# A Persistent α-Fluorocarbanion and Its Analogues: Preparation, Characterization, and Computational Study**

G. K. Surya Prakash, Fang Wang, Nan Shao, Thomas Mathew, Golam Rasul, Ralf Haiges, Timothy Stewart, and George A. Olah**

Fluoromethylated organics are of substantial interest in pharmaceutics, biochemistry, and materials science owing to their unique properties.[1] Nucleophilic fluoromethylation reactions have been used as major synthetic strategies for introducing fluoromethyl building blocks into organic compounds.[2] Recently, α-fluoro(phenylsulfonyl)methane (FSM) derivatives have been extensively studied as monofluoromethyl pronucleophiles in numerous reactions (Scheme 1).[3]
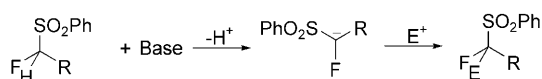
Scheme 1. Nucleophilic monofluoromethylation reactions of an electrophile (E$^+$) by α-fluoro(phenylsulfonyl)methane (FSM) derivatives.

Such nucleophilic fluoromethylation reactions involve α-fluorocarbanions (FCAs) with unique characteristics as the key intermediates. Interestingly, a number of computational studies on α-FCAs have shown that they are electronically, thermodynamically, and sterically different from their parent analogues as a result of the specific electronic effects of fluorine.[4]

Carbanions usually have pyramidal structures, however they deviate from this and assume planar structures when in conjugation with adjacent nitro, carbonyl, or phenylsulfonyl groups.[4,5] The α-fluorine atom, owing to its high electronegativity, can stabilize the carbanions through its strong electron withdrawing effect. However, repulsive force of the vicinal anion–lone pair (derived from the adjacent anionic carbon center and non-bonded 2p lone pairs on the α-fluorine atom) makes fluorine less stabilizing than chlorine, bromine, or some other electron-withdrawing groups (Figure 1) as shown by ready α-fluoride elimination which can lead to complex products.[6] In fact, fluorine is found to destabilize
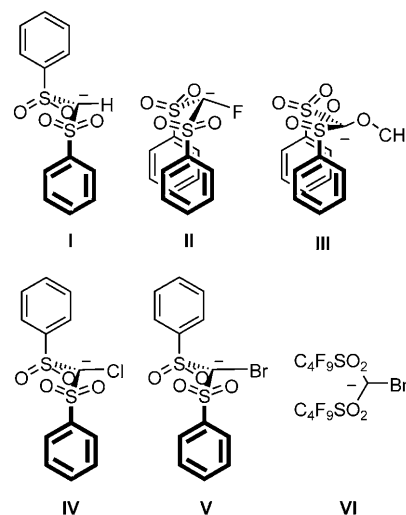
[*] Prof. Dr. G. K. S. Prakash, F. Wang, N. Shao, Dr. T. Mathew, Prof. Dr. G. Rasul, Dr. R. Haiges, T. Stewart, Prof. Dr. G. A. Olah
Loker Hydrocarbon Research Institute and
Department of Chemistry
University of Southern California
University Park, Los Angeles, CA-90089-1661 (USA)
Fax: (+1) 213-740-6679
E-mail: gprakash@usc.edu
olah@usc.edu

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Figure 1. The bis(phenylsulfonyl)methide ion (**I**) and its derivatives.

α-carbanions in many cases.[6–8] Consequently, the structural investigation of FCAs is still a challenge. To our knowledge, α-monofluorocarbanions have not yet been structurally characterized, despite the reports of many computational studies on fluorine-bearing carbanions. Herein, we disclose, for the first time, the preparation, NMR spectroscopic and X-ray structural characterization, and computational studies of the persistent α-fluorobis(phenylsulfonyl)methane (FBSM) anion and its analogues (Figure 1, **I–V**) as a part of our investigations of the synthetic and mechanistic aspects of nucleophilic monofluoromethylations.

