

# Dissociation Constants of 4-Substituted Cubane-1-carboxylic Acids. Evidence for the Field Model for the Polar Effect<sup>1</sup>

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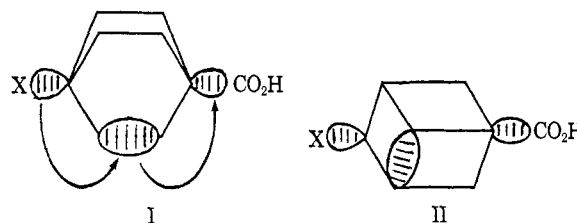
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**Abstract:** The acid dissociation constants of cubane-1-carboxylic acid, 4-bromo-, 4-cyano-, 4-carbomethoxycubane-1-carboxylic acid, and cubane-1,4-dicarboxylic acid have been measured for 50% (weight) aqueous ethanol at 25°. The results for these acids are compared with the results for the corresponding 4-substituted bicyclo[2.2.2]octane-1-carboxylic acids. The  $\log(K/K_H)$  values for both series are similar with  $\rho_1$  (cubane), 1.52, compared to  $\rho_1$  (octane), 1.63. The small differences, which are apparently real, originate in the changed electronegativity of the exocyclic carbon bonding orbital of cubane. These findings suggest that the field model accurately describes the propagation mechanism for the polar effect. There is no evidence for enhanced inductive transmission in either the cubanes with their additional transmission paths or in the octanes with their unique stereochemical relationship between the 1,4 substituents and the C<sub>2</sub>C<sub>3</sub> bond.

Investigations designed to assess the relative merits of the through-bond induction model and the electrostatic field model for the polar effect<sup>2</sup> indicate that the field model offers a better description of the observed influence of monopolar and dipolar substituents.<sup>3</sup> The 4-substituted bicyclo[2.2.2]octane-1-carboxylic acids have been studied in several laboratories during the course of this work.<sup>4</sup> The acids with "electron-withdrawing" substituents, e.g., carbomethoxy, bromo, and cyano in the 4 position, are somewhat stronger, relative to the parent acid, then expected on the basis of the familiar Kirkwood–Westheimer field model for the propagation of dipolar substituent effects.<sup>5</sup> Although the discrepancy between the experimental observations and the calculated value of  $\log(K/K_H)$  is not large, it has received special attention because the bicyclo[2.2.2]octanes occupy a central position in the definition of the Taft  $\sigma_1$  scale<sup>6</sup> and in the experimental work on the propagation mechanism for the polar effect.<sup>3,4</sup> Consequently, several explanations have been advanced for the difference between the experimental and calculated  $\log(K/K_H)$  values. While it seems reasonable to relate the discrepancy to an inadequacy of the quite approximate theory, most investigators have been reluctant to adopt this viewpoint. Rather the discrepancy has been ascribed to an inductive component not considered in the theory,<sup>4a</sup> to an especial interaction between the proximate 1,4 positions of this molecule,<sup>7</sup> or to varia-

tions in solvent–substrate interactions which alter the dielectric environment differently for dipolar substituents than for alkyl or hydrogen substituents.<sup>4b,8</sup> The latter interpretation is supported by the fact that the differences in acid strength among the acids with dipolar groups are predicted by the Kirkwood–Westheimer model<sup>5</sup> and that the results for the ethano and benzo bridged anthroic acids, where solvent structure may be dictated by the dimensions of the molecule rather than by the dimensions of a substituent, do adhere closely to the predictions of the Kirkwood–Westheimer model.<sup>8,9</sup>

Recently, another interpretation for the enhanced acid strength of the bicyclo[2.2.2]octane acids has emerged. The basis for this new suggestion is the important interaction between the lone pair n electrons of 1,4-diazabicyclo[2.2.2]octane as revealed by the photoelectron spectrum.<sup>10,11</sup> The measured ionization potentials for 20 bicyclic diamines, at least in part, support the idea that the exocyclic bonding orbitals at N<sub>1</sub> and N<sub>4</sub> interact *via* the C<sub>2</sub>C<sub>3</sub> bond.<sup>12</sup> Thus, the bicyclo[2.2.2]octane skeleton may have an enhanced inductive transmittivity, I. To test this idea, we have extended an



earlier study of the dissociation constants of cubane-1,4-dicarboxylic acid and bicyclo[2.2.2]octane-1,4-dicar-

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(2) The term polar effect is used to characterize the observed influence of unconjugated, sterically remote substituent on reaction processes. This designation permits the use of the terms inductive effect and field effect for the description of the transmission mechanism.

