Photochemical nucleophile–olefin combination, aromatic substitution (photo-NOCAS) reaction, Part 15. Investigations involving fluoride anion as the nucleophile and the effect of fluorine substitution on the relative stability of the reaction intermediates[1]

Mary S.W. Chan and Donald R. Arnold

Abstract: The scope of the photochemical nucleophile–olefin combination, aromatic substitution (photo-NOCAS) reaction has been extended to include fluoride anion as the nucleophile. The 4-cyanophenyl substituted fluoroalkanes were obtained in moderate yields with 2,3-dimethyl-2-butene and 2-methyl-2-butene reacting as the olefin. The yields were lower with 2-methylpropene, and no photo-NOCAS products were detected when conjugated dienes were used as the olefin. The selectivity of the fluoride anion towards alkenes can be explained in terms of the Hard–Soft-Acid–Base (HSAB) principle. The regiochemistry of this reaction can be described as predominantly following the *anti*-Markovnikov mode of addition. The fluoride anion adds preferentially to the less alkyl-substituted end of an unsymmetrical alkene radical cation to produce the more heavily substituted β-fluoroalkyl radical. Ab initio molecular orbital calculations (MP2/6-31G*//HF/6-31G*) were used to determine the relative stability of the β-fluoroalkyl radical intermediates. The more heavily substituted β-fluoroalkyl radical is NOT the more stable. The addition step is kinetically, rather than thermodynamically, controlled.

Key words: photochemistry, radical ions, electron transfer, alkyl fluorides, nucleophilic addition.

Résumé : On a élargi le domaine d'application de la réaction photochimique de combinaison nucléophile–oléfine avec substitution aromatique («photo-NOCAS») de façon à inclure l'anion fluorure comme nucléophile. Utilisant le 2,3-diméthylbut-2-ène et le 2-méthylbut-2-ène comme oléfine pour la réaction, on a obtenu des rendements modérés de fluoroalcanes substitués par le 4-cyanophényle. Les rendements ont été inférieurs avec le 2-méthylpropène et on n'a observé aucun produit «photo-NOCAS» lorsqu'on a utilisé des diènes comme oléfines. On peut expliquer la sélectivité de l'anion fluorure pour les alcènes en termes du concept des acides et des bases dures et molles. On peut décrire la régiochimie de cette réaction à l'aide du mode d'addition *anti*-Markovnikov. L'anion s'additionne d'une façon préférentielle à l'extrémité la moins substituée par des groupes alkyles du cation radical d'un alcène non symétrique; ceci conduit à la formation préférentielle du radical β-fluoroalkyle le plus substitué. On a fait appel à des calculs d'orbitales moléculaires ab initio (MP2/6-31G*//HF/6-31G*) pour déterminer les stabilités relatives des radicaux β-fluoroalkyles intermédiaires. Le radical β-fluoroalkyle le plus substitué n'est PAS le plus stable. L'étape d'addition est contrôlée d'une façon cinétique plutôt que d'une façon thermodynamique.

Mots clés : photochimie, ions radicaux, transfert d'électron, fluorures d'alkyles, addition nucléophile.

[Traduit par la rédaction]

Introduction

Organofluorine compounds can be found in a variety of industrial applications. Some of these include lubricants, coatings, propellants, pharmaceuticals, blood substitutes, liquid crystals, and textile chemicals (1). One of the more important applications is isosteric replacement, the replacement of a hydrogen atom, hydroxyl group, or another halogen by a fluorine atom. The similarity in size of the fluorine and the hydrogen atom results in negligible steric effects, yet the significant difference in electronegativity produces pronounced effects on the electronic distribution within the molecule. These characteristics make isosteric replacement an ideal structural modification for altering the chemical and biological activities of organic compounds. For this reason, the selective formation of a carbon–fluorine bond has been, and continues to be, the focus of intensive research (2). In this paper, we report a highly selective, one-step synthesis for fluoroalkanes starting from simple alkenes. The fluoro-substituted compounds were obtained from the photochemical nucleophile–olefin combi-

