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Electron Density Distribution in a 1,2-Difluorinated Cubane Derivative

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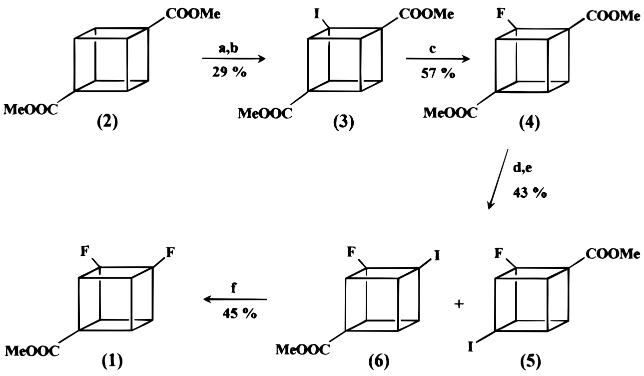
cis-1,2-Difluoroethylene is energetically favored above the corresponding *trans*-isomer because of the strongly electronegative properties of the fluorine substituents.[1] For the same reason, *gauche*-1,2-difluoroethane is more stable than the corresponding *anti*-conformer.[2] A recent proposal for explaining this "cis/gauche-effect" is given by Wiberg and co-workers.[3] According to their calculations, the C−C bond is predicted to be bent. The bending is energetically more favorable in the case of the *cis*-isomer and *gauche*-conformer. Recent structural investigations of 1,2-difluoroethylene have been made using high-resolution infrared spectra.[1b]

To test this explanation we synthesized methyl 3,4-difluorocubane-1-carboxylate (**1**) (Scheme 1). As a consequence of the rigid cage system, the two fluorine substituents are fixed in a *cis*-like orientation in this molecule. Therefore, this cubane derivative should be a model for the *cis*-isomer of difluoroethylene. We would expect the FC−CF cage bond to be the most strongly bent bond and the HC−CF bonds to be more strongly bent than the CH−CH bonds in derivative **1**. To determine the bending of the different bond types in this molecule, we investigated the electron density distribution by high-resolution X-ray analysis at a low temperature from *X*−*X* difference maps.

The synthesis of **1** (Scheme 1) started with the chlorocarbonylation of dimethyl cubane-1,4-dicarboxylate (**2**) by the procedure described by Bashir-Hashemi.[4] Hydrolysis of the acid chloride followed by iododecarboxylation resulted in dimethyl 2-iodocubane-1,4-dicarboxylate (**3**). Dimethyl 2-fluorocubane-1,4-dicarboxylate (**4**) was synthesized by fluorodeiodination of **3** with xenon difluoride. The structure of **4** was established by X-ray analysis[5] of single crystals obtained from chloroform. Subsequently, the isomeric iodides methyl 2-fluoro-4-iodocubane-1-carboxylate (**5**) and methyl 3-fluoro-4-iodocubane-1-carboxylate (**6**) were produced by saponification of one ester group of fluoride **4,** followed by iododecarboxylation. The isomeric iodides were separated from each other by manifold column chromatography. The structure of isomer **5** was established by X-ray analysis.[6] To complete the synthesis of difluoride **1**,[7] iodide **6** was treated with xenon difluoride as described above.

Scheme 1[a]



[a] Reagents and conditions: (a) (i) $(COCl)_2$, *hν*, 30−35 °C, 48 h, (ii) H_2O, CH_2Cl_2; (b) $Pb(OAc)_4$ (1.3 equiv), I_2 (5 equiv), benzene, *hν*, reflux, 2.5 h; (c) XeF_2 (9.2 equiv), *n*-hexane, reflux, 2 h; (d) (i) 2.5 M methanolic KOH (1 equiv), THF, 24 h; (ii) conc HCl; (e) $Pb(OAc)_4$ (1.25 equiv), I_2 (5 equiv), benzene, *hν*, reflux, 2.5 h; (f) XeF_2 (9.1 equiv), *n*-hexane, reflux, 4.5 h.

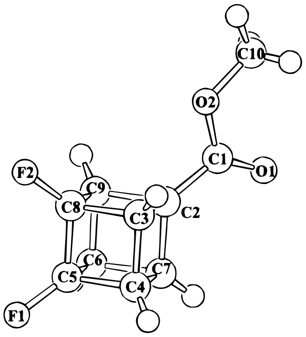


Figure 1. Structure of molecule **1** with the heavy atoms labeled. Some selected bond lengths [Å]: C2−C9 1.577(2); C2−C3 1.567(2); C2−C7 1.562(2); C5−C8 1.554(2); C4−C5 1.550(2); C5−C6 1.554(2); C3−C8 1.551(2); C8−C9 1.549(2); C3−C4 1.572(2); C4−C7 1.568(2); C6−C7 1.568(2); C6−C9 1.569(2).