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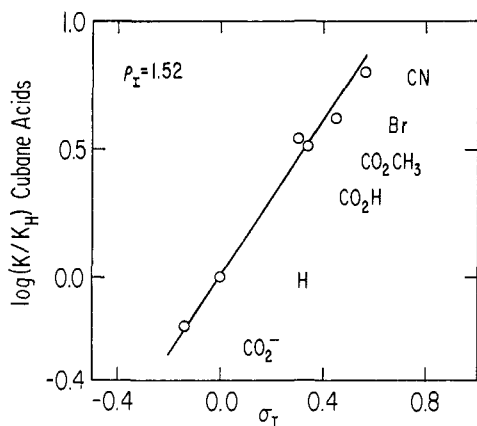


Figure 1. The relationship between  $\log(K/K_H)$  for the 4-substituted cubane-1-carboxylic acids and  $\sigma_I$ .

Table I. Thermodynamic Dissociation Constants for 4-Substituted Cubane carboxylic Acids in 50% (Weight) Aqueous Ethanol at 24.95°

4-Substituent	pK <sub>A</sub>
H	5.94 ± 0.02 (4) <sup>a, b</sup>
CO <sub>2</sub> H	5.43 ± 0.01 (2) <sup>c, d</sup>
CO <sub>2</sub> CH <sub>3</sub>	5.40 ± 0.01 (3)
Br	5.32 ± 0.02 (4)
CN	5.14 ± 0.02 (2)
CO <sub>2</sub> <sup>-</sup>	6.23 ± 0.01 (2) <sup>c, d</sup>

<sup>a</sup> Prior value, 5.95 ± 0.01, ref 8. <sup>b</sup> Number of observations. <sup>c</sup> Reference 8. <sup>d</sup> Statistically corrected.

boxylic acid to include several dipolar substituents. Cubane was selected for comparison with the octane because the distance between the groups in the 1 and 4 positions are identical; however, there is a skew relationship, II, between the exocyclic bonding orbitals at C<sub>1</sub> and C<sub>4</sub> and the C<sub>2</sub>C<sub>3</sub>  $\sigma$  bond diminishing the transmittivity of the cubane. Consequently, differences in substituent effects are to be expected only if the C<sub>2</sub>C<sub>3</sub> linkage plays a role in the transmission of substituent effects.

### Results and Discussion

Conventional methods were used for the synthesis of the acids.<sup>13</sup>

Aqueous ethanol, 50% by weight, was used as the solvent for convenient comparison with the data of other investigations. As in previous studies, the pK of benzoic acid (5.74 ± 0.02) was measured frequently to verify the accuracy of the new constants. The results are summarized in Table I.

The 4-substituted cubane-1-carboxylic acids are each about tenfold stronger acids in 50% aqueous ethanol than the corresponding 4-substituted bicyclo[2.2.2]octane-1-carboxylic acids. To illustrate, the pK for bicyclo[2.2.2]octane-1-carboxylic acid is 6.87 compared to 5.94 for cubane-1-carboxylic acid. The pK for pivalic acid is 6.82 under these conditions. As noted previously,<sup>8</sup> the increased acidity of the cubane acids is related to the increased electronegativity (s character) of the exocyclic carbon bonding orbital in cubane relative to the octane.<sup>14, 15</sup>

(13) The preparation of these acids will be reported subsequently.

(14) The values of  $J^{13C_{CH}}$  for cubane and bicyclo[2.2.2]octane indicate 32 and 27% s character, respectively: P. E. Eaton and T. W. Cole,

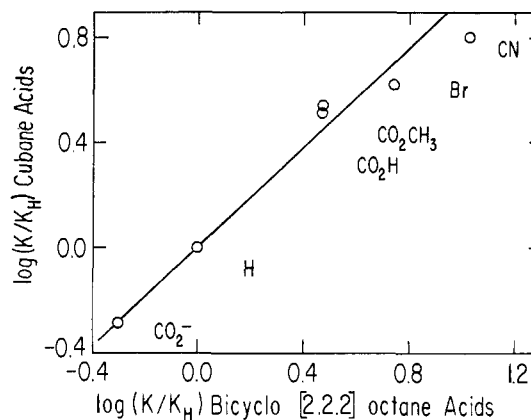


Figure 2. The relationship between  $\log(K/K_H)$  for the 4-substituted cubane-1-carboxylic acids and the 4-substituted bicyclo[2.2.2]octane-1-carboxylic acids.

The relationship between  $\log(K/K_H)$  for the cubanes and  $\sigma_I$  is shown in Figure 1.

Least-squares analysis yields expression 1. The  $\rho_I$

$$\log(K/K_H) = 1.52\sigma_I - 0.02 \quad (1)$$

value, 1.52, is only about 6% less than  $\rho_I$ , 1.63 for the bicyclo[2.2.2]octanes. Consequently, in contrast to the differences in absolute acidity, the  $\log(K/K_H)$  values for the cubane and octane acids differ only modestly. There is no major difference in the transmittivity of the cubane and octane skeletons.

