

Closing Report of Partner 4 Contributions for the M-ERA.Net COR_ID Project

National Research Development and Innovation Office (NN 117633).

Corrosion is unfavourable process with huge economic and environmental adverse effects. Improvement of corrosion resistance of aluminium and its alloys, especially under operating conditions in aeronautical, nautical and automobile industries, is a necessity due to restriction of chromate conversion coatings. In the proposed project we investigate organic corrosion inhibitors and hydrophobic agents in combination with hybrid coatings for various aluminium metal substrates.

The objective of the project is to design multifunctional coatings which would simultaneously act as high-quality corrosion inhibitors and offer additional properties like hydrophobicity. These coatings will be used also for less corrosion resistant Al alloys or secondary Al alloys by industrial partner Talum to improve the functional performance of some of their products.

The design strategy for potential corrosion inhibitors involved the selection of functional groups with appropriate activity for adhesion to clean metal surfaces; and tuning the structure of ponytails (*alkyl vs. perfluoroalkyl, length, and branching*) as a second criterion to achieve (super)hydrophobicity. The effect of *alkyl-* vs *fluorous* tails will be determined when the other parts of these molecules (head- and spacer groups) kept unchanged. *Functional groups such as -N₃, -NH₂, -CO₂H, -OH, -SH, -SS-, -PO₃H₂ and others were considered as targets.* The glucamine derivatives, however, represented multiple functionalized head group among these amphiphiles.

Routine corrosion tests included (1) *sample preparation* via dipping in the clean metals ethanol solution of such amphiphiles or sol-gel development of polymeric matrices; then (2) *evaluation of their performance* using electrochemical polarization cells, and/or saltwater chloride bath.

THROUGH THE PROJECT THE FOLLOWING RESULTS HAVE BEEN ACHIEVED:¹

- POTENTIAL CANDIDATES FOR (I) HYDROPHOBIC COMPOUNDS AND (II) CORROSION INHIBITOR COMPOUNDS BASED ON ALKYL AND PERFLUOROALKYL CHAINS WERE SYNTHESIZED AND TESTED ON ALUMINUM ALLOYS. THE MOST EFFICIENT COMPOUNDS HAVE BEEN VERIFIED. THE MOST CORROSION RESISTANT HYBRID MATRIX HAS BEEN SELECTED AND TESTED IN FIELD MARINE ENVIRONMENT.
- A “VIRTUAL LABORATORY” IS BEING ESTABLISHED TO ENABLE THE CONSTRUCTION OF PARAMETERS USED IN LARGER-SCALE SIMULATIONS, SUCH AS, SEMI-EMPIRICAL BASED MOLECULAR-DYNAMICS.
- PILOT DEVICE FOR LARGE-SCALE TESTING IS UNDER CONSTRUCTION.

PROJECT DETAILS: THE PROJECT GOALS ARE BEING REALIZED THROUGH THE ICME (INTEGRATED COMPUTATIONAL MATERIALS ENGINEERING) PARADIGM CONSISTING OF INTEGRATION OF THREE FUNDAMENTAL DISCIPLINES: MULTI-SCALE MODELING, MULTI-SCALE CHEMICAL SYNTHESIS, AND HIGH-THROUGHPUT ELECTROCHEMICAL AND CORROSION EXPERIMENTAL TESTING AND VERIFICATION.

PARTNERS: (1) JOŽEF STEFAN INSTITUTE, LJUBLJANA, SLOVENIA (COORDINATOR); (2) TALUM D.D. KIDRIČEVO, SLOVENIA; (3) L'ECOLE NATIONALE SUPÉRIEURE DE CHIMIE DE PARIS (ENSCP) AND LE CENTRE NATIONAL DE LA RECHERCHE SCIENTIFIQUE (CNRS), PARIS, FRANCE; (4) EÖTVÖS LORÁND UNIVERSITY, HUNGARY. PROJECT DURATION: 36 MONTHS; TOTAL PROJECT COST: € 597,300; CONTACT DETAILS: JOŽEF STEFAN INSTITUTE; PROF. INGRID MILOŠEV, PH.D.; JAMOVA C. 39, 1000, SLOVENIA; INGRID.MILOSEV@IJS.SI

¹ https://www.m-era.net/success-stories/cor_id-2013-design-of-corrosion-resistant-coatings-targeted-for-versatile-applications

Within the COR_ID network (cf. *supra*) our group had different objectives:

- Synthesis of selected classes of fluoros compounds as potential corrosion inhibitors and/or additives for making anticorrosive protecting sol-gel matrices;
- Development of synthesis processes for the production of selected fluoros compounds at multigram scale; and
- Identifying their possible application in organofluorine chemistry – focused at the fields of Active Pharmaceutical Ingredients (APIs) research and Chiral Recognition.

