Friedel−Crafts Reactions of Fluorinated Allylic Compounds

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Introduction

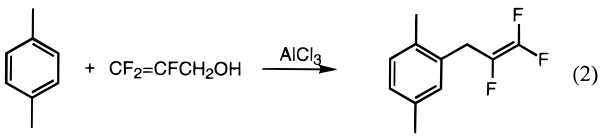
There have been a number of theoretical studies on fluorinated carbocations.[1] In both the 1,1-difluoroallyl and the 1,1,2-trifluoroallyl cation, the majority of the positive charge is at the terminal carbon bearing the fluorine which can back π-bond. Belen'kii[2] has recently reviewed fluorinated allylic intermediates in the reactions of organofluorine compounds. These were predominantly perfluorinated. We were interested in studying the behavior of 1,1-difluoroallyl and 1,1,2-trifluoroallyl carbocations in the Friedel−Crafts reaction.

Results and Discussion

The readily available 2,2,3,3-tetrafluoropropanol can be dehydrofluorinated to the allylic 2,3,3-trifluoropropenol. On treatment with concentrated sulfuric acid the allylic carbocation forms and reacts with water at the fluorinated terminus giving 2-fluoracroyl fluoride, eq 1.[3]

$$CF_2{=}CFCH_2OH \xrightarrow{H_2SO_4} \left[CF_2{=}CFCH_2^+ \longleftrightarrow {}^+CF_2CF{=}CH_2\right] \xrightarrow{H_2O} FC(=O)-CF{=}CH_2 \quad (1)$$

Interest in this allyl carbocation led us to study the reaction of 2,3,3-trifluoropropenol in the Friedel−Crafts reaction. To avoid the problem of hydrolysis that was observed using sulfuric acid, the reaction was performed in xylene using aluminum chloride as the catalyst as shown in eq 2.



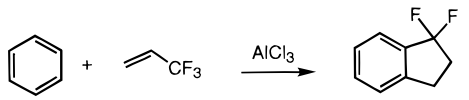
(2)

1

Interestingly, in contrast to the hydrolysis, electrophilic aromatic substitution led to the attachment of the aromatic ring at the CH_2 terminus of the fluorinated carbocation. Only one product, **1**, was observed. The carbon bearing hydrogen, not fluorine, is the one that becomes bound to the ring. It is probable that the relative stability of the intermediate cyclohexadienyl carbocations determines the regiochemistry of the reaction. Intermediate **A** is less stable than intermediate **B** because the electronegative fluorine destabilizes the carbocation. In addition, the substitution product that would result from **A** is thermodynamically less stable than **1**.

A **B**

When Kobayashi and co-workers[4] studied the Friedel−Crafts reaction of 3,3,3-trifluoropropene with benzene and $AlCl_3$, they observed the formation of difluoroindane, as shown in eq 3. The initially formed (difluoroallyl)-benzene was not isolated, nor was its structure determined. It is interesting to note that in the case of **1** a third fluorine on the allyl moiety of 2,3,3-trifluoropropenol suppresses the intramolecular cyclization process.



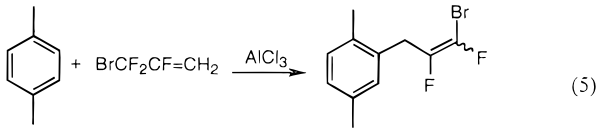
(3)

Treatment of 2,3,3-trifluoropropenol with PBr_3 gives rise to 3-bromo-1,1,2-trifluoro-1-propene, **2**. Reaction of the crude allylic bromide with *p*-xylene in the presence of $AlCl_3$ is rapid and also gives rise to **1**. On attempted purification by distillation, the allylic bromide, **2**, rearranges to the more stable 1-bromo-1,1,2-trifluoro-2-propene, **3**, as shown in eq 4.

$$CF_2{=}CFCH_2Br \xrightarrow{\text{heat}} BrCF_2CF{=}CH_2 \quad (4)$$

2 **3**

Reaction of **3** with $AlCl_3$ and *p*-xylene is complete in 15 min and produces a mixture of *E* and *Z* isomers **4** as shown in eq 5.



