Monday, July 4, 2005		
8:15	**Opening** R. H. Fish, LBNL, Berkeley/USA J.-M. Vincent, LCOO-CNRS, Talence/F	
Chair: R. H. Fish		
8:30	***Plenary Lecture*** **Changing Designer Issues in Fluorous Chemistry** I. T. Horváth**,** Eötvös University, Budapest, Hungary	6
9:30	***Invited Lecture*** **Enantiopure Fluorous Nitrogen Ligands: Synthesis and Applications in Asymmetric Organometallic Catalysis** G. Pozzi, CNR-Istituto di Scienze e Tecnologie Molecolari, Milano, Italy	7
10:10	***Oral Communication*** **Development of Industrial Reaction Processes Using Fluorous Lewis Acid Catalysts** J. Nishikido, The Noguchi Institute, Tokyo, Japan	8
10:30	**Noncovalent Attachment of Nucleotides by Fluorous-Fluorous Interactions** W. Bannwarth, University of Freiburg, Germany	9
10:50	***Coffee break***	
Chair: G. Pozzi		
11:10	***Invited Lecture*** **Styling and Setting of Fluorous Ponytails for Engineered Separations** J. Rábai, Eötvös University, Budapest, Hungary	10
11:50	***Oral Communication*** **Pernitrometalloporphyrins with Fluorous Ponytails as Catalysts in Epoxydation of Alkenes** K. Pamin, Institute of Catalysis and Surface Chemistry, Kraków, Poland	11
12:10	**Fluorous Catalysis With Metal Perfluorocarboxylates** A. Biffis, Dipartimento di Scienze Chimiche, Padova, Italy	12
12:30	**Lunch**	
Chair: D. Bonnet-Delpon		
14:00	***Plenary Lecture*** **Advances in Highly Fluorinated Materials for Diagnosis and Therapy** J. Riess, University of California, San Diego, USA	13
15:00	***Invited Lecture*** **Basic Principles and Recent Advances in Fluorinated Self-Assemblies and Colloidal Systems** M.- P. Krafft, Institut Charles Sadron, Strasbourg, France.	14
15:40	***Oral Communication*** **Gelation of Perfluorocarbons** J.-L. Pozzo, Unversité Bordeaux 1, Talence, France	15
16:00	***Coffee break***	
Chair : M.-P. Krafft		
16:20	***Invited Lecture*** **Self-Assembly Mediated by the Fluorophobic Effect** V. Percec, University of Pennsylvania, Philadelphia, USA	16
17:00	***Oral Communication*** **Spontaneous Resolution Phenomena In Perfluorocarbon-Hydrocarbon Supramolecular Architectures** P. Metrangolo, Department of Chemistry Polytechnic of Milan, Italy	17
17:20	***Poster Session*** *(Wiley VCH prize committee: R. H. Fish, D. P. Curran, J. A. Gladysz)*	
19:30	***Reception City Hall of Bordeaux***	

Tuesday, July 5, 2005		
Chair: D. P. Curran		
8:30	***Plenary Lecture*** **Fluorous Chemistry without Fluorous Solvents: New Catalyst Recovery Protocols based upon Fluoropolymers** J. A. Gladysz, University Erlangen-Nürnberg, Germany	18
9:30	***Invited Lecture*** **Fluoro-alcohols: Effective Solvents for Classical Organic Reactions** D. Bonnet-Delpon, Laboratoire BioCIS, Chatenay Malabry, France	19
10:10	***Oral Communication*** **Fluorous-Derivatised Phase Transfer Catalysts** A. M. Stuart, University of Leicester, Leicester, UK	20
10:30	***Coffee break***	
Chair: J. Otera		
11:00	***Invited Lecture*** **New Synthetic Methods for Natural Products Using Heavy Fluorous Technics** T. Inazu, The Noguchi Institute, Tokyo, Japan	21
11:40	***Oral Communication*** **Chemical Synthesis of Oligodeoxyribonucleotides on a Fluorous Dendron** T. Wada, The University of Tokyo, Japan	22
12:00	**Synthesis of Monofunctional Perfluoropolyethers** G. Fontana, Solvay Solexis, Milan, Italy.	23
12:20	**Lunch**	
Chair: A. M. Stuart		
14:00	***Plenary Lecture*** **Fluorous Organotin Chemistry** J. Otera, Okayama University of Science, Okayama, Japan	24
15:00	***Oral Communication*** **Fluorous-Tagged Glycoside Primer for Saccharide Chain Elongation by Cellular Enzyme** K. Hatanaka,The University of Tokyo, Japan	25
15:20	**Solvation of oxygen, carbon dioxide, carbon monoxide and nitrous oxide in fluorinated liquids** M. F. Costa Gomes, Université Blaise Pascal, France	26
15:40	***St Emilion visit***	
20:00	***Banquet at Chateaux La Couspaude***	

Wednesday, July 6, 2005		
Chair: I. T. Horváth		
8:30	***Plenary Lecture*** **Fluorous Biphasic Catalysis: Oxidation of Alkanes, Alkenes, Alcohols, and Alkenols with Mn(II), Co(II), and Cu(I and II) Fluorous Soluble or Thermomorphic Complexes in the Presence of TBHP/O2 or TEMPO/O2 or H2O2.** R. H. Fish, University of California, Berkeley, USA	27
9:30	***Oral Communication*** **Design and Application of Highly Fluorous Catalysts** B.-J. Deelman, Utrecht University, The Netherlands	28
9:50	**F-TEMPO Radicals: Efficient Mediators for the Oxidation of Alcohols** O. Holczknecht, CNR-Istituto di Scienze e Tecnologie Molecolari, Milano, Italy	29
10:10	**Alternative Solid Supports for Fluorous Catalysis** E. G. Hope, University of Leicester, England	30
10:30	***Coffee break***	
Chair: W. Bannwarth		
10:50	***Oral Communication*** **Perfluorinated Vinyl Sulfoxydes: Efficient Synthons for the Preparation of Fluorinated Tetraazamacrocycles. Applications in Catalysis.** E. Magnier, Université de Versailles-Saint-Quentin, Versailles, France	31
11:10	**Hydrogenation of Styrene and 1-octene catalyzed using Pd(II) complex with monodentate perfluoropyridine in $scCO_2$ and conventional organic solvents** I. Kani, Anadolu University, Turkey	32
11:30	**Fluorous Biphasic Catalysis Without Solvent: Novel Recycling Concept** P. Pollet, Georgia Institute of Technology, Atlanta, USA	33
11:50	**Synthesis of Fluorous Phosphines** G. Vlád, J. Fraga-Dubreuil, N. Farkas, F. Richter, I. T. Horváth, Eötvös University, Department of Chemical Technology and Environmental Chemistry, Hungary	34
12:10	**Lunch**	
Chair: J. A. Gladysz		
14:00	***Invited Lecture*** **Application of Fluorous Technologies in Solution-Phase Synthesis** W. Zhang, Fluorous Technologies, Inc., Pittsburgh, USA	35
14:40	***Oral Communication*** **An Expeditious Synthesis of Bistratamide H Using a New Fluorous Protecting Group** S. Takeuchi, Niigata University of Pharmacy and Applied Life Sciences, Japan	36
15:00	**Association of Fluorous ´Phase-Vanishing´ Method with Visible-light Activation for Benzyl Bromination** J. Iskra, University of Ljubljana, Slovenia	37
15:20	**Fluoroponytailed Carboxylate Complexes with Non-Fluorous Ligands as Pre-Catalysts for the Oxidation of Alkenols and Alcohols Under Fluorous Biphasic or Thermomorphic Modes** M. Contel, Universidad de Zaragoza-C.S.I.C., Spain	38
15:40	***Plenary Lecture*** **Fluorous Mixture Synthesis of Murisolin and Passifloricin Stereoisomer Libraries** D. P. Curran, University of Pittsburgh, USA	39
16:40 17:10	***Future Perspectives Panel Discussion Panel: Fish (Chairman), Horváth, Curran, Yeske, Reiss, Krafft*** **Concluding Remarks / Announcement for next ISOFT**	

Poster Program

CHANGING DESIGNER ISSUES IN FLUOROUS CHEMISTRY

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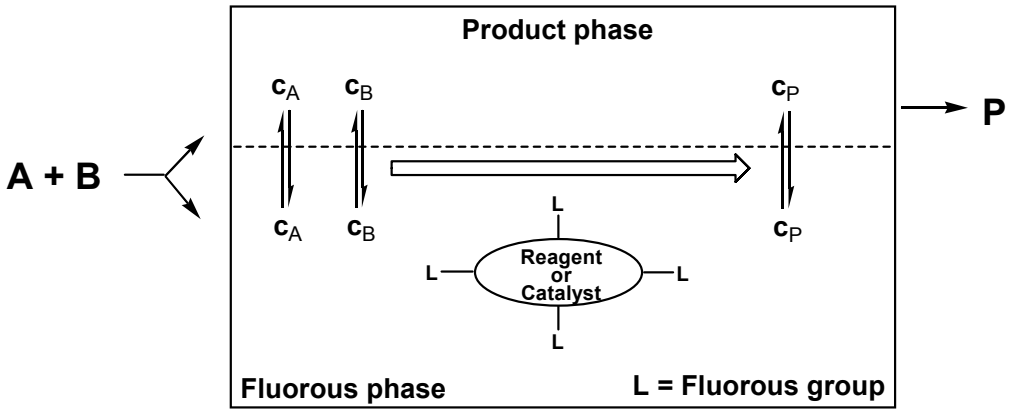
Fluorous chemistry was invented to provide facile separation of the products from reagents or catalysts.[1] Fluorous ponytails of various lengths and structures are the key building components of fluorous reagents and catalysts, which are attached to the reagents or catalysts in appropriate numbers to achieve effective separation.



While a fluorous system is designed to remain inside a laboratory or a production facility, low level leaching to products or accidental releases could result in environmental issues. If such reagents or catalysts enter the environment, the oxidation of the hydrocarbon domains could lead to the formation of fluorous carboxylic acids. Some of these acids have been shown to have negative health and environmental effects. The bioaccumulation could be limited by using shorter (C1-C4) or longer (C10+) fluorous ponytails. The application of C10+ fluorous ponytails could provide good separation, but significantly increases the molecular weight. The combination of shorter (C1-C4) and longer (C10+) fluorous ponytails could lead to commercially attractive reagents and catalysts. The incorporation of oxygen or nitrogen atoms into the fluorous ponytails is another designer tool that could effect simultaneously separation and environmental effects.

[1] I.T. Horváth and J. Rábai, *Science* **1994**, *266*, 72-75 and I.T. Horváth, *Acc. Chem. Res.* **1998**, *31*, 641-650.

ENANTIOPURE FLUOROUS NITROGEN LIGANDS: SYNTHESIS AND APPLICATIONS IN ORGANOMETALLIC CATALYSIS.

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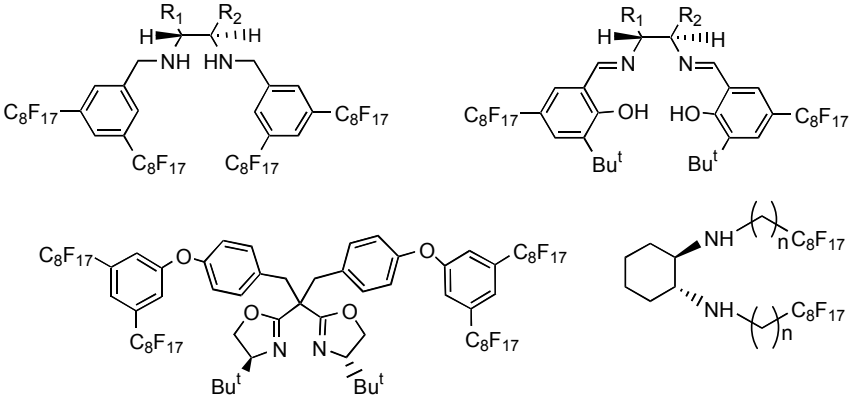
The use of novel reaction media in which homogeneous chiral catalysts can effectively operate and then be easily recovered by simple phase separation is currently attracting considerable interest. Research in this field is also stimulated by the unusual selectivities and increased activities, which are sometimes engendered by the peculiar solvation environment. The molecular structure of the catalyst which, with the notable exception of ionic liquids, must be specifically tailored for use in one of these reaction media, is also utterly important. The development of perfluoroalkyl-substituted (fluorous) chiral ligands to be used in liquid-liquid biphasic systems (or supercritical CO_2), [1] but also in common organic solvents or amphiphilic solvents (BTF) [2] nicely illustrates these points.

In this lecture the ongoing efforts to design and use fluorous chiral ligands for asymmetric organometallic catalysis will be summarised, with emphasis on the work carried out in the author's lab. [3] The synthesis of fluorous nitrogen ligands (Figure 1) and the effect of the perfluoroalkyl chains and reaction media on the activity and selectivity of the corresponding metal complexes in representative enantioselective transformation will be discussed. Recovery and recycling of catalysts based on chiral fluorous nitrogen ligands can be easily achieved, but after a limited number of recycles catalytic activity is usually lost. These are similar results to other supported systems and have to be improved for fluorous catalysts to have wide applications. Therefore, there are still many avenues to be researched in this fast expanding field in order to tailor fluorous ligands to the demanding requirements of recyclable asymmetric catalysts.



[1] Sinou, D. in "Handbook of Fluorous Chemistry" (Gladysz, J. A.; Curran, D.; Horváth; I. T. Eds.), Wiley-VCH, Weinheim, **2004**, 306.
[2] Takeuchi, S.; Nakamura, Y. in "Handbook of Fluorous Chemistry" (Gladysz, J. A., Curran, D., Horváth, I. T. Eds.), Wiley-VCH, Weinheim, **2004**, 316.
[3] Pozzi, G.; Shepperson, I. *Coord. Chem. Rev*. **2003**, *242,* 115.

DEVELOPMENT OF INDUSTRIAL REACTION PROCESSES USING FLUOROUS LEWIS ACID CATALYSTS

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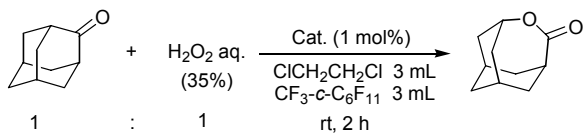
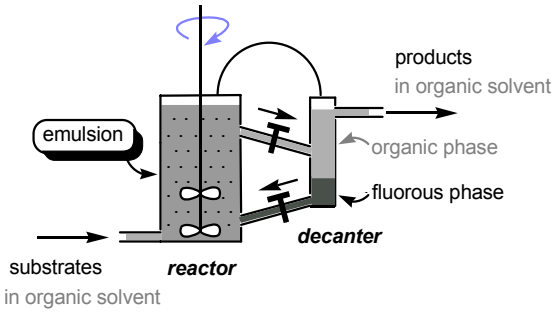
Aluminum chloride, boron trifluoride, *etc.* are known as Lewis acids, but they need to be used stoichiometrically or in excess to achieved high yield and high selectivity. Furthermore, they are rarely recovered and recycled. Thus, even though they are widely used industrially, these Lewis acids cause the production of large amounts of wastes. Our procedure was, first, to develop highly active Lewis acid catalysts, and then to meet the challenge of creating revolutionary organic reaction processes using fluorous solvents, water and supercritical carbon dioxide as reaction media. The key technological aim of the development was to achieve a catalyst recycling system using fluorous Lewis acid catalysts.

We developed a number of fluorous biphasic reactions such as esterification, Diels-Alder reactions, Mukaiyama aldol reactions, Friedel-Crafts reactions,[1] Baeyer-Villiger oxidations with aqueous hydrogen peroxide,[2] transesterifications and direct esterifications[3] catalyzed by $M[N(SO_2R_f)_2]_n$ and $M[C(SO_2R_f)_3]_n$ (M = Yb, Sc, Sn, Hf, Ga, Bi, *etc.*; R_f = *n*-C_8F_{17}, $C_{10}HF_{20}O_3$).



Cat.	cycle	yield(%)	selec.(%)
$Sn[N(SO_2$-*n*-$C_8F_{17})_2]_4$	1	93	99
	4	93	99
$Sc[N(SO_2$-*n*-$C_8F_{17})_2]_3$	1	53	69
$Sc(OTf)_3$	1	31	66

We applied the batch fluorous biphasic reactions to the industrial continuous-flow system.[4] The acetylation of cyclohexanol and Baeyer-Villiger oxidation of 2-adamantanone with 35% aqueous solution of hydrogen peroxide in organic-fluorous biphase were examined to give the corresponding products with high TON using our original continuous-flow system.



