New fluorination of organic compounds using thermodynamically unstable nickel fluorides

Neil Bartlett,*[b]† Richard D. Chambers,*[a] Alex J. Roche,[a] Robert C. H. Spink,[a] Lisa Chacón[b] and J. Marc Whalen[b]
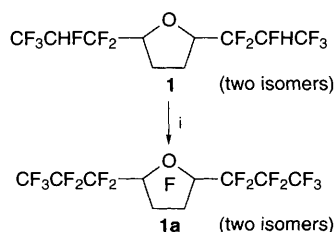
[a] Department of Chemistry, University Science Laboratories, South Road, Durham, UK DH1 3LE
[b] Chemical Sciences Division, LBL, and Department of Chemistry, University of California, Berkeley, California, 94720, USA

Replacement of hydrogen by fluorine in a variety of organic compounds is accomplished with high efficiency in liquid hydrogen fluoride (aHF), at or below 20 °C, using the thermodynamically unstable fluorides $RNiF_3$ and NiF_4, the latter prepared *in situ* from K_2NiF_6 with BF_3.

Fluorocarbon compounds can often be derived from hydrocarbon precursors by well controlled interaction of the latter with elemental fluorine, as pioneered by Margrave and Lagow,[1] and Lagow and his co-workers.[2] Although the convenient reagent cobalt trifluoride, CoF_3, is less potent than elemental fluorine, it has long been employed in the synthesis of highly fluorinated organic compounds.[3] Nevertheless, high temperatures are necessary for the process, depending on the substrate, and this has often resulted in unwanted carbon–carbon bond cleavage. Fluorination *via* the Simons electrochemical cell is also well established,[4] and it is conjectured that higher fluorides of nickel are formed at the anode in this process. The Simons process evidently requires lower activation temperatures than CoF_3, but this route to highly fluorinated organic compounds has generally been most effective with precursors that are soluble in aHF. The recent preparation of the thermodynamically unstable nickel fluorides $RNiF_3$ and NiF_4, and the demonstration that the latter would quantitatively fluorinate perfluoropropene to perfluoropropane below room temperature,[5] indicated that this reagent might be a more easily applied fluorinator than either CoF_3 or the Simons process, for the preparation of highly fluorinated organic compounds. Since K_2NiF_6 is readily available, and the more potent oxidisers NiF_4 and $RNiF_3$ are now conveniently preparable from this reagent in aHF, all three of these materials have been studied in interactions with a variety of organic substrates, using experimental techniques described previously,[5] *i.e.* all manipulations and reactions were performed using transparent fluorocarbon tubing.

To study these systems, we used a model compound **1** that has been shown previously to be very efficiently fluorinated by both CoF_3[6] and the Simons cell process.[7] We have now established that this cyclic ether (which like many oxygen containing species is moderately soluble in aHF) is efficiently fluorinated by $RNiF_3$ at or below, room temperature, to give the perfluorinated compound **1a**. Interaction of $MeCOF$ with $RNiF_3$

was also of interest, since this molecule is efficiently perfluorinated in the Simons process. Although CF_3COF was seen to be formed below 0 °C, further fluorination to the highly volatile products CF_4 and COF_2 easily occurred, and yields of CF_3COF were always low. This indicates that the nickel fluoride formed at the Simons process anode is a less powerful fluorinator than $RNiF_3$.

The oxidative potency of $RNiF_3$ is illustrated by its facile oxidation of MeCN, which is resistant to strong oxidizers.[8] When the initial interaction with MeCN in aHF was at −20 °C to −25 °C (3 h), the carbon–nitrogen bond cleavage was minimal and CF_3CN the major product, but when the interaction was −15 to −20 °C, C_2F_6 and NF_3 were the major products. K_2NiF_6 (in solution in aHF) with MeCN, initiated at −20 to −25 °C proved to be the best perfluorination reagent for MeCN, giving $CF_3CF_2NF_2$ and CF_3CN (2 : 1), with C_2F_6, NF_3 and CF_4 as minor products (*ca.* 1–2% each). The Simons process also yields CF_3CN and $CF_3CF_2NF_2$ with maximum current efficiencies of 40 and 8%, respectively.[9]

The Simons process is much less useful, in general, for the fluorination of compounds which have a low solubility in aHF. Precursor **2**,[10] was selected for the examination of the metal
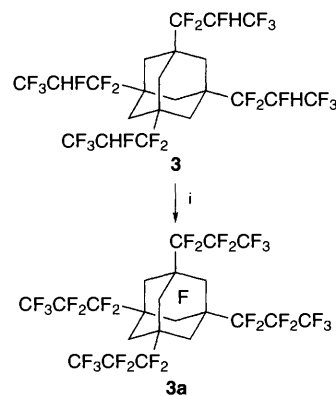
Scheme 2 *Reagents and conditions:* i, $RNiF_3$, aHF, 0 °C, 24 h; ii, NiF_4 (generated *in situ*), aHF, 0 °C, 24 h; iii, K_2NiF_6, aHF, 20 °C, 24 h

