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Journal Title: Acta Crystallographica Section C: Structural Chemistry
Volume: Volume 69, Number 8
Publisher: International Union of Crystallography | 2013-08-15, Pages 910-914
Type of Work: Article | Final Publisher PDF
Publisher DOI: 10.1107/S0108270113017496
Permanent URL: https://pid.emory.edu/ark:/25593/rpkcd

Final published version: http://dx.doi.org/10.1107/S0108270113017496

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Accessed February 17, 2019 5:45 AM EST
Determination of the electron density in methyl (±)-(1S,2S,3R)-2-methyl-1,3-diphenylcyclopropanecarboxylate using refinements with X-ray scattering factors from wavefunction calculations of the whole molecule

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Received 2 May 2013
Accepted 25 June 2013

The molecule of the title compound, C18H18O2, is a substituted cyclopropane ring. The electron density in this molecule has been determined by refining single-crystal X-ray data using scattering factors derived from quantum mechanical calculations. Topological analysis of the electron densities in the three cyclopropane C—C bonds was carried out. The results show the effects of this substitution on these C—C bonds.

Keywords: crystal structure; electron density; molecular modelling.

1. Introduction

The large departure of the bond angles in three-membered cyclopropane rings from tetrahedral angles and the resulting strain energy are of great theoretical interest. The research described in this paper is an attempt to extend the theoretical and quantitative information on the molecular structures and electron-density distributions of cyclopropane molecules available through combining X-ray crystallography and quantum mechanical calculations of a substituted cyclopropane. In their development of invarioms, Dittrich and co-workers have defined a procedure by which Gaussian wavefunctions are used to project theoretical electron densities onto the multipole model (Dittrich et al., 2005). In this method, theoretical structure factors are generated by the program TONTO (Jayatilaka & Grimwood, 2003) from the Gaussian wavefunction, and then least-squares refinements give the populations of the multipoles. We have determined the nature of the electron density in the cyclopropane ring in the title compound, (I), by this method and observed the effects of substitution on the covalent bonding between these C atoms.

2. Experimental

2.1. Synthesis and crystallization

A mixture of trans-β-methylstyrene (2.5 mmol) and AgOTf (0.05 mmol) was weighed into a 25 ml one-necked round-bottomed flask covered with aluminium foil to exclude light. The mixture was dissolved in dichloromethane (2 ml) and stirred at room temperature under an atmosphere of argon. Methyl phenyldiazoacetate (0.5 mmol) in dichloromethane (8 ml) was then added to the solution via syringe pump over a period of 3 h. After addition, the mixture was stirred for an additional 1 h and then concentrated in vacuo. Purification by silica-gel chromatography (using 20:1 v/v hexane–Et2O as the solvent system) gave the product in 64% yield (86 mg) as colorless crystals. 1H NMR (600 MHz): δ 7.11–7.71 (m, 2H), 6.76–7.05 (m, 6H), 7.02–7.06 (m, 2H), 3.65 (s, 3H), 3.08 (d, 1H, J = 7.8 Hz), 2.25 (dq, 1H, J = 7.2 and 6.0 Hz), 1.47 (d, 3H, J = 6.0 Hz); 13C NMR (100 MHz): δ 172.3, 137.0, 136.4, 131.3, 127.9, 127.8, 127.6, 126.9, 126.0, 52.3, 42.4, 37.7, 27.3, 12.9. The spectroscopic data are consistent with the previously reported results (Thompson & Davies, 2007).

2.2. Calculation of structure factors

Nonspherical scattering factors were obtained from theoretical calculations of (I) by following a procedure developed

Figure 1
The molecular structure of (I), with the atom-numbering scheme. Displacement ellipsoids are drawn at the 50% probability level.
by Dittrich et al. (2006). Density functional theory (DFT) calculations were carried out using the B3LYP method in the GAUSSIAN09 suite of programs (Frisch et al., 2009). A Dunning–Huzinaga full double-ζ basis set with 3df and 3dp polarization functions was used (Dunning & Hay, 1977). Calculations were carried out using 1164 basis functions. The wavefunction was calculated for the nuclear configuration geometry from the crystal structure. Electron densities were derived by evaluating the Gaussian orbitals using the programs AIMAII (Keith, 2012) and TONTO (Jayatilaka & Grimwood, 2003). An artificial crystal of (I) (space group $P1$), with a cubic cell edge of 30 Å and the molecule centered at the position $(\frac{1}{2}, \frac{1}{2}, \frac{1}{2})$, was constructed. Structure factors for this crystal were generated by TONTO up to a resolution of $(\sin \theta)/\lambda = 1.15 \ \text{Å}^{-1}$. Thermal smearing was ignored and the contributions of the core electrons were included in structure-factor calculations. Least-squares refinements of the multipole populations parameters with these structure factors, and the fixed geometry from the crystal structure, yielded a multipole model suitable for reproducing the electron density in the molecule. This method provides a means of calculating the atomic electron densities without having to partition individual atoms into pseudo-atoms. These multipole parameters, together with the orientation and symmetry of the local atomic coordinate system, were transferred to the input files for a refinement with the XDLSM program of the XD2006 suite.