Continuous-flow reaction model

Bench-Scale continuous-flow system

The fluorous reverse-phase silica gel-supported Lewis acids which have our fluorous ligands acted as effective catalysts of Baeyer-Villiger oxidation and Diels-Alder reactions in water. Direct esterification of carboxylic acid with alcohol in organic media was also catalyzed. Our fluorous solid catalysts could be recycled by simple filtration after reaction.[5]

[1] Nishikido, J., *et al.*,*Synlett*, **1998**, 1347; **1999**, 1990; Hao, X.; Yoshida, A.; Nishikido, J. *Tetrahedron Lett*. **2005**, *46*, 2697.
[2] Hao, X.; Yamazaki, O.; Yoshida, A.; Nishikido, J. *Tetrahedron Lett*. **2003**, *44*, 4977.
[3] Hao, X.; Yoshida, A.; Nishikido, J. *Tetrahedron Lett*. **2004**, *45*, 781.
[4] Yoshida, A.; Hao, X.; Nishikido, J. *Green Chem.* **2003**, *5*, 554.
[5] Yamazaki, O.; Hao, X.; Yoshida, A.; Nishikido, J. *Tetrahedron Lett*. **2003**, *44*, 8791.

NONCOVALENT ATTACHMENT OF NUCLEOTIDES BY FLUOROUS-FLUOROUS INTERACTIONS

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In aqueous phase, interactions of perfluoro-tags can become very intense.[1]. We have used these interactions to immobilize DNA-fragments noncovalently on fluorous silica gel (FSG) as a basis to develop a simple purification system for synthetic oligonucleotides.[2,3] The procedure is compatible with standard solid-phase synthesis of oligonucleotides. It can be performed on small cartridges in parallel fashion avoiding purifications by polyacrylamide gel electrophoresis (PAGE) or HPLC. Currently, the approach is being extended to the immobilization of RNA and proteins.

[1] Kobos, R.K.; Eveleigh, J.W.; Arentzen, R.; *Trends in Biotechnology* **1989**, 101-105.
[2] Andrushko, V.; Schwinn, D.; Tzschucke, C.C.; Michalek, F.; Horn, J.; Mössner, C.; Bannwarth, W.; *Helv. Chim. Acta* **2005**, *88*, 936-949.
[3] Beller, C.; Bannwarth W; *Helv. Chim. Acta* **2005**, *88*, 171-179.

STYLING AND SETTING OF FLUOROUS PONYTAILS FOR ENGINEERED SEPARATIONS

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Ideal purification processes rely on the transfer of the target compounds and other components to different phases involving e.g. fluorous liquid-organic liquid, fluorous solid-organic liquid, and homogeneous vapour - two immiscible liquid pairs. Here only simple operations are used including extraction (L-L, SPE), filtration (S-L) or distillation to furnish pure products. Since the molecular structure of the compounds determines their bulk properties, the understanding of this correlation is a key for designing molecules with tuned phase characters. To make compounds fluorous the temporary or permanent attachment of longer perfluoroalkyl (R_{fn} = $CF_3(CF_2)_{n-1}$) chains to organic molecules became a general practice of today. The purposeful incorporation of these domains in target molecules is the base for the invention of several techniques, such as fluorous biphasic catalysis, fluorous synthesis and fluorous mixture synthesis. All unique properties of fluorous compounds and phases are governed by complex thermodynamic principles. The state-of-matter (solid, liquid, gas) of compounds are defined by their molecular structure, while some other macroscopic properties including solubility (e.g. thermomorphism) and miscibility can vary very steeply by temperature. Most of the fluorous properties can be learnt by experimental observations, while the specific fluorophilicity can also be predicted with reliable accuracy to the empirical values by using estimated molar volumes and calculated Hildebrand parameters. Structure-fluorophilicity studies revealed that the trifluoromethyl (CF_3-) group have the highest impact on *fluorousness*, it makes the steepest relative increase of fluorophilicities referred to fluorines used per ponytails. Another important parameter is molar volume, which allows dramatic increasing of the fluorous partition coefficient, while the fluorine content and polarity of compound are kept unchanged. This inspired us to design and synthesize novel fluorous model compounds rich in CF_3-groups and initiated a systematic study of the effect of “styling” and “setting” of ponytails on selected properties, including melting point, solubility, fluorophilicty and volatility. Since the state-of-matter of compounds can be a determining factor of engineered separations, it is necessary to have a control on this property at the design stage of these processes. It will be demonstrated, that melting points can be tuned at two levels: *first* with the styling of ponytails by using linear or branching chains, by the presence of hetero atoms in the tails providing conformational flexibility, and *second* with their numbers and setting patterns which ultimately define the degree of symmetry of the final molecules. Syntheses of some novel generation *F*-compounds with defined state-of-matter will also be discussed [1].

[1] Szabó, D.; Bonto, A.-M.; Kövesdi, I.; Gömöry, Á.; Rábai, J. *J. Fluorine Chem.* **2005**, 126, 641-652; and references cited therein.

PERNITROMETALLOPORPHYRINS WITH FLUOROUS PONYTAILS AS CATALYSTS IN EPOXYDATION OF ALKENES

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Oxidation of hydrocarbons catalyzed by metalloporphyrins with molecular oxygen is one of the most attractive transformations in organic synthesis [1]. The major drawback which prevents progress in practical application of the metalloporphyrin catalysts for large scale oxidation is their recycling and re-use. One of the methods to circumvent this problem is the catalysis in fluorous solvents, in particular in a relatively new fluorous biphase system (FBS) that is designed to facilitate the separation of catalysts from reaction mixtures [2]. Thus, we have synthesized the pernitrated metalloporphyrins with ponytails and we have applied these compounds in epoxydation of alkenes with molecular oxygen.

In this work we prepared for the first time pernitrometalloporphyrins with ponytails: $CoTPFP(NO_2)_4(C_6F_{13})_4P$, $FeTPFP(NO_2)_4(C_6F_{13})_4P$, $MnTPFP(NO_2)_4(C_6F_{13})_4P$, $CoTPFP(NO_2)_4(C_8F_{17})_4P$, $CoTPFP(NO_2)_4(C_{10}F_{21})_4P$, and characterized them by UV-Vis, EPR and FTIR spectroscopy. These metallocomplexes are soluble in some perfluorosolvents like perfluoro(methylcyclohexane), perfluorohexane or perfluorodecalin and were applied as catalysts in epoxidation of alkenes in perfluorohexane/CH_3CN biphase system with molecular oxygen and sacrificial aldehyde as the reducing agent [2]. Reactions were carried out at room temperature under O_2 at atmospheric pressure. All synthesized metalloporphyrins were active in the investigated epoxidation reaction. We examined the epoxidation of cyclic and linear olefins. The main product was epoxide. No epoxydation products have been observed in blank experiment without catalyst showing that catalytic activity is associated with metalloporphyrin component. The conversion of substrates and epoxide yields were high, about 90-100% for cyclooctene and cyclohexene. However, these pernitrometalloporphyrins were less active in epoxidation of dodecene and propene which are rather inert linear olefins. The conversions of propene were between 9-15% and of dodecene reached 39-45% wheras epoxide yields were rather high (85-90%). The perfluorohexane phase containing cobalt complex $CoTPFP(NO_2)_4(C_6F_{13})_4P$ was recycled and re-used twice in epoxidation of cyclooctene without decrease of conversion of substrate or yield of epoxide, indicating that the metalloporphyrin does not lose catalytic activity during oxidation process.

Summarizing, we stress that physicochemical and catalytic properties of pernitrometalloporphyrins with ponytails are mainly governed by the strong electron-withdrawing effect of the nitro- and fluoro- substituents.

[1] Połtowicz, J; Haber. J. *J. Mol. Catal*. **2004**, *220*, 43.
[2] Pozzi, G; Montanari, F, Quici, S. Chem. Comm. **1997**, 69

FLUOROUS CATALYSIS WITH METAL PERFLUOROCARBOXYLATES

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Fluorous strategies for the recovery and recycling of homogeneous catalysts have proven to be extremely effective for a variety of catalytic species and reactions. However, the cost of perfluorinated solvents as well as the doubts on their ecocompatibility have recently pushed research towards the development of fluorous separation strategies which minize or even eliminate the need for fluorous solvents.

We have an ongoing program aimed at the application of fluorous recovery and recycling strategies to metal perfluorocarboxylates, which are highly useful catalysts for a number of technologically relevant application.[1-3] In particular, we have developed for such compounds diverse strategies which imply minimal use of fluorous solvents.[2,3]

In this contribution, we would like to illustrate some of our most recent achievements in this field, including 1) a novel approach to fluorous catalysts heterogenization on solid supports, indipendently introduced by our group[2] as well as by others,[4] which we have termed “Bonded Fluorous Phase Catalysis” (BFPC); 2) strategies for the recovery and recycling of fluorous chiral dirhodium(II) carboxylates,[3] which are active and selective catalysts in intermolecular asymmetric cyclopropanation and C-H bond activation reactions; 3) a novel, general protocol for the preparation of heterogenized metal perfluorocarboxylates, making use of fluorous solid ion exchangers.

[1] Biffis, A.; Castello, E.; Zecca, M.; Basato, M. *Tetrahedron* **2001**, *57*, 10391.

[2] a) Biffis, A.; Zecca, M.; Basato, M. poster communication at the Symposium“*Green Solvents for Catalysis”*, Bruchsal (Germany) 13-16 October **2002**; b) Biffis, A.; Zecca, M.; Basato, M. *Green Chem.* **2003**, *5*, 170; b) Biffis, A.; Braga, M.; Basato, M. *Adv. Synth. Catal.* **2004**, *346*, 451;

[3] Biffis, A.; Braga, M.; Cadamuro, S.; Tubaro, C.; Basato, M. *Org. Lett.*, ASAP

[4] a) Tzschucke, C.C.; Markert, C.; Glatz, H.; Bannwarth, W. *Angew. Chem. Int. Ed.* **2002**, *41*, 4501; b) Ablan, C.D.; Hallet, J.P.; West, K.N.; Jones, R.S.; Eckert, C.A.; Liotta, C.L.; Jessop, P.G. *Chem. Commun.* **2003**, 2972; c) Jenkins, P.M.; Steele, A.M.; Tsang, S.C. *Catal. Commun.* **2003**, *4*, 45; d) Yamazaki, O.; Hao, X.; Yoshida, A.; Nishikido, J. *Tetrahedron Lett.* **2003**, 44, 8791.

ADVANCES IN HIGHLY FLUORINATED MATERIALS FOR DIAGNOSIS AND THERAPY

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The basic properties of perfluorocarbons (PFCs) relevant to their use in medicine will be reminded. Exceptionally strong intramolecular binding and weak intermolecular cohesiveness of liquid PFCs result in a unique combination of high O_2- and CO_2-dissolving capacities, extreme hydrophobicity and lipophobicity as well, and high chemical and biological inertness. Injected PFCs are not metabolized and are excreted with the exhaled air.

Poor water solubility of PFC gases allowed the development of stable injectable micron-size gas bubbles that serve as contrast agents for ultrasound diagnosis. The PFC gas compensates for Laplace pressure and arterial pressure, thus opposing dissolution of the microbubbles in the blood. Several such PFC-based microbubble contrast agents have been approved by the EMEA or FDA in the recent years.

Where PFC emulsions for *in vivo* oxygen delivery are concerned, the challenge was to identify a PFC that had a relatively low vapor pressure, yet was readily excreted, capable of producing stable emulsions and easy to manufacture. Perfluorooctyl bromide, a slightly lipophilic PFC, obeys these conditions. Intravascular use supposes the preparation of a stable, sterile, ready-for-use submicron-size PFC-in-water emulsion. Phospholipids are privileged as emulsifiers as they effectively reduce the PFC/water interfacial tension and have a long history of use in pharmaceuticals. Particle growth in such emulsions (which is driven by molecular diffusion) is slowed down by addition of a higher molecular weight PFC such as perfluorodecyl bromide. Heat sterilized PFC emulsions ca. 0.15 μm in size were prepared that are stable for over 2 years. Other emulsion stabilization principles rely on the use of fluorocarbon-hydrocarbon diblocks that modify the interfacial film. *In vivo* oxygen delivery has been established through preclinical experimentation and human clinical trials.

Targeted microbubbles and emulsions are now being investigated that allow molecular imaging of disease using ultrasound or magnetic resonance, as well as drug delivery.

[1] Riess, J.G. *Chem. Rev.* **2001**, *101*, 2797-2919.
[2] Riess J.G. *Tetrahedron* **2002**, *58*, 4113-4131.
[3] Schutt E.G., Klein D.H., Mattrey R.M., Riess J.G., *Angew. Chem. Int. Ed.* **2003**, *42*, 3218.

BASIC PRINCIPLES AND RECENT ADVANCES IN FLUORINATED SELF-ASSEMBLIES AND COLLOIDAL SYSTEMS

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A clear understanding of the basic properties of fluorinated self-assembled systems and interfaces should be valuable to chemists using fluorous phases for synthesis, as these properties determine phase separations, the development of large size interfaces and the possible constitution of micro- or nanoreactors and templates. Many reagents, catalysts and substrates, once fitted with perfluoroalkylated chains for use in fluorous chemistry, are likely to become amphiphilic or to experience enhanced amphiphilic character. Hence, they become susceptible to adsorption at interfaces and to self-association into colloidal systems, including spherical and worm-like micelles, vesicles and fibers, emulsions, microemulsions or other more or less complex colloidal systems. In addition, fluorinated compounds, due to their combined hydro- and lipophobia, and consequent tendency to phase separate from both aqueous and hydrocarbon media, can generate compartmentalization in molecular systems. Interface-driven parameters, which depend largely on the length of the fluorinated moiety, can complicate otherwise simple chemistry.

After a brief reminder of the basic physicochemical properties of fluorocarbons and fluorinated surfactants, we will focus on recent advances on self-assemblies and colloidal systems, e.g. micelles, vesicles, tubules, monolayers and emulsions that comprise fluorinated components. Their present and potential applications, primarily in materials sciences will also be presented.

[1] Special issue of *Curr. Opin. Colloid Interface Sci.* on *Fluorinated Colloids and Interfaces* (M.P. Krafft, ed), **2003**, *8*, 213-314.
[2] M.P. Krafft, in *Handbook of Fluorous Chemistry* (J.A. Gladysz, I. Horváth, D.P. Curran, eds); Wiley-VCH: Weinheim, pp. 478-490, 2004.
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[4] P. Fontaine, M. Goldmann, P. Muller, M.-C. Faure, O. Konovalov, M.P. Krafft, *J. Am. Chem. Soc.* **2005**; *127*, 512-513.
[5] F. Gerber, M.P. Krafft, T.F. Vandamme, M. Goldmann, P. Fontaine, *Angew. Chem. Int. Ed.* **2005**, *44*, 2749-2752.

GELATION OF PERFLUOROCARBONS

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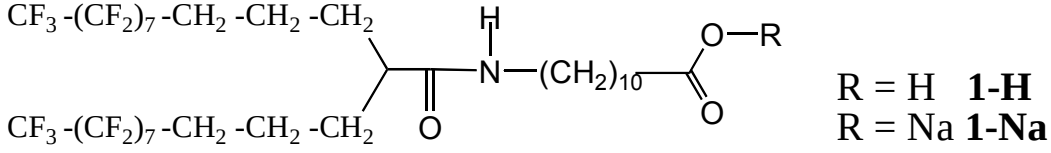
Perfluorocarbons (PFCs) are hydrophobic and lipophobic gas-like liquids that have been extensively studied and used for the preparation of micron- and sub-micron-size fluorous colloidal phases (*F*-colloids).[1] *F*-colloids have found major applications in medicine including, in vivo oxygen delivery (PFC-in-water emulsions), controlled drug delivery (micelles, vesicles, tubules), pulmonary drug delivery (water-in-PFC or HC-in-PFC emulsions) or ultrasound contrast agent (PFC gas emulsion in water). The PFC gels are another class of *F*-colloids that have received special attention (with their potential use as topical delivery barrier cream).[2] To date, most of these PFC gels were obtained using fluorous surfactants in the presence of ~1–20% water.[3] Only a few examples of compounds were shown to gelate "pure PFCs" and, moreover, for each of these compounds gelation is restricted to only one PFC.[4] Now we report on the gelling ability of the charged fluorinated surfactant **1-Na** for a range of PFCs along with AFM observations of unprecedented self-organization of fluorous vesicles into giant three-dimensional periodic structures.



R = H **1-H**
R = Na **1-Na**

[1] Riess, J.G. *Tetrahedron.* **2002**, *58*, 4113-4131.
[2] Krafft, M.P. *Fluorocarbon Gels.* **2001**, *66*, Chap. 10, 195-219.
[3] Krafft, M.-P.; Riess, J.G. *Angew. Chem. Int. Ed.* **2002**, *58*, 4113-4131.
[4] a) perfluorodecaline gel: Höpken, J.; Pugh, C.; Richtering, W.; Möller, M. *Makromol. Chem.* **1988**, *189*, 911-925; b) perfluorooctane gel: George, M.; Snyder, S.L.; Terech, P.; Glinka, C.J.; Weiss, R.G.*J. Am. Chem. Soc*. **2003**, *125*, 10275-10283. c) perfluorotributylamine gel: Loiseau, J.; Lescanne, M.; Colin, A.; Fages, F.; Verlhac, J.-B.; Vincent, J.-.M. *Tetrahedron* **2002**, *58*, 4049-4052.