In accordance with our research plan and the inputs of the COR_ID network partners a series of preselected fluoros compounds of different classes were prepared either by re-syntheses based on reported procedures (Fig.1) or by the new procedures developed during this project. Some of the latter methods are unpublished yet, but they are compiled in the Supplement of this Report.

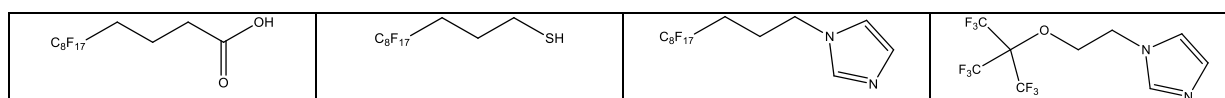


Fig.1 Some examples of compound classes prepared by improved procedures (carboxylic acids, alkanethiols, and imidazoles with linear or branched fluoros ponytails)

Most of the new syntheses developed here are based on the strategy of using perfluoroalkylated building blocks- available commercially or accessible by multistep synthesis using perfluoroalkyl iodides, perfluoroalkane carboxylic acids or nonafluoro-*tert*-butyl alcohol as precursors.

(1) Synthesis of perfluoroalkyl)alkyl azides²

The reaction of *F*-alkylation reagents including (perfluoroalkyl)alkyl halides and sulfonates [$R_n(\text{CH}_2)_m\text{X}$ ($\text{X} = \text{Br}, \text{I}, \text{OTs}, \text{OTf}$)], and a slight excess of NaN_3 in DMSO at 100°C for 5 h, followed by steam distillation, allowed the isolation of azides $R_n(\text{CH}_2)_m\text{N}_3$ in good to excellent yields with high purity (GC assay $\geq 98\%$). Due to the stability of these fluoros azides they can be distilled at atmospheric or lower pressures for further purification. 4-Azidoperfluorotoluene ($p\text{-CF}_3\text{C}_6\text{F}_4\text{N}_3$) and 1-azidooctane were also prepared under similar conditions starting from perfluorotoluene ($\text{CF}_3\text{C}_6\text{F}_5$) or 1-iodooctane, respectively. Steam distillation allowed easy and safe product isolations up to 50 g scale.

Their catalytic hydrogenation in a flow reactor affords the appropriate primary *F*-amines in quantitative yields (cf. Appendix D).

Highlights

- Efficient synthetic route for fluoros-, polyfluoroaryl- and alkyl azides are disclosed here.
- Steam-distillation enabled cost-effective separation of highly volatile fluoros azides.
- Synthesis and isolation of stable fluoros azides can easily be upscaled to safe processes.

(2) 0th Generation Fluoros Secondary Amine Type Dendrimer: Synthesis and Characterization³

Bis(perfluorooctylpropyl)amine and *N*-(benzyloxycarbonyl)iminodiacetic acid di(pentafluorophenyl) ester was heated in $\text{C}_6\text{H}_5\text{CF}_3$ to afford a fluoros diamide with four perfluorooctyl chains, which on deprotection with catalytic hydrogenation in FC-72 (a mixture of perfluorohexanes) solvent gave the appropriate secondary amine in high yield. Although this fluoros secondary amine showed rather low solubility in perfluoroalkanes at room temperature it was found to solubilize colloidal palladium particles in ether, BTF and perfluoroalkanes.