FBSM has been found to be an effective reagent for nucleophilic monofluoromethylations and is superior to (phenylsulfonyl)monofluoromethane (PhSO$_2$CH$_2$F) in many cases. Hu et al. pointed out that the additional phenylsulfonyl group not only stabilizes the formed carbanion, but also increases the nucleophilicity of the fluorinated carbanion by its softening ability.[3b] The stabilization of the carbanion by two phenylsulfonyl groups is supported by the following observations: a) the parent carbanion **I** (Figure 1), studied by Henderson and others,[9] has been readily prepared and proved to be highly thermostable, b) Dubenko et al.[10] have reported the preparation of potassium salts of **IV** and **V**, c) later, Ochiai and co-workers[11] reported that brominated bis(perfluoroalkylsulfonyl) carbanion **VI** also can be crystallized as a fairly stable solid. Based on these studies, we decided to prepare the fluorine-bearing carbanion **II** and study its stability under suitable conditions.

Several attempts were made to obtain a salt of anion **II** in a persistent separable crystalline form. However, none of the products was stable in the solid state under usual conditions (Scheme 2). While monitoring the *t*BuOK mediated depro-
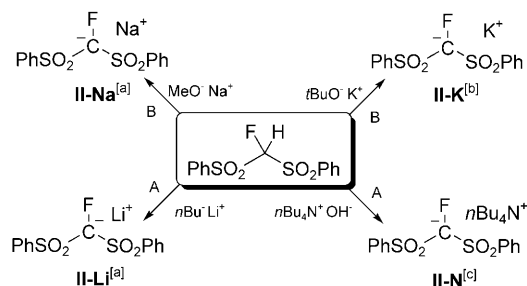
Scheme 2. Preparation of α-fluorobis(phenylsulfonyl)methide ion (**II**) under different conditions: A) THF, room temperature, B) DMF, room temperature. [a] Not stable in the solid state. [b] Not isolated. [c] Stable at ambient temperature for several weeks under an inert atmosphere.

tonation of FBSM by NMR spectroscopy (^{1}H, ^{19}F) the signals for the acidic proton at $\delta = 6.1$ ppm and the doublet F signal at $\delta = -171.9$ ppm disappeared. Appearance of a new sharp singlet at about $\delta = -202$ ppm was observed in the ^{19}F NMR spectrum, indicative of facile deprotonation of FBSM under basic conditions. However, instability of the carbanionic products owing to defluorination restricted their isolation in solid crystalline form. To suppress any probable C−F···M$^+$ interaction[12] and the resulting defluorination, we decided to use appropriate bases with countercations that would weakly coordinate with the fluorine atom. Among the choices, alkyl ammonium hydroxides were found to be most desirable because of their diminished interaction with the substrate, greater commercial availability, and structural variability. We found that reaction of FBSM with tetrabutylammonium hydroxide resulted in the formation of the ionic salt **II-N** which is stable in the solid state for up to few weeks under inert atmosphere.

