)	12	1.525 (8)	1.500 (6)	−0.012	1.517 (6)	−0.017	1.863 (9)
DFT ($SiMe_3$)	–	1.512 (–)	1.493 (–)	−0.009	1.506 (–)	−0.013	1.874 (–)
DFT (SiH_3)	–	1.511 (–)	1.493 (–)	−0.008	1.505 (–)	−0.012	1.861 (–)
ED (SiH_2Me)[a]	–	1.510 (10)	1.490 (12)	−0.010	1.503 (10)	−0.013	1.876 (2)
ED (SiH_3)[b]	–	1.528 (2)	1.490 (4)	−0.019	1.515 (3)	−0.025	1.840 (2)
OH							
X-ray (*gauche*)	18	1.500 (9)	1.518 (11)	+0.009	1.506 (9)	+0.012	1.418 (21)
DFT (*gauche*)	–	1.486 (–)	1.498 (–)	+0.006	1.490 (–)	+0.008	1.400 (–)
N(R)$_2$							
X-ray (N pyr.)	28	1.500 (10)	1.508 (8)	+0.004	1.503 (8)	+0.005	1.444 (7)
MW (N pyr.)[c]†	–	1.499 (8)	1.512 (8)	+0.006	1.504 (8)	+0.008	1.452 (7)
DFT [N pyr,τ(lp) = 0°]	–	1.498 (–)	1.502 (–)	+0.002	1.499 (–)	0.003	1.436 (–)
DFT [N pyr,τ(lp) = 60°]	–	1.499 (–)‡	1.505 (–)	§	1.501 (–)	§	1.436 (–)
DFT [N pyr,τ(lp) = 120°]	–	1.498 (–)¶	1.511 (–)	§	1.503 (–)	§	1.436 (–)
DFT [N pyr,τ(lp) = 180°]	–	1.501 (–)††	1.502 (–)	§	1.501 (–)	§	1.436 (–)
MP2/6-31G* (N pyr.)[d]	–	1.499 (–)	1.500 (–)	+0.001	1.499 (–)	+0.001	1.442 (–)
X-ray (N planar, perp.)	75	1.491 (10)	1.497 (11)	+0.003	1.493 (8)	+0.004	1.454 (15)

References: (*a*) Dakkouri & Hermann (1995); (*b*) Dakkouri & Typke (1987); (*c*) Rall *et al.* (1986); (*d*) Rall *et al.* (1986). † Microwave spectroscopy. ‡ Asymmetric ring, $d_{12} \neq d_{13}$, d_{12} = 1.497 Å, d_{13} = 1.500 Å. § It is not appropriate to quote asymmetry parameters for these rings. ¶ Asymmetric ring, $d_{12} \neq d_{13}$, d_{12} = 1.507 Å, d_{13} = 1.490 Å. †† Asymmetric ring, $d_{12} \neq d_{13}$, d_{12} = 1.500 Å, d_{13} = 1.502 Å.

determinations of the tribromo- and hexabromocyclopropane structures would be beneficial.

The CSD currently records 383 cyclopropane structures having one or more halogen substituents but, apart from the dihalide subsets analysed in Table 1, the majority of these substituents co-occur with other substituents that are also likely to have electronic effects on ring geometry. The only other small subset of note which is free of effects from other substituents is a group of six 1,1,2,3-tetrachlorocyclopropane fragments which have Csp^3 atoms as additional substituents, as well as one similar 1,1,2,3-tribromo compound. The additivity principle means that these tetrahalides should have bond-length asymmetry closely similar to that for monohalides, and analysis of the available data generates δ and Δ values from this tetrachloride subset of +0.009 Å and +0.012 Å, closely similar to the values given in Table 1.

4. Rings bearing methyl, trimethylsilyl, hydroxy and amino substituents

Within the CSD, the only other cyclopropyl substituents that give rise to acceptable numbers of structures for data analysis (and within the restriction that rings do not carry additional substituents which would further affect the ring bond lengths, as described in §2.1) are the methyl, trimethylsilyl, hydroxyl and amino groups. Relevant crystallographic mean bond lengths and ring asymmetry parameters for these four groups are collected in Table 3 and are compared with results from our DFT calculations. Some gas-phase structural data are also included in Table 3.