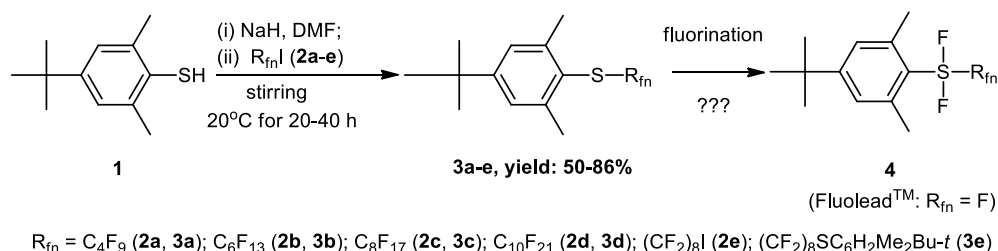
Keywords: fluoros amines, fluoros scavengers, fluoros dendrimers

² Máté Berta, András Dancsó, Anikó Nemes, Zoltán Pathó, Dénes Szabó, József Rábai: Convenient synthesis of pure fluoros alkyl azides at multigram scale, *J. Fluorine Chem.*, Vol. 196: pp. 57-62., 2017; <https://doi.org/10.1016/j.jfluchem.2016.08.005>

³ Anikó Nemes, Gitta Schlosser, Antal Csámpai, Dénes Szabó, József Rábai: Synthesis of 2,2'-azanediylbis[*N,N*-bis(4,4,5,5,6,6,7,7,8,8,9,9,10,10,11,11,11-heptadecafluoroundecyl) acetamide] - a novel fluoros secondary amine with four perfluorooctyl chains, *FLUORINE NOTES / FTORNIE ZAMETKI* 5:(114), 2017; [DOI 10.17677/fn20714807.2017.05.04](https://doi.org/10.17677/fn20714807.2017.05.04)

(3) Synthesis of (2,6-dimethyl-4-*tert*-butylphenyl) perfluoroalkyl sulfides⁴

The synthesis of these sterically hindered aryl perfluoroalkyl sulfides was inspired by the introduction of Fluolead™ as a shelf stable electrophilic fluorination reagent of Umemoto. The sodium salt of 2,6-dimethyl-4-*tert*-butyl-benzenethiol was reacted in dimethyl formamide with a series of perfluoroalkyl iodides and 1,8-diiodoperfluorooctane to afford the corresponding perfluoroalkyl sulfides and 1,8-bis(arythio)perfluorooctane in good yields.

(4) Unusual conversion of a trifluoromethyl-group to an ester group⁵

Based on the unusual reactivity of trifluoromethyl groups in nitrogen containing heterocycles, we synthesized the appropriate porphyrin mono-, di-, tri- or tetra-carboxylic ester derivatives by treatment of the precursor *meso*-tetrakis(trifluoromethyl) porphyrin with an excess of sodium- or potassium alkoxide in the respective alcohol. This method offers an efficient route for the synthesis of lower symmetry *meso*-substituted porphyrins compared to usual preparations utilizing stepwise condensation reactions. The structure of tetrakis(butyloxycarbonyl)porphyrin **5** was determined by X-ray analysis (Fig.1).