(5)

4 *E* and *Z*

Cleavage of the C−F bond occurs when **3** is treated with $AlCl_3$. Formation of the bromofluorocation is not completely unexpected as aluminum chloride has previously been observed to facilitate C−F bond breaking in bromodifluoropropenes.[5] An additional driving force might be the strong aluminum−fluorine bond energy relative to the aluminum−bromine bond.[6] Again, the unsubsti-

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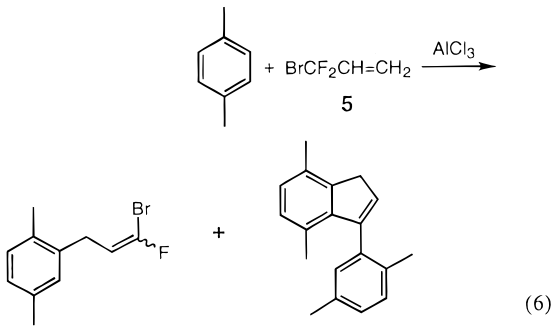
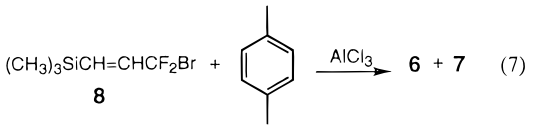
tuted carbon and not the halogenated one is bound to the ring. It is also noted that no cyclization to the indane ring system is observed.

To assess the effect of the fluorine on the central carbon, the reaction of 1-bromo-1,1-difluoro-2-propene, **5**, with *p*-xylene in the presence of $AlCl_3$ was examined. The alkene was rapidly consumed to give rise to the expected bromofluoro adducts (**6**, *E* and *Z*) as well as an unhalogenated substitution product, **7**, eq 6. The amount of **6** that is formed is dependent on the reaction time. The halogenated product is observed initially, but with time is consumed. The bromofluoroalkene, **6**, is an intermediate in the formation of indene **7**; when **6** is treated with $AlCl_3$ in xylene, it is converted to **7**.



6 *E* and *Z* 7 (6)

Reaction of 1-(trimethylsilyl)-3-bromo-3,3-difluoro-1-propene,[7] **8**, with *p*-xylene in the presence of $AlCl_3$ also provides **6** and **7** as shown in eq 7. Like bromofluoropropene, **5**, cleavage of the C−F bond occurs to give the carbocation. Reaction of the allylic ion occurs α to the silyl group which is subsequently removed. The initially formed compound with a silyl group is not observed.



(7)

We were able to effect the desilylation of **8**, by treating it with tetrabutylammonium fluoride in sulfolane. The NMR of the crude reaction mixture showed the presence of **5**. However, on distillation of the propene from the sulfolane, only 1,1-difluoro-3-bromo-1-propene, **9**, was obtained. This is in contrast to the observation of Seyferth and co-workers who found that on distillation of a mixture of **5** and **9** through a glass-helices-packed column, the amount of **5** increased.[8] Reaction of **9** with *p*-xylene in the presence of $AlCl_3$ led to the formation of hydrocarbon **7**.

Increasing the halogen content of the propene shuts down the Friedel−Crafts reaction. Thus, 1,1,2-trichloro-3,3,3-trifluoropropene fails to react with refluxing *p*-xylene in the presence of aluminum chloride.

Conclusion

Although theoretical studies point out that the majority of the positive charge on fluorinated allylic carbocations lies on the fluorinated carbon, reactions of these species with aromatic substrates give products with the non-fluorinated carbon attached to the ring. This suggests that the strongly electron-withdrawing fluorine destabilizes the cyclohexadienyl ion that is the intermediate in the substitution reaction.