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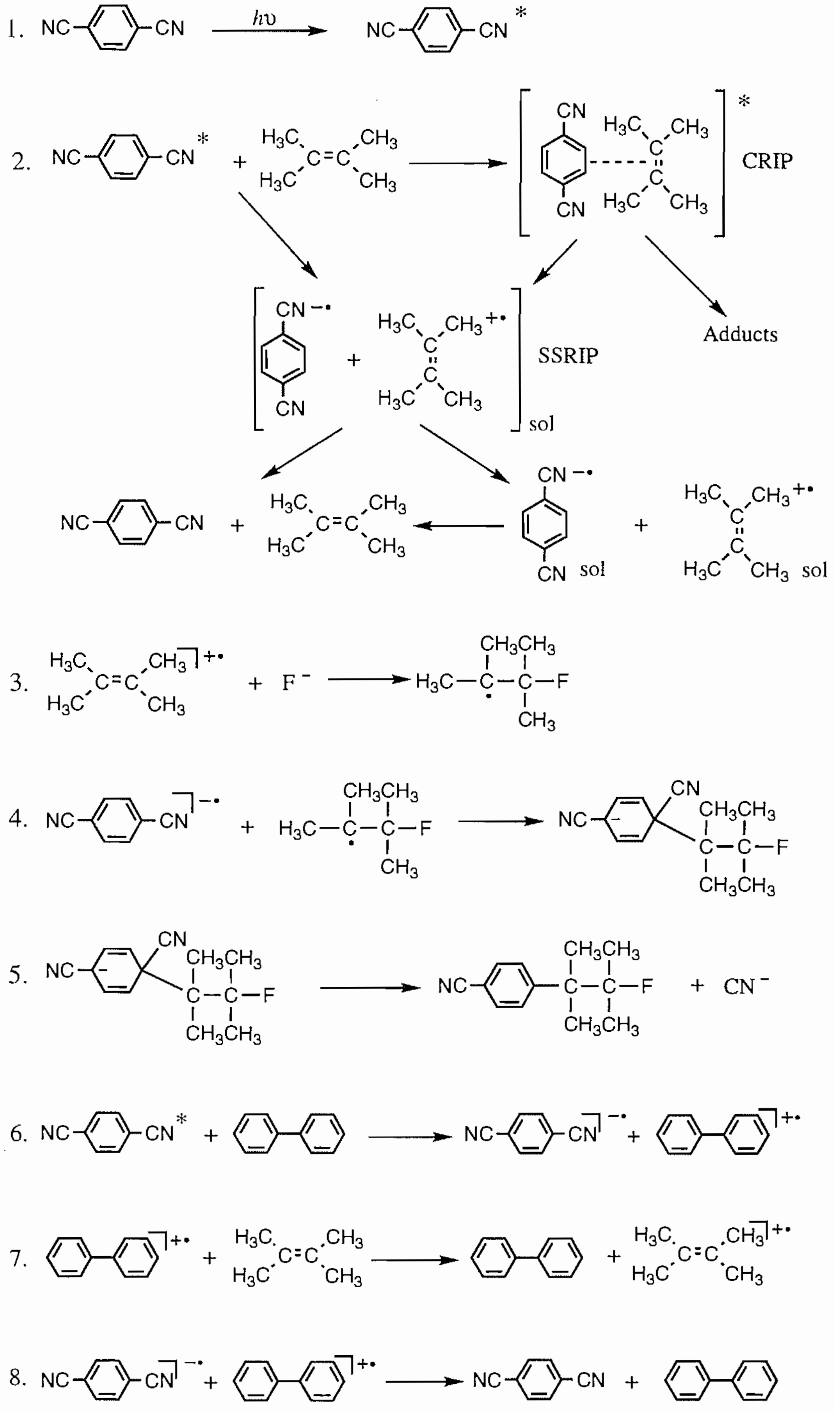
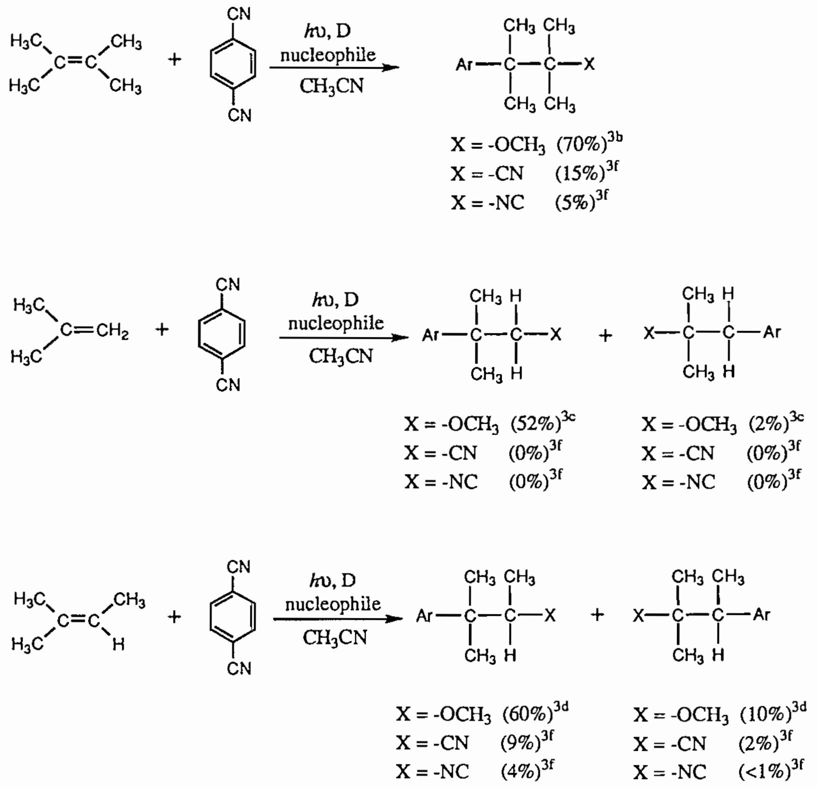
Scheme 1. Mechanism for the photo-NOCAS reaction.



nation, aromatic substitution (photo-NOCAS) reaction with fluoride anion serving as the nucleophile.

The mechanism of the photo-NOCAS reaction had been analyzed and documented (3). The proposed mechanism for the reaction, using 2,3-dimethyl-2-butene as the olefin, is shown in Scheme 1. The scope and limitations of this reaction with regard to the olefin in combination with alcoholic nucleophiles have been extensively investigated; only recently has this study been extended to other nucleophiles (3*f*). Figure 1 summarizes the results of the reaction involving simple alkenes when methanol or cyanide anion serves as the nucleophile. The regiochemistry in all cases can be considered as predominately *anti*-Markovnikov, where the nucleophile adds to the less substituted carbon of the double bond. The reasons for this preference have also been rationalized (3*e*, *f*). In the case of methanol serving as the nucleophile, distonic radical cations that can equilibrate via a bridged structure are initially formed. The regiochemistry is thermodynamically controlled and the product distribution is dependent on the stability of the β-alkoxyalkyl radical intermediates (Scheme 1, step 3). When

Fig. 1. Isolated yields of photo-NOCAS products.



X = -OCH$_3$ (70%)[3b]
X = -CN (15%)[3f]
X = -NC (5%)[3f]

X = -OCH$_3$ (52%)[3c]
X = -CN (0%)[3f]
X = -NC (0%)[3f]

X = -OCH$_3$ (2%)[3c]
X = -CN (0%)[3f]
X = -NC (0%)[3f]

X = -OCH$_3$ (60%)[3d]
X = -CN (9%)[3f]
X = -NC (4%)[3f]

X = -OCH$_3$ (10%)[3d]
X = -CN (2%)[3f]
X = -NC (<1%)[3f]

D = biphenyl Ar = 4-cyanophenyl

cyanide anion reacts as the nucleophile, the β-cyano or β-isocyano alkyl radicals cannot bridge, the regiochemistry is kinetically controlled, and steric factors dominate. Similar experimental and theoretical investigation of the photo-NOCAS reaction with fluoride anion serving as the nucleophile will be described. The olefins chosen for this study were 2,3-dimethyl-2-butene (**1**), 2-methylpropene (**2**), and 2-methyl-2-butene (**3**).

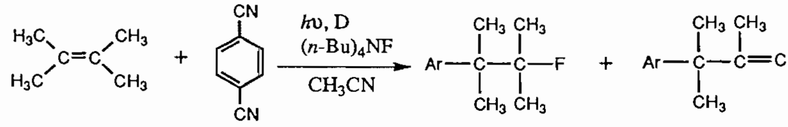
Results

Irradiation of an acetonitrile solution of 1,4-dicyanobenzene (**4**), biphenyl (**5**), tetrabutylammonium fluoride (**6**), and 2,3-dimethyl-2-butene (**1**) resulted in one major 1:1 (alkene:1,4-dicyanobenzene) adduct and one photo-NOCAS product (Reaction [1]). The 1:1 adduct, 3-(4-cyanophenyl)-2,3-dimethyl-1-butene (**7**), was obtained in 28% yield. The yield of the photo-NOCAS product, 3-(4-cyanophenyl)-2-fluoro-2,3-dimethylbutane (**8**), was 22%. The addition of the codonor, biphenyl, increased the efficiency of the reaction, but had no affect on the relative amounts of these reaction products.

