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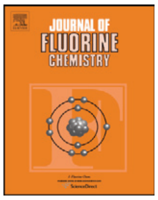

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Editorial

Graham Sandford

Department of Chemistry, Durham University, South Road, Durham DH1 3LE, UK

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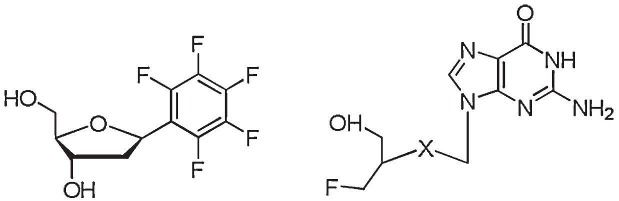
Synthesis and applications of fluorinated nucleoside analogues

Hanna Wójtowicz-Rajchel

Adam Mickiewicz University, Department of Chemistry, Grunwaldzka 6,
60-780 Poznań, Poland

► Highly modified fluorinated analogues of nucleosides are overviewed. ► Synthesis and design of fluorinated carbocyclic nucleosides. ► Aromatic nucleoside isosteres as probes of noncovalent bonding in DNA. ► Fluorinated acyclic nucleosides as antiviral agents and tracers for PET.



Fluorinated analogues of nucleosides

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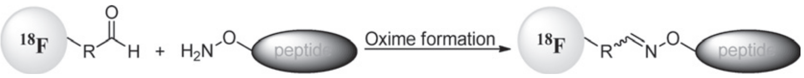
Oxime formation for fluorine-18 labeling of peptides and proteins for positron emission tomography (PET) imaging: A review

Xiang-Guo Li[ac], Merja Haaparanta[b], Olof Solin[cd]

[a]*Laboratory of Synthetic Drug Chemistry, Department of Pharmacology, Drug Development and Therapeutics, University of Turku, FI-20014 Turku, Finland*
[b]*MediCity/PET Preclinical Imaging, Turku PET Centre, University of Turku, Tykistökatu 6A, FI-20520 Turku, Finland*
[c]*Radiopharmaceutical Chemistry Laboratory, Turku PET Centre, University of Turku, Porthaninkatu 3, FI-20500 Turku, Finland*
[d]*Accelerator Laboratory, Åbo Akademi University, Porthansgatan 3, FI 20500 Turku, Finland*

► Methods for ^{18}F-labeling of peptides for PET imaging are reviewed. ► The focus is on ^{18}F-aldehydes as prosthetic groups for peptide labeling. ► Oxime formation is considered as a robust, feasible and practical ^{18}F-labeling method for preclinical and clinical applications.



doi:10.1016/S0022-1139(12)00305-3

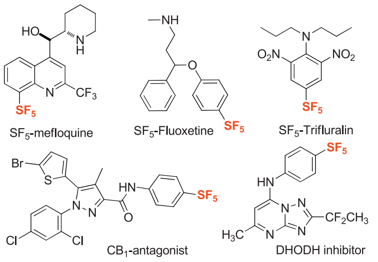
J. Fluorine Chem., 143 (2012) 57

Synthetic chemistry and biological activity of pentafluorosulphanyl (SF_5) organic molecules

Stefano Altomonte[a], Matteo Zanda[ab]

[a]*Kosterlitz Centre for Therapeutics, Institute of Medical Sciences, and John Mallard Scottish PET Centre, University of Aberdeen, Foresterhill, Aberdeen AB25 2ZD, Scotland, UK*
[b]*C.N.R.-Istituto di Chimica del Riconoscimento Molecolare, via Mancinelli 7, 20131 Milano, Italy*

► We review the synthesis of SF_5-compounds, with an emphasis on work published after year 2000. ► We review the reactivity of SF_5-substituted organic molecules. ► We review the biological properties of SF_5-substituted drug candidates.



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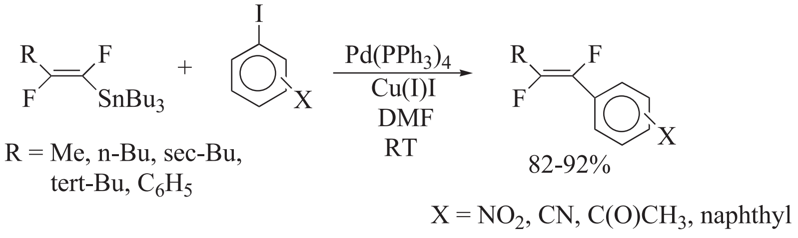
The stereospecific preparation of (E)-1,2-difluoro-1,2-disubstituted alkenes