The complex **II-N** was crystallized from its solution in a THF/toluene/hexane solvent mixture as fine cubes. X-ray crystallographic studies indicated that the fluorinated ion pair **II-N** is significantly different from its parent and brominated analogues in its electronic as well as stereochemical nature (Figure 2). The most remarkable structural characteristic is that **II-N** has a pyramidal structure, the critical pyramidalization angle (Φ) around the carbanion center is found to be 49.9°, whereas a planar structure is adopted by both **I** and **VI**. Considering that the pyramidalization angle of a standard tetrahedral structure is 60°, it is evident that **II-N** is strongly sp^3 (pyramidalized) rather than sp^2 hybridized. On the other hand, the C17−F1 distance of 1.404 Å is considerably longer than the typical C_{sp^3}−F bond length in fluorohydrocarbons (1.32–1.38 Å as in CH$_3$F, CH$_2$F$_2$, CF$_3$H, and CF$_4$). This C−F bond in **II-N** is very close to the "upper limit" of tertiary C−F bonds (1.408 Å).[13] Nevertheless, the C−Br bond of **VI**, 1.884 Å, is much shorter than the regular C−Br bond which is approximately 1.95–1.98 Å. Besides these two differences, the
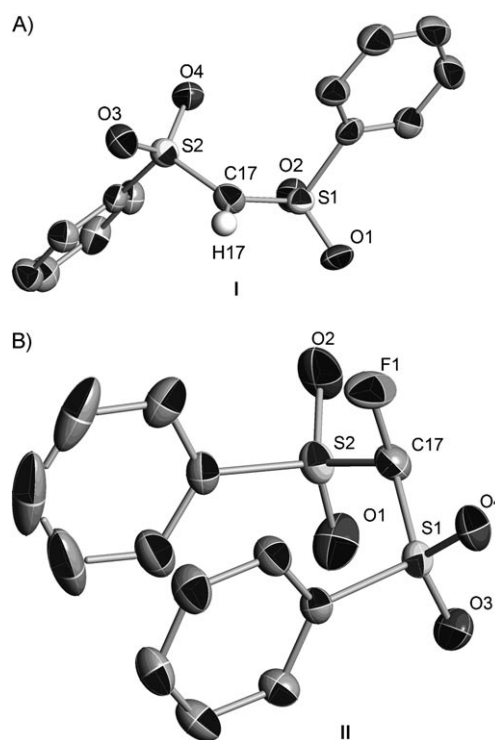

Figure 2. X-ray crystal structures of A) bis(phenylsulfonyl)methide (**I**) and B) α-fluorobis(phenylsulfonyl)methide (**II**) anions.[15]

structure of **II-N** is essentially consistent with the properties of α-sulfonyl carbanions described by Gais and co-workers.[14] For instance, the average S−C17 bond length (1.716 Å) in **II-N** is noticeably shorter than the corresponding one in sulfone[13] whereas the S−O bonds of **II-N** are slightly longer. Further NMR spectroscopy studies of **II** with different counterions (Li$^+$ (**II-Li**), Na$^+$ (**II-Na**), and *n*Bu$_4$N$^+$ (**II-N**)) in [D$_6$]DMSO reveal the liquid-phase behavior of the anion (Table 1).

Table 1: NMR chemical shifts of carbanions **I** and **II** in combination with various cations.

Compound	$\delta_{\alpha\text{-F/H}}$ [ppm]	δ_H [ppm]			δ_{C_x} [ppm][a]
		o-H	*m*-H	*p*-H	
I-H (HBSM)[b]	5.94	7.87–7.89	7.60–7.64	7.73–7.77	71.8
I-N[b]	3.65	two multiplets at 7.30–7.34 (2 H) and 7.70–7.74 (3 H)			63.8
II-H (FBSM)	−171.9	7.93–7.95	7.71–7.75	7.86–7.90	104.4
II-Li	−202.5	7.15–7.17	7.04–7.08	7.19–7.23	127.2
II-Na	−202.8	7.17	7.04–7.08	7.21–7.23	127.1
II-N	−202.3	7.16–7.18	7.04–7.08	7.19–7.23	127.2

[a] Of the carbanionic carbon atom C_x. [b] HBSM = bis(phenylsulfonyl)-methane; **I-N** = I[*n*Bu$_4$N]$^+$.

As expected, the ^{19}F NMR spectroscopy studies showed an upfield shift of approximately 30 ppm for **II** compared to **II-H** (FBSM). The essentially identical ^{19}F chemical shifts for all the salts (**II-Li**, **II-Na**, and **II-N**) clearly indicate the absence of strong interactions between the cations (Li$^+$, Na$^+$, *n*Bu$_4$N$^+$) and the FBSM anion in [D$_6$]DMSO. More interest-

ingly, the signals of the carbanionic carbon atom of **II** in the ^{13}C NMR spectrum showed a downfield shift by 22.7 ppm compared to **II-H** (FBSM). In contrast, the signals of the carbanionic carbon atom of **I-N** has an upfield shift of approximately 8 ppm compared to that in **I-H** (HBSM).