The photo-NOCAS reaction of 2,3-dimethyl-2-butene (**1**) was also attempted using potassium fluoride as the fluoride ion source. These irradiations were identical to the ones involving **6** with the exception that an equal molar amount of KF and 18-crown-6 was added instead. The use of KF as a source of fluoride ion did not affect the identity of the products, but significantly more 1:1 (alkene: 1,4-dicyanobenzene) adducts were observed. For this reason, tetrabutylammonium fluoride (**6**) was used in the subsequent large-scale reactions to improve the yield of the photo-NOCAS products.

A similar irradiation of an acetonitrile solution of **4**, **5**, **6**, and 2-methylpropene (**2**) resulted in a 1:1 (alkene:1,4-dicyanobenzene) adduct and two photo-NOCAS products (Reaction [2]). The 1:1 adduct, 3-(4-cyanophenyl)-2-methylpropene (**9**), was obtained in 8% yield. The *anti*-Markovnikov photo-NOCAS product, 2-(4-cyanophenyl)-1-fluoro-2-methylpropane (**10**), was isolated in 5% yield. A trace amount of the Markovnikov isomer, 1-(4-cyanophenyl)-2-fluoro-2-methylpropane, was identified (gc/ms, ^{1}H and ^{13}C nmr) but it was not isolated. Integration of a gc/ms chromatograph obtained from single ion monitoring for the molecular ion

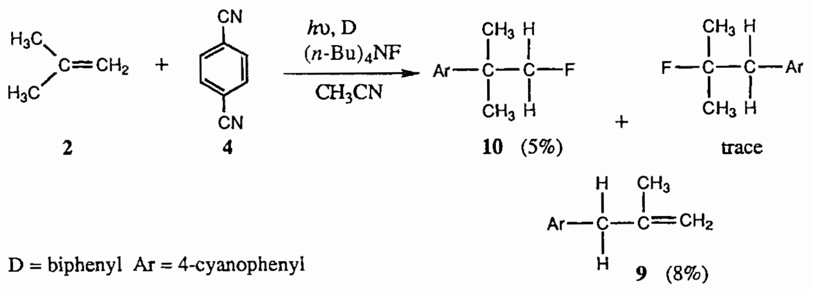
Reaction [1]



1 **4** **8** (22%) **7** (28%)

D = biphenyl Ar = 4-cyanophenyl

Reaction [2]



Reaction [3]

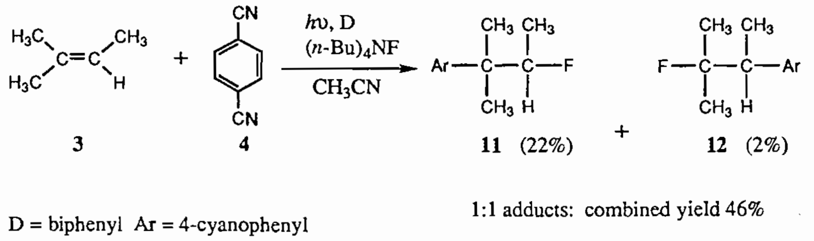


Table 1. Calculated enthalpy change for reaction 2b as a function of theoretical model.

Theoretical model	2-Fluoro-2-methylpropane (au)	1-Fluoro-2-methylpropane (au)	ΔH (kJ/mol)
HF/6-31G*//HF/6-31G*	-256.159 00	-256.148 10	28.62
MP2/6-31G*//HF/6-31G*	-256.855 96	-256.842 52	35.29
MP2/6-31G*//MP2/6-31G*	-256.857 00	-256.843 76	34.76
MP2/6-311+G*//MP2/6-31G*	-256.988 41	-256.975 13	34.87

gave a ratio of 95: 5 (*anti*-Markovnikov:Markovnikov) for the two photo-NOCAS products. This ratio remained constant as a function of irradiation time. Again, the addition of the codonor, biphenyl, increased the efficiency of the reaction, but did not have any affect on the product ratios.

The stability of the radical intermediates resulting from the reaction of the 2-methylpropene radical cation with fluoride anion was estimated by ab initio molecular orbital calculations. The relevant isodesmic reactions, along with enthalpy changes calculated from MP2/6-31G*//HF/6-31G* energies, are shown in Fig. 2. The isodesmic reaction 2a is a direct comparison of the two β-fluoroalkyl radical intermediates resulting from the Markovnikov (**2a**·) and *anti*-Markovnikov (**2b**·) modes of addition. Reactions 2b and 2c separate the effect of alkyl substitution on the fluoro and radical moiety, respectively. The sum of these two reactions shows the combined effect of the two factors on the overall stability of the β-fluoroalkyl radicals (reaction 2d). The isodesmic reaction 2e is an alternative way of separating these two effects. β-Fluoroalkyl radicals do not show a tendency to bridge (4), and the results of the calculations were consistent with this. Geometry optimization starting from a symetrically bridged radical converged to the more stable open radical (**2a**·).

The calculated thermodynamic stability of fluoro-substituted compounds has not been extensively investigated, and the question of an appropriate theoretical model to evaluate the enthalpy changes of these isodesmic reactions should be addressed. Therefore, the influence of the theoretical model on the ΔH of reaction 2b was examined and the results are summarized in Table 1.

Irradiation of an acetonitrile solution of **4**, **5**, **6**, and 2-methyl-2-butene (**3**) resulted in four 1:1 (alkene:1,4-dicyanobenzene) adducts and two photo-NOCAS products (Reaction [3]). The combined yield of the four 1:1 adducts was 46%. The *anti*-Markovnikov photo-NOCAS product, 3-(4-cyanophenyl)-2-fluoro-3-methylbutane (**11**), was isolated in 22% yield; whereas the Markovnikov product, 3-(4-cyanophenyl)-2-fluoro-2-methylbutane (**12**), was obtained in only 2% yield. The ratio of *anti*-Markovnikov to Markovnikov prod-

