

Articles

Manifestations of Bridgehead–Bridgehead Interactions in the Bicyclo[1.1.1]pentane Ring System

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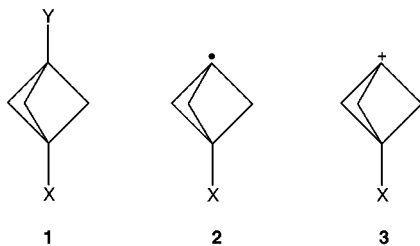
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A series of 3-halo-substituted bicyclo[1.1.1]pentane-1-carboxylic acids **1** (Y = COOH; X = F, Cl, Br, I, and CF₃) as well as the parent compound **1** (Y = COOH, X = H) have been prepared, and a study of some of their properties have been made. It was found that their reactions with xenon difluoride cover a wide range of reactivities. On one hand, the fluoro acid **1** (Y = COOH, X = F) displayed no apparent reaction at all while, on the other, the bromo acid **1** (Y = COOH, X = Br) and parent compound **1** (Y = COOH, X = H) underwent ready reaction with complete disintegration of the ring system. A possible explanation is advanced based on polar kinetic and thermodynamic effects governing the lifetime of an intermediate acyloxy radical species. The relative ease of oxidation of the carboxylates **1** (Y = COO⁻; X = H, F, Cl, Br, I, CF₃, and COOCH₃), as mirrored by their peak oxidation potential values (*E*_p) determined by cyclic voltammetry, also covers a wide range. These data coupled with the dissociation constants (*pK*_a) of some of the acids **1** (Y = COOH; X = H, F, Cl, and CF₃) reflect significantly on the modes of transmission of electronic effects acting through the bicyclo[1.1.1]pentane ring system.

Introduction

Over the years the bridgehead positions of polycycloalkanes have been shown to have considerable utility as probe sites for ascertaining structural and electronic factors underlying various physical and chemical phenomena. In the case of the bicyclo[1.1.1]pentane ring system (**1**) these positions are uniquely disposed being



separated by only ca. 1.85 Å,¹ and hence cross-cage interactions are mandatory. Several striking manifestations of strong bridgehead–bridgehead interactions in this system have now been recorded.^{1–12} Theoretical

considerations have largely centered on through-space interactions between the back- or rear-lobes of the bridgehead bond molecular orbitals which depend sensitively on the electronic characteristics of the substituents or reaction site located at the bridgehead positions.

In this paper we report the surprising course of the reactions between 3-halo and 3-trifluoromethyl-substituted (X) bicyclo[1.1.1]pentane-1-carboxylic acids **1** (X = F, Cl, Br, and CF₃; Y = COOH) and xenon difluoride (XeF₂) which demonstrate further physical and chemical consequences of cross-cage interactions in this small bicyclic ring system. In addition, the dissociation constants of the carboxylic acids **1** (X = H, F, Cl, and CF₃; Y = COOH) have been determined and the electrochemical

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(1) Wiberg, K. B.; Hadad, C. M.; Sieber, S.; Schleyer, P. v. R. *J. Am. Chem. Soc.* **1992**, *114*, 5820 and references therein.

(2) Wiberg, K. B.; Conner, D. S. *J. Am. Chem. Soc.* **1966**, *88*, 4437.

(3) Barfield, M.; Della, E. W.; Pigou, P. E.; Walter, S. R. *J. Am. Chem. Soc.* **1982**, *104*, 3549.

(4) (a) Kaszynski, P.; Michl, J. *J. Org. Chem.* **1988**, *53*, 4593. (b) Wiberg, K. B.; Waddell, S. T. *J. Am. Chem. Soc.* **1990**, *112*, 2194.

(5) Adcock, W.; Krstic, A. R. *Tetrahedron Lett.* **1992**, *33*, 7397.

(6) Toops, D. S.; Barbachyn, M. R. *J. Org. Chem.* **1993**, *58*, 6505.

(7) (a) Maillard, B.; Walton, J. C. *J. Chem. Soc., Chem. Commun.* **1983**, 900. (b) McKinley, A. J.; Ibrahim, P. N.; Balaji, V.; Michl, J. *J. Am. Chem. Soc.* **1992**, *114*, 10631.

(8) Della, E. W.; Grob, C. A.; Taylor, D. K. *J. Am. Chem. Soc.* **1994**, *116*, 6159.

(9) Wiberg, K. B.; McMurdie, N. *J. Am. Chem. Soc.* **1994**, *116*, 11990.

(10) Adcock, W.; Clark, C. I.; Houmann, A.; Krstic, A. R.; Pinson, J.; Savéant, J.-M.; Taylor, D. K.; Taylor, J. F. *J. Am. Chem. Soc.* **1994**, *116*, 4653.

(11) Adcock, W.; Binmore, G. T.; Krstic, A. R.; Walton, J. C.; Wilkie, J. *J. Am. Chem. Soc.* **1995**, *117*, 2758.

(12) Adcock, W.; Krstic, A. R. *Magn. Reson. Chem.* **1997**, *35*, 663.

Table 1. Product Distribution of the Reaction between 3-Substituted (X) Bicyclo[1.1.1]pentane-1-carboxylic Acids **1** (Y = COOH) and Xenon Difluoride

entry no.	X	equiv of XeF ₂	solvent	product distribution proportions, % ^a				
				1 , Y = F	1 , Y = Cl	1 , Y = D	dimer	1 , Y = COOH ^b
1	F	2.5	CD ₂ Cl ₂	0	0	0	0	100
2	F	1.2	CDCl ₃	0	0	0	0	100
3	Cl	3.0	CD ₂ Cl ₂	trace ^c	23	11	3	63
4	Cl	4.0	CDCl ₃	0	20	27	4	49
5	Br	1.5	CD ₂ Cl ₂	0	0	0	0	0
6	CF ₃	2.5	CD ₂ Cl ₂	4	19	7	5	65
7	CF ₃	4.0	CDCl ₃	trace ^c	10	36	4	50

^a Relative proportions determined by ¹H NMR. ^b Unreacted precursor acid. ^c Detected by ¹⁹F NMR.

oxidation of some carboxylates **1** (X = H, F, Cl, Br, I, CF₃, and COOCH₃; Y = COO⁻) also investigated by means of cyclic voltammetry. As we shall see below, the acidity constants (pK_a values) and peak potential data (E_p values) from the latter work bear significantly on the nature and transmission of substituent electronic effects in the [1.1.1] system (**1**).

Results and Discussion

Xenon Difluoride Reactions. All the reactions were carried out in 5 mm NMR tubes and their progress monitored by ¹H NMR. The latter measurements were facilitated by the use of deuterated solvents (CD₂Cl₂ or CDCl₃). The product mixtures were finally characterized by ¹³C NMR. Spectral assignments followed unequivocally from the additivity of chemical shifts utilizing appropriate data from well characterized compounds. One of the reactions, namely, the attempted fluorodecarboxylation of the fluoro acid **1** (X = F, Y = COOH) was also performed on a preparative scale.