SELF-ASSEMBLY MEDIATED BY THE FLUOROPHOBIC EFFECT

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This lecture will discuss selected examples from our laboratory in which the fluorophobic effect has been exploited as an extraordinarily efficient tool to both generate and amplify nonbonding intramolecular and intermolecular interactions in order to mediate unprecedented self-assembly processes. Most examples will discuss the design of supramolecular structure and through the supramolecular structure the engineering of the supramolecular order and function. [1, 2, 3, 4]

[1] Percec, V., Glodde, M., Bera, T.K., Miura, Y., Shiyanovskaya, I., Singer, K.D., Balagurusamy, V.S.K., Heiney, P.A., Schnell, I., Rapp, A., Spiess, H.-W., Hudson, S.D., Huan, H. *Nature* **2002**, *419*, 384.

[2] Percec, V., Glodde, M., Johansson, G., Balagurusamy, V.S.K., Heiney, P.A. *Angew. Chem. Int. Ed.* **2003**, *42*, 4338.

[3] Percec, V., Imam, M.R., Bera, T.K., Balagurusamy, V.S.K., Peterca, M., Heiney, P.A. *Angew. Chem. Int. Ed*. **2005**, in press.

[4] Percec, V., Johansson, G., Ungar, G., Zhou, J. *J. Am. Chem. Soc*. **1996**, *118*, 9855.

SPONTANEOUS RESOLUTION PHENOMENA IN PERFLUOROCARBON-HYDROCARBON SUPRAMOLECULAR ARCHITECTURES

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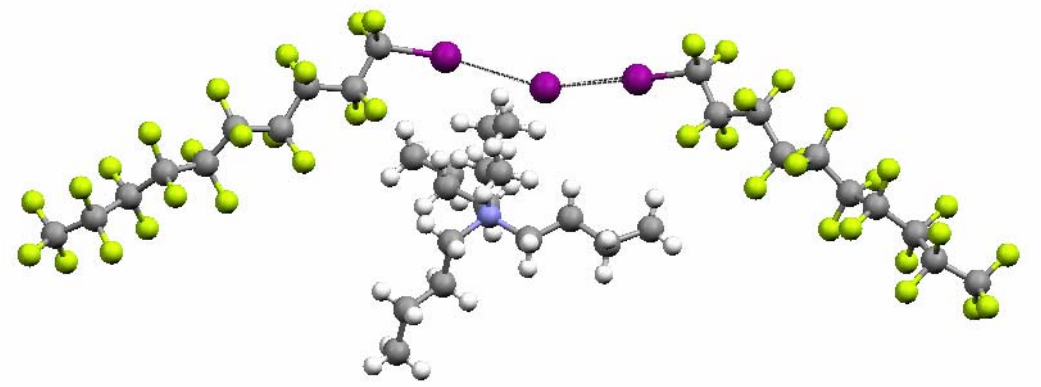
The term halogen bonding (XB) describes any non-covalent interaction involving halogens as electron density acceptors [1]. Bromo- and iodo-substituted perfluorocarbons (PFCs) are nicely tailored to XB-based supramolecular chemistry, and thus behave as particularly robust tectons [2]. The XB-mediated self-assembly of PFCs and hydrocarbons (HCs) revealed to be an efficient strategy in affording new and structurally different hybrid PFC-HC supramolecular architectures [3]. The particular ability of XB in controlling spontaneous resolution phenomena in hybrid PFC-HC supramolecules has been only recently discovered [4]. To date we observed spontaneous resolutions occurring in five crystals of PFC-HC systems affording chiral PFC-HC supramolecular architectures starting from achiral modules. Three of them involved long-chain iodo-PFCs (C_8-C_{10}) with either QUATS or *N,N,N',N'*-tetramethyl-*p*-phenylendiamine as Lewis bases. Their different features with regard to the segregation behaviour and the conformation of the PFC chains will be outlined. Through this approach, for the first time a long chain haloperfluoroalkane has been obtained in the chiral and enantiopure form in the solid state.



Single crystal X-ray structure of the chiral halogen bonded supramolecule TBA-I/I-$(CF_2)_{10}$-I.

[1] Metrangolo, P.; Neukirch, H.; Pilati, T.; Resnati, G. *Acc. Chem. Res.* 2005, **38**, 386.
[2] Metrangolo, P.; Resnati, G. in Halogen Bonding, *Encyclopedia of Supramolecular Chemistry*, Marcel Dekker Inc., New York, **2004**, p. 628.
[3] Metrangolo, P.; Pilati, T.; Resnati, G.; Stevenazzi, A. *Curr. Opin. Colloid Interface Sci.* 2003, **8,** 215.
[4] Neukirch, H.; Guido, E.; Liantonio, R.; Metrangolo, P.; Pilati, T.; Resnati G. *Chem. Commun.* **2005**, 1534.

FLUOROUS CHEMISTRY WITHOUT FLUOROUS SOLVENTS: NEW CATALYST RECOVERY PROTOCOLS BASED UPON FLUOROPOLYMERS

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Conventional fluorous catalysis exploits the temperature-dependent miscibilities of fluorous and organic solvents. Reactions are often conducted at the high-temperature, one phase limit, with product/catalyst separation at the low-temperature, two-phase limit. This talk will focus on recent efforts to eliminate the fluorous solvent requirement. We have found that many fluorous compounds exhibit highly temperature dependent solubilities in organic solvents. Such "thermomorphic" behavior allows fluorous catalysts to be utilized under one phase conditions at elevated temperatures in ordinary organic solvents, and recovered by a simple liquid/solid phase separation at low temperature.[1] It is advantageous to conduct these reactions in the presence of a fluorous support, especially when catalyst quantities are small. This talk will highlight recent refinements involve fluoropolymers such as Teflon.[2] Rhodium-catalyzed hydrosilylations and ruthenium-catalyzed alkene metatheses will be emphasized.

[1] Wende, M.; Gladysz, J. A. *J. Am. Chem. Soc.* **2003**, *125*, 5861.
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FLUORO-ALCOHOLS: EFFECTIVE SOLVENTS FOR CLASSICAL ORGANIC REACTIONS

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Fluorinated alcohols such as hexafluoroisopropanol (HFIP) and trifluoroethanol (TFE) [1] are not considered *stricto sensu* as fluorous media. However, the presence of one or more fluoroalkyl groups brings them specific properties compared to non fluorinated alcohols, what could provoke changes in reaction courses if they are used as solvents. Their properties, with a combination of high hydrogen bonding donor ability, low nucleophilicity, high ionizing power (Table) [2] allowed carrying on reactions which usually require the use of additive reagents or metal catalysts.

Table : Properties of fluorinated alcohols compared to ethanol

	EtOH	TFE	HFIP
b.p. (°C)	78	73.8	58.6
m.p. (°C)	-	-43.5	-5
Density (d)	0.79	1.383	1.605
pKa	15.9	12.4	9.3
Nucleophilicity (N)	0	-2.78	-4.23
Dielectric constant (□)	24.5	26.7	16.7
Ionizing power (Y)	-1.75	1.8	3.82
Hydrogen bond donor (□)	0.83	1.51	1.96
Hydrogen bond acceptor (□)	0.77	0	0
Auto association constant ($dm^3.mol^{-1}$)	0.89	0.65	0.13

Providing they are used as solvents, HFIP and, in a less extent, TFE, are able to facilitate O-O bond and C-O bond cleavages or to facilitate C-C bond formation with no need of metal or acid catalysis.
Examples will be given in oxidation and epoxidation reactions, reactions of oxirane ring opening, cycloaddition reactions and three component reactions.
The procedures offer several advantages like mild and neutral reaction conditions, operational simplicity and ease of isolation of products, good yields of products. In most cases there are no effluents after reaction, and the fluorinated alcohols can be recovered and reused for other reactions [3,4].

[1] HFIP is purchased by Central Glass Co, Ltd (Japan)
[2] Mortimer, J. K.; Abboud, J. L. M.; Abraham, M. H.; Taft, R. W. *J. Org. Chem*. **1983**, *48*, 2877; Schadt, F. L.; Bentley, T. W.; Schleyer P. v. R. *J. Am. Chem. Soc.* **1976**, *98*, 766.
[3] Bégué, J.P. ; Bonnet-Delpon, D. ; Crousse, B. *Synlett*, **2004**, *1*, 18-29.
[4] V. Kesavan, K.S. Ravikumar, B. Crousse, D. Bonnet-Delpon, J.P. Bégué Organic Synthesis , **2003**, *80*, 184-189.

FLUOROUS-DERIVATISED PHASE TRANSFER CATALYSTS

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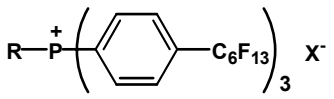
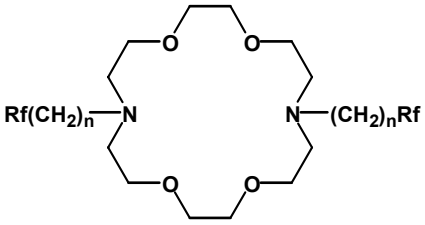
Phase transfer catalysis finds wide industrial applications, but the drive towards cleaner technologies requires the ability to recover, recycle and reuse the phase transfer catalysts.[1] Curran has elegantly shown that product/reagent separation can be readily achieved using fluorous-tagging procedures and fluorous solid-phase extraction on fluorous reverse phase silica gel.[2] We have recently extended this approach to catalyst/product separation [3] and here, we describe the extension of this methodology to phase transfer catalysts.



(1)



(2)

A series of novel aryl phosphonium salts **(1)** and 4,13-diaza-18-crown-6 ethers **(2)** containing fluorous ponytails have been synthesised. All of these perfluroalkylated phase transfer catalysts extract picrate from the aqueous phase into a partially-fluorinated phase, benzotrifluoride. An evaluation of their catalytic applications under liquid-liquid and solid-liquid conditions will be reported, as well as the separation, recovery and recycling results.

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[2] Curran, D. P. *Synlett*. **2001**, *9*, 1488.
[3] Croxtall, B. C.; Hope, E. G.; Stuart, A. M. *Chem. Commun*. **2004**, 2430.

NEW SYNTHETIC METHOD FOR NATURAL PRODUCTS USING HEAVY FLUOROUS TECHNIQUE

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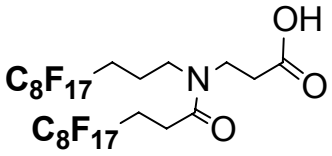
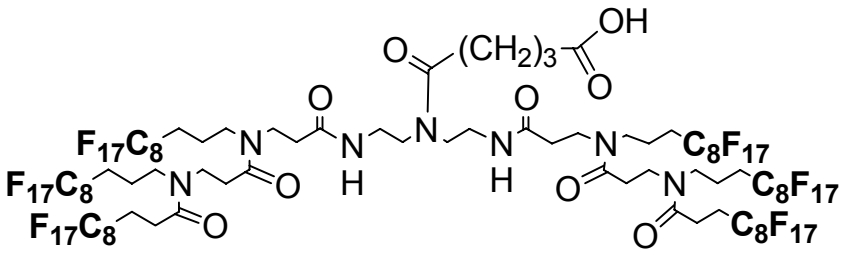
Since Horváth and Rábai introduced the concept of the fluorous biphasic system in 1994, fluorous chemistry has been developed for use in several fields such as combinatorial chemistry, parallel synthesis, and catalytic chemistry. Curran and co-workers elaborated the fluorous synthesis (fluorous-tag method) as a strategic alternative to solid-phase synthesis. The fluorous protecting groups are essential for the fluorous synthesis performance.

Recently, we reported a method for the fluorous oligosaccharide synthesis involving the novel fluorous acyl protective group, the **Bfp** (bisfluorous chain type propanoyl) group and the **Hfb** (hexafluorous chain type butanoyl) group. [1-3] The use of these groups made it possible to rapidly synthesize the several oligosaccharides by minimal column chromatography purification. Each synthetic intermediate was able to be easily purified only by simple fluorous-organic solvent extraction, and monitored by TLC, NMR, and MS.

We also reported the new fluorous support based on Hfb group. Bioactive peptides were synthesized on these fluorous supports by an Fmoc strategy.[4,5]



Bfp-OH



Hfb-OH

[1] Miura, T. ; Hirose, Y. ; Ohmae, M. ; and Inazu, T. ; *Org. Lett.*, **2001**, *3*, 3947-3950.

[2] Miura, T. ; Goto, K. ; Hosaka, D. ; and Inazu, T. ; *Angew. Chem., Int. Ed.*, **2003**, *42*, 2047.

[3] Miura, T. ; Goto, K. ; Waragai, H. ; Matsumoto, H. ; Hirose, Y. ; Ohmae, M. ; Ishida, H.-K. ; Satoh, A. ; and Inazu, T. ; *J. Org. Chem.*, **2004**, *69*, 5348.

[4] Mizuno, M. ; Miura, T. ; Goto, K. ; Hosaka, D. ; and Inazu, T. ; *Chem. Commun.*, **2003**, 972.

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CHEMICAL SYNTHESIS OF OLIGODEOXYRIBONUCLEOTIDES ON A FLUOROUS DENDRON

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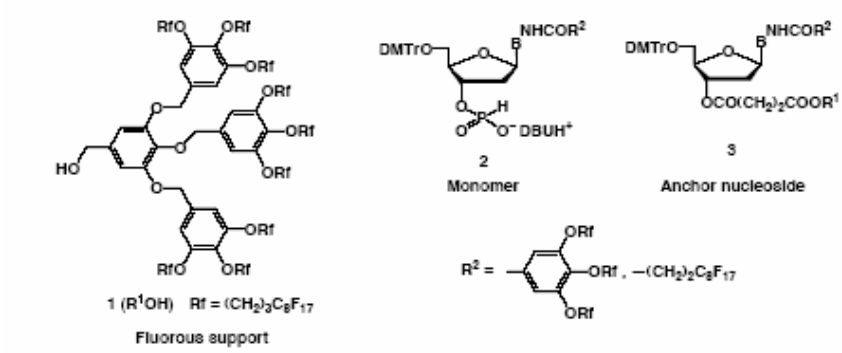
In recent years, a great deal of attention has been focused on small DNA and RNA molecules as therapeutic agents for selective inhibition of gene expression.[1] Oligonucleotide therapeutic agents such as antisense DNAs, ribozymes, and siRNAs act on the target mRNAs and arrest the protein synthesis. In order to meet the glowing demands for these relatively short oligonucleotides, a completely new approach for the large-scale production of DNA and RNA should be developed. Under these circumstances, we have focused on the fluorous chemistry [2] and its application to the solution-phase (fluorous-phase) synthesis of nucleic acids. In the fluorous-phase synthesis of organic compounds involving a fluorous tag, the intermediates can be purified by a simple extraction with a fluorous solvent without using chromatography. In this paper, we wish to describe a novel *H*-phosphonate method [3] for the synthesis of oligonucleotides using a highly-fluorinated dendric molecule **1** (fluorous dendron) as a fluorous support and fluorous protecting groups for nucleobase protection.



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SYNTHESIS OF MONOFUNCTIONAL PERFLUOROPOLYETHERS

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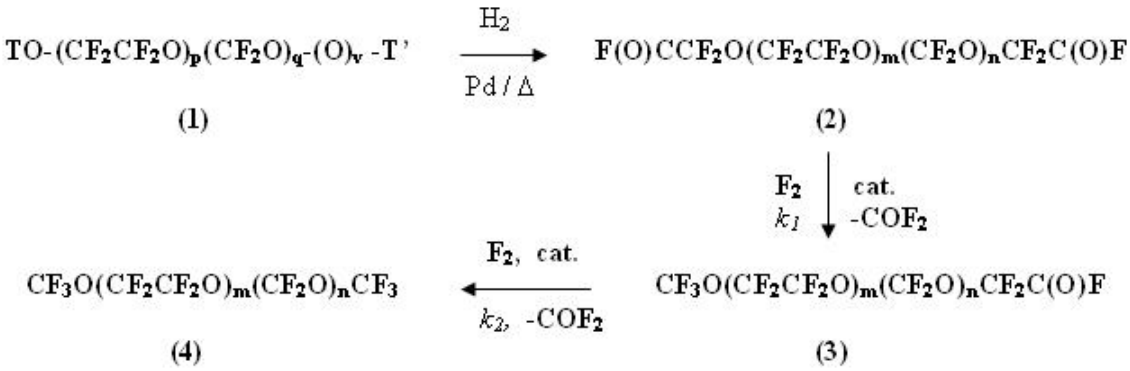
Perfluoropolyethers (PFPEs) are a well-known class of fluids for many industrial applications which can be obtained by reaction of tetrafluoroethylene (TFE) with oxygen in an inert solvent at low temperature using UV irradiation [1]. The reductive cleavage of the peroxide bonds of the peroxidic perfluoropolyether precursor **(1)** with hydrogen over a suitable catalyst yields essentially bifunctional acylfluorides **(2)** which can be converted by specific end group modifications to give valuable functionalized PFPEs such as □□ hydroperfluoropolyethers [2] and PFPE derivatives [3]



In this work, new monoacylfluoride PFPEs **(3)** with different molecular weights have been synthesized by direct fluorination of the PFPE diacylfluorides **(2)** in the presence of catalysts metal fluorides having formula MeFy.zHF (es. CsF, KF) [4]. The fluorination of **(2)** catalyzed by metal fluorides gives PFPEs with terminal groups hypofluorites $–OCF_2CF_2OF$ which by in situ thermal decomposition lead to the formation of the corresponding neutral end groups $–OCF_3$ [5].