For a better understanding of the pyramidal nature of **II**, we carried out computational studies on the anions **I–V**, including optimized conformations, ionization energies, and charge densities. A diagram of gas-phase proton affinities of these anions is illustrated (Figure 3). By defining the heats of formation of the corresponding neutral molecules as 0.0 kcal mol^{-1}, it is found that the gas-phase deprotonation becomes more difficult as the electronegativity of the substituent increases (anion **II–V**). The diagram shows that Cl and Br are able to stabilize the anion (relative to **I**), however, OCH$_3$ and F are destabilizing substituents.

It is also discovered that the "*cis*-pyramidal" conformation (**IIb**; Figure 3), which agrees well with the X-ray determined geometry, is 2.1 kcal mol^{-1} more stable than the "*cis*-planar" conformation (**IIa**) at the B3LYP/6-311 + G-(2d,p)//B3LYP/6-311 + G(2d,p) + ZPE level.[15] Although the *trans*-planar structure **IIc** is found to be the most stable conformation of **II**, it is only 0.9 kcal mol^{-1} more stable than the experimentally observed conformation **IIb**. In contrast, the *trans*-planar structures are favored when the substituent X is H, Cl, or Br. Calculations show that with the methoxy substituent the energy gap between the pyramidal conformation and the planar conformation is only 0.2 kcal mol^{-1}. In other words, the methoxy group is the "critical borderline" substituent showing a clear gradual transition to the pyramidal conformation as an energetically preferred structure.

The partial atomic charges (Q), bond lengths, and pyramidalization angles (Table 2) from the computational studies clearly show the structural and electronic effects the substituents have on the geometry of the anion and the

Figure 3. Gas-phase proton affinities (ionization energy/electronegativity profile) of carbanions **I–V**.

Table 2: Structural parameters (bond order, bond lengths, and charges) associated with disulfonylmethide anions.

X	Bond order[a] X–C$_x$	Bond length [Å]				Mulliken charge				Φ [°]
		S–O	S–C$_x$	X–C$_x$	(X–C$_x$)$_{st}$[b]	Q$_O$	Q$_S$	Q$_{C_x}$	Q$_X$	
H	0.811	1.466	1.690	1.077	1.088–1.099	−0.561	+0.696	−0.240	+0.097	0.0
H[c]	–	1.448	1.670	0.949	1.088–1.099	–	–	–	–	0.0
Br	0.765	1.461	1.713	1.921	1.951–1.983	−0.541	+0.696	+0.093	−0.105	0.0
Br[d]	–	1.435	1.670	1.884	1.951–1.983	–	–	–	–	0.0
Cl	1.023	1.461	1.712	1.761	1.783–1.858	−0.536	+0.476	+0.354	−0.084	0.0
OCH$_3$	0.772	1.464	1.715	1.389	1.405–1.458	−0.522	+0.963	−0.326	−0.310 (O) −0.103 (OCH$_3$)	18.8
F[e]	0.633	1.458	1.731	1.400	1.312–1.408	−0.529	+0.994	−0.066	−0.295	43.3
F[f]	0.644	1.461	1.699	1.381	1.312–1.408	−0.533	+0.707	−0.107	−0.256	0.0
F[g]	–	1.439	1.716	1.404	1.312–1.408	–	–	–	–	49.9

[a] Natural bond order. [b] Bond lengths in similar C$_{sp^3}$–X structures are used as the standard (st). [c] Experimental data. [d] X-ray diffraction data of [(CF$_3$SO$_2$)$_2$CBr]$^-$, taken from Ref. [11]. [e] *cis*-Pyramidal conformation. [f] *trans*-Planar conformation. [g] Experimental data.