The original impetus behind this work was the desire to synthesize 1,3-difluorobicyclo[1.1.1]-pentane **1** (X = Y = F) which was required in connection with a ¹⁹F chemical shift study of an extensive series of 3-substituted (X) bicyclo[1.1.1]pent-1-yl fluorides **1** (Y = F).⁵ Although previous attempts to introduce fluorine at the bridgehead of the bicyclo[1.1.1]pentane system by treatment of the appropriate carboxylic acid with XeF₂ (fluorodecarboxylation)^{13,14} were unsuccessful,^{13b,c,14,15} we were encouraged to try the reaction by the knowledge that the desired difluoride **1** (X = Y = F) has been detected among the products from the photochemical reaction of the fluoro bromide **1** (X = F, Y = Br) with triethylsilane.¹¹ This result was ascribed to disproportionation of two 3-fluorobicyclo[1.1.1]pent-1-yl radicals **2** (X = F). Unfortunately, treatment of a mixture of the fluoro carboxylic acid **1** (X

= F, Y = COOH) and its parent **1** (X = H, Y = COOH) in the ratio 71:29,¹¹ respectively, with 1.5 equiv of XeF₂ in CD₂Cl₂ or CDCl₃ did not lead to the formation of the difluoride **1** (X = Y = F).¹⁶ It was found that on gradual addition of XeF₂ the parent acid was eventually consumed, but surprisingly **1** (X = F, Y = COOH) appeared to remain unchanged even after 4 days at room temperature. The reaction of the former compound apparently occurred via the kinetically labile parent cation **3** (X = H)^{1,8,9} rather than the corresponding radical **2** (X = H)^{1,7} since no obvious products were detected to suggest that the integrity of the ring system was maintained.^{7–9} When the reaction of the carboxylic acid mixture **1** (X = F, Y = COOH and X = H, Y = COOH) was carried out on a preparative scale, it was found that **1** (X = F, Y = COOH) could be recovered in a relatively pure state (>95% by ¹H and ¹³C NMR) from the reaction in good yield (ca. 80%)! This remarkable resistance of the fluoro acid to oxidative decarboxylation on treatment with XeF₂ stands in stark contrast to the result for the parent acid as well as the previously investigated 3-carbomethoxy^{13c,14} and 3-phenyl^{13b,15} derivatives **1** (X = COOCH₃, Y = COOH and X = C₆H₅, Y = COOH, respectively). The latter two compounds both gave good yields of reduction product **1** (X = COOCH₃, Y = H and X = C₆H₅, Y = H(D), respectively) as a result of solvent hydrogen (or deuterium) abstraction by the reactive radical intermediates **2** (X = COOCH₃ and C₆H₅) formed on ready decarboxylation. The unexpected result for **1** (X = F, Y = COOH) prompted us to examine the behavior of some other halo acids **1** (X = Cl, Br, and CF₃; Y = COOH) toward XeF₂. The product distribution of these reactions in CD₂Cl₂ and CDCl₃ are set out in Table 1 together with the results of **1** (X = F, Y = COOH).

Before scrutiny of the data (Table 1) in detail it is instructive to take note of the generally accepted mechanism for fluorodecarboxylation at the bridgehead of polycyclic systems (Scheme 1).^{13c,18}

It can be seen that the first step is the formation of a thermally labile fluoroxenon ester (eq 1). This intermediate has been directly observed and studied in the case of trifluoacetic acid.¹⁹ It subsequently decomposes to give the radical as an intermediate (eqs 2–4). The exact mode of fragmentation of the xenon ester is unknown but there

(13) (a) Patrick, T. B.; Johri, K. K.; White, D. H. *J. Org. Chem.* **1983**, *48*, 4159. (b) Patrick, T. B.; Johri, K. K.; White, D. H.; Bertrand, W. S.; Mokhtar, R.; Kilbourn, M. R.; Welch, M. J. *Can. J. Chem.* **1986**, *64*, 138. (c) Patrick, T. B.; Khazaeli, S.; Nadji, S.; Hering-Smith, K.; Reif, D. *J. Org. Chem.* **1993**, *58*, 705.

(14) Della, E. W.; Head, N. J. *J. Org. Chem.* **1992**, *57*, 2850.

(15) Kaszynski, P.; McMurdie, N. D.; Michl, J. *J. Org. Chem.* **1991**, *56*, 307.

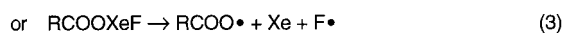
(16) An attempt to obtain the desired difluoride **1** (X = Y = F) by fluorodeiodination¹⁴ was also unsuccessful. Treatment of a mixture of the fluoro iodide **1** (X = F, Y = I) and the parent iodide **1** (X = H, Y = I) in the ratio of 71:29, respectively, with a total of 3.0 equiv of XeF₂ led to the consumption of both iodides, the latter much more rapidly than the former. However, no bicyclo[1.1.1]pentyl products were identified. Only noncharacterizable degradation products were observed. Thus, the reaction outcome displays all the hallmarks of not only the parent cation (**3**, X = H) being a nondiscrete species^{8,9} but also the 3-fluoro cation **3** (X = F) as well. It is noteworthy that the latter species has been calculated (MP2/6-31G*) to be a transition state.⁹ Treatment of the diiodide **1** (X = Y = I) with XeF₂ in CF₂ClCClF₂ also failed to yield **1** (X = Y = F).

(17) (a) Della, E. W.; Pigou, P. E.; Schiesser, C. H.; Taylor, D. K.; *J. Org. Chem.* **1991**, *56*, 4659. (b) Banks, J. T.; Ingold, K. U.; Della, E. W.; Walton, J. C. *Tetrahedron Lett.* **1996**, *37*, 8059.

(18) Tius, M. A. *Tetrahedron* **1995**, *51*, 6605.

(19) Eisenberg, M.; Des Marteau, D. D. *Inorg. Nucl. Chem. Lett.* **1970**, *6*, 29.

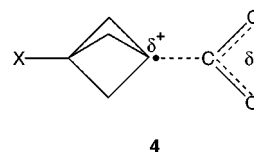
Scheme 1



is some evidence^{20,21} that it is initiated by simple homolytic bond scission (eq 2 or 3) rather than simultaneous multibond fission to give the radical and carbon dioxide directly ($\text{RCOOXeF} \rightarrow \text{R}\cdot + \text{CO}_2 + \cdot\text{XeF}$). The radical is then believed to either yield the fluoride directly (eq 5) or indirectly via a carbocation (eqs 6 and 7). It is important to note that there is no evidence to exclude the possibility that a carbocation may be formed directly from the fluoroxenon ester by heterolytic fission ($\text{RCOOXeF} \rightarrow \text{R}^+ + \text{CO}_2 + \text{Xe} + \text{F}^-$) rather than being formed from the radical by electron transfer (eq 6). Some attempts to observe the expected intermediate ester **1** ($\text{X} = \text{F}$, $\text{Y} = \text{COOXeF}$) by ¹⁹F and ¹²⁹Xe NMR were unsuccessful although the signals of XeF₂ were clearly identifiable (see Experimental Section). These experiments suggest two possibilities. Either XeF₂ fails to react with **1** ($\text{X} = \text{F}$, $\text{Y} = \text{COOH}$), although **1** ($\text{X} = \text{CF}_3$, $\text{Y} = \text{COOH}$) and **1** ($\text{X} = \text{Cl}$, $\text{Y} = \text{COOH}$) do (see later), or XeF₂ reacts with **1** ($\text{X} = \text{F}$, $\text{Y} = \text{COOH}$) but the product rapidly decomposes to **1** ($\text{X} = \text{F}$, $\text{Y} = \text{COO}\cdot$) which abstracts deuterium from the solvent (CD₃CN) to yield **1** ($\text{X} = \text{F}$, $\text{Y} = \text{COOD}$). The latter appears the more likely. In light of the aforementioned result for the parent acid **1** ($\text{X} = \text{H}$) from this study and the known radical nature of the reaction for the 3-carbomethoxy^{13c,14} and 3-phenyl^{13b,15} acid derivatives **1** ($\text{X} = \text{COOCH}_3$, $\text{Y} = \text{COOH}$ and $\text{X} = \text{C}_6\text{H}_5$, $\text{Y} = \text{COOH}$, respectively), the competition between the two mechanistic pathways (radical versus ionic) is obviously finely tuned in this system. Thus, even the presence of a relatively weak electron-withdrawing polar group such as 3-C₆H₅ is sufficient to ensure that a radical course is maintained.