### 2.3. Refinement

Crystal data, data collection and structure refinement details are summarized in Table 1. The program InvariomTool (Hübschle et al., 2007) was used to prepare the master and input files for a multipole refinement with the XDLSM program of the XD2006 suite (Volkov et al., 2006). Full matrix least-squares refinements on $F^2$ using complete multipole expansions were carried out with the program XDLSM using statistical weights. Only reflections with intensities $I > 3\sigma(I)$ were included in the refinement. In the final cycles, all atom positions were refined freely. Positional and displacement (anisotropic for non-H atoms) parameters, but not multipoles, were refined. However, a hexadecapolar level of the multipole expansion was used for all atoms. The introduction of the multipole model improved $R(F)$ from 0.043 to 0.030, using the same weighting scheme $[w = 1/(\sigma^2(F_o^2))]$ as with the spherical atom refinement, and improved the goodness-of-fit value from 2.819 to 1.597.

### 3. Results and discussion

The molecular structure of (I) (Fig. 1) can be derived from that of cyclopropane by replacing two H atoms on C2 by a methyl formate group and a phenyl ring, one H atom on C3 with a methyl group, and one H atom on C4 with a phenyl ring. The conformation of this compound is of interest. The phenyl rings across the C—C bond give rise to 1,3-steric repulsion, which favors a staggered arrangement in an unbridged C—C bond. The steric repulsion between these groups might influence the electron density in the bond and is likely to have an effect on the geometry of the molecule. The electronic interaction between the substituents and the ring is also of interest. Methyl, phenyl and methyl formate groups might be expected to withdraw electron density and weaken the C—C bonds.

A large number of basis functions for atoms with a large number of electrons are needed to yield accurate results. This
The ring does not have propane form the geometry of an equilateral triangle [see, for example, Hartman & Hirshfeld (1966)]. In cyclopropane (I), the ring does not have C₃ symmetry but has two normal C–C bonds [1.5421 (4) Å and 1.5338 (4) Å] and one short bond [1.5019 (4) Å; Table 3]. The shortest C–C bond occurs between the hydride-substituted C atoms distal to the formate group, while the longest bonds are to the C atom bonded to methyl formate. The basicity of the CO₂ group is expected to group, while the longest bonds are to the C atom bonded to methyl formate. The basicity of the CO₂ group is expected to bond-critical points (Table 2). The result is reflected in the atomic charges and electron densities at the bond-critical points (Table 2). The second (3, 1 critical point is /C0/C1/C1/C1 69, 910–914). The existence of a (3, 1 critical point /C0/C1/C1/C1 69, 910–914). The existence of a (3, 1 critical point is insufficient evidence for chemical bonding between these two atoms (Haaland et al., 2004), but it does show that electron density accumulates preferentially along this direction, thereby stabilizing this short contact.

The C–C bonds are expected to be weakened by strain. The characteristic C–C bond length in cyclopropane is 1.50 Å, shorter than the normal C–C bond length of 1.54 Å (Cambridge Structural Database, Version 5.34; Allen, 2002). The three C atoms in a symmetrically substituted cyclopropane form the geometry of an equilateral triangle [see, for example, Hartman & Hirshfeld (1966)]. In cyclopropane (I), the ring does not have C₃ symmetry but has two normal C–C bonds [1.5421 (4) Å and 1.5338 (4) Å] and one short bond [1.5019 (4) Å; Table 3]. The shortest C–C bond occurs between the hydride-substituted C atoms distal to the formate group, while the longest bonds are to the C atom bonded to methyl formate. The basicity of the CO₂ group is expected to reduce the electron density in the two C–C bonds attached to this C atom, lengthening these two bonds (and shortening the distal bond). This effect is reflected in the atomic charges and electron densities at the bond-critical points (Table 2). The shortest bond occurs where the phenyl and methyl substituents are trans, for which repulsion between these 1,4-bonded atoms will be less. The molecular graph is shown in Fig. 2. Bond-critical points were located between the nuclei. Another two bond-critical points were located that are not normally associated with chemical bonds. The distance between atoms H6 and C12 is only 2.709 (7) Å and a (3,–1) critical point exists between them. The second (3,–1) critical point is associated with a weak intramolecular hydrogen bond (C11–H11A · · · O2; Table 4). The existence of a (3,–1) critical point is insufficient evidence for chemical bonding between these two atoms (Haaland et al., 2004), but it does show that electron density accumulates preferentially along this direction, thereby stabilizing this short contact.