The conversion of initial acylfluoride terminal groups to give end units $–OCF_3$ is quantitative. Yield and selectivity to monoacylfluorides **(3)** with respect to neutral PFPE products **(4)** depend on the conversion of initial $–CF_2C(O)F$ end groups, on temperature as well as on the catalyst. After hydrolysis and purification of the reaction mixtures by fractional distillation, pure products as well as fractions with more than 90% molar content of PFPE monocarboxylic acids **(5)** with a number average molecular weight from 350 to 1500 have been isolated in very good yields:

$$\mathbf{CF_3O(CF_2CF_2O)_m(CF_2O)_nCF_2COOH} \qquad \mathbf{(5)}$$

These new monofunctional perfluoropolyethers are useful intermediates for the preparation of valuable additives and fluorinated materials for many high technological and industrial sectors.

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[2] Fontana, G.; Spataro, G.; Marchionni, G. *Fluid Phase Equilibria* **2000**, *174*, 41-50.
[3] Tonelli, C.; Gavezzotti, P.; Strepparola, E. *J. Fluorine Chem*. **1999**, *95*, 51-70.
[4] Fontana, G.; Navarrini, W., U.S. Patent **2004**, No. 0147780 (to Solvay Solexis).
[5] Fontana, G.; Navarrini, W., U.S. Patent **2004**, No. 0147778 (to Solvay Solexis).

FLUOROUS ORGANOTIN CATALYSTS

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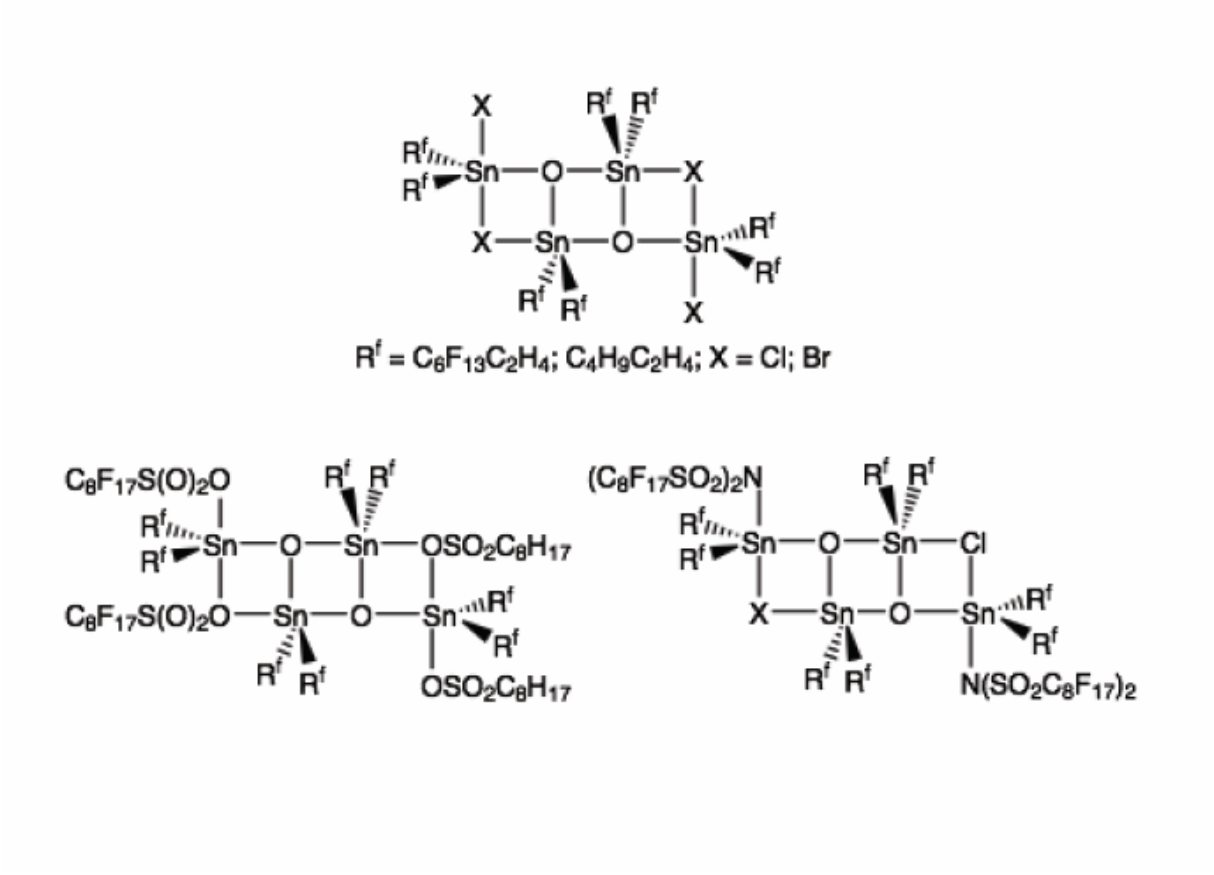
A variety of fluoroalkyltin compounds as shown below are synthesized. These compounds exhibit unusual solubility in organic and fluorous solvents. Their use for highly efficient (trans)esterfication and acetylation will also be the subject of this lecture.



[1] Otera, *J. Acc. Chem. Res.* **2004**, *37*, 288.

FLUOROUS-TAGGED GLYCOSIDE PRIMER FOR SACCHARIDE CHAIN ELONGATION BY CELLULAR ENZYME

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Facile synthesis of oligosaccharides could be accomplished by combining chemical synthetic methods with cellular biosynthetic processes. This strategy involves the preparation of saccharide primers (amphiphilic glycoside derivatives) by simple synthetic means, and subsequent incorporation of these primers into cells that serve as substrates for glycosylation by cellular enzymes. The cellular uptake of primers and release of glycosylation products to the culture medium by cells depend not only on the saccharide moiety and number of hydrophilic groups, but also on the hydrophobic aglycon unit.

Fluorinated compounds can also act as viable building blocks for oligosaccharide synthesis by cellular enzymes. In this research, the incorporation of fluorine to the lipophilic aglycon unit of the lactoside primer was carried out to further establish the role of the aglycon unit in priming oligosaccharide synthesis. Moreover, the incorporation of a fluorous tag is perceived to facilitate the extraction of the glycosylated product from the culture medium by using a fluorous solvent.

Lactoside (Lac), galactoside (Gal) and glucoside (Glu) primers with different fluorous-tags, perfluorohexylhexyl (F6) or perfluorodecylethyl (F10), were prepared and were examined in mouse B16 melanoma cells for their feasibility as substrate for oligosaccharide biosynthesis. The synthesis of the fluorous-tagged lactoside primers was accomplished by glycosylation of lactose peracetate with perfluorohexylhexanol, or with perfluorodecylethanol, followed by deacetylation. Synthesis of the fluorous-tagged galactoside and fluorous-tagged glucoside primers was carried out in a similar manner.

After 48-h incubation of cells with the primer, the lipids were extracted from the cell homogenates and the culture media and analyzed by HPTLC. New bands were extracted from the HPTLC plate and analyzed by MALDI TOF mass spectrometry. Results showed that incorporation of the lactoside primers (Lac-F6 or Lac-F10) gave monosialylated products. Treatment of the glycosylated products with α-(2→3) neuraminidase from *Arthrobacter ureafaciens* in phosphate buffer (pH 7.3) for 16 h at 37 ^{o}C confirmed that the product is α-(2→3) sialylated lactoside which is the same oligosaccharide as GM3 – the glycosphingolipid predominantly expressed on the cell surface of B16 melanoma cells, and effective on several important bioactivities. Treatment of B16 cells with the galactoside primer (Gal-F6) likewise gave a monosialylated product. On the other hand, Gal-F10 primer and the glucoside primers (Glu-F6 and Glu-F10) were not glycosylated.

This research demonstrates for the first time that fluorous-tagged compounds could be taken-up by the cell and take part in the biosynthetic machinery to afford the sialylated oligosaccharides without the need for a series of protection and deprotection steps usually required for chemical synthesis. The efficient extraction of the sialylated products with fluorous solvents is in progress.

SOLVATION OF OXYGEN, CARBON DIOXIDE, CARBON MONOXIDE AND NITROUS OXIDE IN FLUORINATED LIQUIDS

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The solvation of four gases — oxygen, carbon dioxide, carbon monoxide or nitrous oxide — in fluorinated organic liquids, with potential for bio-medical applications (perfluorohexylethane, $C_6F_{13}C_2H_5$, perfluorooctane, C_8F_{18} and perfluorobromooctane, $C_8F_{17}Br$), were studied in terms of molecular interactions, solution structure and thermodynamics.

An original experimental study of the gas solubility as a function of temperature, at pressures close to atmospheric, is reported. These measurements allow the calculation of thermodynamic quantities related to the solution process, such as free energies, that provide macroscopic information about the energetic and structural (entropic) contributions [1]. It is observed that the solubility of the three solutes decrease with temperature (corresponding to an exothermic solvation) and that nitrous oxide is the more soluble gas, followed by carbon dioxide. Carbon monoxide is the less soluble species in all the fluorinated liquids studied.

At the atomic scale, the same systems were investigated using molecular simulation techniques. These tools give access to the structural aspects of solvation through the solute-solvent radial distribution functions. The free energy routes of statistical mechanics provide values for the solutes' chemical potentials, which can be compared to the experimental results to validate the force-field models used in the simulations [2,3].

Apart from their applications in pharmacology and bio-medicine, the gaseous solutes chosen present different molecular characteristics: for example, carbon monoxide is slightly dipolar, carbon dioxide is purely quadrupolar, and nitrous oxide is both. The nature of the solute-solvent interactions in solution can be elucidated, in terms of the strength of the interactions and also of the role of structural effects (cavity formation in the solvents, organisation of the solvation shell). The solvation of these gases can then be understood in molecular terms and the behaviour of the fluorous solutions more accurately predicted.

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FLUOROUS BIPHASIC CATALYSIS: OXIDATION OF ALKANES, ALKENES, ALCOHOLS, AND ALKENOLS WITH Mn(II), Co(II), AND Cu(I AND II) FLUOROUS SOLUBLE OR THERMOMORPHIC COMPLEXES IN THE PRESENCE OF TBHP/O_2 OR TEMPO/O_2 OR H_2O_2

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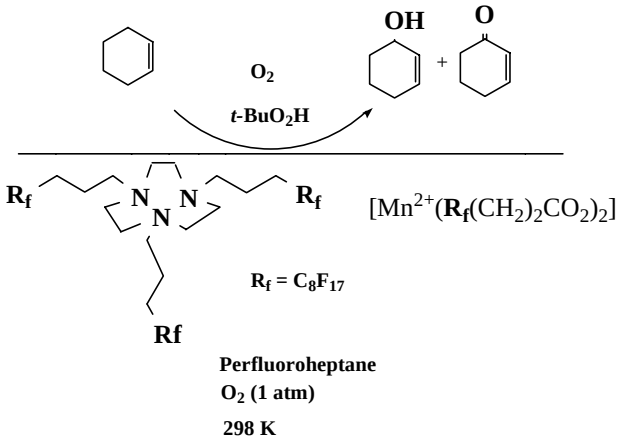
One of the main problems that persists in homogeneous catalysis is the separation of the precatalyst from the resulting products. More than a decade ago, Horváth and Rábai published a seminal paper that described a new and novel biphasic catalysis technique that elegantly separates the precatalyst from the products of catalysis; they named it Fluorous Biphasic Catalysis (FBC).[1] The FBC technique has now been adapted for almost every classic organic reaction, including homogeneous oxidation chemistry.[2] I will focus on the FBC oxidation studies that have been conducted at LBNL, and in collaboration with colleagues at Bordeaux, Zaragoza, and Rehovot.

I will present several FBC scenarios that encompasses the use of fluoroponytailed ligands with sparingly soluble fluoroponytailed metal carboxylates to form fluorocarbon soluble complexes of Mn(II), Co(II), Cu(II), and Cu(I). Moreover, the reverse situation, where the fluorocarbon soluble metal carboxylate phase switches the non-fluoroponytailed ligand from the hydrocarbon layer to the fluorocarbon layer by the *insitu* formation of a fluoroponytailed metal carboxylate-ligand complex, where M= Cu(II). The focus of these FBC oxidation studies was alkanes, alkenes, alcohols, and alkenols; a typical FBC oxidation scenario is shown in the Scheme. I will also discuss the thermomorphic properties of several of the Mn(II) and Cu(II) complexes, which entails the solubilization of a solid fluoroponytailed metal carboxylate-ligand complex in a non-fluorous solvent at higher temperatures, while at RT, the solid precipitates. Finally, I will introduce a novel concept for an FBC gas to liquid scenario for methanol synthesis from CO/H2 in collaboration with SUNY Stony Brook and Zaragoza colleagues.



[1] Horváth, I.T.; Rábai, J. *Science* **1994**, *266*, 72 and refs. therein.

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DESIGN AND APPLICATION OF HIGHLY FLUOROUS CATALYSTS

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Highly fluorous homogeneous catalysts have been developed that can be recycled efficiently using flourous biphasic separation techniques. For fluorous separation techniques to compete effectively with aqueous biphasic separation, catalyst recycling efficiencies have to be > 99.9%.

This talk focuses on some specific applications and discusses recently developed theoretical tools to direct the synthesis and design of catalysts with improved fluorous phase affinity.

F-TEMPO RADICALS: EFFICIENT MEDIATORS FOR THE OXIDATION OF ALCOHOLS

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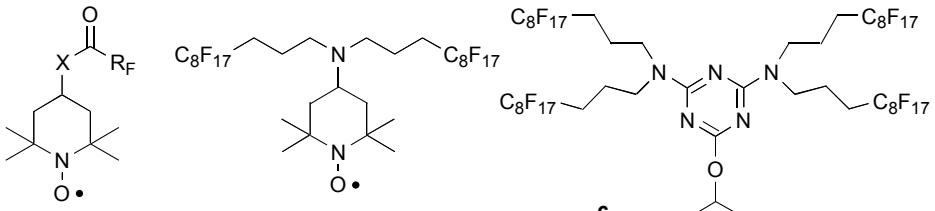
Selective oxidation of primary alcohols to aldehydes or secondary alcohols to ketones can be carried out conveniently with cheap and safe primary oxidants in the presence of nitroxyl radicals, in particular 2,2,6,6-tetramethylpiperidine-1-oxyl (TEMPO).[1] Nitroxyl radicals are relatively expensive and, although used in small amounts (1-10 mol%), their separation from the products often requires lengthy workup procedures. This means efficient recovery and recycling are important issues. Several groups have addressed these problems by designing heterogeneous variants of TEMPO, e.g. via anchoring TEMPO to inorganic supports, [2] or by using soluble polymer-supported TEMPO.[3]
Recyclable TEMPO radicals can be designed without recourse to polymeric supports with all their drawbacks: in this contribution, the preparation of TEMPO derivatives bearing perfluoroalkyl substituents (F-TEMPOs, Figure 1) and their activity as catalysts in the oxidation of alcohols are described. The influence of the linkage between the TEMPO moiety and the fluorous domain on the selectivity of the catalytic system, the use of various primary oxidants, including molecular oxygen, and the recoverability of the different catalysts are also discussed.
F-TEMPOs obtained from easily available precursors have found to be efficient mediators for the oxidation of a variety of alcohols, affording results very similar to those obtained with TEMPO. Reactions were performed in conventional organic solvents under mild, homogeneous or liquid-liquid aqueous-organic conditions. Fluorous separation techniques were then applied to isolate the fluorous-tagged radicals from the organic products. Promising results were obtained using popular primary oxidants such as aqueous NaOCl and [bis(acetoxy)iodo]benzene (BAIB). With the latter, the heavy fluorous radical **6** could be reused up to six times in the oxidation of 1-octanol showing only minor loss of catalytic activity.[4]
F-TEMPOs thus share the advantages usually associated with the use of polymer-supported TEMPO derivatives (simplified workup procedures, quick recovery, recyclability) without some of their common limitations (lack of versatility, mass transfer limitations, poor accessibility to the active site). Results obtained provide further guidelines for the rational design of other fluorous nitroxyl radicals and open new vistas for a possible development of “all-fluorous” catalytic systems involving F-TEMPOs. In this context, the combination of F-TEMPOs with a recyclable fluorous version of BAIB [5] and the use of molecular oxygen as the primary oxidant are worth investigating.