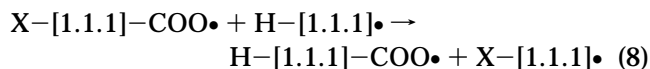
With these mechanistic details in mind the complex pattern of reactivity indicated by the results listed in Table 1 brings to light several noteworthy features. First, it can be seen that except for **1** ($\text{X} = \text{Br}$, $\text{Y} = \text{COOH}$), which will be discussed separately below, there is a general reluctance of the acids **1** ($\text{X} = \text{F}$, Cl , and CF_3 , $\text{Y} = \text{COOH}$) to be consumed by reaction with XeF₂. This result is in marked contrast to the ready decarboxylation of the other 3-substituted acids **1** ($\text{X} = \text{C}_6\text{H}_5$ and COOCH_3 , $\text{Y} = \text{COOH}$) noted above. If the common view is accepted that the reaction involves the formation of an acyloxy radical species (eq 2 or 3), the apparent lack of reactivity of the acids listed in Table 1 can be explained by the rate of the usually very rapid fragmentation step (eq 4)²² being significantly retarded. Thus, the fate of the acyloxy

radical is then governed by a competition between hydrogen (or deuterium) atom abstraction from the solvent versus fragmentation. The former reaction simply regenerates the precursor carboxylic acid. It is important to note that there is precedence in the literature for the electrostatic field influence of electron-withdrawing dipolar substituents being an important factor in significantly reducing decarboxylation rates of alkyl acyloxy radicals.²³ The strong deactivation by F, Cl and CF₃ suggests charge transfer in the transition state as shown in structure **4**.



4

However, because the strong electrostatic field effects (σ_{F}) of F, Cl, and CF₃ are virtually identical (see below), the completely unreactive fluoro-acid suggests an additional factor is involved besides a kinetic polar effect. In an attempt to shed light on the matter we have calculated energies (Table 2) for the reactants and products of the isodesmic reaction shown (eq 8).



The effect of the substituents on the energy (kcal/mol) of the reaction determined at the same level of theory (UHF/6-31G* and UMP2/6-31G**//UHF/6-31G*) are as follows: 2.70 (F), 0.28 (Cl), -0.77 (CF₃) and 3.29 (F), 0.23 (Cl), -1.19 (CF₃), respectively. The energy for F was 2.86 kcal/mol when estimated from energies obtained with geometries fully optimized at the UMP2/6-31G* level of theory. Clearly decarboxylation of the fluoro acyloxy radical of **1** ($\text{X} = \text{F}$, $\text{Y} = \text{COO}\cdot$) is thermodynamically less favorable than the other radicals of **1** ($\text{X} = \text{H}$, Cl , or CF_3 , $\text{Y} = \text{COO}\cdot$). Thus, both kinetic and thermodynamic factors appear responsible for the remarkable behavior of the fluoro acid. Defining the predominant origin of the latter factor requires consideration of the relative importance of stabilizing through-space interactions ($\sigma_{\text{CX}}^* - \sigma$; homohyperconjugation) in the product radical¹⁰ versus polar ground-state stabilization/destabilization energies.²⁴ There are two components to the latter phenomenon: (i) an electronegativity effect which impinges significantly on the degree of nonbonded repulsion between the bridgehead positions as evidenced by the change in length of the bridgehead to bridgehead distance (C1 to C3) on bridgehead substitution.^{9,11,25} This will be stabilizing for σ -electron-withdrawing groups ($\text{F} > \text{Cl} > \text{CF}_3$; see later). It should be noted that this effect is expected to be much more pronounced for the closed shell structures at the bridgehead (precursor acyloxy radical) than for the open shell species (product bridgehead radicals). (ii) a Coulombic effect due to electrostatic destabilization of the starting or parent structure (**1**, $\text{Y} = \text{CO}_2\cdot$) due to unfavorable dipole-dipole through-space interactions between $\text{C}^{\delta+}-\text{X}^{\delta-}$ and $\text{C}^{\delta+}\text{OO}^{\delta-}$. The mag-

(20) Bardin, V. V.; Yagupolskii, Yu. L. Xenon Difluoride. In *New Fluorinating Agents in Organic Synthesis*; German, L., Zemskov, S., Eds.; Springer-Verlag: Berlin, New York, 1989; Chapter 1.

(21) Gregorcic, A.; Zupan, M. *J. Org. Chem.* **1979**, *44*, 4120.

(22) Hilborn, J. W.; Pincock, J. A. *J. Am. Chem. Soc.* **1991**, *113*, 2683 and references therein.

(23) Traylor, T. G.; Sieber, A.; Kiefer, H.; Clinton, N. *Intra-Sci. Chem. Rep.* **1969**, *3*, 289.

(24) Nau, W. M. *J. Org. Chem.* **1996**, *61*, 8312 and references therein.

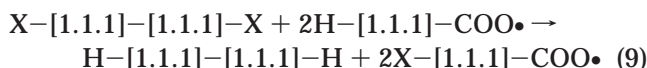
(25) Wiberg, K. B. *Tetrahedron Lett.* **1985**, *26*, 599.

Table 2. Calculated Energies^{a,b}

molecule ^c	UHF/6-31G*	UMP2/6-31G*	UMP2/6-31G*/UHF/6-31G*	ZPVE
H-[1.1.1]-COO•	-380.894675	-381.972753	-381.972839	80.7
F-[1.1.1]-COO•	-479.751611	-480.997161	-480.997059	75.5
Cl-[1.1.1]-COO•	-839.8012296		-841.011627	74.5
CF ₃ -[1.1.1]-COO•	-716.521213		-718.230260	84.5
H-[1.1.1]•	-193.264893	-193.894170	-193.892097	70.6
F-[1.1.1]•	-292.117949	-292.914454	-292.911339	65.7
Cl-[1.1.1]•	-652.171432		-652.930952	64.7
CF ₃ -[1.1.1]•	-528.891226		-530.150144	73.5

^aTotal energies in hartrees. ^bZero-point vibrational energy (ZPVE; kcal/mol) computed at the UHF/6-31G* level. ^c1,3-Disubstitutedbicyclo[1.1.1]pentanes ≡ X-[1.1.1]-Y.

nitude of this effect can be estimated by calculating the isodesmic energy of reaction 9 which effectively segregates the polar

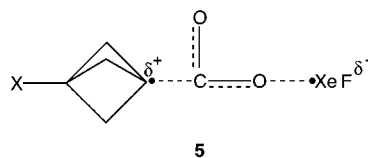


field influence from radical stabilization energy in the product²⁴ and, as well, from the electronegativity effect in the precursor. The similar energies (kcal/mol) of reaction 9 (2.91(F), 3.58(Cl), and 3.75(CF₃)) determined at the RHF/6-31G* (X-[1.1.1]-[1.1.1]-X, calculated energies (hartrees): -386.663319 (H), -584.38183 (F), -1304.482133 (Cl), -1057.922376 (CF₃)) and UHF/6-31G* (see Table 2) level of theory are in accord with various empirical scales of electrostatic field effects of these substituents (see later).

The energetics of reaction 9 for X = F, coupled with the fact that resonance stabilization of the product radical by F is obviously small,¹⁰ leads us to conclude that the unfavorable thermodynamic factor for this substituent (from reaction 8) is governed by a large decrease in the strain energy (>6 kcal/mol) of 1 (X = F, Y = COO•) relative to the parent system 1(X = H, Y = COO•). This is due to the very electronegative fluorine removing electron density from the carbon bridgehead orbital and, thus, significantly reducing 1,3 nonbonded repulsion^{9,25} (the calculated C1–C3 bond distance in 1 (Y = COO•) is 1.865 and 1.823 Å for X = H and F, respectively). This decrease is less pronounced in the radical and translates into a strengthening of the C–COO• bond in 1 (X = F, Y = COO•)(C1–COO• bond distances are 1.497 and 1.491 Å for X = H and F, respectively). It is pertinent to note that high-level ab initio calculated bond dissociation energies of bicyclo[1.1.1]pentanes (1)¹¹ indicate that the C–H bond strength is increased by ca. 4 kcal/mol on 3-fluoro substitution of 1 (X = F, Y = H). Moreover, an electrochemical study of 1-halo- and 1,3-dihalobicyclo[1.1.1]pentanes¹⁰ revealed a significant increase in the strength of the bridgehead C–Br and C–I bonds when H at the other bridgehead is replaced by fluorine. It should be noted that the calculated energy of reaction 8 for Cl (0.23 kcal/mol) appears far too positive in the light of the aforementioned electrochemical study¹⁰ which suggests that a 3-chloro substituent strongly stabilizes (ca. 5.0 kcal/mol) the bicyclo[1.1.1]pent-1-yl radical. Additionally, the calculated energy of reaction 9 for Cl (3.58 kcal/mol) indicates a substantial destabilization of the precursor 1 (X = Cl, Y = COO•) by a polar field effect which augments the resonance stabilization of the product radical contributing to the isodesmic energy of reaction 8.