Substitution of a fluorine on the central carbon of the allylic cation plays a very important role. When fluorine (or bromine) is present only on the terminal carbon, further electrophilic substitutions can occur to give cyclic products. However, the fact that the allylic compounds with a fluorine on the central carbon do not cyclize while those with no fluorine on the central carbon of the allyl carbocation undergo cyclization clearly points to the destabilizing effect of β-fluorine on carbocations. This is further supported by the observation that 2-fluorocrotyl chloride is not solvolyzed even after prolonged heating at high temperature.[9]

Experimental Section

1-Bromo-1,1-difluoroprop-2-ene was obtained from Oakwood Products, Inc. ^{1}H NMR, ^{19}F NMR, and ^{13}C NMR were recorded at 300, 282, and 75 MHz, respectively. All chemical shifts are reported downfield (positive) of the standard: $CFCl_3$ for ^{19}F, and tetramethylsilane for ^{1}H and ^{13}C NMR spectra. Elemental analyses were performed by Atlantic Microlab, Inc., Norcross, GA. The HRMS was performed by Mass Spectrometry Facility at NCSU.

1,1,2-Trifluoro-3-bromo-1-propene (2). 2,3,3-Trifluoropropenol (7.0 g, 62 mmol) was cooled to −5 to −10 °C, and PBr_3 (2.4 mL, 25 mmol) was slowly added with stirring. After the addition was completed, the bath was removed. The reaction mixture was allowed to warm to room temperature and stirred overnight. The two layers were separated, and the crude product, **2**, was characterized by NMR: ^{1}H NMR δ 4.10 (ddd, 1 H, J = 24.4, 3.6, 2.4 Hz); ^{19}F NMR δ −98.6 (dd, J = 65.8, 33.0 Hz), −115.9 (ddt, J = 115.6, 66.0, 5.1 Hz), −174.8 (ddt, J = 114, 33.0, 21.3 Hz).

1-Bromo-1,1,2-trifluoro-2-propene (3). This product was obtained upon heating and attempted distillation of **2**: yield (4.5 g; 64%); bp 65 °C; ^{1}H NMR δ 5.15 (dd, 1H, J = 42.9, 4.6 Hz), 5.02 (ddt, 1H, J = 14.0, 4.6, 1.6 Hz); ^{13}C NMR δ 156.6 (dt, J = 261, 31.0 Hz), 111.1 (td, J = 301, 44.4 Hz), 93.5 (dt, J = 13.8, 3.3 Hz); ^{19}F NMR δ −56.7 (d, J = 19.2 Hz), −117.7 (m); HRMS (EI, *m*/*e*) calcd for $C_3H_2BrF_3$ 173.9292, found 173.9294.

3-Bromo-3,3-difluoropropenyltrimethylsilane (8). (1,3-Dibromo-3,3-difluoro-1-(trimethylsilyl)propane)[7b] (12 g, 38 mmol) in ether (15 mL) was treated with DBU (8.7 mL, 58 mmol) and stirred at room temperature for 30 min. The solid was filtered out and the filtrate washed with water (2 × 25 mL) and dried over magnesium sulfate. The crude product was purified by vacuum distillation, bp 42 °C (15 mmHg) (lit.[7a] 66−68 °C (52 mmHg)); yield (6.8 g; 77%); ^{1}H NMR δ 6.39 (td, 1H, J = 18.7, 1.8 Hz), 6.19 (td, 1H, J = 18.7, 8.8 Hz), 0.13 (s, 9H); ^{13}C NMR δ 138.6 (t, J = 24.2 Hz), 135.7 (t, J = 5.0 Hz), 117.2 (t, J = 302 Hz), 1.9; ^{19}F NMR δ −47.7 (d, J = 9.7 Hz).

General Procedure for the Friedel−Crafts reaction. To a solution of the alkylating agent (2.2 mmol) in xylene (1.3 mL, 11 mmol), was added $AlCl_3$ (0.30 g, 2.3 mmol) in portions at 10 °C under N_2. The reaction mixture was stirred for 10 min and was partitioned between methylene chloride (10 mL) and water (10 mL). The aqueous phase was washed with another 10 mL of methylene chloride, and the combined organic layers were dried over magnesium sulfate. The crude products were purified by column chromatography on silica gel using petroleum ether as the eluent.