1 X = O, R = n-C_7F_{15}
2 X = O, R = n-$C_8F_{17}CH_2CH_2$
3 X = NH, R = n-C_7F_{15}
4 X = NH, R = n-$C_8F_{17}CH_2CH_2$

5

6

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ALTERNATIVE SOLID SUPPORTS FOR FLUOROUS CATALYSIS

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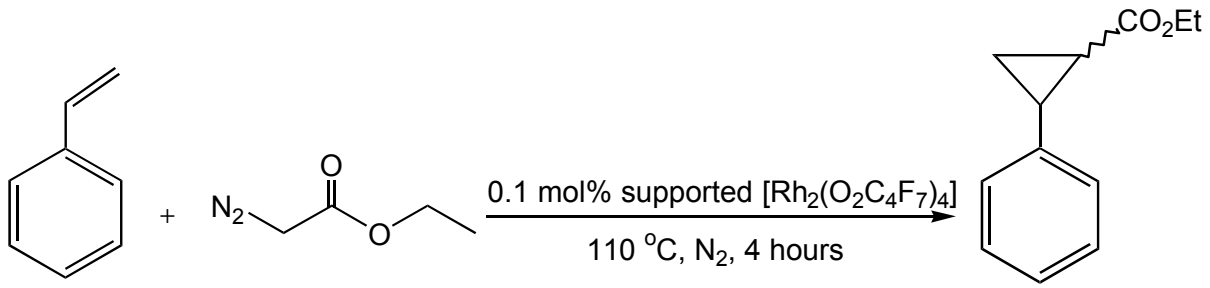
Fluorous silica gel has been used as a solid support for heterogenising homogeneous catalysts [1] and for fluorous solid phase extraction.[2] However, the silica framework contains free hydroxyl groups, which can bind destructively to many effective homogeneous transition metal catalysts, compromising either catalytic activity or catalyst recycle.[3] Here, we are evaluating two, alternative, inert solid supports (fluorous zirconium phosphonates, perfluoroalkylated polystyrenes) for catalysis/solid phase extraction.

In this presentation, the synthesis of amorphous perfluoroalkylated zirconium phosphonates and perfluoroalkylated polystyrene beads will be described, along with initial results from a test catalytic reaction; cyclopropanation of styrene using dirhodium perfluorobutyrate as catalyst. The work will compare the activity of the catalyst under homogeneous conditions with those from the catalyst supported on both fluorous and non-fluorous solid supports, along with recovery, recycle and rhodium leaching levels. In addition, the efficacy of these materials as supports for catalyst recovery and recycle using solid-phase extraction will be presented.



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PERFLUORINATED VINYL SULFOXYDES: EFFICIENT SYNTHONS FOR THE PREPARATION OF FLUORINATED TETRAAZAMACROCYCLES. APPLICATIONS IN CATALYSIS

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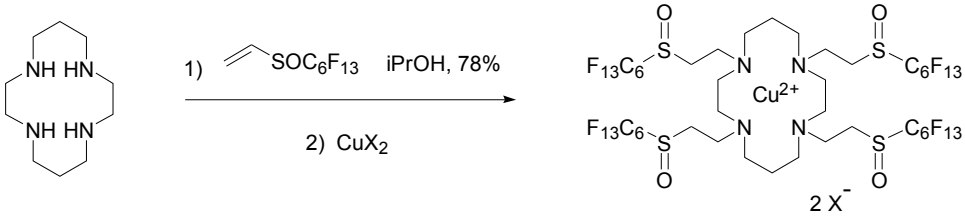
We have recently described the straightforward preparation of perfluoroalkyl sulfoxides and sulfones, on multi-gram scale.[1] These molecules possess multiple reactivity: dienophiles in Diels-Alder reactions,[2] but also good acceptors for the Michael reaction. This chemical behaviour makes these compounds efficient synthons for the introduction of long perfluorinated chains and the synthesis of perfluorinated ligands.

Tetraazacyclotetradecane (cyclam) and its derivatives are well known and efficient ligands of transition metal cations. The properties (solubility, metal bonding) of the macrocycle could be modified by the functionnalization of the nitrogen atoms. One of the easiest way to achieve this chemical modification is the Michael addition.[3]

The goal of this study is to take profit of the high reactivity of perfluoroalkyl vinyl sulfoxide to synthesize new perfluorinated azamacrocycles in order to develop catalytic fluorous chemistry, after complexation with a transition metal (scheme).



The preparation of different perfluorinated macrocycles and our first results of oxidation reaction in fluorous biphasic catalysis will be presented.

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HYDROGENATION OF STYRENE AND 1-OCTENE CATALYZED USING Pd(II) COMPLEX WITH MONODENTATE PERFLUOROPYRIDINE IN $ScCO_2$ AND CONVENTIONAL ORGANIC SOLVENTS

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The fluorous pyridine [1,2], $NC_5H_4COOCH_2(CF_2)_7CF_3$, is prepared in two step from nicotinic acid and then reacted with $Pd(OAc)_2$ to gave soluble and active catalyst in supercritical carbon dioxide ($scCO_2$) [3]. We evaluated its hydrogenation activity using styrene and 1-octene as model reactions. Nitrogen donor Pd(II) compound examined for both supercritical carbon dioxide and organic solvents (toluene, acetone and methanol). Different substrate/catalyst molar ratios were studied for the hydrogenation of olefins at 80 ^oC and 102 bar in $scCO_2$. Also the effect of temperature at 102 bar, and the effect of pressure at 80 ^oC were analyzed for the same reactions. The product of 1-octene was mostly n-octane together with isomerization products. Styrene converted to single product ethyl benzene. The synthesis of the catalyst is reproducible, as shown by reaction activity studies on different batches of catalyst. $scCO_2$ is a more effective, green reaction medium for styrene and 1-octene compared with conventional organic solvents.

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FLUOROUS BIPHASIC CATALYSIS WITHOUT SOLVENT: NOVEL RECYCLING CONCEPT

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The regulations and needs for maintaining the ecologic equilibrium of our planet have made the scientific community facing new challenges. Efficiently synthesizing chemical commodities or high added value products is not satisfactory anymore; the synthetic processes must minimize the impact on the environment and/or society and remain economically competitive.

Homogeneous catalysis is technically superior to the heterogeneous catalysis but is reluctantly use in industry due to often strenuous separations and contaminations of the product. Numbers of concept have been devised in order to achieve homogenous catalysis while ease the separation—ideally mimic the heterogeneous separation. Fluorous Biphasic Catalysis is a wonderful tool which allows the reaction to proceed in homogeneous conditions while the separation deals with a biphasic system.[1] Unfortunately, fluorous solvents are environmentally persistent, they are expensive and do possess small solubility in organic which lead to leaching phenomena.

Our concept relies on using a minimum amount of fluorous phase which will be immobilized—minimize leaching—and will be recycled as normal fluorous phase—to limit the actual amount of fluorous compound. The inter-disciplinary approach of the problem combined the Gas Expanded Liquid (GXLs) technology and the fluorous chemistry. “Fluorous silica” in which fluorous tails have been chemically bond to the silica core provides a fluorophile surface in place of fluorous phase. The critical ‘switch’ which will turn on/off the immobilization of the fluorinated-tagged catalyst onto the fluorous silica surface is CO2. Gas expanded liquids are unique, extremely tunable, and possess hybrid properties from both gases and liquids. CO2 expanded organic solvents are fluorophilic and can induced miscibility of organic and fluorous phases under moderate CO2 pressure (Figure 1). CO2 is the trigger that allows the fluoro-tagged catalyst to be reversibly immobilized and recycled, while permitting the reaction to process under homogeneous conditions.

Figure 1. Biphasic system FC75-toluene 0b of CO2, in the middle 32b, and in the right monophasic

Hydrogenation is a powerful reaction that has been used to highlight the potential of this novel concept. Eliminating the fluorous solvent phase, reducing the need for organic phase from the CO2 benefit and recycling the costly and/or toxic catalyst combined with the easy separation constitute a step-toward sustainable and “green” technology.

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SYNTHESIS OF FLUOROUS PHOSPHINES

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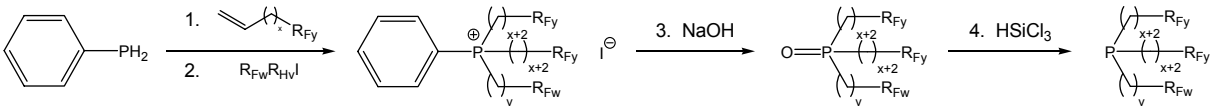
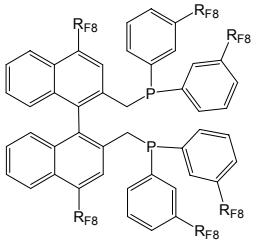
Fluorous catalysts could offer facile product separation for many homogeneous catalytic reactions. One of the most effective ways to make an organometallic catalyst soluble in the fluorous phase is the incorporation of perfluoroalkyl-group(s) into the ligands of the catalyst.[1] Since phosphines are frequently used as ligands, we have been developing novel and efficient synthetic protocols for the preparation of fluorous soluble phosphines.

We have already reported the stepwise incorporation of individual perfluoroalkyl-alkyl groups, which provided an opportunity to fine-tune the electron-density on the phosphorus center by varying the length of the alkyl-spacer between the phosphorus atom and the perfluoroalkyl-group.[2] We have used another approach involving the radical addition of two perfluoroalkyl-olefines to phenylphosphine followed by an alkylation of the resulted bis(perfluoroalkyl-alkyl)phenylphosphine with the appropriate fluorous iodoalkane. The phenyl-group of this phosphonium-salt can be selectively removed leading to a fluorous phosphine oxide, the reduction of which yields the target phosphine.



BINAPHOS and BINAS are among the most efficient diphosphine ligands for rhodium-catalyzed asymmetric hydroformylation in homogeneous or biphasic conditions, respectively.[3] In order to combine the efficiency of the BINAPHOS ligand with the advantages of facile fluorous biphasic separation, we have developed a synthesis for the corresponding fluorous BINAPHOS ligand.



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APPLICATION OF FLUOROUS TECHNOLOGIES IN SOLUTION-PHASE SYNTHESIS

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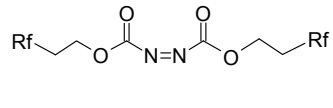
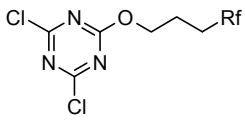
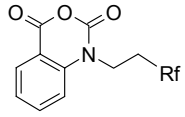
Fluorous synthesis has been recently introduced as a "beadless" combinatorial technology. It employs perfluoroalkyl chains instead of resins as "phase tags" to facilitate the separation process. The separation is performed by strong and selective interactions between fluorous molecules with fluorous sorbents in solid-phase extraction or chromatography formats. Traditional solution-phase reaction conditions and facile phase-tag separations are successfully integrated into fluorous synthesis. Major advantages of fluorous synthesis include: fast homogeneous reaction kinetics; easy purification by fluorous separations as well as conventional methods such as chromatography; no large excess of fluorous reagents required for the completion of the reaction; and recoverable of fluorous species.
This presentation describes the recent effort at FTI on the development of fluorous compounds including reagents (e.g. F-DEAD and F-phosphine for Mitsunobu reactions), scavengers (e.g. F-thiol for electrophiles, F-iscyanate and F-isatoic anhydride for nucleophiles), protecting groups (e.g. F-Boc, F-Cbz, F-Fmoc, and F-silanes), tags (e.g. F-FluoMar and F-sulfonyl fluoride), building blocks (e.g. F-benzaldehydes and F-amino acids), and their applications in parallel and mixture synthesis of drug-like small molecule and natural product libraries including hydantoins, dihydropteridinones, and mappcines. Combination of fluorous synthesis with microwave heating, Pd-catalyzed coupling reactions, multi-component reactions, and comparison of fluorous synthesis with conventional solution-phase and solid-phase synthesis are also highlighted.



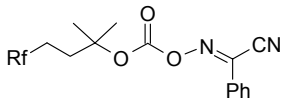
F-DEAD



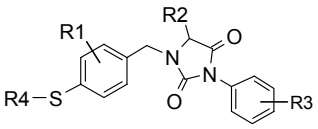
F-dichlorotriazine



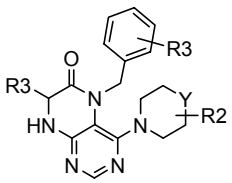
F-isatoic anhydride



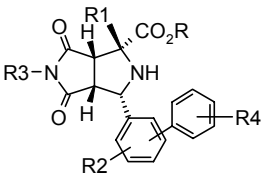
F-Boc-ON



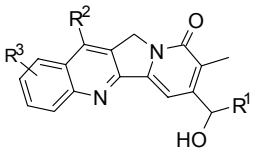
functionalized hydantoins



functionalized dihydropteridinones



biaryl-substituted proline analogs



mappcine analogs

Rf = perfluoroalkyl group

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AN EXPEDITIOUS SYNTHESIS OF BISTRATAMIDE H USING A NEW FLUOROUS PROTECTING GROUP

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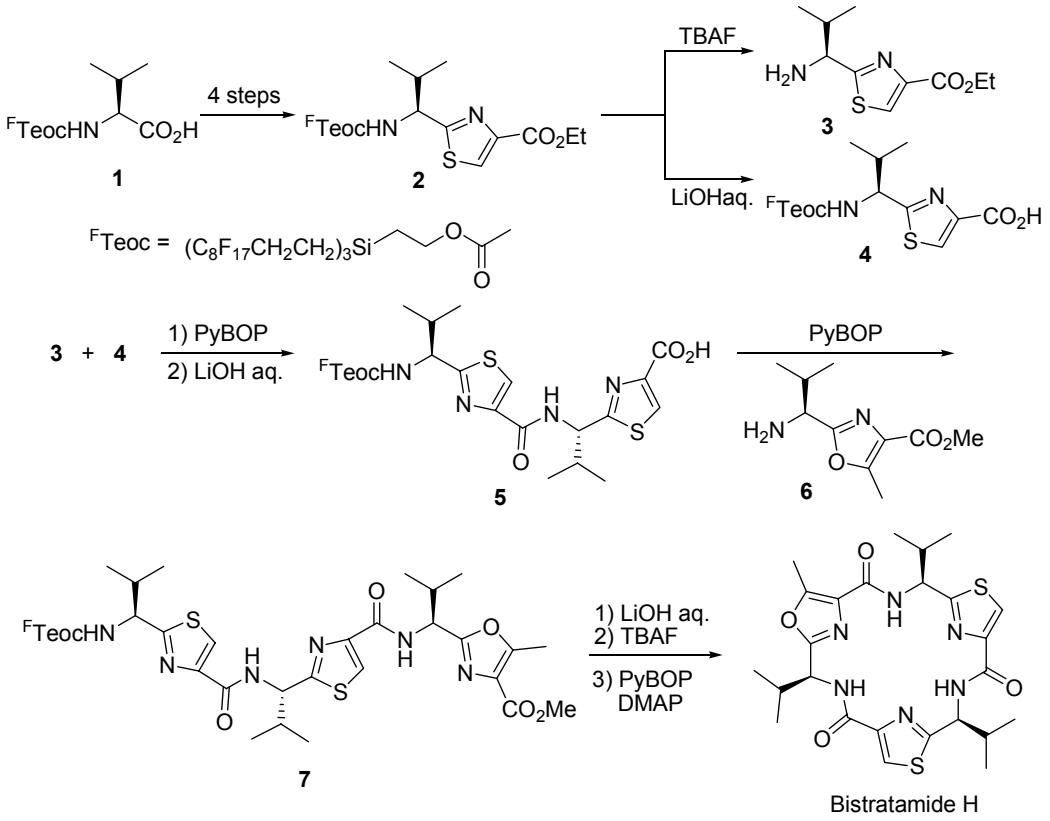
Bistratamides are cyclic tri- or tetra-peptides of amino acids that include heterocycles such as thiazole and oxazole. They were isolated from ascidian *Lissolinum bistratum* and shown to have bioactivities such as anti-tumor and anti-cancer effects. Shin's and Kelly's groups have recently synthesized some of bistratamides in a normal way of peptide synthesis [1]. Here we would like to report an examination of an expeditious synthesis of bistratamide H by using a novel fluorous protecting group, 2-(tris(perfluorodecyl)silyl)ethoxycarbonyl (^{F}Teoc), a fluorous version of 2-(trimethyl)ethoxycarbonyl group as follows.