An alternative explanation for the strong deactivation by X = F, Cl, and CF₃ relative to X = H in the reaction

of 1 (Y = COOH) with XeF₂ can be advanced based on the idea that the rate-determining step of the reaction involves simultaneous multibond scission (eqs 2 (or 3) and 4 occur in one step) of the initially formed fluoroxenon ester. If the transition state for such a mechanistic scenario has significant charge separation as depicted in structure 5 then similar polar kinetic and thermodynamic factors to those described above would prevail in deter-



mining reactivities. However, our inability to identify the formation of a fluoroxenon ester in the case of 1 (X = F, Y = COOH) makes this an unlikely possibility.

The idea that 1 (X = F, Y = COO•) is much more resistant to decarboxylation than the parent (X = H, Y = COO•) prompted us to effect oxidative decarboxylation (Ag⁺/S₂O₈²⁻)²⁶ on a mixture of the acids in a biphasic system (H₂O/cyclohexane)²⁷ in an attempt to purify the fluoro compound. We found after 15 min at 70 °C that the parent acid is completely destroyed while the 3-fluoro derivative (1; X = F, Y = COOH) can be recovered almost quantitatively. If it is assumed that both acids are oxidized, then the result suggests that decarboxylation of 1 (X = F, Y = COO•) is too slow to compete with hydrogen abstraction from c-C₆H₁₂ (1.4 × 10⁶ M⁻¹ s⁻¹ in CCl₄ for C₆H₅COO• at 24 °C).²⁸ Given that the rate of decarboxylation of the cyclopropane carboxyl radical is of the order of 10⁹ s⁻¹ at 80 °C²⁹ (ca. 10⁸ s⁻¹ at 25 °C)²⁹ and, therefore, the parent 1 (X = H, Y = COO•) is probably fairly similar, this is a most dramatic substituent effect. However, a caveat to this interpretation is that oxidation of the fluoro acid 1 (X = F, Y = COOH) relative to the parent 1 (X = H, Y = COOH) by Ag⁺/S₂O₈²⁻ may be very slow (see electrochemical study below).

Second, as noted above the complete consumption of the bromo acid 1 (X = Br, Y = COOH) is exceptional among the halo acids listed in Table 1. Here the strong deactivating kinetic polar effect is apparently overwhelmed by the thermodynamic factor. It is known that 3-bromo substitution strongly stabilizes (>10 kcal/mol)¹⁰ the bicyclo[1.1.1]pent-1-yl radical and, therefore, is mani-

(26) Anderson, J. M.; Kochi, J. K. *J. Am. Chem. Soc.* **1970**, *92*, 1651.

(27) (a) Cyclohexane is a very effective hydrogen atom donor.^{27b} (b) Quiclet-Sire, B.; Zard, S. Z. *J. Am. Chem. Soc.* **1996**, *118*, 9190 and references therein.

(28) Chateaufneuf, J.; Luszyk, J.; Ingold, K. U. *J. Am. Chem. Soc.* **1988**, *110*, 2886.

(29) Fujimori, K.; Hirose, Y.; Oae, S. *J. Chem. Soc., Perkin Trans. 2* **1996**, 405.

fested by a considerable weakening of the C–COO• bond in **1** (X = Br, Y = COO•). Because the reaction leads to the formation of only uncharacterizable degradation products, fragmentation of the bicyclic ring system via a kinetically labile bridgehead cation species is implied (see above). This is explained by the known ready decomposition of the 3-bromobicyclo[1.1.1]pent-1-yl radical **2** (X = Br) to give [1.1.1]propellane³⁰ which subsequently reacts with hydrogen fluoride.³¹

Third, the product distributions for the reactions of 3-chloro- and 3-trifluoromethyl acids **1** (X = Cl and CF₃, Y = COOH, respectively) are noteworthy for two reasons (Table 1): (i) The reaction of alkyl radicals with CH₂Cl₂ (or CD₂Cl₂) and HCCl₃ (or DCCl₃) usually leads to exclusive H-atom abstraction.³² This chemoselectivity is governed primarily by the stability of the incipient radical.^{32b} However, it can be seen that the reactions of the 3-chloro- and 3-trifluoromethylbicyclo[1.1.1]pent-1-yl radicals **3** (X = Cl and CF₃, respectively) with the respective solvents are not chemoselective. Note that Cl-atom abstraction competes significantly against H-atom abstraction in both solvents. In fact the former is the dominant pathway in CD₂Cl₂. Since it is known that both enthalpic and polar factors are important in determining the rates of H-atom abstraction,³³ we ascribe this unusual result to the latter phenomenon. It should be noted that we have already drawn attention to the importance of kinetic polar effects in the chemical behavior of the 3-fluoro radical species **3** (X = F).¹¹ (ii) Given that dimerization of highly reactive bicyclo[1.1.1]pent-1-yl radicals^{7,17} is a most unlikely result, the formation of significant amounts of dimer (X = Cl, CF₃, and COOCH₃) is perplexing. We can only speculate that this observation implies the formation of a xenon ester ((X–[1.1.1]–COO)₂Xe) which undergoes multiple bond homolytic fission with extrusion of CO₂ and subsequent cage dimerization of the bicyclopentyl radicals within the coordination sphere of xenon. Interestingly, xenon bis-(trifluoroacetate) decomposes on standing to give Xe, CO₂, and C₂F₆.¹⁹

Finally, we wish to report that treatment of the half-ester (**1**; X = COOCH₃) with XeF₂ (3.5 equiv) in CD₂Cl₂ gave a product mixture which contained a significant amount (27%) of the known fluoride **1** (X = COOCH₃, Y = F) together with the deuterium derivative **1** (X = COOCH₃, Y = D; 27%), the dimer (5%), and unreacted precursor acid (41%). This contrasts with the results obtained previously in CHCl₃^{13c} and CH₂Cl₂¹⁴ in which only the reduction product **1** (X = COOCH₃, Y = H) was isolated. Note also that a significant amount of the fluoride **1** (X = CF₃, Y = F) was found in the product mixture from treatment of the trifluoromethyl acid **1** (X = CF₃, Y = COOH) with XeF₂ in CD₂Cl₂ (Table 1).

pK_a Measurements. The pK_a values for some 3-substituted (X) bicyclo[1.1.1]pentane-1-carboxylic acids **1** (X = H, F, Cl, and CF₃; Y = COOH) were determined and are given in Table 3.

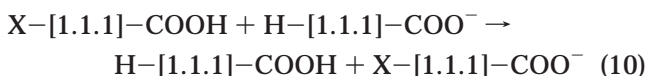
Table 3. Acidities of 3-Substituted (X) Bicyclo[1.1.1]pentane-1-carboxylic Acids **1 (Y = COOH) in 50% (by weight) Aqueous Ethanol at 25 °C**

X	pK _a ^{a,c}	pK _a ^{b,c}
H	5.63 ± 0.05 (0.00)	5.71 ± 0.06 (0.00)
F	4.84 ± 0.04 (0.79)	4.90 ± 0.07 (0.81)
Cl	4.69 ± 0.14 (0.94) ^d	4.66 ± 0.08 (1.05)
CF ₃	4.75 ± 0.06 (0.88)	4.82 ± 0.05 (0.89)

^a Determined by conductometry. ^b Determined by potentiometric titration. ^c ΔpK_a values in parentheses. ^d Extrapolated to time zero.