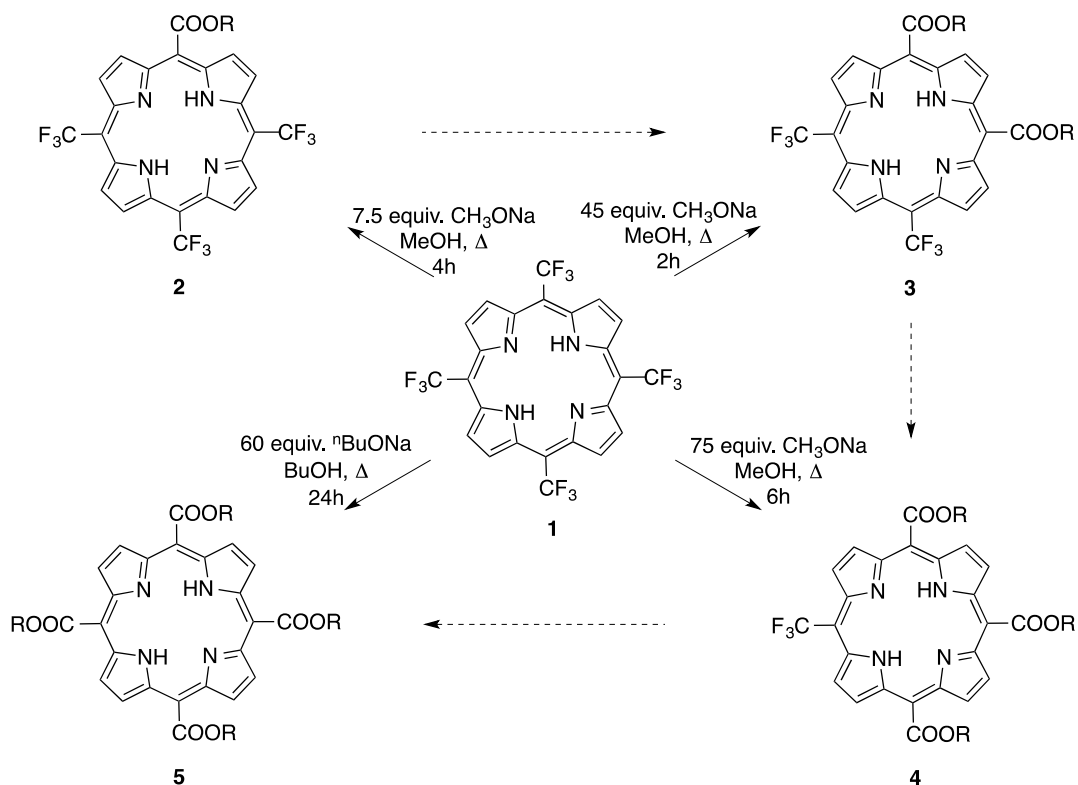


Fig.1 A special case of C(sp³)-F bond activation in fluororous porphyrin system

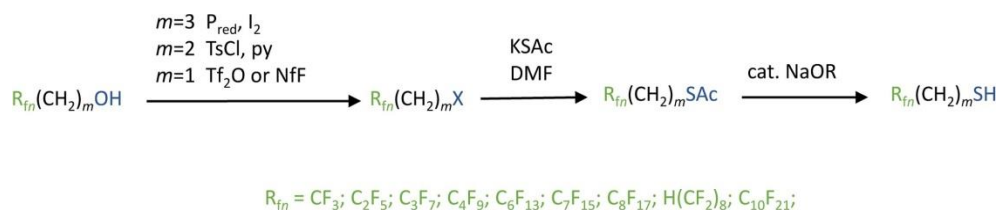
(C-F bond activation has drawn a lot of attention in the past, and the case of C(sp³)-F bonds is particularly interesting as those are the strongest single bonds carbon makes with any other element (Cf. J.-D. Hamel and J.-F. Paquin, Chem. Commun., 2018, **54**, 10224-10239; DOI: [10.1039/C8CC05108A](https://doi.org/10.1039/C8CC05108A)).

⁴ Antal Harsányi, Gitta Schlosser, József Rábai: Synthesis of Sterically Hindered Fluorous Aryl Perfluoroalkyl Sulfides, FLUORINE NOTES / FTORNIE ZAMETKI 5:(114), 2017; DOI [10.17677/fn20714807.2017.05.01](https://doi.org/10.17677/fn20714807.2017.05.01)

⁵ Anikó Nemes Anikó, Egmont Mérés, István Jalsovszky, Dénes Szabó, Zsolt Böcskei, József Rábai: Unusual reactivity of trifluoromethyl groups in meso-tetrakis(trifluoromethyl)porphyrin, J. Fluorine Chem., 203: pp. 75-80., 2017; <https://doi.org/10.1016/j.jfluchem.2017.05.009>

(5) Preparation of (perfluoroalkyl)alkane thiols from fluorous alkyl thioacetates⁶

Convenient and robust synthesis of (perfluoroalkyl)alkane thiols [(C_nF_{2n+1}(CH₂)_mSH); *m/n* = 3/4, 6, 8, 10; *m/n* = 2/6; *m/n* = 1/1, 2, 3, 7, 8H] was developed starting from commercially available fluorous alcohols. The intermediate (perfluoroalkyl) alkyl iodides and/or sulfonates were reacted with potassium thioacetate in DMF, and the resulting thioacetates were deacetylated by a Zemplén reaction. The (perfluoroalkyl)alkane thiols were obtained in good overall yields and high purity.

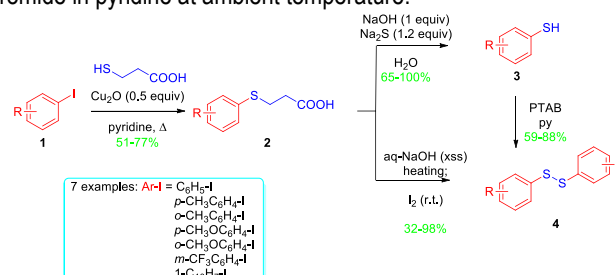


Highlights

- Adaption of Zemplén [deacylation](#) for [thioacetates](#).
- Effective stoichiometric synthesis of thioacetates from [iodides](#) and/or [sulfonates](#).
- Pure perfluoroalkyl thioacetates and [thiols](#) are accessible without [chromatography](#).