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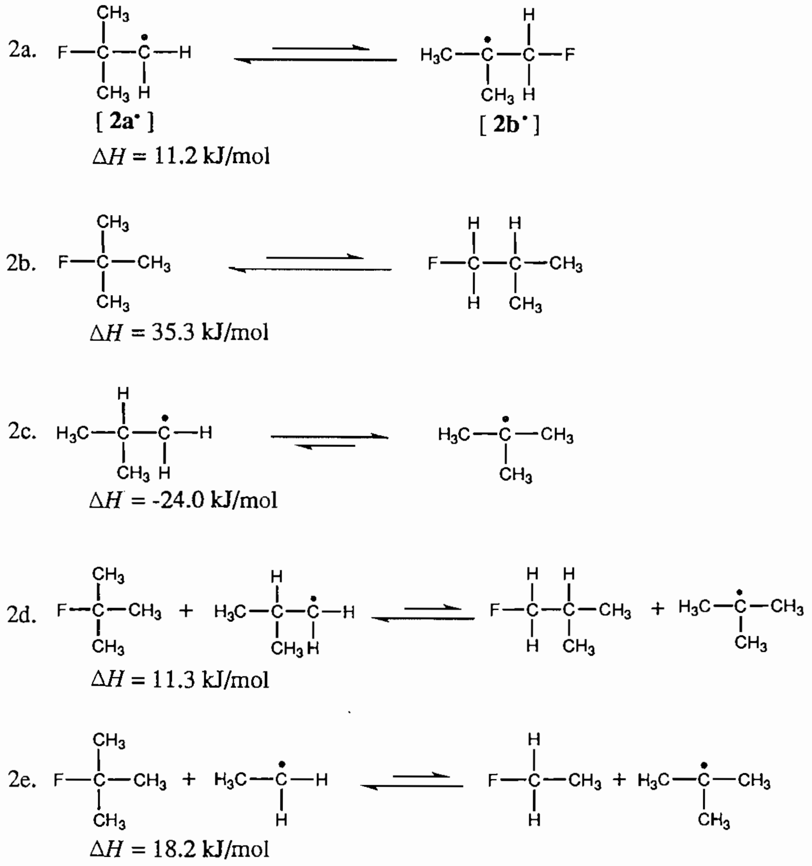
[3] The total energies, selected geometrical parameters, charge and spin distributions of all species in this figure are available as supplementary material, and can be purchased from: The Depository of Unpublished Data, Document Delivery, CISTI, National Research Council Canada, Ottawa, Canada K1A 0S2.

Fig. 2. Isodesmic reactions for 2-methylpropene reaction intermediates.[3]



ucts was found to be 89:11 by integration of a gc/ms chromatograph obtained by single ion monitoring for the molecular ion. This ratio is independent of irradiation time. The addition of a codonor, biphenyl, increased the efficiency of the reaction but had no effect on the product ratios.

The stability of the radical intermediates for this reaction was also evaluated by ab initio molecular orbital calculations. Figure 3 shows the relevant isodesmic reactions and their enthalpy changes. The analysis for this alkene is identical to that described above for the 2-methylpropene reaction. Again, there was no evidence for bridging of the β-fluoroalkyl radical intermediate for this alkene.

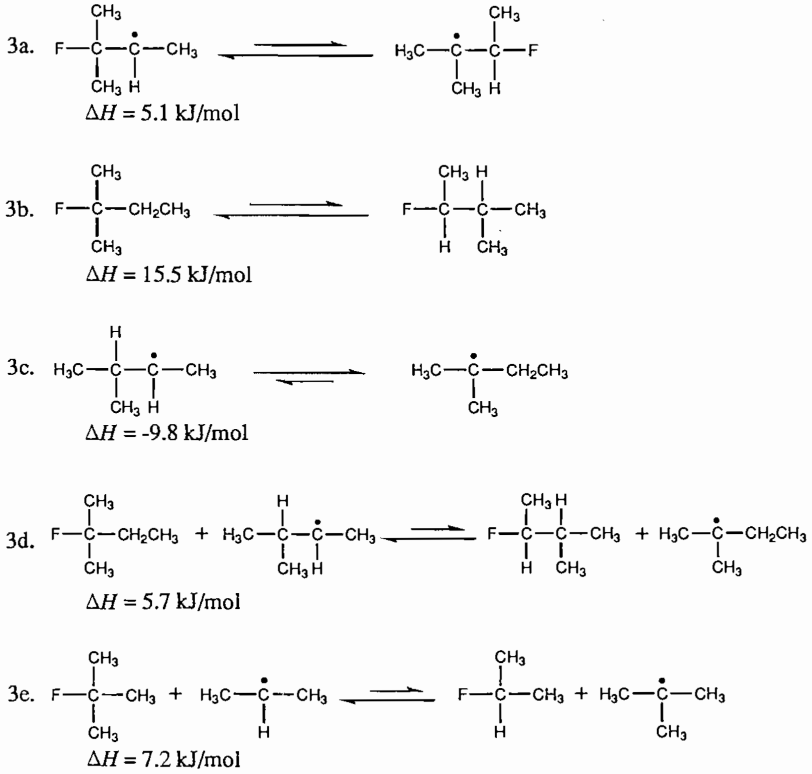
The feasibility of the photo-NOCAS reaction with fluoride anion serving as the nucleophile and conjugated dienes serving as the olefin was also investigated. The dienes chosen for this study were 1,3-butadiene, 2-methyl-1,3-butadiene, 4-methyl-1,3-pentadiene, 2,4-dimethyl-1,3-pentadiene, and 2,5-dimethyl-2,4-hexadiene. Irradiation of an acetonitrile solution of 1,4-dicyanobenzene (**4**), biphenyl (**5**), diene, and tetrabutylammonium fluoride (**6**) did not result in any photo-NOCAS products. The mass spectrum obtained from the gc/ms chromatographs of these reaction mixtures suggested that 1:1 (diene:1,4-dicyanobenzene) adducts and dimers of the dienes were the major products.

Discussion

The results of this study illustrate that the photo-NOCAS reaction with fluoride anion serving as the nucleophile is feasible. The photo-NOCAS products incorporating fluoride anion were obtained in reasonable yields with little attempt to optimize the reaction conditions. The fluoride anion has been shown to react as a nucleophile ($n_{CH_3I} = 2.7$) (5) and as a base (pK_a of HF = 3.2) (6). Therefore, it is not surprising that deprotonation of the alkene radical cation, where the fluoride anion behaves as a base rather than a nucleophile, is a major competing reaction. In fact, the 1:1 adducts resulting from the coupling of the allylic radical and the radical anion of 1,4-dicyanobenzene (Scheme 1, step 10) were the major product(s) in all of the reactions studied. This type of adduct is commonly observed when irradiations are carried out in the absence of a nucleophile (3*a*,*b*). Even though radical cations are known to be highly acidic species (7), there is direct evidence that the fluoride anion enhances the deprotonation step. The radical cation of 2-methylpropene does not deprotonate easily; the resultant allylic radical is primary on both ambident ends (Scheme 1, step 9). The 1:1 adduct (**9**) resulting from the deprotonation of the radical cation followed by coupling with the radical anion of the 1,4-dicyanobenzene is only observed in trace amounts in the absence of added base (8). The fluoride anion reacting as a base is also the major competing pathway in the preparation of alkyl fluorides by normal (S_N1, S_N2) nucleophilic substitution (5*b*, 9).