Gem-dimethyl derivatives dominate the CSD 'methyl subset', and the crystallographic results show δ and Δ values that are effectively zero within the e.s.d.s of the mean bond lengths {σ(mean) = σ(sample)/[N(obs)]$^{1/2}$ in Table 3}. The DFT results for monomethylcyclopropane support this conclusion, although the general level of ring bond lengths is lower than the crystal structure means. This is likely to be due to some slight elongation of bond lengths in the crystal structures arising from eclipsed non-bonded repulsions: the *gem*-dimethyl derivatives in crystal structures may have a variety of other C-substituents at the vicinal ring C atoms, but the DFT results have only H-substituents and are not affected by such considerations.

By contrast, —Si$(CH_3)_3$ is a strong σ-donor group and induces clear asymmetry in the ring bond lengths (Table 3), with the distal bond significantly shorter than the vicinal bonds giving rise to appreciable (negative) δ and Δ values. The sense of asymmetry is opposite that for the σ-accepting halogens, as predicted by Clark *et al.* (1984). The DFT results again support

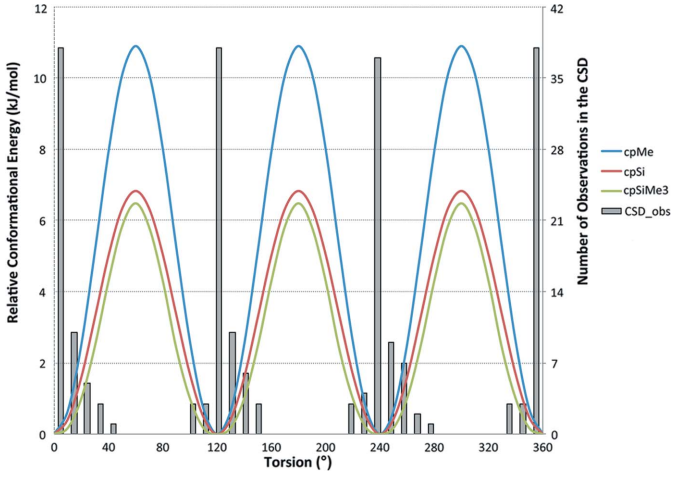

Figure 2
Conformational energy maps for rotation of CH_3 (cpMe), SiH_3 (cpSi) and $Si(CH_3)_3$ (cpSiMe3) substituents on cyclopropane (DFT: B3PW91/aug-cc-pVTZ) and conformations of $Si(CH_3)_3$ substituents on cyclopropane as observed in ten crystal structures from the CSD containing 63 independent fragments. Torsion angles are M—C(cp)—C—H for cpMe, M—C(cp)—Si—H for cpSi and M—C(cp)—Si—C for cpSiMe3, where M is the midpoint of the distal bond (Fig. 1).

the X-ray data analysis, and also show that a similar effect can be expected from pure silyl substituents, $-SiH_3$. In both cases though the DFT bond lengths are slightly shorter than their crystallographic counterparts, again most likely reflecting eclipsed non-bonded repulsion effects in the crystal structure sample. The available electron diffraction data (Table 3) also reinforce our current results.

The DFT calculations also examined the energetically preferred conformations of $-CH_3$ and $-Si(R)_3$ substituents with respect to the cyclopropane ring, in terms of the $M-C-C,Si-R$ torsion angles, where M is the midpoint of the distal ring bond (Fig. 1). Fig. 2 shows that the minimum energy forms always have the substituent R atoms staggered with respect to the ring, a feature which is clearly observed in the crystal structure data, *e.g.* for $Si(Me)_3$ groups as shown in Fig. 2 for which the torsion angles from the CSD are superimposed on the DFT energy curves.