1-(2′,3′,3′-Trifluoro-2′-propenyl)-2,5-dimethylbenzene (1): yield (0.39 g; 90%); ^{1}H NMR δ 7.08 (m, 3 H), 3.63 (dt, 2 H, J = 22.1, 3.3 Hz), 2.33 (s, 3 H), 2.29 (s, 3 H); ^{19}F NMR δ −105.8 (dd,

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J = 87.9, 32.1 Hz), −124.2 (ddt, J = 115, 86.8, 4.8 Hz), −172.7 (m). Anal. Calcd for $C_{11}H_{11}F_3$: C, 65.98; H, 5.54. Found: C, 65.91; H, 5.60.

(*Z* and *E*)-1-(3′-Bromo-2′,3′-difluoro-2′-propenyl)-2,5-dimethylbenzene (4): yield (0.38 g; 66%); ^{1}H NMR δ (major) 7.34 (m, 3 H), 3.98 (dd, 2 H, J = 21.5, 5.1 Hz), 2.65 (s 3 H), 2.60 (s, 3 H); (minor) 7.34 (m, 3 H), 3.88 (dd, 2 H, J = 21.7, 2.6 Hz), 2.66 (s, 3 H), 2.62 (s, 3 H); ^{19}F NMR δ (major) −124.7 (dt, J = 133, 6.1 Hz), −137.6 (dt, J = 134, 22.0 Hz), (minor) −106.9 (d, J = 14.1 Hz), −125.9 (m). Anal. Calcd for $C_{11}H_{11}BrF_2$: C, 50.59; H, 4.24. Found: C, 50.79; H, 4.36.

(*Z* and *E*)-(3′-Bromo-3′-fluoro-2-propenyl)-2,5-dimethylbenzene (6). The amount of this compound could be increased by quenching the reaction after 5 min. ^{1}H NMR ($CDCl_3$) δ 7.14 (s, 1 H), 7.11 (s, 1 H), 7.04 (br, 2 H), 7.02 (br, 2 H), 5.70 (dt, 1 H, J = 12.8, 7.5 Hz), 5.22 (dt, 1 H J = 30.5, 7.8 Hz), 3.45 (dd, 2 H, J = 7.8, 2.5 Hz), 33.37 (d, 2 H, J = 7.5 Hz), 2.38 (s, 6 H), 2.34 (s, 3 H), 2.33 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 136.5, 136.4, 134.3 (d, J = 210 Hz), 134.2 (d, J = 209 Hz), 133.9, 133.7, 130.3, 130.2, 129.4, 129.2, 127.4, 111.0 (d, J = 12.6 Hz), 108.8 (d, J = 16.0 Hz), 31.5 (d, J = 3.7 Hz), 29.6 (d, J = 2.5 Hz), 20.9, 19.0, 18.7; ^{19}F NMR ($CDCl_3$) δ −71.8 (d, J = 13.6 Hz), −76.4 (d, J = 30.5 Hz). Anal. Calcd for $C_{11}H_{12}BrF$: C, 54.34; H, 4.97. Found: C, 54.25; H, 4.97.

Hydrocarbon (7). The reaction was allowed to proceed overnight; **6** was consumed and **7** was isolated: yield (0.45 g; 83%) ^{1}H NMR δ 7.17 (m, 3 H), 7.03 (m, 2 H), 6.39 (t, 1 H, J = 2.1 Hz), 3.46 (d, 1 H, J = 2.3 Hz), 6.45 (d, 1 H, J = 2.3 Hz), 2.47 (s, 3 H), 2.42 (s, 3 H), 2.22 (s, 3 H), 1.94 (s, 3 H); ^{13}C NMR δ 146.5, 143.0, 142.0, 138.8, 134.6, 133.2, 130.9, 130.4, 130.2, 129.9, 129.3, 129.1, 127.9, 126.0, 36.9, 20.9, 19.4, 18.3, 18.2; HRMS (EI, *m*/*e*) calcd for $C_{19}H_{20}$ 248.1565, found 248.1557.

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Supporting Information Available: ^{1}H and ^{13}C NMR spectra of compound **7**. This material is available free of charge via the Internet at http://pubs.acs.org.

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