Scheme 1 *Reagents and conditions:* i, $RNiF_3$, aHF (initiated at −28 < T < −20 °C for 2.5 h), 24 h
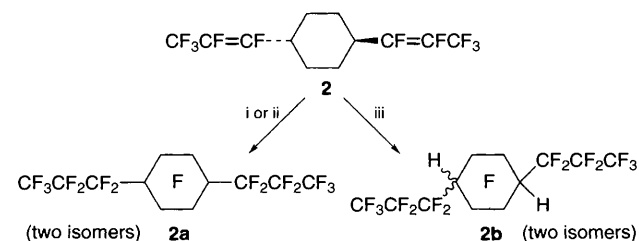
Scheme 3 *Reagents and conditions:* i, NiF_4 (generated *in situ*), aHF, 20 °C, 24 h

fluoride fluorinations for this reason, and also because the fluorination of these cyclohexyl derivatives in vapour phase fluorinations over CoF_3, always undergo some fragmentation. In addition **2** has tertiary carbon–hydrogen bonds which are much more difficult to substitute with fluorine than the hydrogen ligands of a CH_2 group. Separate interactions of **2** with $RNiF_3$, NiF_4 and K_2NiF_6 were carried out to probe their relative effectiveness in carrying through the fluorination. Although $RNiF_3$ in interaction with **2** in aHF at 20 °C gave largely the perfluorinated product **2a**, this compound can also be produced more easily and with even less contamination, by the *in situ* generation of NiF_4 from K_2NiF_6 with BF_3 below 0 °C. When a solution of K_2NiF_6 in aHF was added to an aHF solution of **2** at 0 °C, the rapid precipitation of a red–brown lower fluoride of nickel[5] indicated that fluorination of **2** had occurred, and ^{19}F NMR and GLCMS confirmed the product to be **2b**. This indicates that the more readily replaceable protons in organic compounds can probably be exchanged for fluorine by aHF solutions of the commercially available K_2NiF_6 at ordinary temperatures. When tertiary protons, or other less labile hydrogen ligands need to be substituted, the greater fluorinating power of NiF_4 can then be provided simply by the addition of BF_3.

Previous work in this laboratory[11] had attempted the vapour phase fluorination over CoF_3 of the adamantane derivative **3**, to yield the desired product **3a**. However fragmentation dominated, and **3a** was never observed. However, with either $RNiF_3$ or NiF_4 (generated *in situ*) at 20 °C or below, the fluorination of **3** proceeded efficiently to give **3a**, with no other significant product observed. In contrast, K_2NiF_6 with **3**, did not act as a fluorinator.

Thus we have discovered a new approach to the synthesis of highly fluorinated compounds, that proceeds remarkably efficiently at room temperature or below. The reactions of **1**, **2** and **3** were carried out on a small scale and we have not established

yields, but it is important to emphasise that no significant other products were present, providing that an excess of fluorinating agent was used.

Footnote

† Visiting Professor, University of Durham.

References

1 J. L. Margrave and R. J. Lagow, *Prog. Inorg. Chem.*, 1979, **26**, 161, and references cited therein.
2 See *e.g.* R. J. Lagow, T. R. Bierschenk, T. J. Juhlke and H. Kawa, in *Synthetic Fluorine Chemistry*, ed. G. A. Olah, R. D. Chambers and G. K. S. Prakash, J. Wiley, New York, 1972, ch. 5, p. 97 and references cited therein.
3 M. Stacey and J. C. Tatlow, *Adv. Fluorine Chem.*, 1960, **1**, 166 and references cited therein; R. E. Banks and J. C. Tatlow, *Fluorine, the First Hundred Years*, ed. R. E. Banks, D. W. A. Sharpe and J. C. Tatlow, Elsevier, 1986, p. 267, 337 and references cited therein.
4 Y. W. Alsmeyer, W. V. Childs, R. M. Flynn, G. G. I. Moore and J. C. Smeltzer, in *Organofluorine Chemistry*, ed. R. E. Banks, B. E. Smart and J. C. Tatlow, Plenum Press, 1994, ch. 5, p. 121 and references cited therein.
5 B. Zemva, K. Lutar, L. Chacon, M. Fele-Beuermann, J. Allman, C. Shen and N. Bartlett, *J. Am. Chem. Soc.*, 1995, **117**, 10025.
6 R. D. Chambers, B. Grievson, F. G. Drakesmith and R. L. Powell, *J. Fluorine Chem.*, 1985, **29**, 323.
7 R. D. Chambers, R. W. Fuss and M. Jones, *J. Fluorine Chem.*, 1990, **49**, 409.
8 A. A. A. Emara and G. J. Schrobilgen, *J. Chem. Soc., Chem. Commun.*, 1987, 1644.
9 N. Watanabe and M. Haruta, *Kenkyu Hokoku Asahi Garasu Kogyo Gitjutsu Shoreikai*, 1975/76, **27**, 1; 1974, **25**, 11.
10 R. D. Chambers and R. C. H. Spink, forthcoming publication.
11 R. C. H. Spink, unpublished results.

Received, 1st February 1996; Com. 6/00781C