Our DFT calculations for cyclopropanol (Table 3) show a minimum energy form with the $M-C-O-H$ torsion angle close to 110°, *i.e.* the *gauche* conformation (Fig. 3). This form shows a slightly elongated distal bond (1.498 Å) compared with the vicinal bonds at 1.486 Å. This asymmetry (δ = + 0.006 Å, Δ = + 0.008 Å) is typical for a weak σ-acceptor, being close to values exhibited by single Cl or Br substituents but much less than asymmetry parameters calculated for monofluorocyclopropane (Table 1). DFT results for cyclopropanol calculated by Rademacher (2003) using the B3LYP method yield a distal bond length of 1.521 Å and vicinal bonds of 1.502 Å, *i.e.* δ = + 0.009 Å, Δ = + 0.013 Å. The averaged crystal structure data for hydroxy substituents (attached to rings that do not carry additional electron donor or acceptor substituents, see §2.1) are also given in Table 3 and are closely similar to the DFT results, with δ = + 0.009 Å, Δ = + 0.012 Å. Despite the well known problems of positioning H atoms in X-ray structures, all of the O—H protons in the structures analysed in Table 3 lie within 30 to 40° of the ±*gauche* positions, with no examples adopting the higher-energy *cis* or *trans* conformations which have torsion angles of 0 or 180° (see Fig. 3).

Cyclopropylamine has been the subject of numerous theoretical and experimental studies, with existing results collected and reviewed by Rall *et al.* (1986). We have used DFT to study the conformational and geometrical characteristics of cyclopropylamine having a pyramidal N atom. Conformational analysis was carried out in terms of the position of the N-lone pair (lp) with respect to the ring, as defined by the torsion angle τ(lp) = M—C1—N—(lp) and the results shown in Fig. 4 and Table 3. The global energy minimum occurs when the lone pair is in the *cis*-bisecting position at τ(lp) = 0° (Fig. 4), with other higher-energy positions at τ(lp) = 60 and 180°, and a local minimum at 120°. DFT bond lengths for all four of these conformers are given in Table 3 and show minimal asymmetry between the vicinal and distal bonds. The conformations at τ(lp) = 60, 120 and 180° lose the symmetry for the vicinal bond lengths, with very significant differences being observed at τ(lp) = 120° (footnote ¶, Table 3). Our new DFT results for a pyramidal amino-N are highly comparable to previous theoretical data, especially the MP2/6-31G* results at τ(lp) = 0° presented by Rall *et al.* (1986). The averaged crystal structure data for both pyramidal and planar amino substituents (attached to rings that do not carry additional electron donor

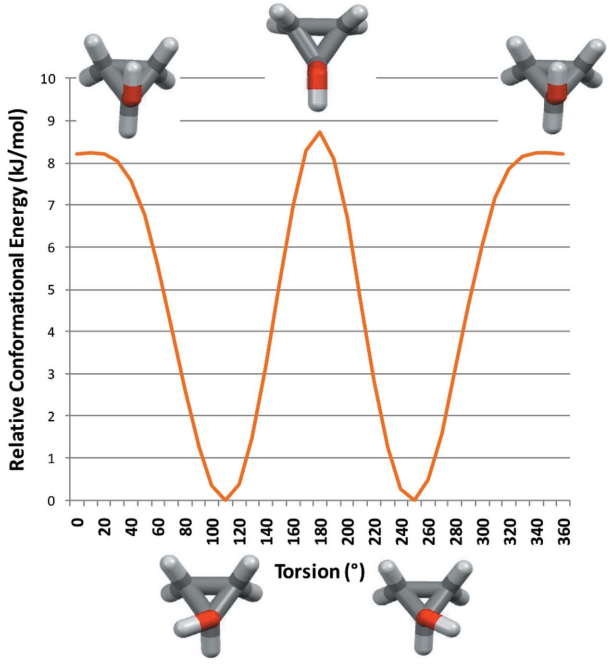

Figure 3
Conformational energy map (DFT: B3PW91/aug-cc-pVTZ) for hydroxy substituents on cyclopropane. The torsion angle is M—C(cp)—O—H, where M is the midpoint of the distal bond (Fig. 1).