Unfortunately, a value for the bromo acid could not be obtained due to its rapid solvolysis. A similar but more tractable problem was also encountered with the corresponding chloro compound. Thus, the uncertainty associated with the measurement of this particular acid is greater than that for the other compounds (Table 3). An inspection of the results reveals that the acidity differences (ΔpK_a's) clearly do not parallel the electronegativity order of the substituents (F > Cl > CF₃).³⁴ The observed order is more in accord with expectations based on their polar field effects (σ_F values (CH₃OH): F, 0.41; Cl, 0.43; CF₃, 0.42),³⁵ namely, F ~ Cl ~ CF₃. Other empirical scales also suggest small differences in electrostatic field effects for these groups.³⁶ Thus, the substituent influence on the acidities of **1** (X = F, Cl, and CF₃; Y = COOH) can be ascribed exclusively to the direct through-space interaction of the substituent dipole with the negative charge in the carboxylate ion. This situation corroborates an earlier deduction of Applequist et al.³⁷ that the acidities of such acids could be described satisfactorily in terms of an electrostatic field model, and agrees with conclusions drawn recently from a study of hexafluorinated bicyclo[1.1.1]pentane-1,3-dicarboxylic acids.³⁸

It is of interest to note that the order of the calculated (RHF/6-31+G*) effects of the substituents on the energy (ΔE(kcal/mol): F, –6.3; Cl, –8.3; CF₃, –8.5) of the isodesmic reaction (eq 10) in a vacuum is in reasonable agreement with the aforementioned experimental order.



Most pertinently, the calculated values parallel precisely the σ_F parameters in nonpolar solvents (c-C₆H₁₂ or CCl₄: F, 0.39; Cl, 0.43; CF₃, 0.44)³⁵ which are more likely to mirror the gas phase environment. Finally, it is worth noting that the above picture is similar to one finally painted for the acidities of 4-substituted (X) bicyclo[2.2.2]octane-1-carboxylic acids.³⁹ Data from this latter system underpin the empirical parameters (σ₁ ≡ σ_F) which characterize polar field effects of substituents.

Electrochemical Measurement. The discovery that oxidative decarboxylation of bicyclo[1.1.1]pentane-1-car-

(30) (a) Della, E. W.; Taylor, D. K. *J. Org. Chem.* **1994**, *59*, 2986. (b) Taylor, D. K. Ph.D. Dissertation, The Flinders University of South Australia, Adelaide, 1993.

(31) Adcock, J. L.; Gakh, A. A. *J. Org. Chem.* **1992**, *57*, 6206.

(32) (a) Free Radicals in Organic Chemistry; Fossey, J., Lefort, D., Sorba, J., Eds.; Wiley: New York, 1995; p 129. (b) Bernardi, F.; Bottoni, A. *J. Phys. Chem. A* **1997**, *101*, 1912 and references therein.

(33) Dolbier, W. R., Jr. *Chem. Rev.* **1996**, *96*, 1557 and references therein.

(34) Marriott, S.; Reynolds, W. F.; Taft, R. W.; Topsom, R. D. *J. Org. Chem.* **1984**, *49*, 959.

(35) Adcock, W.; Abeywickrema, A. N. *J. Org. Chem.* **1982**, *47*, 2957.

(36) (a) Hansch, C.; Leo, A.; Taft, R. W. *Chem. Rev.* **1991**, *91*, 165 and references therein. (b) Reynolds, W. F.; Gomes, A.; Maron, A.; McIntyre, D. W.; Tamin, A.; Hamer, G. K.; Peat, I. R. *Can. J. Chem.* **1983**, *61*, 2376.

(37) Applequist, D. E.; Renken, T. L.; Wheeler, J. W. *J. Org. Chem.* **1982**, *47*, 4985.

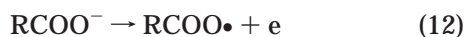
(38) Levin, M. D.; Hamrock, S. J.; Kaszynski, P.; Shtarev, A. B.; Levina, G. A.; Noll, B. C.; Ashley, M. E.; Newmark, R.; Moore, G. G. I.; Michl, J. *J. Am. Chem. Soc.* **1997**, *119*, 12750.

(39) Koppel, I. A.; Mishima, M.; Stock, L. M.; Taft, R. W.; Topsom, R. D. *J. Phys. Org. Chem.* **1993**, *6*, 685.

boxylic acids **1** (Y = COOH) on treatment with XeF₂ (see above) varies markedly with the electronic character of the 3-substituent (X) suggested that an electrochemical study of the corresponding carboxylate anions (**1**, Y = COO⁻) might be fruitful in providing insight into the mechanism outlined in Scheme 1, in particular, on the intermediacy of the RCOO• radical. The first stage of the anodic oxidation of carboxylates (Kolbe reaction)⁴⁰ involves the transfer of one electron to the electrode from RCOO⁻ with subsequent formation of the radical (R•) and CO₂ (eq 11).



The question of whether this process is concerted (eq 11) or stepwise (eq 12 and 13) is a subject of continuing debate.⁴¹



We reasoned that if as suggested above the 3-fluoro-bicyclo[1.1.1]pentane-1-carboxyl radical **1** (X = F, Y = COO•) has a significant lifetime it might be possible to observe it as an intermediate in the Kolbe reaction. Thus, by using very fast scan rates in a cyclic voltammetry experiment the usual irreversible anodic reaction of a carboxylate might become reversible and, therefore, provide quantitative information on the rate of fragmentation of RCOO• (eq 13).²²

The experiments were carried out in acetonitrile in the presence of 0.1M n-Bu₄NBF₄ at a glassy carbon electrode. The carboxylates were prepared in the electrochemical cell by addition of a slightly less than stoichiometric amount of n-Bu₄NOH to the appropriate carboxylic acid so as to avoid oxidation of OH⁻. All the cyclic voltammograms of the carboxylates at a scan rate of 0.2 V/s gave respectable single irreversible anodic waves which correspond to a one-electron stoichiometry as previously observed for some aryl acetates.⁴² Unfortunately, a discrepancy between the peak-width and the variation of the peak potential with the scan rate placed limitations on the investigation. Thus, the assignment of the mechanism (concerted versus stepwise) is uncertain. No reversibility was observed on going to a very high scan rate in the case of the fluoro carboxylate **1** (X = F, Y = COO⁻).

The peak potential data (*E*_p) for the carboxylates of **1** (X = H, F, Cl, Br, I, CF₃, and COOCH₃; Y = COO⁻) are listed in Table 4.

It can be seen that there is a striking variation in the ease of oxidation of the compounds. The importance of an electron-withdrawing electrostatic field influence is highlighted by the deactivating effect of most of the substituents (X = F, Cl, CF₃, and COOCH₃). However,

(40) (a) Kolbe, H. *Ann. Chem.* **1849**, 69, 257. (b) Wurtz, A. *Ann. Chim. Phys.* **1855**, 44, 291.

(41) (a) Ebersson, L. *Acta Chem. Scand.* **1963**, 17, 2004. (b) Ebersson, L. *Electrochim. Acta* **1967**, 12, 1473. (c) Vijh, A. K.; Conway, B. E. *Chem. Rev.* **1967**, 67, 623 (d) Coleman, J. P.; Lines, R.; Utley, J. H. P.; Weedon, B. C. L. *J. Chem. Soc., Perkin Trans. 2* **1974**, 1064. (e) Kraeutler, B.; Bard, A. J. *J. Am. Chem. Soc.* **1978**, 100, 2239. (f) Kraeutler, B.; Bard, A. J. *J. Am. Chem. Soc.* **1978**, 100, 4903. (g) Schäfer, H. J. *Angew. Chem., Int. Ed. Engl.* **1981**, 20, 911. (h) Vassiliev, Y. B.; Grinberg, V. A. *J. Electroanal. Chem.* **1990**, 283, 359. (i) Vassiliev, Y. B.; Grinberg, V. A. *J. Electroanal. Chem.* **1991**, 308, 1.

(42) Andrieux, C. P.; Gonzalez, F.; Savéant, J.-M. *J. Am. Chem. Soc.* **1997**, 119, 4292.