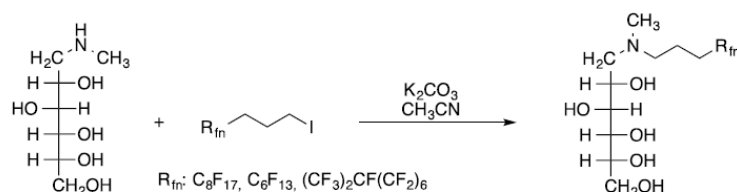
(6) 3-(Arylthio)propionic Acids as Odorless Aryl Mercaptan Surrogates⁷

The reaction of aryl iodides, 3-mercaptopropionic acid, and Cu₂O in refluxing pyridine resulted in the formation of 3-(arylthio)propionic acids in good to excellent yield. The latter 3-(arylthio)propionic acids — as novel aryl mercaptan equivalents — gave aryl mercaptans or diaryl disulfides, respectively, on reductive (Na₂S) or oxidative (I₂) cleavage in alkaline media. The symmetrical disulfides can also be prepared by oxidizing their precursor mercaptans with phenyltrimethylammoniumtribromide in pyridine at ambient temperature.



(7) Synthesis of fluorous glucamine derivatives⁸

As a spin-off studying the synthesis of fluorous corrosion inhibitor candidates- we developed an effective method for the preparation of chiral fluorous glucamines, which at one hand turned out to be effective corrosion inhibitors, while at the other hand they can be used as novel agents for crystallization or extraction enantiomeric resolution methods.



⁶ Bálint Menczinger, Anikó Nemes, Csongor Szijjártó, József Rábai: Preparation of (perfluoroalkyl)alkane thiols via Zemplén deacylation of fluorous (perfluoroalkyl)alkyl thioacetates, J. Fluorine Chem. 210: pp. 70-77., 2018; <https://doi.org/10.1016/j.jfluchem.2018.02.014>

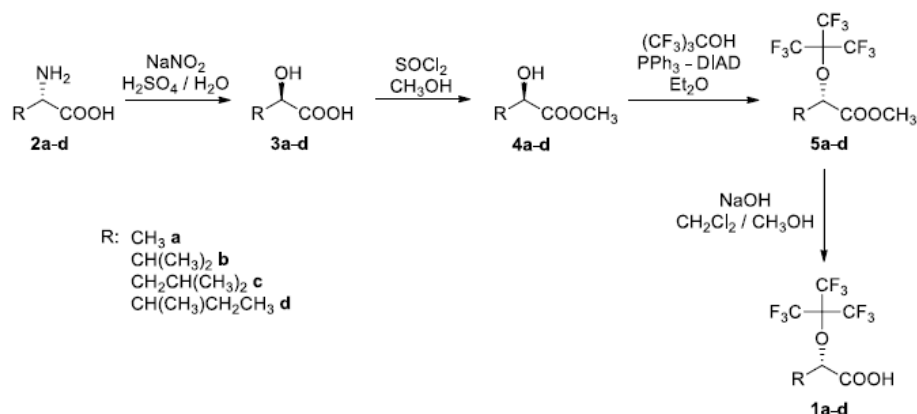
⁷ Bálint Menczinger, Anikó Nemes, Antal Csámpai, József Rábai: Synthesis of 3-(Arylthio)propionic Acids from Nonactivated Aryl Iodides and their Use as Odorless Aryl Mercaptan Surrogates, SYNOPEN 2:(1) pp. 64-71, 2018; DOI: 10.1055/s-0036-1591771

⁸ József Rábai, Dénes Szabó, Bálint Menzinger, Norbert Baris, Gitta Schlosser & the JSI team (Sloven), Unpublished results, 2019. Several joint papers with Ingrid Milošev, Tina Bakarič, Dolores Zimerl, Monika Žnidaršič, and Peter Rodič will be published.