In this method, most of the fluorous intermediates including the precursor were isolated by fluorous liquid-liquid extraction. Optimization of the reactions was carried out by monitoring the reactions with TLC. In addition, the optical purity of the fluorous intermediate was checked by HPLC with a chiral column to avoid racemization of the intermediate products.

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ASSOCIATION OF FLUOROUS ˝PHASE-VANISHING˝ METHOD WITH VISIBLE-LIGHT ACTIVATION FOR BENZYL BROMINATION

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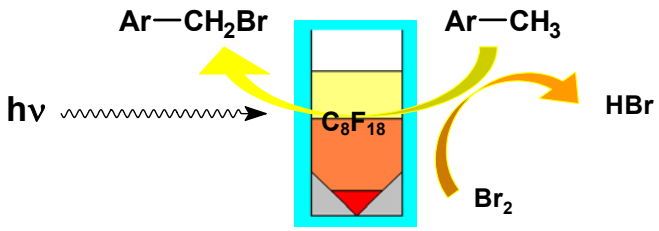
Benzyl bromination is one of the synthetic methodologies widely used for the functionalization of alkyl aromatics through the nucleophilic substitution of benzyl bromine. A classical direct method is radical bromination utilizing NBS with the use of radical initiators and CCl_4 as a solvent. Due to a heavy environmental burden created by the Wohl-Ziegler bromination there is a lot of interest in providing more environmentally benign method.[1,2,3]

Molecular bromine has some advantages and would offers a better alternative to the use of NBS. Furthermore, activation of radical bromination requires only visible light. In order to achieve a selective radical reaction over an electrophilic one, the concentration of bromine needs to be low and thus the amount of solvent used for the reaction is high. The approach taken by Curran *et al.* offers a unique possibility to use fluorous solvent as a bulk membrane for the slow diffusion of the molecular bromine into the reaction mixture.[4] So-called ˝phase-vanishing˝ reaction was already used in many cases and is useful for very reactive reagents and exothermic reactions. [5]

To achieve benzyl bromination in highly concentrated solutions, we combined slow addition of bromine to the reaction phase by “phase-vanishing” method with its concomitant activation for radical reaction by visible-light. Interesting results were obtained that reveal the role of phase transfer in the reaction process. Benzyl bromination was observed in various solvents including methanol and acetonitrile. The substituent on the aromatic ring effects the course of bromination and three different processes were observed: benzyl bromination, bromination at the aromatic ring and bromination on the side chain of the substituent.



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FLUOROPONYTAILED COPPER(II) CARBOXYLATE COMPLEXES WITH NON-FLUOROUS LIGANDS AS PRE-CATALYSTS FOR THE OXIDATION OF ALKENOLS AND ALCOHOLS UNDER FLUOROUS BIPHASIC OR THERMOMORPHIC MODES

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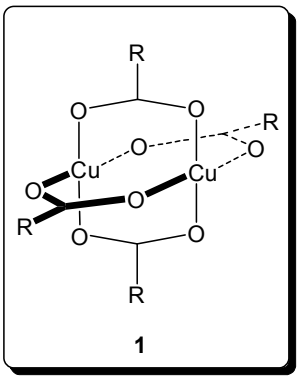
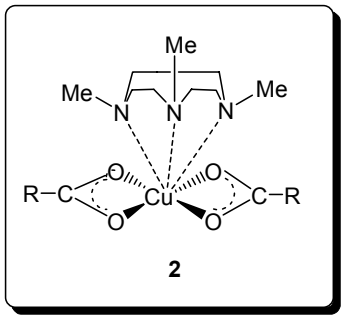
In this fluorous biphasic catalysis (FBC) contribution, we will present the synthesis and characterization of new fluoroponytailed copper (II) complexes that also contain non-fluorous ligands, and define their role, as precatalysts, in the oxidation of alkenols and alcohols under FBC conditions, or as thermomorphic solids (soluble at higher temperatures in organic solvent). The dimeric complex, $[Cu(\{C_8F_{17}(CH_2)_3\}CHCO_2)_2]$, **1**, was found to be soluble in perfluorocarbons.[1] The catalytic activity of **1** under FBC conditions[2] for the oxidation of alkenols and alcohols to aldehydes was demonstrated, and will be presented. Furthermore, addition of non-fluorous nitrogen ligands, such as N-1,4,7-trimethyl-TACN or N,N,N',N",N"-pentamethyldiethylenetriamine to trifluoromethylbenzene solutions of **1** afforded novel fluorous soluble derivatives, **2** and **3**, respectively, whose tentative structures were elucidated by EPR and IR spectroscopic analysis.



1



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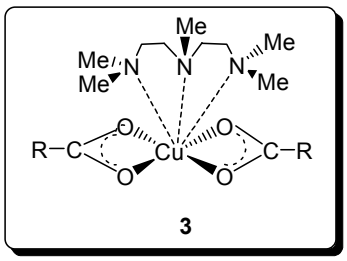

3

R = $-CH\{(CH_2CH_2CH_2)C_8F_{17}\}_2$

While **2** and **3** can catalyze the FBC oxidation of 4-nitrobenzyl alcohol to the 4-nitrobenzaldehyde, their thermomorphic properties were more interesting to study. Thus, solid **3** was soluble in a mixture of chlorobenzene and toluene (1:3) at 80 °C, while insoluble at room temperature, in these same solvents. This thermomorphic property of **3** was used to perform the oxidation of 4-nitrobenzyl alcohol, with TEMPO and O_2, at 90 °C in chlorobenzene/toluene, with recovery of precatalyst **3**, by cooling to room temperature.[3] The mechanisms of these FBC/thermomorphic oxidations will also be discussed.

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FLUOROUS MIXTURE SYNTHESIS OF MURISOLIN AND PASSIFLORICIN STEREOISOMER LIBRARIES

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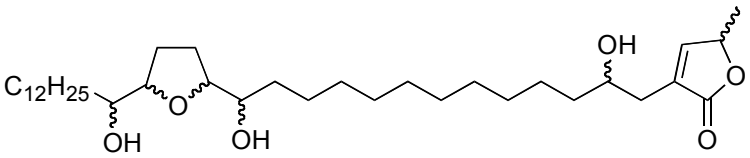
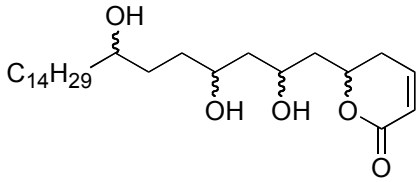
Because it separates primarily by fluorine content, fluorous reverse phase silica gel can be used in a chromatographic mode to separate fluorous molecules from each other. This separation forms the basis of new mixture synthesis techniques in which members of a series of substrates are tagged with different fluorous tags, mixed, carried through a series of reactions, and then separated based on the tag prior to detagging. Recent fluorous mixture syntheses of stereoisomer libraries of murisolins and passifloricins will be highlighted.



murisolins



passifloricins

POSTER PROGRAM

AN INDICATOR-DISPLACEMENT ASSAY FOR HISTAMINE UNDER FLUOROUS TRIPHASIC CONDITIONS

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A synthetic receptor, which is bound through noncovalent interactions to an indicator, can function as a chemosensor.[1] Using a “classical” one-phase methodology the fundamental requirement is that the displacement of the indicator by an analyte results in a change of its optical properties. In such an Indicator-Displacement Assay (IDA) the indicator is attached to the binding site of the host through non-covalent interactions such as electrostatic interactions, hydrogen bonding or coordination bonds. While IDAs have been used to detect various analytes their applicability in highly polar solvents such as water is limited due to competition with the indicator for host binding. There is thus a great challenge in searching for new methodologies allowing the use of water with these systems.

We previously reported a reversible phase-switching methodology between hydrocarbon and perfluorocarbon phases based on the reversible coordination of pyridyl tags on a highly fluorous copper(II)-carboxylate complex.[2] We wish now to describe the application of such a highly sensitive reversible phase-switching process for the detection of histamine under triphasic $H_2O/CH_2Cl_2/C_6F_{14}$ conditions. We will demonstrate that the fluorous phase can act as an effective barrier against water enabling detection and titration of histamine in water solution.

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HIGHLY FLUORINATED LC MATERIALS FOR SURFACE MODIFICATION

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The development of highly fluorinated compounds is of great interest in academic and industrial fields. In fact, the wide use of these materials is due to their unique physico-chemical properties. This type of compounds is well known for coating surface, i.e., for marine protection. In this kind of application, the surface properties of materials is important but also the ability of surface reconstruction. In order to find out the influence of F-alkylated moiety on the microorganized systems like LC, we have prepared and charaterized new series containing the following main segments :

-an hydrophobic and oleophobic part (the fluorinated tail) with different lengths
-a spacer oligomethylenic
-a connector (linked to the mesogenic core) which can improve the LC properties

All these compounds are well defined and can be easily obtained from commercial raw materials such as 2-(F-alkyl)ethyl iodide or 2-(F-alkyl)iodide with a purity higher than 98 %. In this work, we report the preparation, characterization and evaluation of physical properties of these new materials. The relation structure - surface modification of the bulk will be illustred.

PREPARATION OF FLUOROALKYL PYRIDINE DERIVATIVES FROM 2-AZADIENES AND DIENOPHILES

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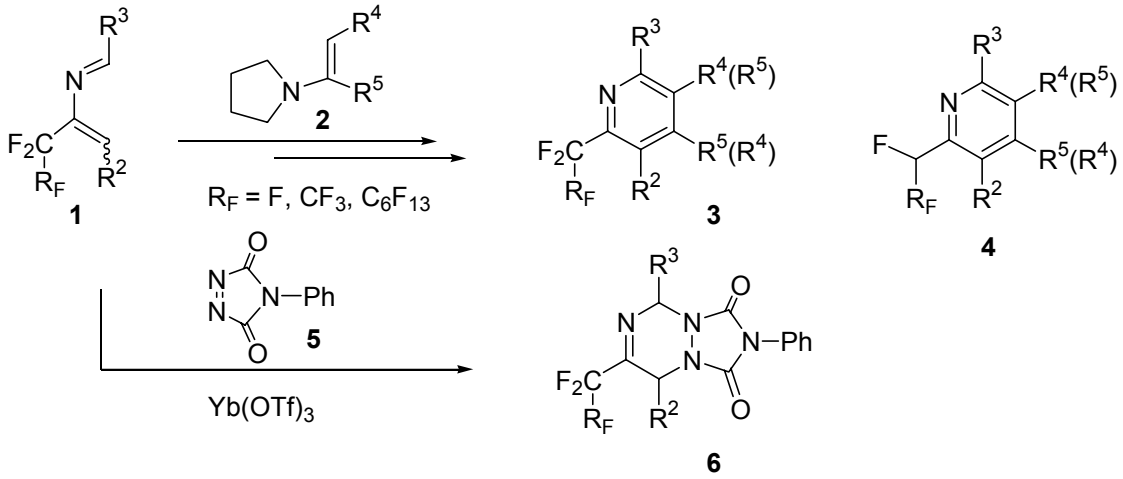
Functionalized 2-azadienes systems are efficient synthons in Organic Synthesis for the preparation of nitrogen heterocyclic compounds [1] through cycloaddition reactions and special interest has been focused on the incorporation of a fluorine-containing group into organic molecules [2] for the preparation of fluorinated building blocks with biological activity and commercial applications.

In this communication, we report the preparation of fluoroalkyl pyridine derivatives through a [4+2] cycloaddition strategy involving fluoroalkyl substituted 2-azadienes [3] **1** with dienophiles **2** and **5**. Reaction of 3-fluoroalkyl-2-azadienes **1** with enamines **2a** (R^4 R^5=$(CH_2)_4$) or **2b** (R^4=H; R^5=^{i}Pr) gave pyridine derivatives **3** or/and also dehydrofluorinated compounds **4,** whereas catalyzed reaction with dienophile **5** gave bicyclic pyridine derivatives **6**.



Acknowledgements:
The present work has been supported by the Dirección General de Investigación del Ministerio de Ciencia y Tecnología (MCYT, Madrid, DGI, PPQ2003-00910) and by the Universidad del País Vasco (UPV-GC/2002).

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FLUOROUS GOLD(I) CATALYZED HYDROSILYLATION

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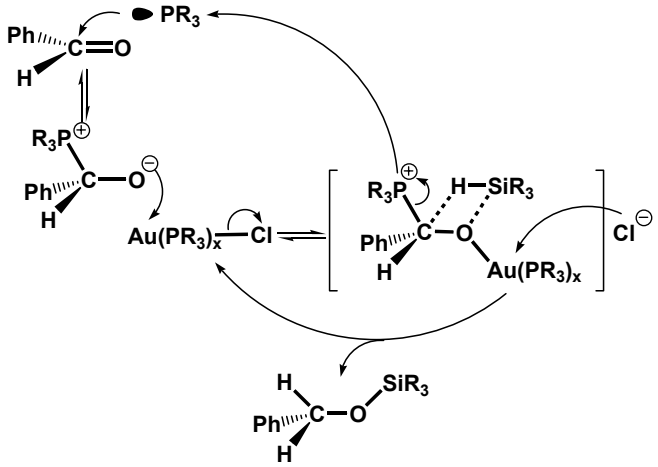
The application of gold compounds in catalysis has been rapidly growing, as gold could be a green replacement of toxic heavy metals. In order to provide facile product separation and catalyst recycling, we have developed a fluorous [1] gold catalyst.

Several fluorous-soluble phosphine-modified gold(I) compounds have been synthesized, characterized, and used for the catalytic hydrosilylation of various aldehydes. The facile separation of the fluorous gold(I) catalyst was demonstrated by recycling the fluorous phase. Hydrosilylations with the fluorous gold(I) catalyst in the absence of fluorous solvents were also studied. The catalyst recycling was based on the temperature dependent solubility of the fluorous gold(I) catalyst [2, 3].

In situ IR and NMR studies suggest a novel mechanism for the catalytic hydrosilylation of aldehydes in the presence of gold compounds:



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H_2O_2/FLUORO-ALCOHOL SYSTEM FOR DIRECT AND SELECTIVE SYNTHESIS OF ANTIMALARIAL 1,2,4,5-TETRAOXANES

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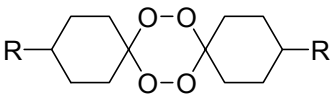
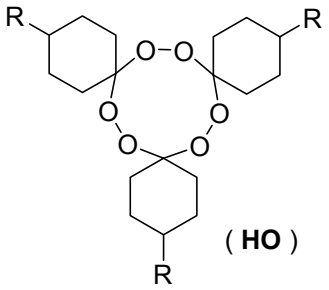
Malaria causes or contributes to millions of deaths per year worldwide. Resistance of parasites to conventional drugs like chloroquine is a severe problem in dealing with malaria. Artemisinin and its semi-synthetic derivatives with endoperoxide functional group represent a new class of antimalarials, active against a chloroquine-resistant seves of parasite *Plasmodium falciparum*.[1] This boosted the research into cyclic peroxides as a group of potential anti-malarial agents and 1,2,4,5-tetraoxanes among them. Synthesis of tetraoxanes by acid-catalyzed oxidative cyclization is potentially a useful method due to its simplicity. Yet, during the synthesis of dispiro-1,2,4,5-tetraoxanes (TO) hexaoxonane (HO) is also formed.[2] Consequently, a different method had to be applied - mainly ozonolysis of O-methyloximes.[3]

We took fluoro-alcohols (1,1,1-trifluoroethanol - TFE and 1,1,1,3,3,3-hexafluoro-2-propanol - HFIP) as solvents that activate hydrogen peroxide and in these conditions tetraoxanes were selectively formed directly from ketone, 30% H_2O_2 and acid as a catalyst.[4] Besides cyclic ketones also dialkyl ketones were used as the starting compounds and 3,3,6,6-tetraalkyl-1,2,4,5-tetraoxanes were isolated as the only products.



(**TO**)



(**HO**)

By using fluoroalcohols as solvents, non-symmetric TOs were also synthesised directly in a one-pot procedure by the in-situ formation of *gem*-dihydroperoxide from carbonyl compound and H_2O_2 followed by acid-catalyzed cyclization step with another ketone. The only compound formed was non-symmetric TO in high yield.