Table 4. Peak Potentials of **1 (Y = COO⁻)**

X	<i>E</i> _p ^{a,c}
H	1.15
F	1.47
Cl	1.38
Br	0.90
I	0.39
CF ₃	1.37
COOCH ₃	1.22

^a Solvent, acetonitrile. ^b At 0.2 V/s, in V vs SCE. ^c Accurate to ±5 mV.

the poor correlation between the *E*_p values and polar field constants (*σ*_F)³⁵ strongly indicates that other factors are at play as well. In this respect, the impressive difference (1.08 V) between the *E*_p values for the fluoro and iodo carboxylates (Table 4; X = F and I) is illuminating since it is reminiscent of the large difference (0.72 V) between the peak reduction potentials of 1-fluoro-3-iodobicyclo[1.1.1]pentane **1** (X = F, Y = I) and 1,3-diiodobicyclo[1.1.1]pentane **1** (X = Y = I).¹⁰ By means of dissociative electron-transfer theory the latter result has been shown¹⁰ to be due to stabilizing through-space interactions (homohyperconjugation) largely in the product radical derived from the diiodide and, as well, stabilization of the starting fluoro iodide due to the very electronegative fluorine reducing 1,3 nonbonded repulsion. Thus, if it is assumed that the loss of CO₂ occurs in the rate-determining step of the anionic oxidation (concerted (eq 11) or stepwise (eq 13)) a qualitative appreciation of the *E*_p trends (Table 4) can be achieved by consideration of the aforementioned three factors (polar field effect, homohyperconjugation (*σ*^{*}_{C-X-σ}), and 1,3-nonbonded repulsion). Finally, it is of interest to note that there is a distinct parallelism between the oxidizability of the carboxylates **1** (Y = COO⁻) and the ease of oxidative decarboxylation of the corresponding acids **1** (Y = COOH) with XeF₂. Hence, it is not surprising that similar factors appear to govern both processes.

Experimental Section

Synthesis of Compounds. Literature procedures were followed in the preparation of 3-chlorobicyclo[1.1.1]pentane-1-carboxylic acid **1** (X = Cl, Y = COOH),³⁰ 3-bromobicyclo[1.1.1]pentane-1-carboxylic acid **1** (X = Br, Y = COOH),³⁰ 3-iodobicyclo[1.1.1]pentane-1-carboxylic acid **1** (X = I, Y = COOH),^{30b} 3-carbomethoxybicyclo[1.1.1]pentane-1-carboxylic acid **1** (X = COOCH₃, Y = COOH),⁴³ 1-iodo-3-trifluoromethylbicyclo[1.1.1]pentane **1** (X = CF₃, Y = I),³¹ and bicyclo[1.1.1]pentane-1-carboxylic acid **1** (X = H, Y = COOH).^{43a} The latter compound was also synthesized from methyl 3-iodobicyclo[1.1.1]pentane-1-carboxylate **1** (X = COOCH₃, Y = I)¹⁴ following procedures recently described for the preparation of bicyclo[2.2.1]heptane-1-carboxylic acid from methyl 4-iodo-bicyclo[2.2.1]heptane-1-carboxylate.⁴⁴ A mixture of 3-fluorobicyclo[1.1.1]pentane-1-carboxylic acid **1** (X = F, Y = COOH) and the parent acid **1** (X = H, Y = COOH) in the ratio 71/29 (respectively) was available from another study.¹¹ A further sample of this mixture was obtained following the published procedure.¹¹ The 3-fluoro- and parent acid in the new sample were in the ratio 85/15, respectively.

3-(Trifluoromethyl)bicyclo[1.1.1]pentane-1-carboxylic Acid **1 (X = CF₃, Y = COOH).** A solution of 1-iodo-3-(trifluoromethyl)bicyclo[1.1.1]pentane **1** (X = CF₃, Y = I),³¹ 1.0 g, 3.82 mmol) in anhydrous ether (50 mL) was cooled to -80

(43) (a) Della, E. W.; Tsanaktsidis, J. *Aust. J. Chem.* **1986**, 39, 2061. (b) Kaszynski, P.; Michl, J. *J. Org. Chem.* **1988**, 53, 4593.

(44) Adcock, W.; Clark, C. I. *J. Org. Chem.* **1995**, 60, 723.

$^{\circ}\text{C}$ under nitrogen and treated with 4.94 mL of 1.7 M *tert*-butyllithium (2.2 mol equiv) in pentane. After being maintained at this temperature for 30 min with stirring, the reaction mixture was quenched quickly with excess dry CO_2 gas. Sufficient water was then added to dissolve all solids, and the crude reaction mixture was extracted (2×30 mL) to remove organic impurities. The aqueous phase was carefully acidified with dilute hydrochloric acid and after being saturated with sodium chloride was subjected to continuous extraction with diethyl ether. After the ether extract was dried (MgSO_4), the solvent was removed in vacuo to afford the crude acid as a white solid. Sublimation ($125\text{ }^{\circ}\text{C}/0.1$ mm) followed by recrystallization from dichloromethane afforded the title compound (540 mg, 84%) as white needles: mp $152\text{--}153\text{ }^{\circ}\text{C}$; $^1\text{H NMR}$ (CDCl_3) δ 9.89 (bs, 1H), 2.28 (s, 6H); $^{13}\text{C NMR}$ (CDCl_3 , relative to Me_4Si) δ 37.02 (C1, q, $^4J_{\text{C-F}} = 2.0$ Hz), 50.08 (C2, q, $^3J_{\text{C-F}} = 2.2$ Hz), 37.18 (C3, q, $^2J_{\text{C-F}} = 39.4$ Hz), 122.30 (CF₃, q, $^1J_{\text{C-F}} = 275.6$ Hz), 174.90 (COOH); $^{19}\text{F NMR}$ (CDCl_3 , relative to FCCl_3) δ -73.81 ; HRMS (EI) calcd for $\text{C}_7\text{H}_7\text{F}_3\text{O}_2$ 180.0398, found 179.0317 ($M^+ - 1$), calcd for ($M^+ - 1$) 179.0320, found 135.0405 ($M^+ - 45$), calcd for ($M^+ - 45$) 135.0542.

1-Fluoro-3-phenylbicyclo[1.1.1]pentane 1 (X = F, Y = C₆H₅). A solution of butyllithium in hexane (22 mL, 1.6 M, 35.2 mmol) was added to a solution of crude 1-iodo-3-phenylbicyclo[1.1.1]pentane⁴⁵ **1** (X = F, Y = C₆H₅; 4.5 g, 16.7 mmol) in dry THF (170 mL) at $-70\text{ }^{\circ}\text{C}$ over a period of 40 min. The mixture was stirred at -60 to $-70\text{ }^{\circ}\text{C}$ for 1.5 h. Then it was cooled to $-90\text{ }^{\circ}\text{C}$, and a solution of *N*-fluorodibenzene-sulfonamide (5.5 g, 17.5 mmol) in THF (40 mL) was added over a period of 30 min. The mixture was stirred for 1 h at $-90\text{ }^{\circ}\text{C}$ and then was allowed to warm to $-10\text{ }^{\circ}\text{C}$ over a period of 2 h. Aqueous NH_4Cl was added at $-10\text{ }^{\circ}\text{C}$, the mixture was extracted with ether (3×200 mL), the extract was washed with water (2×100 mL), aqueous $\text{Na}_2\text{S}_2\text{O}_3$, water, and finally concd. NaCl , and it was then dried over MgSO_4 . The solvent was distilled off through a short column. Column chromatography on silica gel with pentane as the eluent yielded pure 1-fluoro-3-phenylbicyclo[1.1.1]pentane **1** (X = C₆H₅, Y = F; 0.35 g, 2.2 mmol, 13%). $^1\text{H NMR}$ δ 2.33 (d, 6H, $^3J_{\text{H-F}} = 2.4$ Hz), 7.16–7.30 (m, 5H). $^{19}\text{F NMR}$ δ -149.98 (septet, $^3J_{\text{H-F}} = 2.4$ Hz). $^{13}\text{C}\{^1\text{H}\}$ NMR (CD_3CN) δ 31.72 (d, $^3J_{\text{H-F}} = 46.5$ Hz), 56.05 (d, $^2J_{\text{C-F}} = 20.8$ Hz, CH₂), 76.34 (d, $^1J_{\text{C-F}} = 323$ Hz), 127.70, 127.85, 129.32, 137.70 (d, $^5J_{\text{C-F}} = 27$ Hz). Anal. Calcd for $\text{C}_{11}\text{H}_{11}\text{F}$: C, 81.48; H, 6.79. Found: C, 81.34; H, 6.86.