stereochemistry of the products derived from the anion. Opposite partial charges are found on the central carbon (C$_x$) and the substituents X when X is H, Cl, and Br, resulting in Coulombic attractions, whereas negative partial charges on both C$_x$ and the substituent X (when X = F or OCH$_3$ groups) undoubtedly cause repulsions. A trend that F and OCH$_3$ bear

more negative charges than Cl and Br reveals the important role played by the electronegativity of the substituents in the electronic properties of the anions. It is important to mention that the anions are greatly stabilized by the oxygen atoms on sulfonyl groups, although the substituents X also have considerable influence on the structures of the anion. This influence can be strongly supported by two facts: a) Each oxygen atom bears more than 0.5 negative charges and the NAO bond order study shows partial single bond character of the S–O bonds in all structures. b) The calculated bond lengths agree extremely well with the experimentally determined results.

As mentioned above (from the results of X-ray crystallographic studies), our calculations also show that the C_x–X bond lengths in **I**, **IV–VI** are significantly shorter than the standard C_x–X bonds, which can be rationalized by the Coulombic attractions. In contrast, the computational C–F bond distances are found to be considerably longer than the regular C–F bonds in analogous organic compounds. This result is also consistent with the data obtained from X-ray crystallographic analysis. In addition, the extremely low C–F bond orders of both **IIb** (0.633) and **IIc** (0.644), theoretically support the properties of C–F bonds in FCAs and account for the defluorination observed in the solid state. The measured chemical shift deviation is in good agreement with the calculated values in the idealized gas phase (**I-H** to **I-N** and **II-H** to **II-N**). Except in the case of FBSM, all carbanionic carbons show clear upfield shifts. Calculations show a gradual increase in chemical shift deviation (from the neutral to the carbanionic carbon) with the increasing electronegativity of the substituents ($\Delta\delta = Br(-24\ ppm) < Cl(-18\ ppm) < OCH_3(-12\ ppm) < F(+14\ ppm)$, Figure 4). Probably, the electronegativity of the substituent plays a major role. The gradual decline in the pyramidalization angles from 49.9° to 0.0° with decrease in electronegativity ($F > OCH_3 > Cl > Br$) clearly shows the gradual transition in hybridization of the C_x from sp^3 to typical sp^2.

Based on these results, a detailed structural picture of FBSM anion can be illustrated (Figure 5). In terms of MO theory, maximum orbital overlap occurs between one of the 2p orbitals on C_x and a 3p orbital on each of the S atoms since all three orbitals are parallel to each other. Although one of the 2p orbitals on the fluorine and the 2p orbital on C_x are in the same plane, the maximum overlap is not possible because these two orbitals are not parallel. Similarly, there are also four 2p orbitals on the two oxygen atoms interacting with the 3p orbitals on S. The sum of these combinations forms π-type MOs, and the bonding orbital is illustrated as **IIb**-HOMO−33 (Figure 5). Moreover, the **IIb**-HOMO−14 shows the overlap
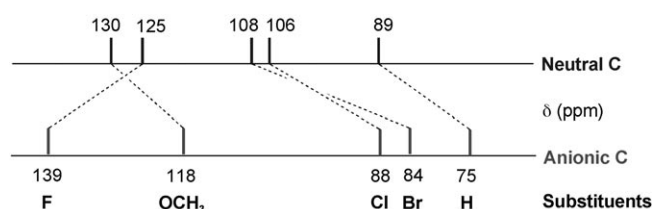