The addition of fluoride anion to the radical cation of unsymmetrical alkenes shows high regioselectivity. The regiochemistry can be described as predominately following the *anti*-Markovnikov mode of addition, where the nucleo-

Fig. 3. Isodesmic reactions for 2-methyl-2-butene reaction intermediates.[3]



phile (fluoride) adds preferentially to the less substituted olefinic carbon to produce the more heavily alkyl-substituted radical. At this point, one may be tempted to conclude that the regioselectivity is governed by the relative stability of the β-fluoroalkyl radical intermediates. However, the theoretical calculations show that this is not the case. For both unsymmetrical alkenes studied, the radical resulting from the Markovnikov addition of fluoride is the more stable of the two alternative β-fluoroalkyl radicals (isodesmic reactions 2a and 3a). Nucleophilic addition to the alkene radical cation is highly exothermic, this results in an early transition state, and the product distribution is determined before the relative stability of the alternative intermediate radicals becomes important. These experimental and theoretical results indicate that the fluoride anion behaves like the cyanide anion: the addition is kinetically controlled, steric and polar factors dominate.

Contrary to expected trends, the ab initio molecular orbital calculations indicate that the primary radical (**2a**·) is 11 kJ/mol more stable than the tertiary radical (**2b**·) (isodesmic reaction 2a). The validity of the level of theory employed for these calculations is a question that should be addressed. The MP2/6-31G*//HF/6-31G* theoretical model was shown to be sufficient for estimating the relative stability of ethers (3*e*) and alkyl radicals (the ΔH of reaction 2c is -15.9 kJ/mol calculated from experimentally determined heats of formation (10)). However, there is little information with regard to fluoro-substituted compounds. Calculations on fluorinated aromatic compounds suggest that electron correlation and diffuse functions were not important for evaluating the enthalpy change of isodesmic reactions (11). The isodesmic reaction 2b compares the relative stability of a primary and a tertiary fluoro-substituted alkane. The enthalpy change of this reaction was calculated at various theoretical levels, and the results are reported in Table 1. Including electron correlation (MP2) in the form of single-point energy calculations produces notable differences in the ΔH value. However, including electron correlation in the optimization procedure and further increasing the basis set to 6-311+G* in the single-point calculations did not change the ΔH value significantly. These results suggest that the MP2/6-31G*//HF/6-31G* level of theory is sufficient for estimating the relative stability of fluoro-substituted compounds using isodesmic reactions.

The relative stabilities of the β-fluoroalkyl radicals were further investigated by calculating the enthalpy change of isodesmic reactions 2b–2e and 3b–3e. Reaction 2b indicates that a tertiary substituted fluoroalkane is 35 kJ/mol more stable than a primary substituted fluoroalkane, whereas a tertiary alkyl radical is more stable than a primary alkyl radical by only 24 kJ/mol (reaction 2c). Obviously the effect of the fluoro substitutent dominates when the two effects are combined (reaction 2d). The isodesmic reaction 2e is an alternative method of separating these two effects. The general agreement between reactions 2a, 2d, and 2e is reassuring. In the case of 2-methyl-2-butene, the comparison is now between a secondary β-fluoroalkyl radical and a tertiary β-fluoroalkyl radical. Still, the effect of the fluoro substitutent dominates: the secondary radical is more stable than the tertiary radical by 5 kJ/mol (isodesmic reaction 3a). The energy difference between a secondary and a tertiary alkyl radical is 10 kJ/mol (reaction 3c), and that between a secondary and tertiary substituted fluoroalkane is 16 kJ/mol (reaction 3b). The sum of these two reactions (reaction 3d) agrees well with the relative stability of the two β-fluoroalkyl radicals (reaction 3a). The tendency for fluoro substituents to cause abnormal behavior as compared to their hydrocarbon analogs has been well documented and this effect has been used to advantage in organic synthesis and mechanistic studies (12).

The attempted photo-NOCAS reaction with fluoride anion reacting as the nucleophile did not result in the desired products when conjugate dienes were employed as the olefin. This behavior is related to that observed when cyanide anion was used as the nucleophile. The nitrogen atom of the ambident cyanide anion reacts as a nucleophile to produce isonitrile products only with alkenes. No trace of the isonitrile products were found when conjugate dienes were used. This selectivity was explained in terms of the hard–soft-acid–base (HSAB) principle. The fluoride anion falls into the hard category (13). Relatively speaking, the radical cations of alkenes can be considered as harder than those of conjugated dienes. Therefore, the hard fluoride anion nucleophile prefers to react with hard alkene radical cations. The photo-NOCAS reaction incorporating fluoride as the nucleophile is then limited to hard electrophiles.

Conclusions

The fluoride anion can serve as an effective nucleophile in the photo-NOCAS reaction. The 4-cyanophenyl substituted fluoroalkanes were obtained in reasonable yields with monoalkenes. The reaction is not effective with conjugated dienes. This reactivity can be explained in terms of the HSAB principle; the hard fluoride anion prefers to react with the relatively harder alkene radical cation.

The reaction is regioselective, with the fluoride anion adding preferentially to the less substituted end of an unsymmetrical alkene. The product ratios are not a reflection of the relative stability of the alternative β-fluoroalkyl radical intermediates; the addition is kinetically controlled, and the product ratio is determined before the relative stability of the resulting radicals becomes important; steric and polar effects dominate.

The degree of alkyl substitution on the carbon atom bearing the fluorine substituent produces substantial differences in stability. This can be attributed to the highly electronegative nature of the fluorine atom. In fact, the effect of alkyl substitution on a fluoroalkane is larger than on a carbon radical center. Consequently the more heavily substituted β-fluoroalkyl radical in not the more stable of the two possible intermediates for the unsymmetrical alkenes studied.