3-Fluorobicyclo[1.1.1]pentane-1-carboxylic Acid 1 (X = F, Y = COOH). **Method A.** By use of the procedure of Carben et al.,⁴⁶ sodium periodate (5.13 g, 0.024 mol) and water (10 mL) were added to a solution of 1-fluoro-3-phenylbicyclo[1.1.1]pentane **1** (X = F, Y = C₆H₅; 300 mg, 0.00185 mol) in acetonitrile (17.5 mL) and dichloromethane (3.5 mL). Ruthenium trichloride hydrate (15 mg) was then added to the vigorously stirred reaction mixture. After stirring for 3 days at room temperature, the reaction mixture was filtered and the filter cake washed with dichloromethane (50 mL). After the combined extracts were dried (MgSO_4), the solvent was removed in vacuo to afford the crude product which was sublimed ($80\text{ }^{\circ}\text{C}/0.1$ mm) twice to give a white solid (90 mg, 37%), mp $117\text{--}118\text{ }^{\circ}\text{C}$; HRMS (EI) calcd for $\text{C}_6\text{H}_7\text{FO}_2$ 130.0430, found 129.0351 ($M^+ - 1$), calcd for ($M^+ - 1$) 129.0352. ^1H , ^{13}C , and $^{19}\text{F NMR}$ spectra were identical to those previously reported¹¹ which were obtained from a mixture of the fluoro acid **1** (X = F, Y = COOH) and the parent **1** (X = H, Y = COOH).

Method B. By use of a modified literature procedure,^{26,47} a solution of ammonium persulfate (0.5 g, 0.0022 mol) in deoxygenated water (10 mL) was added to a vigorously stirred mixture (200 mg; see above) of 3-fluorobicyclo[1.1.1]pentane-1-carboxylic acid (85%) and bicyclo[1.1.1]pentane-1-carboxylic acid (15%) in cyclohexane (20 mL) and deoxygenated water

(15 mL) containing silver nitrate (40 mg) maintained at $70\text{ }^{\circ}\text{C}$. The resulting mixture was allowed to stir at that temperature for 15 min before the heating was stopped and the mixture allowed to cool with stirring for 1 h. The cyclohexane was separated, and the aqueous layer was thoroughly extracted (4×20 mL) with dichloromethane. The extracts were combined and dried over magnesium sulfate, and the solvents were evaporated in vacuo to afford the fluoro acid **1** (X = F, Y = COOH) as a white solid (170 mg) almost quantitatively. The physical and chemical properties of this compound were identical to the sample reported above.

General Procedure for Treatment of 3-Substituted (X) Bicyclo[1.1.1]pentane-1-carboxylic Acids 1 (Y = COOH) with XeF₂. To a solution of the carboxylic acid (15–20 mg) in 0.7 mL of CD_2Cl_2 or CDCl_3 at $0\text{ }^{\circ}\text{C}$ in a 5 mm NMR tube was added granular XeF_2 (45–75 mg). The tube was allowed to warm to room temperature and left to stand overnight to ensure complete reaction before being analyzed by ^1H and $^{13}\text{C NMR}$. The known spectral properties of the acids **1** (Y = COOH; X = F,¹¹ Cl,³⁰ Br,³⁰ CF₃,⁴⁸ and COOCH_3 ⁴³), the fluorides **1** (Y = F; X = Cl, CF₃, and COOCH_3)⁵, and several 1-substituted (X) bicyclo[1.1.1]pentanes **1** (Y = H; X = Cl,⁴⁹ CF₃,⁵⁰ and COOCH_3 ⁵¹) facilitated the assignments. The ^{13}C chemical shifts of the methylene carbons (C2) of the various products were unambiguously assigned by additivity methodology utilizing appropriate ^{13}C SCS data (Cl, 6.09 ppm; CF₃, -2.26 ppm; COOCH_3 , 0.56 ppm). The calculated values for the dimers were determined from the ^{13}C chemical shift data for the parent [2]-staffane.⁵² The relevant NMR data for the reactions of the various acids in CDCl_3 and CD_2Cl_2 are listed in Table 5. See Table 1 and text for product distributions.

Treatment of a Mixture of 3-Fluorobicyclo[1.1.1]pentane-1-carboxylic Acid 1 (X = F, Y = COOH) and Bicyclo[1.1.1]pentane-1-carboxylic Acid 1 (X = H, Y = COOH) with XeF₂. Xenon difluoride (563 mg, 3.33 mmol) crystals were added gradually to a well stirred solution of the aforementioned mixture of acids (279 mg; 71/29, respectively; ca. 2.2 mmol) in CD_2Cl_2 (3.0 mL) under N_2 . The mixture was allowed to stir overnight at room temperature before the solvent was evaporated in vacuo to afford a residue which was subsequently sublimed. The spectroscopic properties of this product (136 mg; >95% pure by $^1\text{H NMR}$) were identical to those reported above for the pure fluoro acid **1** (X = F, Y = COOH). No parent acid **1** (X = H, Y = COOH) was detected.

Procedure for the Attempted Observation of the Fluoroxenon Ester of 1 (X = F, Y = COOH). To a solution of the fluoro acid **1** (X = F, Y = COOH; 9 mg, 0.069 mmol) in CD_3CN (0.7 mL) maintained at $-20\text{ }^{\circ}\text{C}$ under N_2 was added granular XeF_2 (14 mg, 0.083 mmol), and the mixture was stirred for 5 h at $-20\text{ }^{\circ}\text{C}$. $^{19}\text{F NMR}$ revealed a singlet and doublet corresponding to XeF_2 ($\delta(\text{rel } \text{CFCl}_3)$: 131.7 ppm, $J_{\text{XeF}} = 5644$ Hz). Stirring the mixture for a further 1 day at $-20\text{ }^{\circ}\text{C}$ left the situation unchanged. The solution was then allowed to warm to room temperature, but no new ^{19}F and $^{129}\text{Xe NMR}$ resonances appear after 3 h at this temperature. $^{129}\text{Xe NMR}$ gave only the signal for XeF_2 .⁵³ Further warming to $40\text{ }^{\circ}\text{C}$ (1 h) and then to $60\text{ }^{\circ}\text{C}$ (2 h) led to no new ^{129}Xe signals. However, at the latter temperature the XeF_2 signals in ^{129}Xe and $^{19}\text{F NMR}$ slowly decrease (the latter by reference to the singlet resonance of **1** (X = F, Y = COOH)). No new $^{129}\text{Xe NMR}$ peaks appear, but new $^{19}\text{F NMR}$ signals appear in a variety of places.

Similar experiments carried out in CD_2Cl_2 and $\text{CCl}_2\text{FCF}_2\text{-Cl}$ were unsuccessful. Solubility may have been a problem in the former solvent.⁵⁴

(48) This study.

(49) Della, E. W.; Taylor, D. K. *Aust. J. Chem.* **1991**, *44*, 881.

(50) Krstic, A. R. Ph.D. Dissertation, Flinders University of South Australia, Adelaide, 1995.