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RECYCLBLE MOLECULAR THERMOMORPHIC CATALYSTS FOR ATOM TRANSFER RADICAL ADDITIONS AND POLYMERIZATION

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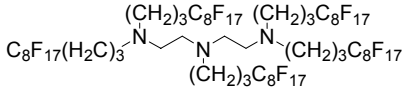
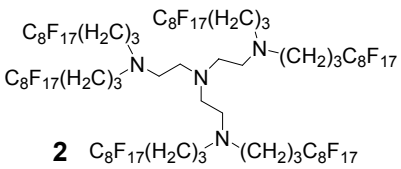
The search for “ideal recoverable catalysts” is a major concern of modern chemistry.[1] We have been interested in developing molecular recyclable catalysts for Atom Transfer Radical Additions and Polymerizations (ATRA, ATRP). We previously reported the first example of a molecular recyclable catalyst for ATRA that was based on the thermomorphic behaviour of a Fluorous Biphasic System (FBS).[2] The fluorous polyamine ligands **1** and **2** were prepared and their CuCl complexes used as catalysts for the preparation of lactones. Efficient recycling of the catalyst was achieved by simple hydrocarbon/perfluorocarbon extraction, leading to low copper contamination of the final products. This FBS also proved to be effective for catalyst recovery in ATRP.[3]
We recently developed a simple non-fluorous recyclable catalyst for ATRP using the tetramine ligand **3**.[4] Compound **3** exhibits an exceptionally large temperature-dependent solubility in 1,4-dioxane, its solubility increasing ca. ~10^4-fold between 23 and 50°C. The CuBr/**3** complex was shown to catalyze the ATRP of methyl methacrylate with excellent controls of the molar masses and polydispersities. Due to the thermoresponsive character of CuBr/**3** polymerizations were carried out in homogeneous conditions while catalyst recovery (> 95 %) was achieved by a simple filtration after lowering the temperature to 10°C. Very low residual copper contamination (~200 ppm) was measured in the final polymer. The catalyst has also been recycled two times without significant loss of activity.



1



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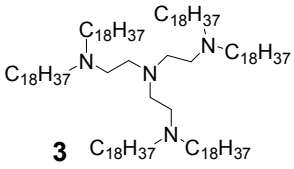

3

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REVERSIBLE HYDROCARBON/PERFLUOROCARBON PHASE-SWITCHING OF PYRIDYL TAGGED MOLECULES

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The search for rapid and efficient protocols for the purification of organic compounds is a major concern of modern chemistry.[1] This research area has received special attention during the past decade with the advent of combinatorial synthesis and automated organic synthesis that require straightforward separation protocols. In addition to the heterogeneous and homogeneous macromolecular systems, homogeneous molecular approaches have been developed in which the phase separation is driven by a small functional group called a phase tag.[2]

We discovered that pyridyl groups may be used as masked phase tags for the hydrocarbon/perfluorocarbon phase-switching of fluorine-free pyridyl-tagged molecules.[3] We showed that rather large and polar molecules such as *meso*-pyridyl substituted porphyrins are very effectively extracted into perfluorocarbons by pyridine coordination to a fluorous dicopper(II)-carboxylate complex. Due to the high lability of the coordination bonds, release of the tagged molecules into the hydrocarbon phase is achieved by simply adding THF in excess to the biphasic system, the THF acting as a competitive ligand.

Recently, as a case study for application of this novel phase-switching technique, a *bis*-monopyridyl benzyl alcohol tag was synthesized and used to prepare an analytically pure hydantoin.[4] After each step, the product was recovered in high yield and purity using the straightforward liquid-liquid extraction/recovery procedure.

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APPLICATION OF THE "PHASE-VANISHING METHOD" TO CYCLOPROPANATION OF ALKENES

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The “phase-vanishing (PV) method” utilize unique properties of the fluorous phase, which can divide otherwise miscible two phases. The PV method, which capitalizes on the diffusion of reagents through the fluorous phase, does not need any dropping funnels, heating/cooling baths, and even thermometers. Using the PV method, we carried out various organic reactions including bromination of olefins with Br_2, demethylation of aryl methyl ethers with BBr_3, bromination and chlorination of alcohols with PBr_3 or $SOBr_3$ and PCl_3 or $SOCl_2$ respectively, and the Friedel-Crafts acylation of aromatic compounds with $SnCl_4$. [1] Recent work demonstrates that the PV method has been modified to use gases [2] or a reagent reservoir with greater density than the fluorous phase, such as 1,2-dibromoethane. [3]

Here we will show an application of the PV method to cyclopropanation of olefins. While PV cyclopropanation of olefins using CH_2I_2 / Et_2Zn gave poor results, CH_2I_2 / Et_3Al systems afforded the cycloprapane derivatives in good yields. We also discuss about alternative fluorous media other than FC-72 available for the PV method.

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SYNTHESIS OF OLIGOSACCHARIDE AND PEPTIDE, GLYCOPEPTIDE USING FLUOROUS SUPPORT

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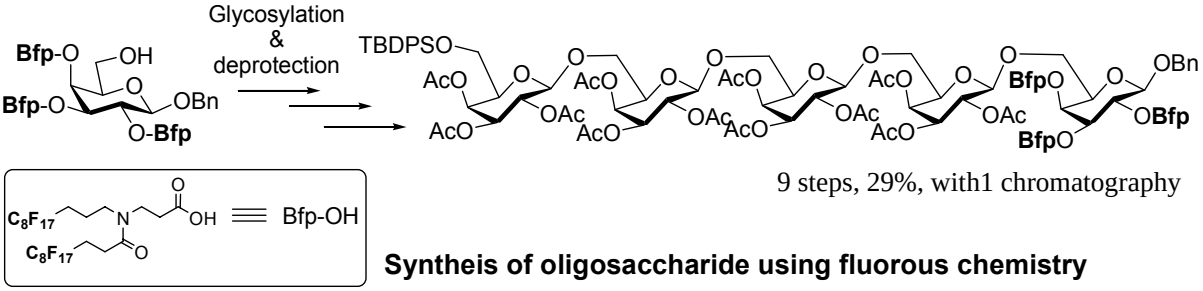
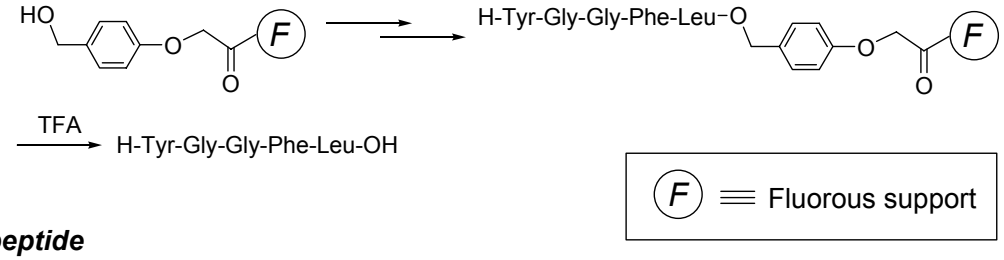
Novel acyl-type fluorous protecting group (Bfp) [1] and fluorous support [2, 3] as a heavy fluorous tag were prepared, and these fluorous tags made it possible to synthesize oligosaccharide with minimal column chromatography purification.



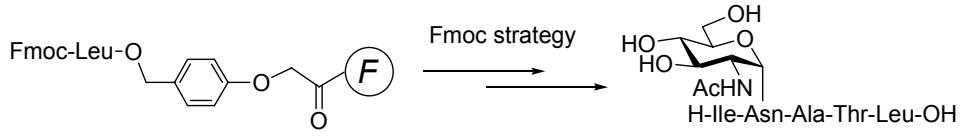
Syntheis of oligosaccharide using fluorous chemistry

Furthermore, rapid synthesis of peptides and glycopeptides were achieved on a fluorous support with suitable linker corresponding to the C-terminal form.

C-terminal COOH peptide



Glycopeptide



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REGIOSELECTIVE SYNTHESIS OF FLUORINATED *A*- AND *B*-AMINOPHOSPHORUS DERIVATIVES FROM *p*-TOLYLSULFONYL OXIMES

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The chemistry of 2*H*-azirines has been extensively explored because of the high reactivity of this ring towards nucleophilic and electrophilic reagents as well as for their photochemical and thermal behaviour [1]. In this way, we disclosed the first asymmetric synthesis of 2*H*-azirines derived from phosphine oxides and phosphonates by alkaloid- and solid-supported amines-mediated Neber reaction of tosyloximes [2].

Following our studies on the synthetic applications of this heterocycles, here we disclose the synthesis of functionalized aziridines **3** through addition of Grignard reagents to 2*H*-azirines **2**, generated *in situ* from fluorine containing *p*-tolylsulfonyl oximes derived from diphenylphosphine oxide **1** (R= Ph) and diethyl phosphonate **1** (R= OEt). We also explore the use of these aziridinyl derivatives **3** as versatile key intermediates for the regioselective synthesis of fluorinated *α*- and *β*-aminophosphorus derivatives **4** and **5** [3] (Figure 1).

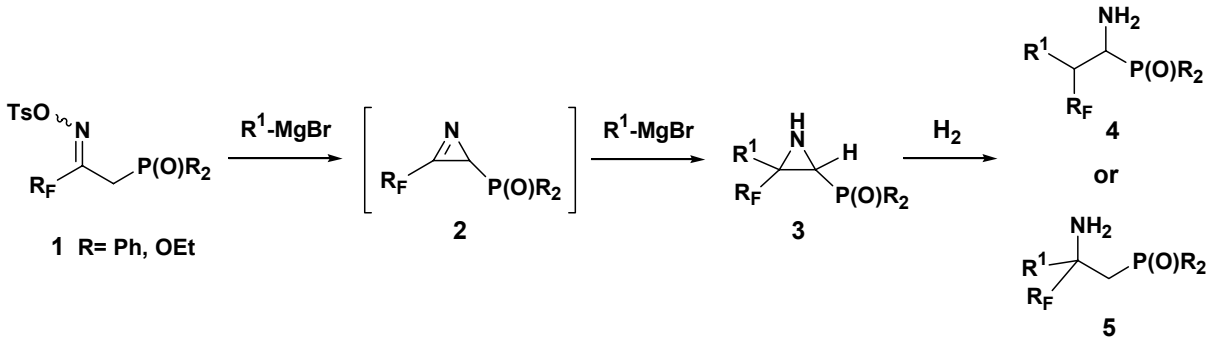

Figure 1

Acknowledgements:
The present work has been supported by the Dirección General de Investigación del Ministerio de Ciencia y Tecnología (MCYT, Madrid, DGI, PPQ2003-00910) and by the Universidad del País Vasco (UPV-GC/2002).

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POLYFLUORINATED BAYTRON

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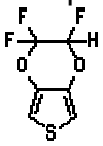
Baytron® M (3,4-Ethylenedioxythiophene (EDT, EDOT,) (**1**) is a monomer for the synthesis of the latest generation of conductive polymers, which is used in capacitors, antistatic coatings for plastics and glass, organic light-emitting diodes (OLEDS).[1-4] It is available in ton scale from H.C. Starck GmbH, a subsidiary of the BayerMaterialScience Group. Fluorinated analogues of Baytron® M were unknown up to now. However the introduction of fluorine atoms in the ethylene chain of **1** is of great interest and could radically change the electronic properties of polymer material by the introduction of the strong electron-withdrawing group and might have significant impact on the transparency, conductivity, and thermal stability of the resulting polymer. The known method of the synthesis of **1**, which involves the reaction of the corresponding derivatives of dihydroxythiophene with 1,2-dibromoethane [5] cannot be transferred automatically to the synthesis of 3,4-tetrafluoroethylenedioxythiophene. In the case of 1,2-dibromoperfluoroethane the mixture of inseparable products is the result of the reaction.

1



2

We have found a way for the preparation of 3,4-polyfluoroalkylenedioxythiophenes on the example of a new 3,4-trifluoroethylene analogue (**2**).

The later was obtained by the reaction of dimethyl 3,4-dihydroxy-2,5-thiophenecarboxylate, as a starting material with trifluorochloroethylene as a reactant, in DMSO as a solvent, in the presence of NaOH as a base → the following water-alkaline hydrolysis of methyl ester of the bicycle obtained in the first step with the formation of the corresponding free carboxylic acid at the thiophene ring → and the decarboxylation of the carboxylic group at the thiophene ring of the product formed in the second step using Cu-powder in quinoline as a promoter. The details of the different approaches to the synthesis of 3,4-polyfluoroethylenedioxythiophene, the reaction's conditions and the properties of **2**, as well as its electrochemical properties, will be discussed.

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FLUOROUS CHROMIUM REAGENTS FOR PREPARATION OF ORGANIC COMPOUNDS

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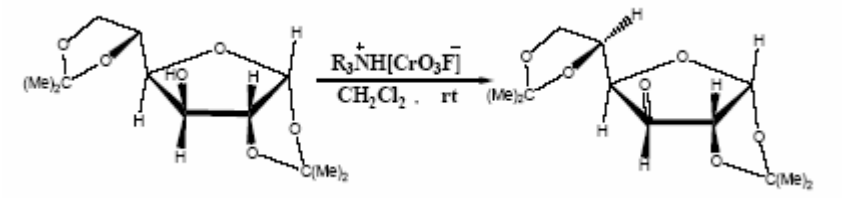
Development of oxidizing agents based upon higher-valent transition metal oxo derivatives has been the objective of many research laboratories and a host of such reagents derived from ruthenium, osmium, iron, manganese, molybdenum, vanadium and chromium have all proven to be capable of oxidation. In particular, there is continued interest in the development of new chromium(VI) reagents for the effective and selective oxidation of organic substrates under mild conditions. In recent years, significant improvements were achieved by the use of new oxidizing agents, such as pyridinium fluorochromate,[1] caffeinilium chlorochromate,[2] isoquinolinium fluorochromate,[3] and tetramethylammonium fluorochromate.[4] We have now investigated the synthetic potential of trialkylammonium fluorochromates, $R_3NH[CrO_3F]$, (TriAAFC) and we have found that these reagents have certain advantages over similar oxidizing agents in terms of amounts of oxidant and solvent required, easier working up and high yields. The results obtained with trialkylammonium fluorochromates are very satisfactory and show the new reagents as valuable additions to the existing oxidizing agents. Trialkylammonium fluorochromates have also been used for oxidations of carbohydrates such as 1,2:5,6-Di-O-isopropylidine-α-D-Glucofuranose to its relative ketosugar like by use of the equimolar ratio of the reagent.



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SYNTHESES AND X-RAY CRYSTAL STRUCTURES OF TWO MIXED ANIONIC FLUOROUS COMPLEXES

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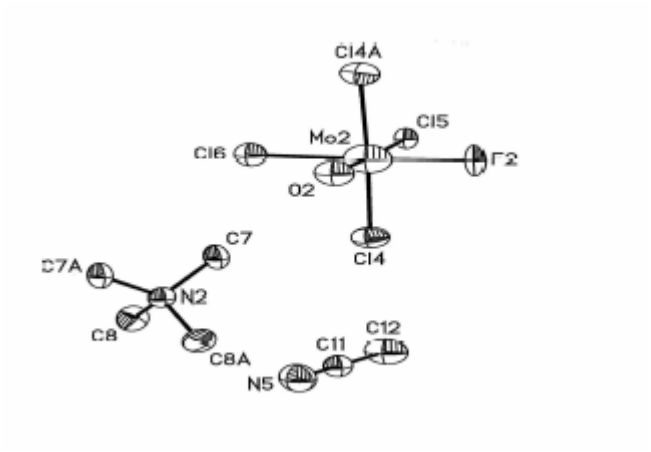
In recent years, many compounds found that have not configurations predicted by VSEPR model. These systems named as “Non-VSEPR” compounds. On the base of ligands similarity this compounds classified as “Homoleptic” and “Heteroleptic” systems. These terms mean that systems have one kind of ligands named Homoleptic and systems that have different kinds of ligands named Heteroleptic. Because of the simplicity of homoleptic systems, these systems have been studied more than heteroleptic systems.[1,2] We report here the synthesis and structures of two heteroleptic mixed-anionic systems of molybdenum and tungsten compounds. The structures of these two systems were determined by X-ray crystallography. The coordination geometries are similar in two complexes. In these crystals there are two crystallographically distinct anions, both have cis geometry. Experimental data showed the Non-VSEPR structures that have good agreement with sd^5 hybridation rather than sp^3d^2.



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FLUOROUS SYNTHESIS OF β,β-DIFLUORINATED CYCLIC QUATERNARY α-AMINOACIDS.

