

FLUORINE CHEMISTRY FOR FLUOROUS CHEMISTRY

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Fluorous chemistry [1] has become a new discipline, the history and paradigms of which are summarized in a recent Handbook [2]. Main streams include fluororous biphasic catalysis, fluororous synthesis and fluororous mixture synthesis, which are recently being supplemented with thermomorphic and confined fluororous systems.

All branches of fluororous chemistry are based on the unique properties of perfluoroalkanes and related solvents, such as chemical inertness, immiscibility with water and most hydrocarbons, low refractive index and as a consequence low intermolecular forces. Noteworthy is the fact that the substitution of hydrogen by fluorine is the sole methodology to reduce the electronic polarizability and to make the molecule hard and to lower the boiling point [3].

Fluorophilic compounds represent a subclass of fluororous ones, displaying a fluororous partition coefficient, $P_{FBS} > 1$, measured between a *c*-CF₃C₆F₁₁-toluene solvent pair at 25°C temperature; while all fluororous compounds have at least one perfluoroalkyl-chain or 'fluorous ponytail' (e.g. R_{fn} = C_nF_{2n+1}, n = 1-10) in each molecule. Fluorophilic compounds can be designed effectively using the simple 'like dissolves like' rule or more complex mathematical expressions derived from thermodynamic models [1, 4]. Both the present practice and the future development of fluororous chemistry should be affected by the awareness of the environmental and health issues of the involved perfluoroalkyl-species, since the presence of perfluorooctanesulfonate (PFOS) and perfluorooctanecarboxylate (PFOA) in the environment have been detected globally, including blood plasma of nonoccupationally exposed humans too (Scheme 1) [5].

Problem 1^o "**Bioaccumulation of perfluorinated C8 derivatives**"

Problem 2^o "**Fluorocarbon's persistence and global warming potential (GWP)**"

Scheme 1. Strategic Issues for Fluorous Chemistry Development

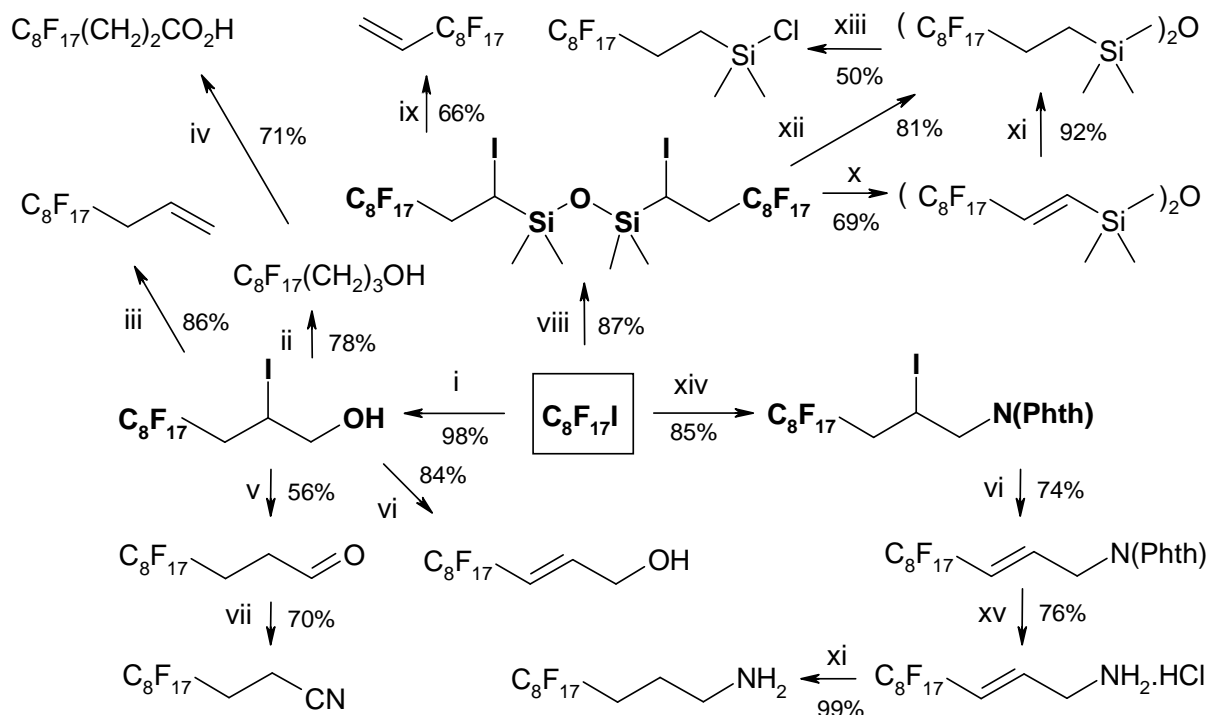
The first problem calls for the introduction of either shorter fluororous ponytails and/or the development novel generation ponytails based on fluorine chemistry examples. CF₃-group chemistry has been identified by us and others as a promising strategy for this purpose. The second issue could be solved by the substitution of other solvents for fluorocarbons or using no solvents, whenever possible. The purposeful selection and application of non-volatile fluororous ionic liquids, stationary fluororous liquid phases, confined fluororous nanodroplets, self assembled fluororous monolayers and solid superstoichiometric poly(carbon fluorides) {[CF_{1.12±0.03}]_n} could be useful choices.