(51) Della, E. W.; Taylor, D. K. *Aust. J. Chem.* **1990**, *43*, 945.(52) Murthy, S. G.; Hassenrück, K.; Lynch, V. M.; Michl, J. *J. Am. Chem. Soc.* **1989**, *111*, 7262.(53) Schrobilger, G. J.; Holloway, J. H.; Granger, P.; Brevard, C. *Inorg. Chem.* **1978**, *4*, 980.(54) Dukat, W. W.; Holloway, J. H.; Hope, E. G.; Townson, P. J.; Powell, R. L. *J. Fluorine Chem.* **1993**, *62*, 293.(45) Kaszynski, P.; Friedli, A. C.; Michl, J. *J. Am. Chem. Soc.* **1992**, *114*, 601.(46) Carlsen, P. H. J.; Katsuki, T.; Martin, V. S.; Sharpless, K. B. *J. Org. Chem.* **1981**, *46*, 3936.(47) Jacobsen, N.; Torssell, K. *Liebigs Ann. Chem.* **1972**, *763*, 135.

Table 5. ^1H , ^{13}C , and ^{19}F NMR Chemical Shifts of CH_2 , CH_2 , and F, Respectively, of Reactants and Products of the Reaction between **1** ($\text{Y} = \text{COOH}$) and XeF_2

reactant 1 ($\text{Y} = \text{COOH}$)	products 1	solvent	^1H NMR (δ , ppm)	^{13}C NMR (δ , ppm)	^{19}F NMR (δ , ppm)
$\text{X} = \text{Cl}$ (17 mg) ^a	$\text{X} = \text{Cl}, \text{Y} = \text{Cl}$	CDCl_3	2.46 (6H)	58.21	
	$\text{X} = \text{Cl}, \text{Y} = \text{D}$	CDCl_3	2.47 (6H)	62.49 (62.93) ^f	
	$\text{X} = \text{Cl}, \text{Y} = \text{C}_5\text{H}_6\text{Cl}$	CDCl_3	2.16 (6H)	56.89	
	$\text{X} = \text{Cl}, \text{Y} = \text{C}_5\text{H}_6\text{Cl}$	CDCl_3	2.03 (12H)	56.72 (55.84) ^f	
$\text{X} = \text{Cl}$ (15.8 mg) ^b	$\text{X} = \text{Cl}, \text{Y} = \text{Cl}$	CD_2Cl_2	2.48 (6H)	57.80	
	$\text{X} = \text{Cl}, \text{Y} = \text{D}$	CD_2Cl_2	2.50 (6H)	62.08	
	$\text{X} = \text{Cl}, \text{Y} = \text{C}_5\text{H}_6\text{Cl}$	CD_2Cl_2	2.18 (6H)	56.47	
	$\text{X} = \text{Cl}, \text{Y} = \text{F}$	CD_2Cl_2	2.06 (12H)	56.30	
$\text{X} = \text{CF}_3$ (14.0 mg) ^c	$\text{X} = \text{CF}_3, \text{Y} = \text{Cl}$	CDCl_3	2.30 (6H)	50.17	-166.83
	$\text{X} = \text{CF}_3, \text{Y} = \text{D}$	CDCl_3	2.36 (6H)	55.43 (54.58) ^f	-74.51
	$\text{X} = \text{CF}_3, \text{Y} = \text{C}_5\text{H}_6\text{CF}_3$	CDCl_3	2.00 (6H)	48.43	-71.86
	$\text{X} = \text{CF}_3, \text{Y} = \text{F}$	CDCl_3	1.85 (12H)	47.75 (47.89) ^f	-75.15
$\text{X} = \text{CF}_3$ (13.7 mg) ^d	$\text{X} = \text{CF}_3, \text{Y} = \text{Cl}$	CD_2Cl_2	2.32 (6H)	49.71	-75.75
	$\text{X} = \text{CF}_3, \text{Y} = \text{D}$	CD_2Cl_2	2.39 (6H)	55.02	-69.20
	$\text{X} = \text{CF}_3, \text{Y} = \text{C}_5\text{H}_6\text{CF}_3$	CD_2Cl_2	2.03 (6H)	47.27	-73.14
	$\text{X} = \text{CF}_3, \text{Y} = \text{F}$	CD_2Cl_2	1.89 (6H)	46.62	-70.49
		CD_2Cl_2	2.44 (6H)	52.24	-73.78
		CD_2Cl_2	(2.55 Hz)	(22.0 Hz)	-73.35
$\text{X} = \text{COOCH}_3$ (16.1 mg) ^e	$\text{X} = \text{COOCH}_3, \text{Y} = \text{Cl}$	CD_2Cl_2	2.35 (6H)	52.48	-152.04
	$\text{X} = \text{COOCH}_3, \text{Y} = \text{D}$	CD_2Cl_2	2.08 (6H)	50.99	
	$\text{X} = \text{COOCH}_3, \text{Y} = \text{C}_5\text{H}_6\text{COOCH}_3$	CD_2Cl_2	1.91 (12H)	50.10 (50.31) ^f	
	$\text{X} = \text{COOCH}_3, \text{Y} = \text{F}$	CD_2Cl_2	2.37 (2.45 Hz)	54.94 (21.8 Hz)	-149.53

^a $\text{XeF}_2 = 74$ mg (4 equiv). ^b $\text{XeF}_2 = 52.8$ mg (3 equiv). ^c $\text{XeF}_2 = 52.5$ mg (4 equiv). ^d $\text{XeF}_2 = 44.9$ mg (2.5 equiv). ^e $\text{XeF}_2 = 53.9$ mg (3.5 equiv). ^f Calculated value.

pK_a Measurements. Conductivity water prepared by passing distilled water through Milli Quf apparatus was used for both conductivity measurements and titrations. U.S.P. absolute ethanol was refluxed with magnesium ethoxide under nitrogen for 24 h and distilled. Titrations were monitored by pH measurements with Orion 81–72 Sure-Flow electrode and Orion 701A Ionalyzer. The titrations were performed at 25 °C under a stream of nitrogen. Standard aqueous ethanol buffers used for electrode calibration covered the pH range 2.8–7.7.⁵⁵ Each titration was repeated three times at different concentrations between 7×10^{-4} and 5×10^{-3} M. Conductance of aqueous ethanol solutions (50 wt %) was measured at 25 °C in a thermostated cell with platinum-coated electrodes and a cell constant of 1. Fresh stock solutions of the acids, made by weight, were sequentially diluted (8×10^{-3} to 9×10^{-5} M), and conductance measurements were repeated three times for each acid.⁵⁶ Nonlinear regression analysis of titration curves was performed with Axum software.⁵⁷

Cyclic Voltammetry. The measurements were carried out as previously described.^{10,42}

Computations. All calculations were carried out utilizing the GAUSSIAN 94 program package.⁵⁸ The enthalpies of

proton abstraction (kcal/mol) for **1** ($\text{Y} = \text{COOH}$; $\text{X} = \text{H}$ (354.6), F (348.3), Cl (346.3), and CF_3 (346.1) were calculated at the HF level of theory using the 6-31+G* basis set for both neutral and anionic forms.

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(55) Galster, H. *pH Measurement: Fundamentals, Methods, Applications, Instrumentation*; VCH: New York, 1991.

(56) Albert, A.; Serjeant, E. P. *The Determination of Ionization Constants*; Chapman and Hall Ltd: New York, 1971.

(57) Axum 4.0 for Windows; 1995, TriMetrix, Inc.

(58) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Gill, P. M. W.; Johnson, B. G.; Robb, M. A.; Cheeseman, J. R.; Keith, T.; Peterson, G. A.; Montgomery, J. A.; Raghavachari, K.; Al-Laham, M. A.; Zakrzewski, V. G.; Ortiz, J. V.; Foresman, J. B.; Cioslowski, J.; Stefanov, B. B.; Nanayakkara, A.; Challocombe, M.; Peng, C. Y.; Ayala, P. Y.; Chen, W.; Wong, M. W.; Andres, J. L.; Replogle, E. S.; Gomperts, R.; Martin, R. L.; Fox, D. J.; Binkley, J. S.; Defrees, D. J.; Baker, J.; Stewart, J. J. P.; Head-Gordon, M.; Gonzalez, C. and Pople, J. A. *Gaussian 94*, Revision D, Gaussian, Inc.: Pittsburgh, PA, 1995.