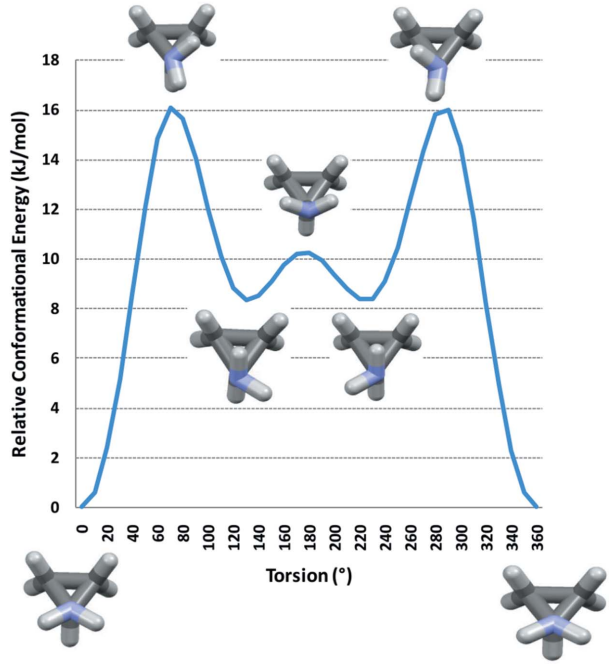

Figure 4
Conformational energy map (DFT: B3PW91/aug-cc-pVTZ) for pyramidal amino substituents on cyclopropane. The torsion angle is M—C(cp)—N—lp, where M is the midpoint of the distal bond (Fig. 1) and lp is the calculated position of the lone pair on N.

or acceptor substituents) are well aligned with the theoretical work, having δ and Δ values in the narrow range of +0.003 to +0.005 Å. These asymmetry parameters are very small, and at the level of the e.s.d.s for a well refined modern crystal structure. The results would classify the amino group as a very weak σ-acceptor in this context, a conclusion also reached by Rall *et al.* (1986). We note that all of the pyramidal NR_2 groups in the crystal structure subset adopt the minimum energy conformation with $\tau(\mathrm{lp}) = 0^\circ$. The more significant asymmetry suggested by Clark *et al.* (1984) for a perpendicular planar amino substituent is not observed in crystal structures, where the bisected planar-amino conformation predominates.

5. Conclusion

In agreement with previous theoretical calculations and experimental studies on individual compounds, the current work has shown that σ-acceptor substituents, such as the halogens, on cyclopropane rings lead to significant lengthening of the ring bond distal to the point of substitution and a shortening of the vicinal ring bonds. The asymmetry parameters δ and Δ increase in the order Br $\simeq$ Cl < F and there is excellent agreement between DFT results and mean values obtained from crystal structures in the CSD. The bond-length asymmetry in the case of σ-acceptor substituents is in the opposite sense to that observed for π-acceptors (Cruz-Cabeza & Allen, 2011). The current work suggests that the crystal structure of *cis*-1,2,3-tribromocyclopropane (FITSUW: Schrumpf & Jones, 1987*b*) is an outlier in the analysis and would benefit from a re-determination. Similar considerations also apply to the hexabromo compound (FITTAD: Schrumpf & Jones, 1987*b*).

DFT analyses of the ring asymmetry effects arising from CH_3, SiH_3, $Si(CH_3)_3$, OH and NH_2 substituents show clear negative values of δ and Δ for SiH_3 and $Si(CH_3)_3$ with the substituents being staggered with respect to the ring. These results are reinforced by crystal structure data for cyclopropyl-$Si(CH_3)_3$ compounds and are as expected for σ-donors. Data for OH substituents from both DFT and crystal structures show small positive asymmetry of the ring bond lengths, indicating weak σ-acceptor activity for $-$OH. For NH_2 substituents, both the DFT and experimental observations show even smaller positive asymmetry parameters, suggestive of very weak σ-acceptor effects in this case. Both computational and experimental data analyses indicate that CH_3 substituents have no discernible effect on the ring geometry.

This study, and the earlier study of π-acceptor substitution of cyclopropane (Cruz-Cabeza & Allen, 2011), has shown an excellent level of agreement between the DFT results and those obtained by careful analysis of available crystal structures in the CSD. As far as the DFT analysis is concerned, this supports the view of Jalkanen *et al.* (2008) that the B3PW91/aug-cc-pVTZ is an appropriate level of theory for calculations involving cyclopropane. However, despite the large number of structures of substituted cyclopropanes now available in the CSD, it remains difficult to locate structures in which asymmetry in the ring bond lengths is solely due to a single substituent type, hence restricting the chemical diversity of substituents available for the type of comparative analysis attempted here.

AJCC thanks De Nederlandse Organisatie voor Wetenschappelijk Onderzoek (NWO) for a VENI fellowship and the Pfizer Institute for Pharmaceutical Materials Sciences (Cambridge, UK) for funding during the initial phase of the project. We thank Professor Peter Jones (Universität Braunschweig) for his valuable comments.

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