Figure 4. Calculated ^{13}C NMR chemical shifts of the α-C (carbanionic carbon) in **I–V** and the corresponding neutral molecules.
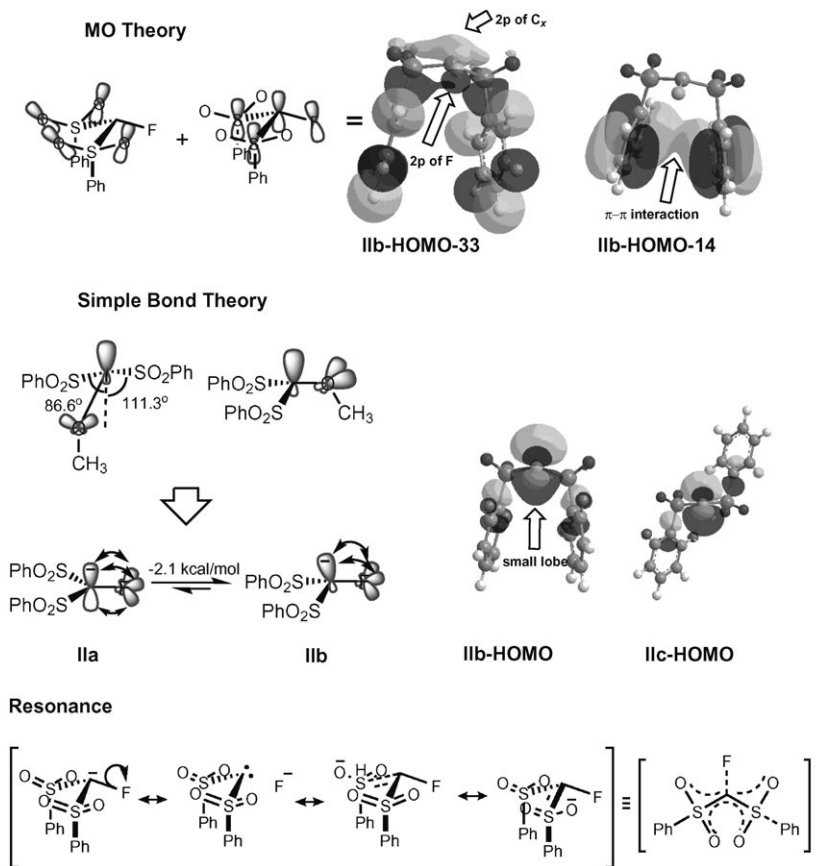

Figure 5. Orbital representation of the FBSM anion based on molecular orbital (MO) theory and bond theory.

between the two π orbitals on the phenyl groups, which may partially cancel out the instability caused by the additional steric repulsion in the *cis* conformation. The structure of **IIb** can be explained by simple bond theory as well. To "localize" the lone pairs on the fluorine atom and their relation to the anionic sp^3 orbital on C_x, the anion **III** (Figure 1) is used as a model structure since the positions of the lone pairs on the methoxy oxygen atom can be determined by viewing in the direction of the O–CH$_3$ bond. According to the calculation, the O–CH$_3$ bond is roughly periplanar to the anionic sp^3 orbital on C_x which means the two lone pairs on oxygen are gauche to the sp^3 orbital. Consequently, the lone pairs on the FBSM anion **IIb** are supposed to have a similar conformation to the methoxy oxygen atom in **III**. The planar structure causes more electronic repulsion owing to the strong interaction of the two lobes of the 2p orbital with all three lone

pairs on F. Nevertheless, in the pyramidal structure **IIb**, there are only two of these lone pairs experiencing similar repulsion. To some extent, this explanation can be supported by the MO theory results as well (note that the two lobes of the 2p orbital in **IIb**-HOMO have slightly different sizes where as the two lobes of the 2p orbital in **IIc**-HOMO have the same size; Figure 5). The anion **IIb** can be described as a resonance hybrid of the various resonance structures (Figure 5) which rationalizes many of the properties exhibited by the anion.

In conclusion, the preparation and structural characterization of the first persistent FCA that is, α-fluorobis(phenylsulfonyl)methide and related anions with a tetrabutylammonium countercation have been achieved. The critical role of electron-withdrawing substituents in modulating the properties of bis(phenylsulfonyl)methide anions and the resulting pyramidalization that occurs with highly electronegative α-substituents, such as F and OCH_3, have been established by high-level theoretical calculations, further supported by X-ray crystallographic studies of the α-fluorobis(phenylsulfonyl)methide salt.

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[15] CCDC 728306 (FCA **II**) and CCDC728307 (parent anion **I**) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif. The details of the X-ray studies and calculations are included in the supporting information.