Long Lu, Donald J. Burton

Department of Chemistry, The University of Iowa, Iowa City, IA 52242, USA

► Stereospecific synthesis of (E)-1,2-difluoro-1-substituted aryl-alkene. ► Stereospecific synthesis of (Z)-RCF=CFSnBu$_3$. ► Stereospecific Si/Sn exchange of (Z)-1,2-difluoro-2-substituted vinylsilanes. ► Preparation of (Z)-1,2-disubstituted vinyl silanes from F_2C=CFCL



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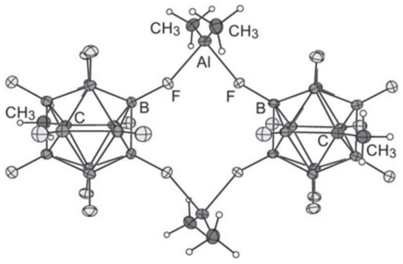
Synthesis, structure, and reactivity of AlMe$_2$(1-Me-CB$_{11}$F$_{11}$): An AlMe$_2^+$ cation-like species bonded to a superweak anion

Sergei V. Ivanov, Dmitry V. Peryshkov, Susie M. Miller, Oren P. Anderson, Anthony K. Rappé, Steven H. Strauss

Department of Chemistry, Colorado State University, Fort Collins, CO 80523, USA

► Synthesis of [AlMe$_2$(1-Me-CB$_{11}$F$_{11}$)]$_2$. ► X-ray structure of [AlMe$_2$(1-Me-CB$_{11}$F$_{11}$)]$_2$, which consists of AlMe$_2^+$ cation-like species bonded to two F atoms from two 1-Me-CB$_{11}$F$_{11}^-$ superweak anions. ► [AlMe$_2$(1-Me-CB$_{11}$F$_{11}$)]$_2$ undergoes rapid exchange on the NMR timescale with both AlMe$_3$ and [N(n-Bu)$_4$][1-Me-CB$_{11}$F$_{11}$].



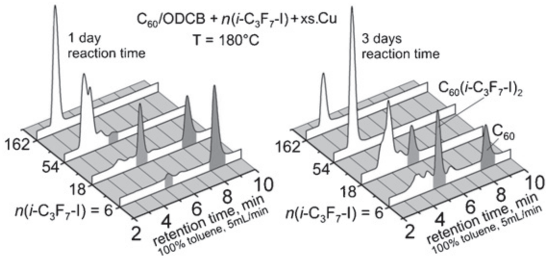
J. Fluorine Chem., 143 (2012) 103

Solution-phase perfluoroalkylation of C$_{60}$ leads to efficient and selective synthesis of bis-perfluoroalkylated fullerenes

Igor V. Kuvychko, Steven H. Strauss, Olga V. Boltalina

Department of Chemistry, Colorado State University, Fort Collins, CO 80523, USA

► Efficient perfluoroalkylation of C$_{60}$ with R$_F$I reagents under homogeneous conditions. ► Strong effect of reagent ratio, reaction time, and copper promoter on product composition. ► Selective synthesis of bisadducts is based on "low-conversion" reaction regime.



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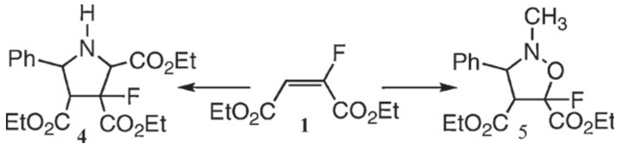
[3+2] Cycloaddition reactions of diethyl (*E*)-2-fluoromaleate

Timothy B. Patrick, Mehrdad Shadmehr, Akbar H. Khan, Rajiv K. Singh, Bethel Asmelash

Department of Chemistry, Southern Illinois University, Edwardsville, IL 62026, USA

► The fluoromaleate **1** is prepared easily in 89% yield. ► The fluoromaleate reacts with nitornes to give fluoro isoxazolidines. ► The fluoromaleate reacts with imines to give fluoropyrrolidones. ► Stereochemistry and regiochemistry is determined by proton NMR.



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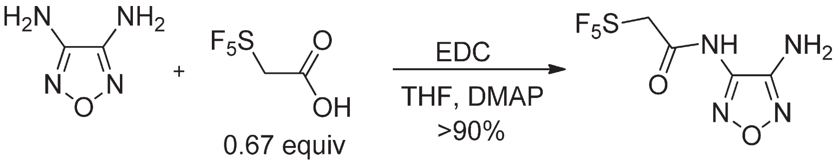
Energetic materials containing fluorine. Design, synthesis and testing of furazan-containing energetic materials bearing a pentafluorosulfanyl group

Henry Martinez, Zhaoyun Zheng, William R. Dolbier Jr.