Computational details

The GAUSSIAN 94 package of programs (14) was employed for all ab initio molecular orbital calculations. The geometries of the open-shell systems were fully optimized at the unrestricted Hartree–Fock level with the 6-31G* basis set.[4] Single-point energies were calculated to second order in Møller–Plesset perturbation theory (MP2) (16) using the 6-31G* basis set at the HF/6-31G* optimized geometries, and were corrected for spin contamination where appropriate. Unless otherwise noted, all of the structures were optimized using the Berny optimization procedure (17) without symmetry constraints and were confirmed, by harmonic frequency analyses, to be minima on their respective potential energy surfaces. The charge and spin density distributions were obtained from Mulliken population analysis (18).

Experimental

General information

Progress of the reactions was monitored by using a Hewlett–Packard (HP) 5890 gas chromatograph with a BD-1701 fused silica WCOT column (20 m × 0.25 mm, 0.4 μm film thickness) and a flame ionization detector (gc/fid). An HP 3392A integrator is interfaced with the gc/fid to obtain peak areas. An HP 5890 gas chromatograph with a 5% phenyl methyl silicone fused silica WCOT column (25 m × 0.20 mm, 0.33 μm film thickness) interfaced with an HP 5970 mass selective detector (gc/ms) was also used for product analysis. Exact Mass determinations were obtained using a CEC 21-110 mass spectrometer. The mass spectra are reported as *m/z* (relative intensity). The ^{1}H and ^{13}C nmr spectra were obtained from a Bruker 250 or 400 MSL spectrometer. Spectra were recorded in parts per million and frequencies are relative to tetramethylsilane. Infrared spectra (ir) were recorded on a Nicolet 205 spectrometer and are reported in wave numbers (cm^{-1}). Separation of the reaction mixtures was carried out using a combination of the following chromatographic methods: preparative, centrifugally accelerated, radial, thin-layer chromatography (chromatotron),[5] using 1, 2, or 4 mm plates prepared with thin-layer chromatography (tlc) grade silica gel (with binder and fluorescent indicator, Merck 7749); dry column flash chromatography (dcfc) (19) packed with tlc grade silica gel (with binder, Rose Scientific Ltd. 81632); preparative thin-layer chromatography using precoated silica gel plates (2 mm thickness, Merck 5717).

Materials

Acetonitrile was distilled twice, first from sodium hydride and then from phosphorus pentoxide. It was then passed through a column of basic alumina, refluxed over calcium hydride for 24 h (under a nitrogen atmosphere), fractionally distilled, and stored over 3Å molecular sieves. 1,4-Dicyanobenzene (Aldrich) was purified by treatment with activated carbon in methylene chloride, followed by recrystallization from 95% ethanol. Biphenyl was recrystallized three times from methanol before use. Tetrabutylammonium fluoride (Aldrich) was dried at 55°C under vacuum for 24 h just prior to use. 2-Methylpropene (Matheson), 2,3-dimethyl-2-butene (Aldrich), and 2-methyl-2-butene (Aldrich) were used as received.

Irradiations

Irradiations were carried out on acetonitrile solutions of 1,4-dicyanobenzene (**4**), the alkene, tetrabutylammonium fluoride (**6**), and biphenyl (**5**) (serving as a codonor). These solutions were irradiated in either 2 cm inner diameter Pyrex tubes or

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[4] For an in-depth discussion of theoretical methods and basis sets see ref. 15.

[5] Purchased from Harrison Research, Palo Alto, Calif.

5 mm Pyrex nmr tubes, which were degassed by either nitrogen or alkene ebullition. The samples were irradiated at 10°C using a CGE 1 kW medium-pressure mercury vapor lamp contained in a water-cooled quartz immersion well. The yields of the reaction products were calculated based on the amount of 1,4-dicyanobenzene consumed.

Reaction of 2,3-dimethyl-2-butene with 1,4-dicyanobenzene and tetrabutylammonium fluoride

A solution of 1,4-dicyanobenzene (**4**) (1.0401 g, 0.0081 mol), biphenyl (**5**) (1.2151 g, 0.0079 mol), and tetrabutylammonium fluoride (**6**) (3.7161 g, 0.014 mol) in acetonitrile (160 mL) was degassed by nitrogen ebullition. 2,3-Dimethyl-2-butene (**1**) (2.0 mL, 0.017 mol) was added to the reaction mixture, and the solution was irradiated for 24.0 h. Removal of the solvent yielded the crude photolysate. Initial separation of the irradiation mixture was achieved by dcfc using an ether–hexanes gradient. Further purification of the products 3-(4-cyanophenyl)-2,3-dimethyl-1-butene (**7**) and 3-(4-cyanophenyl)-2-fluoro-2,3-dimethylbutane (**8**) was carried out by repeated chromatography (chromatotron) using 100% hexanes as the eluant. Final separation of the 1:1 (alkene:1,4-dicyanobenzene) adduct from the fluoride adduct was achieved by preparative tlc using a 2.5% ether – hexanes gradient (developed twice).

3-(4-Cyanophenyl)-2,3-dimethyl-1-butene (7)

The yield of **7** was 28%. The ^{1}H nmr spectrum agrees well with previously reported results (3*a*): ^{1}H nmr (250.13 MHz, $CDCl_3$) δ_{TMS}: 1.43 (s, 6H, H's of methyl groups adjacent to aryl-substituted carbon), 1.50 (s, 3H, H's of vinylic methyl group), 4.94 (d, 1H, $^2J_{H\text{-}H}$ = 1.2 Hz, vinylic hydrogen), 5.01 (d, 1H, $^2J_{H\text{-}H}$ = 1.2 Hz, vinylic hydrogen), 7.41 (d, 2H, $^3J_{H\text{-}H}$ = 8.5 Hz, H's adjacent to alkyl-substituted aryl carbon), 7.58 (d, 2H, $^3J_{H\text{-}H}$ = 8.5 Hz, H's adjacent to cyano-substituted aryl carbon); ^{13}C nmr (62.90 MHz, $CDCl_3$) δ: 20.09 (q, vinylic methyl group), 28.08 (q, methyl groups adjacent to aryl-substituted carbon), 44.42 (s, aryl-substituted carbon), 109.61 (s, quaternary aryl carbon, cyano substituted), 110.78 (t, terminal olefinic carbon), 119.13 (s, CN), 126.98 (d, aromatic CH adjacent to alkyl-substituted aryl carbon), 132.02 (d, aromatic CH adjacent to cyano-substituted aryl carbon), 151.08 (s, quaternary aryl carbon, alkyl substituted), 154.15 (s, alkyl-substituted olefinic carbon).