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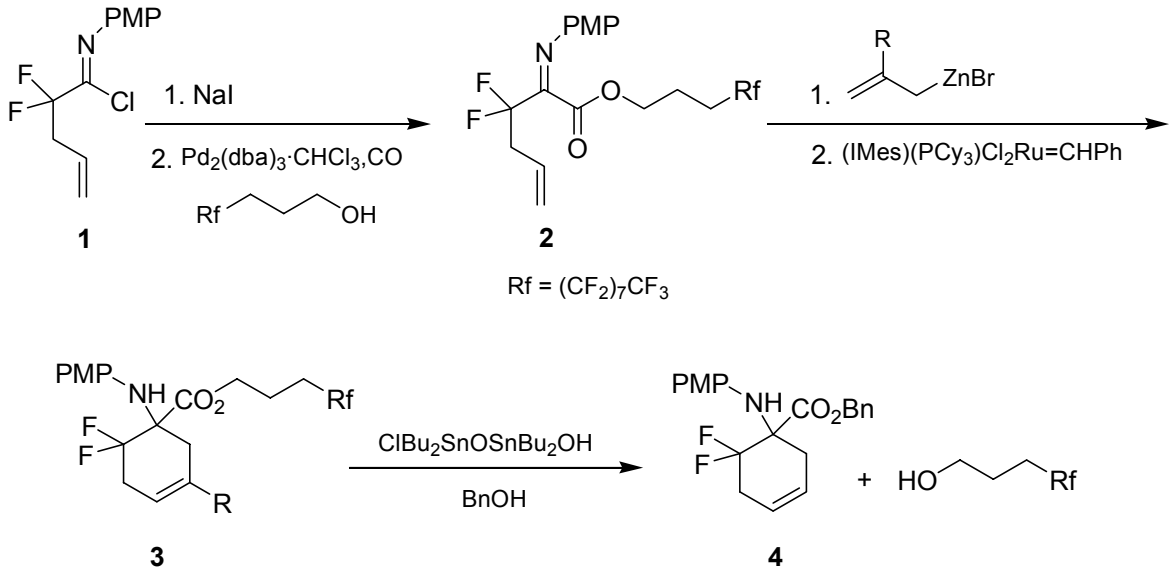
We wish to report the fluorous synthesis of β,β-difluorinated cyclic quaternary □-aminoacids using as a key step a ring closing metathesis reaction (RCM). The introduction of the fluorous tag was performed in imidoyl chloride **1** by means of alcoxycarbonilation of the corresponding iodide following the method developed by Uneyama,[1] in the presence of the prefluorinated alcohol. Fluorous imino ester **2** was treated then with the corresponding organozinc derivative and the resulting dienes were heated in refluxing toluene in the presence of second generation Grubbs catalyst affording α-amino acids **3** in high yield. The cleavage of the fluorous tag was accomplished by using a transesterification method mediated by CHTD ($ClBu_2SnOSnBu_2OH$),[2] giving rise to the protected amino acids **4** and the prefluorinated alcohol used as a fluorous tag.

In all the reactions carried out that contain the fluorinated tag, the purification was made by fluorous solid phase extraction (FSPE), affording the desired products with high purity and yield, which demonstrate the efficiency of SPE in the purification of the final products. In addition, the technique allows the easy recover of the perfluorinated alcohol used as a fluorinated tag.



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METHOD OF SYNTHESIS α,ω DIPHENYLPERFLUORALKANES

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The hydrocarbons containing two aromatic cycles connected by bridges from difluoromethylene groups - diarylperfluoralkanes are investigated a little. It is known some diphenyl perfluor alkanes. It is described two methods of production of diphenylperfluoralkanes. One of them is based on replacement of chlorine in diphenylchloralkanes on fluorine by action of fluorinating agents, for example trifluoride antimony.However this way has production only diphenyl perfluor alkanes with one or to two difluoromethylene groups between phenylic radicals. As the atoms of chlorine which are taking place in α-position to a benzene ring routinely easily come into exchange reaction.

The second method of synthesis diphenyl perfluor alkanes are driven in to compounds with two and three difluoromethylene groups is based on replacement of carbonyl atoms of oxygen in aromatic tri- and diketene on fluorine under action of sniphur tetrafluoride**.**

The dibenzoylperfluoralkanes with various number difluoromethylene groups can be easily obtained at interaction corresponding aliphatic perfluordicaboxylic acids with phenyl magnesium bromide.

In this paper is described fluorination of the aromatic diketenes by sniphur tetrafluoride. These two reactions have resulted in the development of general methods for the synthesis of diphenylperfluoralkanes with a number of difluoromethylene groups higher than 3. Interaction diketenes with sulfur tetrafluoride was executed according to the scheme:

$$C_6H_5CO(CF_2)COC_6H_5 + SF_4 \rightarrow C_6H_5(CF_2)_{x+1}C_OC_6H_5 + SOF_2 + SF_4 \rightarrow$$

$$C_6H_5(CF_2)x + 2\,C_6H_5 + SOF_2 \qquad X = 2, 3, 4.$$

Conclusions

1. The general method of synthesis α,ω– diphenylperfluoralkanes by action of sniphur tetrafluoride on α,ω– diphenylperfluoralkanes easily received{obtained} of perfluordicarboxylic acids is developed. By such way are synthesized 1,4-diphenylperfluorbutane ; 1,5-diphenylperfluorpentane; 1,6- diphenylperfluorhexane.
2. The conditions of synthesis 1,2-diphenylperfluoethane from benzyl and sniphur tetrafluoride are specified.
3. The replacement of atoms of oxygen in diketenes on the fluorine occurs serially and at reduction of duration of reaction with sniphur tetrafluoride, in a case for example dibenzoylperfluorpropane alongside with 1,5-diphenylperfluorpentane is formed mainly 1-phenyl-4-benzoylperfluorbutane.

THE SYNTHESIS OF PENTAFLUORIDE OF PHOSPHORUS BY FLUORINATION OF PENTAOXIDE PHOSPHORUS BY ELEMENTARY FLUORINE

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The problem of making of soft fluorinating agents for fluororganic synthesis to which it is necessary to relate and phosphorus pentafluoride is actual.
In laboratory practice for reception PP5 routinely use an exchange reaction between pentachloride phosphorus and such fluorides as AsF3HF, C6H5COF and 5FP5, use of the last provides rather high yield of a finished product.
The purpose of research were improvement of a technique of synthesis and making clean phosphorus pentafluoride. The pentafluoride phosphorus was received using interaction P205 with elementary fluorine. This synthesis highly was complicated owing to reaction of formation of the fluorine phosphoryl going in parallel of the basic reaction.
The starting reagents - fluorine and P205 carefully has been refined from fluorine hydride and a moisture accordingly. The purification of fluorine from fluorine hydride (HF) has been made by freeze-out at the temperature a minus 95°C (with use of solid acetone and the subsequent adsorption on fluorine sodiums. The reaction of interaction of phosphorus pentoxide with elementary fluorine was carried out in nickeliferous equipment at the temperature 300-400°C and 15 % excess of fluorine. The formed reactionary gas was missed through the heated column of after-burning filled by the fluorinated nickeliferous grid at the temperature 250-300 °C.
Further gas entered in system of the condensation. This system has incorporated of three tandem quartz traps working at freezing temperatures of ethyl acetate (-87,4°C), acetone (-94,6°C) and ethanol (-112°C). Traps were cooled by liquid nitrogen. The finite product was pentafluoride phosphorus condensed in two last condensers. And the basic quantity pentafluoride phosphorus collected in the condenser having temperature-112°C. Gas analyzed a mass - spectrometric method. The impurity level in synthesized pentafluoride phosphorus was slight and did not exceed 0,5 - 1 %. The yield pentafluoride phosphorus has made 75 % from theoretical
The analysis of the formed condensates in the first two the condensers having temperature - 87,4°C and - 94,6°C accordingly, has specified content in them mainly fluorine hydride.
At fluorination of phosphorus pentoxide by elementary fluorine significant temperature effect for speed of interaction has been noticed.

DEVELOPMENT OF OXYGEN SENSING SYSTEM BY STATIONARY QUENCHING METHOD USING ZnTFPP

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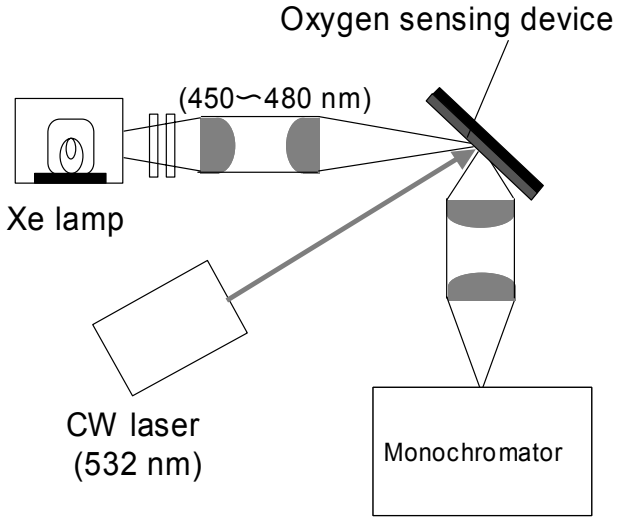
Determination of oxygen concentration is of importance in various fields of chemical, clinical analysis and environmental monitoring. Several oxygen detection systems using luminescence quenching by oxygen have been developed. Many sensing dyes for these systems are luminescent organic dyes, such as polycyclic aromatic hydrocarbons and transition metal complexes. As the most organic dyes, however, do not show the luminescence at room temperature, the novel oxygen sensor based on T-T absorption quenching using pulse laser has been developed. The conventional laser flash photolysis system is adopted for oxygen sensing and non-luminescent dyes can be used in this system. As the triplet lifetime of the dye decreases with oxygen concentration, oxygen concentration is given by the measurement of triplet lifetime of the dye. This system, however, is inconvenient because of the large scale apparatus like a pulse laser. In this study, a new oxygen sensing system by T-T absorption at steady state quenching using CW laser is developed.

Figure shows the outline of the oxygen sensing system using CW Nd-YAG lase as an excitation light. A xenon arc lamp was used as a monitoring light. Oxygen pressure in a gas stream was controlled by the flow rates of oxygen and nitrogen gases. The intensity of the transmittance of the ZnTFPP-PS film was measured by using digital storage oscilloscope through monochromator.



T-T absorption spectrum of ZnTFPP-PS film observed with CW laser system was almost same as that of conventional transient absorption spectrum, attributed to the T_1-T_n absorption. As the maximum T-T absorption was observed at 470 nm, oxygen sensitivity is measured at 470 nm in the following experiments. Effect of the oxygen concentration on the T-T absorption intensity of ZnTFPP-PS film was measured. The intensity of T-T absorption at 470 nm was about 0.8 under nitrogen and decreased with the oxygen concentration, indicating that the excited triplet state of ZnTFPP-PS film was quenched by the oxygen and the steady state T-T absorption reached the new equilibrium state.

SYNTHESIS AND AIR-WATER INTERFACE OF SULFOBETAINE FLUOROSURFACTANTS

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The development of highly fluorinated compounds mainly of surfactant type are of great interest in numerous fields like surface modifications (i.e. AFFF). We present in this work the synthesis and characterization of new compounds of sulfobetaine type in fluorinated series. As structural point of view, these amphiphilic compounds have the main chemical segments:

-a highly fluorinated chain
-an hydrocarbon spacer
-a polar sulfobetaine head

The overall compounds are synthetized in three steps from raw materials, ie, 2-F-alkylethyliodide or directly from F-alkyliodide. These compounds are monodisperse. The air-water interface properties have been investigated from tensiometric method. We present also the critical micellar concentrations and adsorption kinetic for each surfactant. A correlation between the length of the hydrocarbon spacer and the corresponding surface properties will be discussed. The results are described and compared to hydrocarbon or fluorocarbon homologues.

DEVELOPMENT OF FLUOROUS LEWIS ACID-CATALYZED REACTIONS IN A FLUOROUS BIPHASIC SYSTEM AND AN APPLICATION TO CONTINUOUS-FLOW REACTION SYSTEM

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We have already found that *lanthanide(III), tin(IV), and hafnium(IV) bis(perfluoroalkanesulfonyl)amides* would be highly active catalysts of Lewis acid-promoted reactions such as (direct) esterification, transesterification, Diels−Alder reactions, Friedel−Crafts reactions, and Baeyer−Villiger reactions with aqueous hydrogen peroxide in a fluorous biphasic system.[1-3]

In a fluorous biphasic batch system, a fluorous phase containing fluorous Lewis acid catalyst described above was readily recovered and reused by phase separation without loss of catalytic activity after the reactions (Figure 1). We applied this batch system to a continuous-flow reaction system. Our continuous-flow system is as follows (Figure 2).[4] At first, fluorous solvent is poured into the reactor followed by adding the catalyst such as ytterbium(III) bis(perfluorooctanesulfonyl)amide, which is immobilized in the fluorous solution because of its insolubility in general organic solvent. Next, organic solution containing organic substrates and reagents as the mobile organic phase is continuously flowing into the stationary fluorous phase in the reactor with vigorous stirring. The reaction proceeds in the resultant emulsion. After the reaction, the emulsion mixture is automatically introduced to the decanter where organic/fluorous phases are separated. Then, the upper organic phase is overflowing and lower fluorous phase is recycled. Thus, the substrates can be converted to the products through this continuous-flow system. We performed acetylation of cyclohexanol in toluene and GALDEN® SV135 (Solvay Solexis K.K.) catalyzed by ytterbium(III) bis(perfluorooctanesulfonyl)amide to give cyclohexyl acetate with high TON (≈ 22,000).

Figure 1

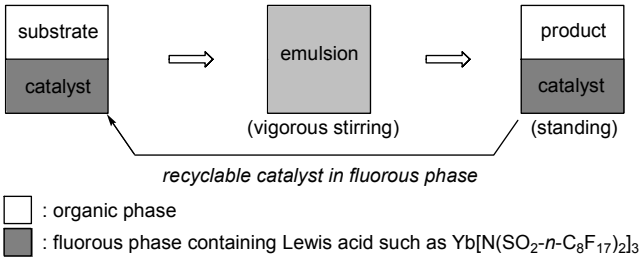
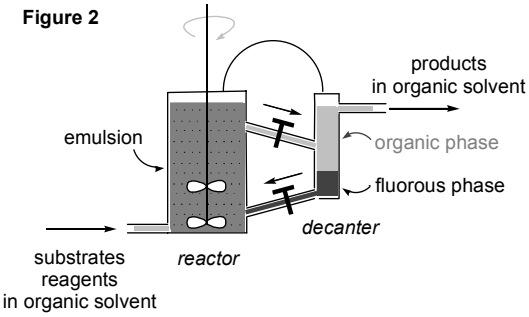


Figure 2



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DEVELOPMENT OF SYNTHETIC APPROACHES TO POLYFUNCTIONAL COMPOUNDS WITH PENTAFLUOROSULFANYL (SF_5) GROUPING.

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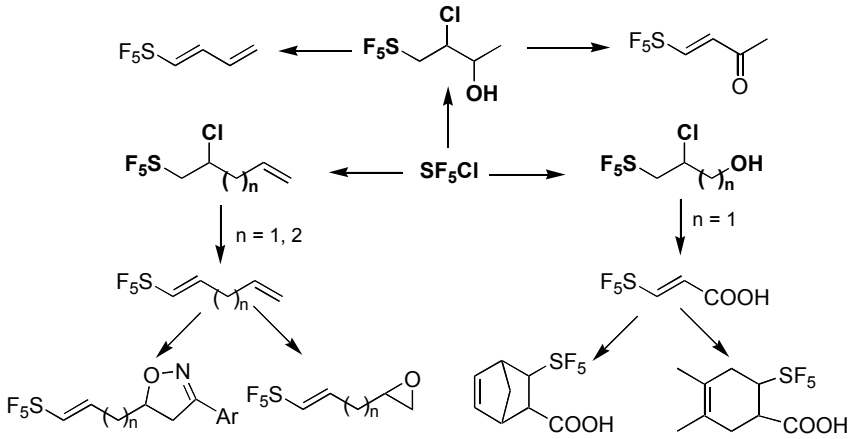
As part of a program concerned with the synthesis and characterization of new pentafluorosulfur derivatives, we became interested in the development of synthetic approaches to various unsaturated compounds with pentafluoro-λ^6-sulfanyl terminal groupings. Organic compounds in which pentafluoro-λ^6-sulfanyl group is present are of special interest because they often possess the advantageous properties of the parent compound, SF_6, among which are a high group electronegativity, large steric bulk, a nonfunctional hexacoordinate stereochemistry, and high thermal and hydrolytic stability. The synthesis and chemistry of these compounds are the subjects of ongoing studies.[1-3]



Sulfur chloride pentafluoride (F_5SCl) has been utilized in reactions with variety of unsaturated compounds. We have investigated the development of some novel reaction systems with (F_5SCl). Using the reaction between the sulfur chloride pentafluoride (F_5SCl) and unsaturated alcohols or 1,4-, 1,5-alkadienes (in gas phase) under irradiation of ultra-violet light leads to products of addition of F_5SCl to the double bounds in good yields. These adducts were used as useful precursors for preparation of new unsaturated, cyclyc and heterocyclic compounds with pentafluorothio groups. The structure of synthesized new compounds, were characterized by ^1H, ^{13}C, and ^{31}P NMR data and in some cases by single crystal X-ray crystallography. The details of the synthesis, spectroscopic properties and X-ray data will be discussed.

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