Department of Chemistry, University of Florida, PO Box 117200, Gainesville, FL 32611-7200, United States



► Pentafluorosulfanylacetic acid is a useful building block for preparation of new furazan energetic materials. ► SF_5-substituted furazans have densities greater than materials containing either moiety alone. ► SF_5-substituted furazans have enhanced energetic properties when compared to materials containing either moiety alone. ► The low nucleophilicity of aminofurazans makes synthesis of derivatives challenging.

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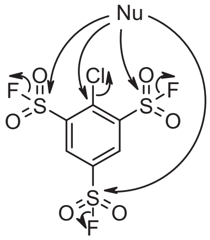
Interaction of 2,4,6-tris(fluorosulfonyl)chlorobenzene with O-, N-, S-, C-nucleophiles and F-anion

Andrey A. Filatov, Vladimir N. Boiko, Yurii L. Yagupolskii

Institute of Organic Chemistry, National Academy of Sciences of Ukraine, 5 Murmanskaya St., UA-02094 Kiev-94, Ukraine

► Selective reactions of 2,4,6-tris(fluorosulfonyl)chlorobenzene with a O-, N-, S-, C-nucleophiles. ► Excess of nucleophile commonly led to SO_2F groups implication in the reaction. ►Fluoride-anion source gave anionic σ-complex with two fluorine atoms in the *hem*-position. ► Reduction with zinc/AcOH conveniently led to 1,3,5-tris(fluorosulfonyl)benzene.



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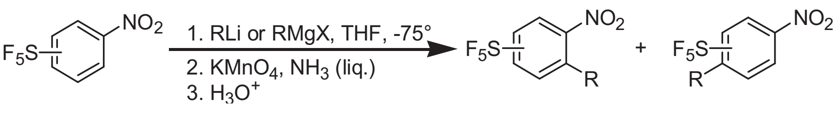
Oxidative nucleophilic substitution of hydrogen in nitro(pentafluorosulfanyl)benzenes with alkyl Grignard and lithium reagents

Norbert Vida, Petr Beier

Institute of Organic Chemistry and Biochemistry, Academy of Sciences of the Czech Republic, Flemingovo nám. 2, 166 10 Prague, Czech Republic

► Oxidative nucleophilic substitution of hydrogen in nitro(pentafluorosulfanyl)benzenes with Grignard and lithium reagents was investigated. ► Addition of potassium permanganate in liquid ammonia significantly increases the yield of ONSH products. ► ONSH reaction take place in *ortho*- and *para*-positions relative to the nitro group.



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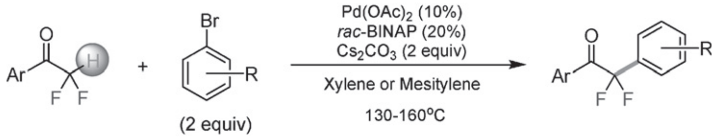
Palladium catalyzed direct α-arylation of α,α-difluoroketones with aryl bromides

Chen Guo[a], Ruo-Wen Wang[a], Feng-Ling Qing[a,b]

[a] *Key Laboratory of Organofluorine Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, 345 Lingling Lu, Shanghai 200032, China*

[b] *College of Chemistry, Chemical Engineering and Biotechnology, Donghua University, 2999 North Renmin Lu, Shanghai 201620, China*



► The palladium-catalyzed direct α-arylation of α,α-difluoroketones was developed. ► *rac*-BINAP and Cs$_2$CO$_3$ promoted the reaction efficiently. ► A variety of α-aryl-α,α-difluoroketones can be prepared by this practical method.

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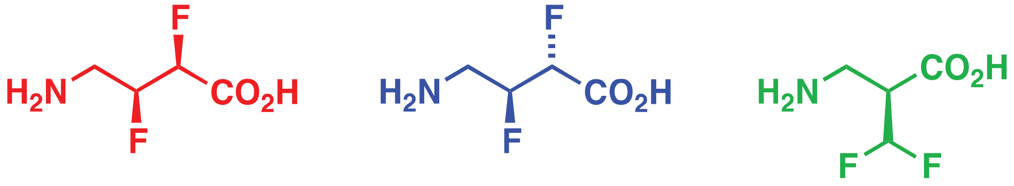
Synthesis of difluorinated β- and γ-amino acids: Investigation of a challenging deoxyfluorination reaction

Zhiyong Wang, Luke Hunter

School of Chemistry, The University of New South Wales, Sydney 2052, Australia



► Fluorinated β- and γ-amino acids have been synthesised. ► All possible stereoisomers can be selectively accessed. ► The key transformation is a modest-yielding deoxyfluorination of a vicinal fluorohydrin. ► Several fluorinating reagents were investigated including DeoxoFluor™, PBSF and XtalFluor-E®.