3-(4-Cyanophenyl)-2-fluoro-2,3-dimethylbutane (8)

The yield of **8** was 22%: infrared (Nicolet 205) ν: 2989(s), 2229(s), 1608(m), 1506(m), 1474(m), 1377(s), 1098(m), 844(s); ^{1}H nmr (250.13 MHz, $CDCl_3$) δ_{TMS}: 1.22 (d, 6H, $^3J_{H\text{-}F}$ = 22.0 Hz, H's of methyl groups adjacent to fluoro-substituted carbon), 1.42 (s, 6H, H's of methyl groups adjacent to aryl-substituted carbon), 7.55 (d, 2H, $^3J_{H\text{-}H}$ = 9.1 Hz, H's adjacent to alkyl-substituted aryl carbon), 7.60 (d, 2H, $^3J_{H\text{-}H}$ = 9.1 Hz, H's adjacent to cyano-substituted aryl carbon); ^{13}C nmr (62.90 MHz, $CDCl_3$) δ: 23.59 (q, d, $^2J_{C\text{-}F}$ = 24.8 Hz, methyl groups adjacent to fluoro-substituted carbon), 24.14 (q, d, $^3J_{C\text{-}F}$ = 5.7 Hz, methyl groups adjacent to aryl-substituted carbon), 45.12 (s, d, $^2J_{C\text{-}F}$ = 20.0 Hz, aryl-substituted carbon), 98.74 (s, d, $^1J_{C\text{-}F}$ = 175.5 Hz, fluoro-substituted carbon), 109.99 (s, quaternary aryl carbon, cyano substituted), 119.04 (s, CN), 128.80 (d, aromatic CH adjacent to alkyl-substituted aryl carbon), 131.31 (d, aromatic CH adjacent to cyano-substituted aryl carbon), 151.61 (s, quaternary aryl carbon, alkyl substituted); ms *m/z*: 40(25), 61(7), 116(30), 130 (20), 144(100), 145(95), 205(1). Exact Mass calcd. for $C_{13}H_{16}FN$: 205.1267; found: 205.1262.

Reaction of 2-methylpropene with 1,4-dicyanobenzene and tetrabutylammonium fluoride

2-Methylpropene (**1**) was bubbled into a solution of 1,4-dicyanobenzene (**4**) (1.5572 g, 0.012 mol), biphenyl (**5**) (1.9684 g, 0.013 mol), and tetrabutylammonium fluoride (**6**) (3.8249 g, 0.015 mol) in acetonitrile (240 mL). This reaction mixture was irradiated for 50.5 h. The solvent was then removed to afford the crude photolysate. Initial separation of the reaction mixture was achieved by dcfc using a solvent gradient of hexanes and ether. 1,4-Dicyanobenzene (**4**) (0.9318 g, 0.0073 mol) was recovered in this manner (40% conversion). Subsequent purification of the products 3-(4-cyanophenyl)-2-methylpropene (**9**) and 2-(4-cyanophenyl)-1-fluoro-2-methylpropane (**10**) was carried out by repeated chromatography (chromatotron) with 100% hexanes and 0.25% ether – hexanes as eluants, respectively.

A trace amount of 1-(4-cyanophenyl)-2-fluoro-2-methylpropane was also detected. Evidence for this compound consisted of a doublet at 2.95 ppm ($^3J_{H\text{-}F}$ = 21.7 Hz) in the ^{1}H nmr spectrum, indicative of the aryl-substituted methylene group, and, a doublet at 26.69 ppm ($^2J_{C\text{-}F}$ = 24.8 Hz) in the ^{13}C nmr spectrum, indicative of methyl groups adjacent to a fluoro-substituted carbon. Integration of a gc/ms chromatograph obtained from single-ion monitoring mode for the molecular ion (*m/z* = 177) gave a ratio of 95:5 (*anti*-Markovnikov: Markovnikov) for the two photo-NOCAS products.

3-(4-Cyanophenyl)-2-methylpropene (9)

The yield of **9** was 8%: ^{1}H nmr (250.13 MHz, $CDCl_3$) δ_{TMS}: 1.66 (s, 3H, CH_3), 3.36 (s, 2H, methylene group), 4.72 (s, 1H, vinylic hydrogen), 4.86 (s, 1H, vinylic hydrogen), 7.29 (d, 2H, $^3J_{H\text{-}H}$ = 8.5 Hz, H's adjacent to alkyl-substituted aryl carbon), 7.58 (d, 2H, $^3J_{H\text{-}H}$ = 8.5 Hz, H's adjacent to cyano-substituted aryl carbon); ^{13}C nmr (62.90 MHz, $CDCl_3$) δ: 22.06 (q, CH_3), 44.64 (t, aryl-substituted methylene carbon), 110.07 (s, quaternary aryl carbon, cyano substituted), 113.23 (t, terminal olefinic carbon), 119.09 (s, CN), 129.71 (d, aromatic CH adjacent to alkyl-substituted aryl carbon), 132.16 (d, aromatic CH adjacent to cyano-substituted aryl carbon), 143.56 (s), 145.44 (s). These spectral data agree well with previously reported results (20).

2-(4-Cyanophenyl)-1-fluoro-2-methylpropane (10)

The yield of **10** was 5%: infrared (Nicolet 205) ν: 2974(s), 2898(m), 2229(s), 1608(m), 1507(m), 1473(m), 1370(m), 1020(s), 839(s); ^{1}H nmr (250.13 MHz, $CDCl_3$) δ_{TMS}: 1.37 (d, 6H, $^4J_{H\text{-}F}$ = 1.8 Hz, H's of methyl groups), 4.38 (d, 2H, $^2J_{H\text{-}F}$ = 47.6 Hz, H's of fluoro-substituted methylene group), 7.49 (d, 2H, $^3J_{H\text{-}H}$ = 8.5 Hz, H's adjacent to alkyl-substituted aryl carbon), 7.63 (d, 2H, $^3J_{H\text{-}H}$ = 8.5 Hz, H's adjacent to cyano-substituted aryl carbon); ^{13}C nmr (62.90 MHz, $CDCl_3$) δ: 24.61 (q, d, $^3J_{C\text{-}F}$ = 5.8 Hz, methyl groups), 39.81 (s, d, $^2J_{C\text{-}F}$ = 18.1 Hz, aryl-substituted carbon), 90.65 (t, d, $^1J_{C\text{-}F}$ = 178.0 Hz, fluoro-substituted carbon), 110.35 (s, quaternary aryl carbon, cyano substituted), 118.86 (s, CN), 127.02 (d, aromatic CH adjacent to alkyl-substituted aryl carbon), 132.12 (d, aromatic

CH adjacent to cyano-substituted aryl carbon), 151.13 (s, d, $^{3}J_{\text{C-F}}$ = 2.9 Hz, quaternary aryl carbon, alkyl substituted); ms *m/z*: 38(13), 40(12), 116(48), 144(100), 145(17), 177(32). Exact Mass calcd. for $C_{11}H_{12}FN$: 177.0954; found: 177.0955.