The X-ray analysis of the difluoride **1** was carried out at −55 °C, and 5506 reflections were recorded in the range of $\theta = 2-55°$. The crystals are triclinic with the space group *P*1 possessing two molecules in the unit cell.[8a] Figure 1 is a drawing of molecule **1** with the heavy atoms labeled. As occurs in the methyl 4-halocubanecarboxylates,[9] the fluorine-substituted bonds (av 1.552(2) Å) are shortened compared with the average length (1.569(2) Å) of the CH−CH bonds.

The electron density distribution in the cage bonds of **1** is obtained from the difference density maps shown in Figure 2.

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(3) (a) Wiberg, K. B.; Murcko, M. A.; Laidig, K. E.; MacDougall, P. J. *J. Phys. Chem.* **1990**, *94*, 6956−6959. (b) Wiberg, K. B.; Hadad, C. M.; Breneman, C. M.; Laidig, K. E.; Murcko, M. A.; LePage, T. J. *Science* **1991**, *252*, 1266−1272.

(4) (a) Bashir-Hashemi, A. *Angew. Chem.* **1993**, *105*, 585−586; *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 612. (b) Bashir-Hashemi, A.; Li, J.; Gelber, N.; Ammon, H. *J. Org. Chem.* **1995**, *60*, 698−702.

(5) For **4**: colorless prisms (0.4 × 0.3 × 0.2 mm), monoclinic space group *C*2/*m*, $a = 13.798(3)$, $b = 6.489(2)$, and $c = 5.885(1)$ Å, $\beta = 92.38(2)°$, at 293 K, $Z = 2$, $R(F) = 0.045$, $wR(F^2) = 0.134$, GOF = 1.09.

(6) For **5**: colorless needles (0.5 × 0.18 × 0.1 mm), orthorhombic space group $Pna2_1$, $a = 25.718(2)$, $b = 5.733(1)$, and $c = 6.557(1)$ Å, at 218 K, $Z = 4$, $R(\mathrm{F}) = 0.024$, $wR(F^2) = 0.066$, GOF = 1.16.

(7) For **1**: mp 110−111 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 3.71 (s, 3H, OCH_3), 3.97−4.00 (m, 1H, cage), 4.16−4.22 (m, 2H, cage), 4.40−4.43 (m, 2H, cage); ^{19}F NMR (90 MHz, $CDCl_3$) δ −154.8, −156.3; FTIR (KBr) 2957 (w−m), 2922 (w−m), 1725 (s), 1445 (m), 1350 (s), 1294 (s), 1204 (s), 1140 (s), 1118 (m−s), 1090 (m−s), 1053 (m−s) cm^{-1}; MS (EI) *m*/*z* 183 (1), 167 (16), 139 (90), 138 (47), 127 (33), 120 (26), 119 (100), 114 (38); HRMS (EI) calcd for $C_9H_5OF_2^+$ ($M^+ - OCH_3$) 167.0308, obsd 167.0271; calcd for $C_8H_5F_2^+$ ($M^+ - CO_2CH_3$) 139.0359, obsd 139.0330; MS (CI^+, isobutane) 199 ($M^+ + H$).

(8) For **1**: (a) Colorless prisms (0.4 × 0.25 × 0.2 mm), triclinic space group *P*1, $a = 6.056(1)$, $b = 6.574(1)$, and $c = 10.593(2)$ Å, $\alpha = 91.74(1)°$, $\beta = 101.80(1)°$, $\gamma = 91.69(1)°$ at 218 K, $Z = 2$, $R = 0.044$, $wR(F^2) = 0.107$, GOF = 2.02. The lowest possible temperature was not chosen, since on further cooling phase transition started. (b) Collected reflections 5506, independent reflections 2636 ($\theta = 2- 55°$, Mo Kα radiation, $R_{\mathrm{int}} = 0.029$). The obtained structure model was first refined anisotropically for all non-hydrogen atoms and isotropically for the hydrogen atoms in the range $\sin \theta/\lambda = 0-0.66$ using 1533 reflections. The *R*-factors for this refinement were $R(F) = 0.043$ and $wR(F^2) = 0.102$. To determine the coordinates of the non-hydrogen atoms precisely, the structure was refined with anisotropic displacement parameters for these atoms and with fixed hydrogen atoms in the high order range $\sin \theta/\lambda = 0.6-1.15$ using 963 reflections. The *R*-factors for this high order refinement were $R(F) = 0.027$ and $wR(F^2) = 0.061$. From this structure model thus received, F_{calcd} were obtained in the range $\sin \theta/\lambda = 0-0.66$ and the difference density maps were calculated from $\Delta(F_{\mathrm{obsd}} - F_{\mathrm{calcd}})$.