### Table 2

<table>
<thead>
<tr>
<th>Property</th>
<th>X-ray refinement</th>
<th>Gaussian wavefunction</th>
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<tr>
<td>C2–C3</td>
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<tr>
<td>ρ(r) (e Å⁻³)</td>
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<td>1.54</td>
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<tr>
<td>Bond path (Å)</td>
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<td>Bond-angle degree (°) C4–C2–C3</td>
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<td>67.27</td>
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<tr>
<td>Ellipticity, ε</td>
<td>0.609</td>
<td>0.529</td>
</tr>
<tr>
<td>V²ρ(r) (e Å⁻⁵)</td>
<td>–4.589</td>
<td>–2.875</td>
</tr>
<tr>
<td>λ₁</td>
<td>–10.157</td>
<td>–10.679</td>
</tr>
<tr>
<td>λ₂</td>
<td>–6.31</td>
<td>–6.99</td>
</tr>
<tr>
<td>λ₃</td>
<td>11.88</td>
<td>7.39</td>
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<tr>
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<tr>
<td>Ellipticity, ε</td>
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### Table 3

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<th>C2–C3</th>
<th>C3–C4</th>
<th>C4–C5</th>
<th>C5–C6</th>
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</thead>
<tbody>
<tr>
<td>1.5338 (4)</td>
<td>1.5019 (5)</td>
<td>1.5421 (4)</td>
<td>1.5209 (4)</td>
</tr>
<tr>
<td>1.5348 (4)</td>
<td>1.5492 (4)</td>
<td>1.5700 (5)</td>
<td>1.5989 (4)</td>
</tr>
<tr>
<td>1.5375 (4)</td>
<td>1.5395 (5)</td>
<td>1.5700 (5)</td>
<td>1.5989 (4)</td>
</tr>
<tr>
<td>1.5380 (4)</td>
<td>1.5395 (5)</td>
<td>1.5700 (5)</td>
<td>1.5989 (4)</td>
</tr>
</tbody>
</table>

**organic compounds**
A difference electron-density map in the plane of the cyclopropane ring is shown in Fig. 3. It is evident from this plot that there is an accumulation of charge over the entire cyclopropane triangle area and beyond the C—C bonds. Critical points (CP), due to C—C bonding, are displaced by 0.031–0.041 Å from the C—C internuclear axes. The electron densities at the critical points for the C—C bonds, calculated by XD2006, are in the range 1.48–1.61 e Å$^{-3}$. The largest peak, and the shortest bond path, occur between atoms C3 and C4. The smallest bond-path angle (63.85°) corresponds to the internuclear angle C4—C2—C3 and the longest C—C bonds. These distances indicate that the carboxylate group withdraws some of the valence density from these bonds, thereby lengthening them and decreasing the angles between them. These bond-path angles are greater than the bond angles, but still substantially smaller than the tetrahedral angle normally associated with C—C bonds.

The electron density is at a minimum near the center of the plane of the three C atoms and this point is a (3,+1) critical point of the electron density. The bond ellipticities give a measure of how much electron density accumulates normal to the direction of the bond. Single bonds in linear alkanes typically have ellipticities close to 0. The

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**Figure 3**
A deformation electron-density map of (I), in the plane of the C atoms belonging to the cyclopropane group. Contours are drawn at 0.02 e Å$^{-3}$ intervals. Solid lines represent positive contours and dashed lines negative contours. The charge is concentrated in the plane of this ring, with the largest bonding concentrations lying outside the triangle shown. The charge drops off more quickly perpendicular to this plane, resulting in a flattened shape. The local charge concentrations are greatest between atoms C3—C4, distal to the carboxylate group.

---

**Figure 4**
A contour plot of the negative Laplacian $[-\nabla^2 \rho(r)]$ of the charge density in the symmetry plane of the cyclopropane. Solid lines represent positive contours and dashed lines negative contours.

---

**Figure 5**
A relief plot of the negative Laplacian $[-\nabla^2 \rho(r)]$ of the charge density in the symmetry plane of the cyclopropane. The bonded concentrations between atoms C3 and C4 are the largest.

---

**Figure 6**
A positive deformation density isosurface (0.009 e Å$^{-3}$), viewed in the plane of the ring.
organic compounds

3

Table 4
Hydrogen-bond geometry (Å, °).

\[
\begin{array}{cccccc}
D & H & A & D & H & A \\
C4—H4 & 1.011 (9) & 2.453 (11) & 2.8877 (6) & 105.2 (6) \\
C11—H11A & 0.939 (11) & 2.485 (9) & 3.1200 (7) & 125.0 (8) \\
C17—H17 & 0.972 (7) & 2.530 (6) & 3.4020 (6) & 149.2 (5) \\
\end{array}
\]

Symmetry code: (i) \( x, -y + \frac{1}{2}, z \).

Support of this research by the National Institutes of Health is gratefully acknowledged. Its contents are solely the responsibility of the authors and do not necessarily represent the official views of the NIH. The authors acknowledge an NSF MRI-R2 grant (No. CHE-0958205) and the use of the resources of the Cherry L. Emerson Center for Scientific Computation. We express our appreciation to Huw Davies for advice related to this manuscript. We acknowledge Birger Dittrich and Christian Hübchle for discussions and for shell scripts which made the computations less time consuming.

Supplementary data for this paper are available from the IUCr electronic archives (Reference: QS3027). Services for accessing these data are described at the back of the journal.

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4. Conclusion

These results show a cyclopropane group with an asymmetric and highly flattened bonding charge density. Lengthening of the C2—C4 and C2—C3 bonds and shortening of the C3—C4 bond, due to the withdrawal of electron density by the carboxylate group, is reflected by the electron densities at the bond-critical points. The spread out density is likely to have been enhanced by the proximity of the two phenyl rings and the carboxylate group.

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