APPENDIX (Preliminary Results Disclosed as Conference Contributions: Posters & Lectures)

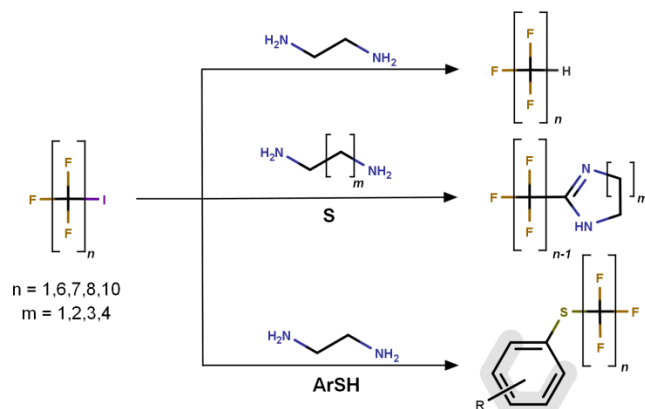
(A) Synthesis of chiral α -nonafluoro-*tert*-butyloxy substituted carboxylic acids⁹

Naturally occurring α -amino acids are used as the precursors of the multigram synthesis of novel α -(nonafluoro-*tert*-butyloxy)-carboxylic acids (**1a-d**). These products can be simply isolated (e.g. steam distillation) and purified without chromatography. Although they originally were designed as chiral NMR shift reagents, their unique physical properties could also allow of making novel (super)hydrophobic surfaces on metals (SAMs) via adsorption from their ethanol solution.



(B) Synthesis of fluorous heterocyclic amidines and fluorous aryl sulphides¹⁰

Perfluoroalkyl iodides were easily converted into fluorous heterocyclic amidines in an excess of 1,2-diaminoethane (ED) and sulfur (Figure, 2nd line). The formed ED*HI-ED as a heavy liquid facilitated the phase separation of the title fluorous products. Without sulfur omega-hydroperfluoroalkanes were obtained (Figure, 1st line)



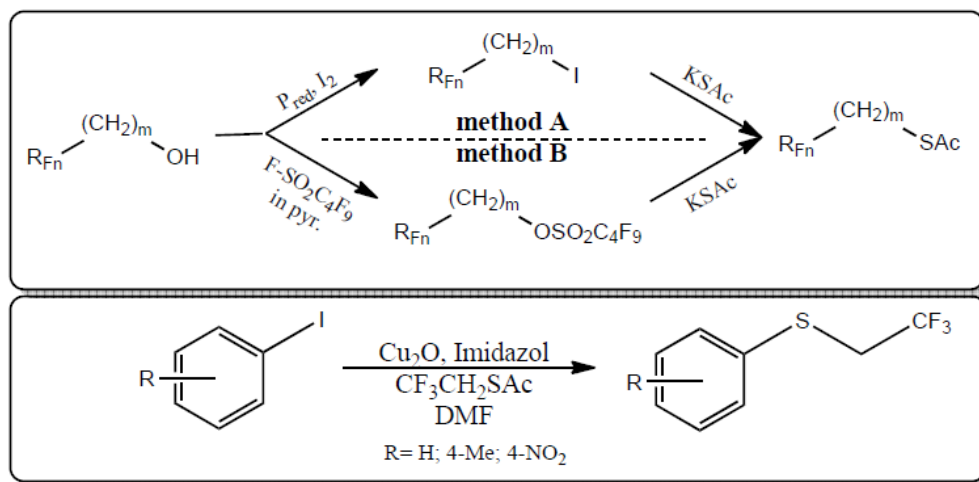
We developed an efficient method for the perfluoroalkylation of thiophenols using ethylenediamine as solvent and base, where perfluoroalkyl iodides (F(CF₂)_nI, n=1,4,6,8,10) served as a source of the perfluoroalkyl chains. As a competitive reaction the reduction of the 1-iodoperfluoroalkane also took place, however in the case of trifluoromethyl iodide, this reaction was considerably slower than the alkylation of the mercaptan (Figure, 3rd line). Using only a slight excess of the trifluoromethyl source, excellent yields of aryl trifluoromethyl sulfides were obtained after a simple extraction from the reaction mixture.

⁹ Anikó Nemes, Tamás Csóka, Szabolcs Béni, Dénes Szabó, József Rábai; New fluorine containing chiral NMR shift reagents; Poster_64. 22nd International Symposium on Fluorine Chemistry, July 22-27, 2018, Oxford, UK.