Saturated fluorocarbons (R_FH) and fluorocarbon halides (R_FX, X = I, Br, Cl), acid fluorides (R_FCOF) and sulfonyl fluorides (R_FSO₂F) are amongst the most frequently used fluororous solvents and precursors.

Telomer iodides *n*-C_nF_{2n+1}I with even carbon numbers are more easily accessible than those with odd carbon numbers, due to their production schemes (**a** & **b**); since the syntheses of telogenes like CF₃I and (CF₃)₂CFI are more complex and expensive.

- (a) $C_2F_4 + IF_5 \cdot 2I_2 + MoF_6$ (cat) at $75^\circ C \rightarrow C_2F_5I$ (JP 73 52 706)
 (b) $C_2F_5I + C_2F_4 + (i\text{-}PrO_2CO)_2$ at $55^\circ C \rightarrow CF_3(CF_2)_xI$, $x = 3, 5, 7$, etc. (JP 73 42 852)

Although many fluororous reagents have recently become commercially available and thus facilitate the practice of fluororous chemistry, there is a need for their cost effective syntheses. We chose perfluoroalkyl iodides and divinyltetramethyldisiloxane, allyl alcohol and *N*-allylphthalimide, respectively, for the syntheses of $R_{fn}C_2$ and $R_{fn}C_3$ derivatives. The radical chain addition of perfluoroalkyl iodides to alkenes followed by functional group transformations afforded the reagents shown below (Scheme 2).



- (i) $CH_2=CHCH_2OH$, AIBN, $K_2S_2O_8 \cdot H_2O$, (ii) $N_2H_4 \cdot H_2O$, Raney-Ni, (iii) P_{red} , heating, (iv) Jones oxidn., (v) $AgNO_3$, $t\text{-}BuOH \cdot H_2O$, (vi) Et_2NH , Et_2O , r.t., (vii) $CF_3C(O)O \cdot NHCOCF_3$, pyridine, heating; (viii) $(CH_2=CHSiMe_2)_2O$ /AIBN, (ix) Bu_4NF/THF , (x) Et_2NH , reflux, (xi) H_2/Pd , (xii) $NaBH_4$ /diglyme, (xiii) PCl_3 , (xiv) *N*-allylphthalimide, AIBN, *iso*-octane, (xv) N_2H_4/CH_3OH , reflux; HCl.

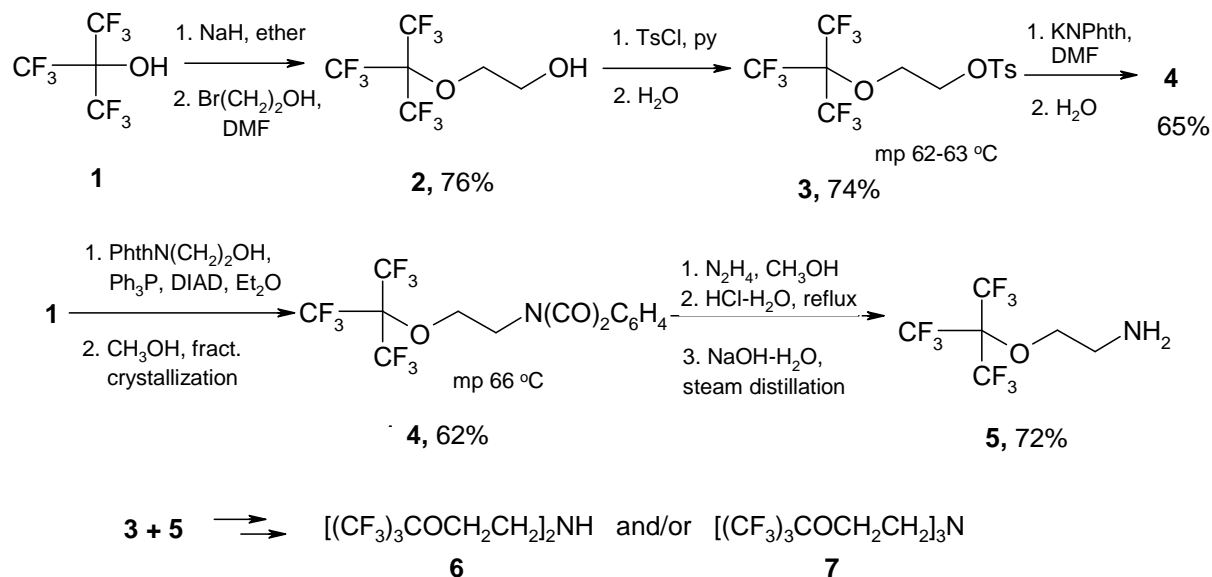
Scheme 2. An entry to fluororous propanols, propanals, propenols, propenes, ethenes, propionitriles, propylamines, allylamines, propanoic acids, silanes and siloxanes.