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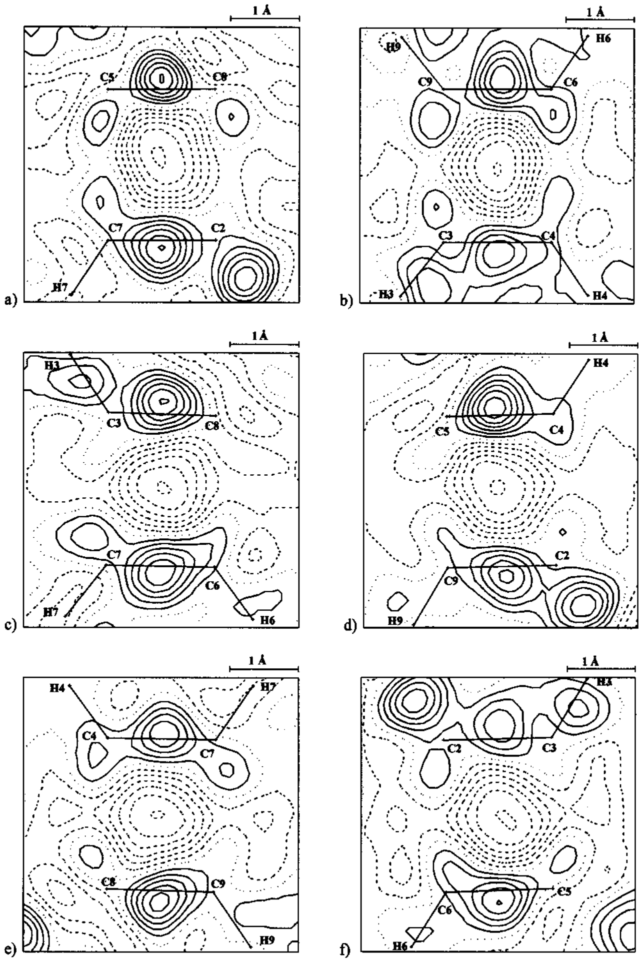

Figure 2. Electron density difference maps (0.17−0.35(6) e/Å^3) in the diagonal planes; contour interval 0.05 e/Å^3: (a) C2, C7, C5, C8; (b) C3, C4, C6, C9; (c) C3, C8, C6, C7; (d) C2, C9, C4, C5; (e) C4, C7, C8, C9; and (f) C2, C3, C5, C6.

The maxima of the electron densities are of the order of 0.17−0.35 e/Å^3. They were determined from low-order reflections ($\theta < 28°$) using the $X-X$ method by high-order refinement of the non-hydrogen atoms.[8b]

All of the cage bonds are bent (av $d = 0.14$ Å, $\delta = 10.2°$) (Table 1), as is expected for the cubane cage. The bending is of the same order of magnitude as found in dimethyl cubane-1,4-dicarboxylate.[10] For several bond types of **1**, parameters characterizing the bending of the bonds are given in Table 1 and illustrated in Figure 3.

Table 1. Parameters of Bond Bending in **1**

bond type	d [Å]	δ [deg]
HC−CH (av)	0.12	8.70
HC−CF (av)	0.16	11.66
FC−CF	0.16	11.63
HC−C(COOMe) (C2−C9, C2−C3 av)	0.17	12.20
HC−C(COOMe) (C2−C7)	0.12	8.74
cage bonds (av)	0.14	10.16

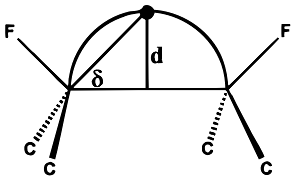

Figure 3. Parameters characterizing the bending of the bonds in **1**: **d** is the length of the perpendicular line dropped from the maximum of the electron density to the internuclear axis; δ is the angle between the internuclear axis and the connection line between the atomic position and the maximum of the electron density.

The CF−CF bond and the CH−CF bonds are more bent (av $d = 0.16$ Å, $\delta = 11.6°$) than the CH−CH bonds (av $d = 0.12$ Å, $\delta = 8.7°$). The degree of bending is of the same order of magnitude for the difluoro-substituted bond (CF−CF) and the monofluoro-substituted (CF−CH) bonds. The bonds (C2−C9, C2−C3) influenced by the π-accepting property of the methyl carboxylate group are two of the most strongly bent bonds (av $d = 0.17$ Å, $\delta = 12.2°$) in the cubane derivative **1**.

Hence, there is evidence for the rule that strong electronegative substituents increase the bending of the bonds to which they are attached. From our data (Table 1), we only observe that fluorine-substituted bonds are more strongly bent than CH−CH bonds, but no difference in bending between monofluorinated and difluorinated cage bonds could be detected. The bond possessing the two *cis*-like positioned fluorine substituents, as a model for the *cis*-difluoroethylene isomer, is one of the most strongly bent bonds in the cubane derivative **1** ($d = 0.16$ Å, $\delta = 11.6°$).

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Supporting Information Available: Synthetic experimental descriptions and details of the spectroscopic and X-ray structural data; ^{1}H NMR, ^{19}F NMR, IR, mass spectra, and elemental analysis of **3**, **4**−**6**; positional and thermal parameters, bond lengths and bond angles, and crystallographic information for **3**, **4**, and **1**, as well as further details about the electron density distribution of **1** (16 pages, print/PDF). An X-ray crystallographic file, in CIF format, is available via the Web only. See any current masthead page for ordering information and Web access instructions.

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