¹⁰ (a) Kristóf Hegedüs, József Rábai, 1,2-Diaminoethane as a versatile reagent in the transformation of perfluoroalkyl iodides. Poster_67. 22nd International Symposium on Fluorine Chemistry, July 22-27, 2018, Oxford, UK; (b) Kristóf Hegedüs, József Rábai: 1,2-Diaminoethane as a versatile reagent in the transformation of perfluoroalkyl iodides -[P4.44], 18th Tetrahedron Symposium: New Developments in Organic Chemistry, Book of Abstracts, 2017; (c) Kristóf Hegedüs, Máté Berta, András Dancsó, József Rábai: Reactions of perfluoroalkyl iodides with α,ω -diaminoalkanes in the presence or absence of sulfur, F-2016 All-Russian Conference "Fluorine Chemistry" marking the 110th anniversary of Professor Ivan L. Knunyants June 26-30, 2016, Moscow. INEOS RAS. Poster; cf. P-07, 2016

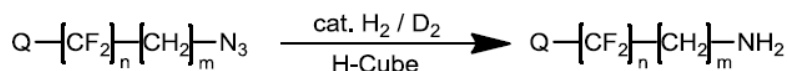
(C) Synthesis of aryl (perfluoroalkyl)alkyl sulfides including aryl trifluoromethyl sulfides¹¹

We synthesised (perfluoroalkyl)methyl thioacetates in good yields from the precursor (perfluoroalkyl)methyl alcohols. And we found that 2,2,2-trifluoroethyl thioacetate can be used as reagent in copper-mediated coupling reactions. This work also shows that if we choose benzylamine as solvent it could play the role of the base and the ligand instead of other additives (imidazole). The adaptation of this reaction to longer (perfluoroalkyl)methylthio ($n \neq 1$) group will be published in the near future.



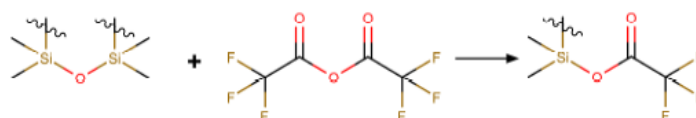
(D) Preparation of fluorous amines by the reduction of azides in a flow reactor¹²

Hydrogenation and deuteration of (perfluoroalkyl)alkyl azides provided the appropriate fluorous azides in quantitative yields. These reactions were optimized in a flow reactor system (H-Cube by ThalesNano). We attempted to find the optimal reaction conditions (i.e. 99+% conversion by highest flow rate) by varying the catalyst (Pd/C, Pd(OH)₂, Pt/C, Rh/C, Ru/C, Raney-Ni) and the reaction conditions in terms of pressure, temperature, flowrate and concentration of the reactant.



(E) Preparation of dialkyl and trialkylsilyl trifluoroacetates and perfluoroalkanoates¹³

The cleavage reaction of siloxanes was performed by using trifluoroacetic anhydride or its homologues, to afford highly reactive silylation reagents, with potential application in the analysis of silicon based hybride matrices, relevant to this project. The formed perfluoroalkane carboxylic acid silyl esters were isolated by distillation using a cryotrap in high yielded and purity. The Si-O-Si bond cleavage reaction occurs at 160 °C in a Pyrex pressure tube if high purity anhydrides are used. In the presence of acid catalyst it takes place under milder condition (25-50 °C, 1 atm). The reaction of hexamethyldisiloxane and perfluoroalkancarboxylic anhydrides gave the appropriate trimethylsilyl esters ($Me_3SiOCOR_n$, $R_n = CF_3, C_2F_5, C_3F_7$).



¹¹ (a) Bálint Meczinger, József Rábai: Synthesis of aryl (perfluoroalkyl)alkyl sulphides; Poster_58. 22nd International Symposium on Fluorine Chemistry, July 22-27, 2018, Oxford, UK.; (b) Bálint Meczinger, József Rábai: Synthesis of (perfluoroalkyl)alkyl thioacetates and aryl (perfluoroalkyl)alkyl sulfides -[P2.19], 18th Tetrahedron Symposium: New Developments in Organic Chemistry, Book of Abstracts, 2017; (c) Bálint Meczinger, Csongor Szijártó, József Rábai: A simple method for the preparation of (perfluoroalkyl)alkyl thioacetates as novel sulfur transfer reagents for the synthesis of aryl (perfluoroalkyl)alkyl sulfides from aryl iodides, 18th European Symposium on Fluorine Chemistry, 7-12 August, 2016, Kyiv, Ukraine, 2016

¹² Máté Berta, András Dancsó, József Rábai: Improved synthesis of fluorous azides and amines, F-2016 All-Russian Conference "Fluorine Chemistry" marking the 110th anniversary of Professor Ivan L. Knunyants June 26-30, 2016, Moscow.