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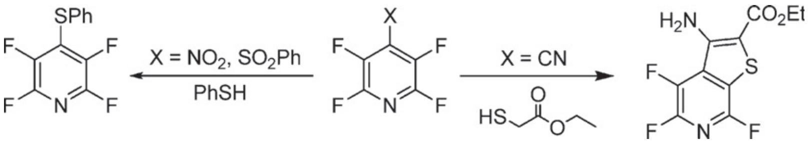
Reactions of 4-substituted tetrafluoropyridine derivatives with sulfur nucleophiles: S$_N$Ar and annelation processes

Mark A. Fox[a], Graham Sandford[a], Rachel Slater[a], Dmitrii S. Yufit[b], Judith A.K. Howard[b], Antonio Vong[c]

[a] *Department of Chemistry, Durham University, South Road, Durham DH1 3LE, UK*

[b] *Chemical Crystallography Group, Department of Chemistry, Durham University, South Road, Durham DH1 3LE, UK*

[c] *GlaxoSmithKline Pharmaceuticals, New Frontiers Science Park, Third Avenue, Harlow, Essex CM19 5AW, UK*



► 4-Tetrafluoropyridine derivatives react with sulfur nucleophiles. ► Ipso substitution of 4-nitro and 4-phenylsulfonyl substituents occur. ► Thieno[2,3-c]pyridine products formed from 4-cyano-tetrafluoropyridine.

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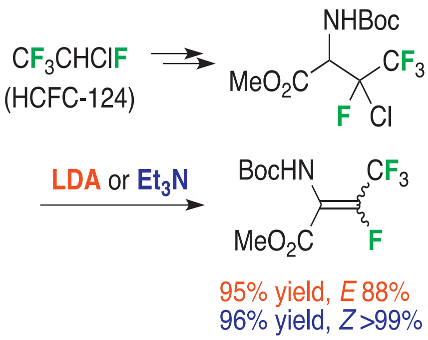
Stereodivergent formation of fluorine-containing enamides

Shin Ota[a], Tomoko Kawasaki-Takasuka[a], Takashi Yamazaki[a], Toshio Kubota[b]

[a] *Division of Applied Chemistry, Institute of Engineering, Tokyo University of Agriculture and Technology, Koganei 184-8588, Japan*

[b] *Department of Biomolecular Functional Engineering, Ibaraki University, Nakanarusawa 4-12-1, Hitachi 316-851, Japan*



► Convenient reaction of HCFC-124 with aromatic imines protected by Boc or Ts groups on nitrogen. ► Smooth conversion of aromatic groups in the above products to the methyl ester in two steps. ► Stereodivergent construction of fluorinated enamides just by selection of a base.

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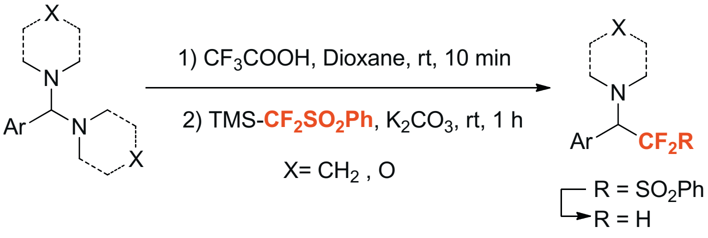
Nucleophilic difluoromethylation of *N*,*N*-acetals with $TMSCF_2SO_2Ph$ reagent promoted by trifluoroacetic acid: A facile access to α-difluoromethylated tertiary amines

Weizhou Huang, Chuanfa Ni, Yanchuan Zhao, Bing Gao, Jinbo Hu

Key Laboratory of Organofluorine Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, 345 Ling-Ling Road, Shanghai 200032, China

► Nucleophilic difluoromethylation of *N*,*N*-acetals with $TMSCF_2SO_2Ph$ is developed. ► Iminium species could be in situ generated from *N*,*N*-acetals and CF_3COOH. ► Potassium carbonate activates the $TMSCF_2SO_2Ph$ during difluoromethylation.