Similar yields can be obtained with the use of shorter perfluoroalkyl iodides as well, including straight chain $n\text{-}C_4F_9I$, $n\text{-}C_6F_{13}I$ and the branched chain $(CF_3)_2C(CF_2)_4I$, without significant alteration of the above reaction conditions. Work-up procedures are based on the inherent fluororous nature of products, since fluororous chemistry was invented to provide facile separation of the products from reagents or catalysts [5a].

Telomer alcohols $H(CF_2CF_2)_nCH_2OH$ have two reaction sites and can be used for the synthesis of functionalized perfluoroalkyl iodides {e.g. $CH_3CO_2CH_2(CF_2)_8I$ }. Such fluororous derivatives could be useful intermediates for materials science applications.

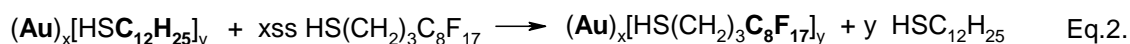
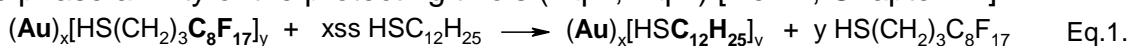
Perfluoroalkanecarboxylic acids $R_{fn}CO_2H$, and **perfluoroalkanesulfonyl halides** $R_{fn}SO_2X$ ($X = F, Cl$) with smaller carbon numbers also have large potential for the synthesis of novel fluororous tags and non-nucleophilic fluororous anions for ionic liquids.

Nonafluoro-*tert*-butyl alcohol (CF₃)₃COH has been demonstrated by us and others to be a valuable CF₃-rich fluorous precursor. Some derivatives include a multiplicity of this building block per molecule, but due to symmetry reasons they display only one high intensity singlet in their ¹⁹F NMR spectra. This property can be exploited for the design and synthesis of novel magnetic resonance imaging (MRI) diagnostics. Our preliminary results with this novel fluorous alcohol are shown below (Scheme 3).



Scheme 3. Sequential synthesis of 1° (5), 2° (6) and 3° (7) fluorous-ethyl amines.

Fluorous monolayer protected gold clusters can be synthesized using the Brust-Schiffrin method, which is based on the reduction of gold(I) in the presence of an excess of thiol. We observed, that the place displacement reaction of the surface layer of fluorous **F-(Au_x)** or organophilic **ORG-(Au_x)** gold clusters with an excess of *n*-C₁₂H₂₃SH or C₈F₁₇(CH₂)₃SH, respectively, results in the transfer of the gold nano-clusters from one layer to the other layer of a fluorous biphasic system according to the phase affinity of the protecting thiols (Eq.1, Eq.2) [Ref. 2, Chapter 14].



We synthesized a series of MPC's and studied their thermal stability with TG method. Decomposition temperatures are: Au_x(HSC₁₂H₂₅)_y 270°C, Au_x(HSC₁₂H₂₅CH₂CH₂C₈F₁₇)_y 239°C, Au_x(HSC₁₂H₂₅CH₂C₆F₁₃)_y 215°C and Au_x(HSC₁₂H₂₅CH₂C₇F₁₅)_y 191°C. The lower the latter temperature the easier is the deposition of gold particles onto porous supports.

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