¹³ Máté Berta, András Dancsó, József Rábai: Siloxane bond cleavage with perfluoroalkane carboxylic anhydrides-[P3.80], 18th Tetrahedron Symposium: New Developments in Organic Chemistry, Book of Abstracts, 2017

(F) The principles of fluororous chemistry has been disclosed to the Russian fluorine community¹⁴ Some rules and protocols were disclosed there and illustrated with sequential and/or coherent syntheses of target *fluorophilic* compounds starting from commercially accessible *F*-building blocks such as perfluoroalkyl iodides, perfluoroalkane carboxylates, telomeric *F*-alcohols and their derivatives.

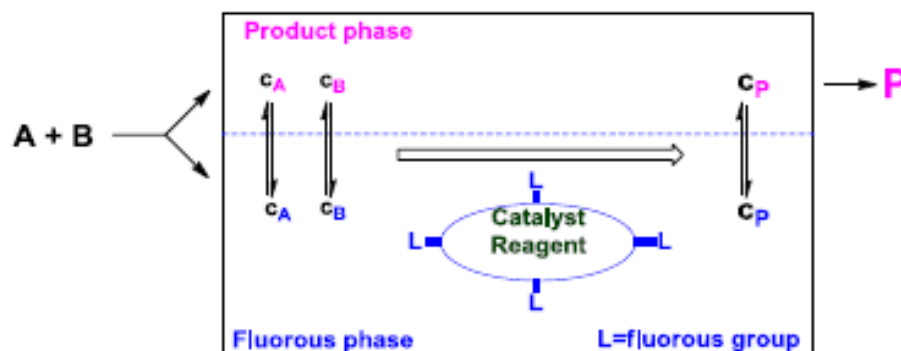


Figure 1. The original drawing of an *fluorous biphasic system*. The lower phase consists of a fluorocarbon type solvent and a *fluorous* catalyst or *fluorous* reagent which is designed to be preferentially soluble there; while the upper phase could be any immiscible liquid including hydrocarbons as well.

Since the CF_3 -group was predicted and observed as the most effective *fluorophilic* substituent (J. Rábai et al. *J. Fluorine Chem.* **2001**, *108*, 95-109), the introduction of nonafluoro-*tert*-butylalcohol – first synthesized and reported by I.L. Knunyants and B.L. Dyatkin (*Izv Nauk SSSR, Ser. Khim.*, **1964**, *5*, 923-925) – and its use as a *fluorous* building block became evident. In addition, the $(\text{CF}_3)_3\text{C}$ -group as opposed to the classical longer *perfluoroalkyl*-groups ($\text{C}_n\text{F}_{2n+1}$, R_{fn} , $n > 6$) does not have any negative environmental concerns (A.S.W. Lo and I.T. Horváth, I. T., *Green Chem.*, **2015**, *171*, 4701-4714).

(G) Some results of the corrosion tests including novel inhibitors has been disclosed¹⁵



Figure 1: Images of bare AlSi9Cu3 aluminium alloy before immersion, bare alloy after immersion, and alloys coated with different types of inhibitor coatings after immersion for 7 days in 0.6 M NaCl.

Note the last two bars were treated with $\text{R}_{18}(\text{CH}_2)_3\text{CO}_2\text{H}$ (perfluoro A) and $3,5-(\text{R}_{18})_2\text{C}_6\text{H}_3\text{CO}_2\text{H}$ (perfluoro B), respectively.

¹⁴ József Rábai, Practice of fluororous biphasic chemistry, Plenary Lecture, F-2016 All-Russian Conference “Fluorine Chemistry” marking the 110th anniversary of Professor Ivan L. Knunyants June 26-30, 2016, Moscow.

¹⁵ Ingrid Milošev, Tina Bakarič, Dolores Zimerl, Monika Žnidaršič, Peter Rodič, József Rábai, Jernej Iskra; Alkyl and Perfluoro Compounds as Corrosion Inhibitors for Aluminium Alloys Containing Si, Regional Symposium on Electrochemistry South-East Europe, Balatonkenese, 11-15 June, 2017