Reaction of 2-methyl-2-butene with 1,4-dicyanobenzene and tetrabutylammonium fluoride

A solution of 1,4-dicyanobenzene (**4**) (1.6289 g, 0.013 mol), biphenyl (**5**) (1.8685 g, 0.012 mol), and tetrabutylammonium fluoride (**6**) (6.1549 g, 0.024 mol) in acetonitrile (240 mL) was degassed by nitrogen ebullition. 2-Methyl-2-butene (**3**) (3.0 mL, 0.028 mol) was added to the reaction mixture, and the solution was irradiated for 24.0 h. Removal of the solvent yielded the crude photolysate. Initial separation of the irradiation mixture was achieved by dcfc using an ether–hexanes gradient. 1,4-Dicyanobenzene (**4**) (0.4193 g, 0.0033 mol) was recovered in this manner (74% conversion). Four 1:1 adducts (combined yield of 46%) were also separated from the reaction mixture by dcfc. The identity of these products was deduced by the mass of the molecular ion (*m/z* = 171) and the fragmentation pattern in the mass spectrum. Subsequent purification of the fluoride adducts was carried out by repeated chromatography (chromatotron) using 100% hexanes as the eluant. Final separation of the two isomers was attempted by preparative tlc using a 1.0% ether – hexanes gradient (developed 12 times). Integration of a gc/ms chromatograph obtained from single-ion monitoring mode for the molecular ion (*m/z* = 191) gave a ratio of 89:11 (*anti*-Markovnikov: Markovnikov) for the two photo-NOCAS products.

3-(4-Cyanophenyl)-2-fluoro-3-methylbutane (11)

The yield of **11** was 22%: infrared (Nicolet 205) ν: 2985(s), 2924(m), 2229(s), 1608(m), 1507(m), 1453(m), 1382(m), 1067(s), 841(s); ^{1}H nmr (250.13 MHz, $CDCl_3$) δ_{TMS}: 1.10 (d, d, 3H, $^{3}J_{\text{H-H}}$ = 6.1 Hz, $^{3}J_{\text{H-F}}$ = 24.4 Hz, H's of methyl group adjacent to fluoro-substituted carbon), 1.38 (s, 6H, H's of methyl groups adjacent to aryl-substituted carbon), 4.66 (q, d, 1H, $^{3}J_{\text{H-H}}$ = 6.1 Hz, $^{2}J_{\text{H-F}}$ = 47.0 Hz, methine proton), 7.50 (d, 2H, $^{3}J_{\text{H-H}}$ = 8.5 Hz, H's adjacent to alkyl-substituted aryl carbon), 7.61 (d, 2H, $^{3}J_{\text{H-H}}$ = 8.5 Hz, H's adjacent to cyano-substituted aryl carbon); ^{13}C nmr (100.61 MHz, $CDCl_3$) δ: 16.23 (q, d, $^{2}J_{\text{C-F}}$ = 24.2 Hz, methyl groups adjacent to fluoro-substituted carbon), 24.07 (q, d, $^{3}J_{\text{C-F}}$ = 5.3 Hz, methyl group adjacent to aryl-substituted carbon), 24.25 (q, d, $^{3}J_{\text{C-F}}$ = 4.7 Hz, methyl group adjacent to aryl-substituted carbon), 42.83 (s, d, $^{2}J_{\text{C-F}}$ = 18.7 Hz, aryl-substituted carbon), 96.36 (s, d, $^{1}J_{\text{C-F}}$ = 176.5 Hz, fluoro-substituted carbon), 110.48 (s, quaternary aryl carbon, cyano substituted), 119.10 (s, CN), 127.89 (d, aromatic CH adjacent to alkyl-substituted aryl carbon), 132.10 (d, aromatic CH adjacent to cyano-substituted aryl carbon), 151.32 (s, quaternary aryl carbon, alkyl substituted); ms *m/z*: 47(2), 104(8), 116(35), 144(100), 145(10), 191(8). Exact Mass calcd. for $C_{12}H_{14}FN$: 191.1110; found: 191.1105.

3-(4-Cyanophenyl)-2-fluoro-2-methylbutane (12)

The yield of **12** was 2%. Spectral information obtained from a 7:3 (**12**:**11**) mixture: ^{1}H nmr (250.13 MHz, $CDCl_3$) δ_{TMS}: 1.26 (d, 6H, $^{3}J_{\text{H-F}}$ = 22.0 Hz, H's of methyl groups adjacent to fluoro-substituted carbon), 1.34 (d, 3H, $^{3}J_{\text{H-H}}$ = 7.3 Hz, H's of methyl group adjacent to aryl-substituted carbon), 2.96 (q, d, 1H, $^{3}J_{\text{H-H}}$ = 7.3 Hz, $^{3}J_{\text{H-F}}$ = 19.5 Hz, methine proton), 7.35 (d, 2H, $^{3}J_{\text{H-H}}$ = 8.3 Hz, H's adjacent to alkyl-substituted aryl carbon), 7.59 (d, 2H, $^{3}J_{\text{H-H}}$ = 8.3 Hz, H's adjacent to cyano-substituted aryl carbon); ^{13}C nmr (62.90 MHz, $CDCl_3$) δ: 15.57 (q, d, $^{3}J_{\text{C-F}}$ = 5.7 Hz, methyl group adjacent to aryl-substituted carbon), 24.90 (q, d, $^{2}J_{\text{C-F}}$ = 24.7 Hz, methyl group adjacent to fluoro-substituted carbon), 25.76 (q, d, $^{2}J_{\text{C-F}}$ = 24.8 Hz, methyl group adjacent to fluoro-substituted carbon), 49.08 (s, d, $^{2}J_{\text{C-F}}$ = 21.7 Hz, aryl-substituted carbon), 96.51 (s, d, $^{1}J_{\text{C-F}}$ = 172.1 Hz, fluoro-substituted carbon), 110.49 (s, quaternary aryl carbon, cyano substituted), 118.97 (s, CN), 129.67 (d, aromatic CH adjacent to alkyl-substituted aryl carbon), 131.85 (d, aromatic CH adjacent to cyano-substituted aryl carbon), 148.44 (s, quaternary aryl carbon, alkyl substituted); ms *m/z*: 61(90), 77(20), 103(27), 116(21), 129(19), 130(100), 156(34), 191(5).

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