Another important point emerges from a more detailed examination of the data. The relationship between  $\log(K/K_H)$  for the cubanes and the octanes is shown in Figure 2.

The experimental data do not precisely adhere to a linear relationship. In particular the cubanes with bromide and cyanide substituents are somewhat less acidic than expected on the basis of the results for the octanes. On the other hand, the cubanes with carboxylic acid and ester groups appear slightly more acidic than expected. The experimental deviations are small, but apparently real. It is well accepted that changes in hybridization alter the effective bond moments ( $\mu_{CX} - \mu_{CH}$ ).<sup>16-19</sup> Accordingly, some differences in substituent effects are anticipated. The observed pattern is similar to the variations in dipole moments for monosubstituted cyclopropanes and cyclobutanes compared to monosubstituted adamantanes.<sup>20</sup> The changes in acidity are, accordingly, accommodated within the framework of the electrostatic field model. On the basis of these observations we conclude that there is no special inductive path, I, involving the C<sub>2</sub>C<sub>3</sub> bond of the octane. Rather, substituent effects are propagated with nearly equal efficiency in the cubanes and octanes as predicted by the

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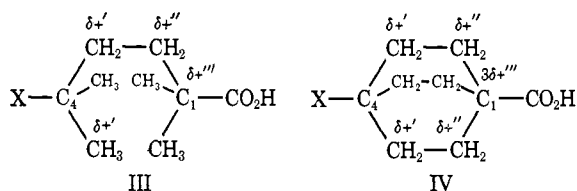
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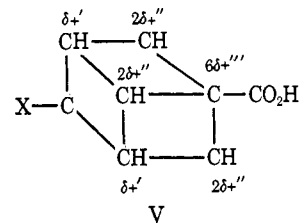
field model. Substituent effects are not identical in the series. However, the deviations may be attributed with some confidence to the influence of changed hybridization on group moments.

In earlier work, it was pointed out that the similar values of  $\log(K/4K_2)$  for bicyclo[2.2.2]octane-1,4-dicarboxylic acid (0.767) and cubane-1,4-dicarboxylic acid (0.798) were compatible with the field model because the distance between the acid groups is the same ( $\pm 0.05$  Å) in these molecules.<sup>8</sup> On the other hand, the results are incompatible with the inductive model because there are 6 three-bond paths in cubane compared to only 3 three-bond paths in the octane.<sup>8</sup>

The observations for the dipolar groups, Figures 1 and 2, reinforce the previous conclusion. The values of  $\log(K/K_H)$  for the cubanes and octanes are sensibly the same. This finding is incompatible with the inductive model which, in its usual form, requires a dependence on the number of paths.<sup>3,8</sup> To illustrate, although the methylene and methyl groups of III are



polarized to an equivalent extent ( $\delta^{+}$ ), only the polarization of the methylene group, according to the inductive model, can be propagated to the reaction site. The propagation of charge to  $C_1$  is enhanced threefold in IV with its three additional connecting links. In cubane, V, there are six connecting links leading to a charge ( $6\delta^{+'''}$ ) at  $C_1$  compared to the charge ( $3\delta^{+'''}$ ) at  $C_1$  of the octane. Consequently, the inductive model requires that substituent effects propagated more effectively in the cubanes. Clearly, our results are incon-



sistent with this prediction.<sup>21</sup> Rather the observations are compatible with the predictions of the field model with its key dependence on the fact that the substituents and the acid groups are equidistant in the octanes and cubanes.

### Experimental Section

The preparation of the cubane acids will be reported subsequently by T. W. Cole. The acids were sublimed, recrystallized, and dried *in vacuo* prior to determination of the dissociation constants. The melting points of the acids are cubane-1-carboxylic acid, 125–126°; cubane-1,4-dicarboxylic acid, 225°; 4-carbomethoxycubane-1-carboxylic acid, 182–183°; 4-bromocubane-1-carboxylic acid, 210° dec; 4-cyanocubane-1-carboxylic acid, 200° dec.

The methods used for the purification of the solvents and reagents employed in the determination of the dissociation constants have been reported previously.<sup>4b,8</sup>

The thermodynamic dissociation constants of the monobasic acids were determined by potentiometric titration.<sup>23</sup> Observations were made using independently prepared solutions of the acids and reagents to randomize experimental error. The dissociation constant for benzoic acid was determined frequently throughout the measurements. The  $pK_A$  value for benzoic acid was  $5.74 \pm 0.02$ , in good agreement with previous results.<sup>8,24</sup>

(21) The charge distributions predicted by the CNDO/2 model do not resemble the predictions of the simple induction model. Hermann has shown that the CNDO/2 model can be molded with the Kirkwood-Westheimer approach to yield a contemporary physical picture of substituent effects in the bicyclo[2.2.2]octanes.<sup>22</sup>

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