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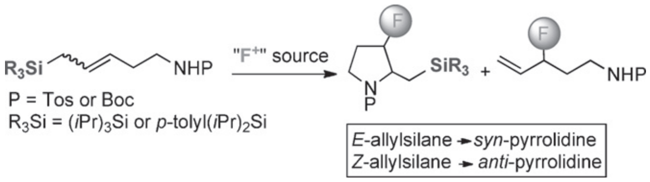
Metal free fluoroamination of allylsilanes: A route to 3-fluoropyrrolidines

Lorraine E. Combettes, Oscar Lozano, Véronique Gouverneur

University of Oxford, Chemistry Research Laboratory, 12 Mansfield Road, Oxford, OX1 3TA, United Kingdom



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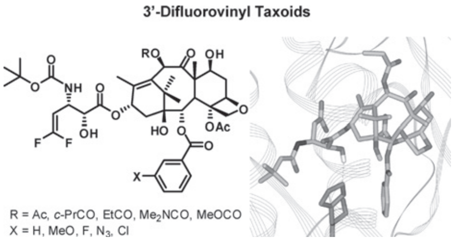
Synthesis and biological evaluation of novel 3′-difluorovinyl taxoids

Larissa Kuznetsova[a], Liang Sun[a], Jin Chen[a], Xianrui Zhao[a], Joshua Seitz[a], Manisha Das[a], Yuan Li[a], Jean M. Veith[c], Paula Pera[c], Ralph J. Bernacki[c], Shujun Xia[d], Susan B. Horwitz[d], Iwao Ojima[ab]

[a]*Department of Chemistry, State University of New York at Stony Brook, Stony Brook, NY 11794-3400, United States*
[b]*Institute of Chemical Biology & Drug Discovery, State University of New York at Stony Brook, Stony Brook, NY 11794-3400, United States*
[c]*Department of Experimental Therapeutics, Grace Cancer Drug Center, Roswell Park Memorial Institute, Elm and Carlton Streets, Buffalo, NY 14263, United States*
[d]*Department of Molecular Pharmacology, Albert Einstein College of Medicine, Bronx, NY 10461, United States*

► A series of 3′-difluorovinyl taxoids were strategically designed to block the metabolism by P-450 3A4 enzyme and synthesized. ► Difluorovinyl taxoids exhibit up to 3 orders of magnitude higher potency against MDR cell line as compared to paclitaxel. ► Difluorovinyl taxoids induced GTP-independent tubulin polymerization much faster than paclitaxel. ► Molecular modeling study indicates that a difluorovinyl taxoid binds to β-tubulin consistent with the REDOR-Taxol structure. ► Difluorovinyl group's unique stereoelectronic property may account for the high potency of difluorovinyl taxoids.



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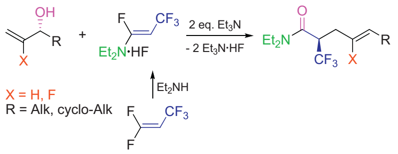
Synthesis of α-trifluoromethylated amides by Eschenmoser–Claisen-type rearrangement of allylic alcohols

Justyna Walkowiak[a], Magdalena Tomas-Szwaczyk[a], Günter Haufe[b], Henryk Koroniak[a]

[a]*Adam Mickiewicz University, Faculty of Chemistry, Grunwaldzka 6, 60-780 Poznań, Poland*
[b]*Organisch-Chemisches Institut, Westfälische-Wilhelms Universität, Corrensstraße 40, 48149 Münster, Germany*



► One-pot, stereospecific synthesis of α-trifluoromethyl-γ,δ-unsaturated amides by a Eschenmoser–Claisen-type rearrangement. ► Chirality transfer from carbon C-3 of the enantiomerically enriched allylic alcohol to C-2 of the corresponding carboxamide. ► General mechanism of action of the pentafluoropropene-diethylamine adduct towards different alcohols.

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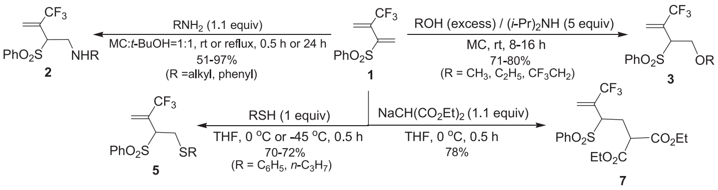
Regioselective addition reactions of 3-phenylsulfonyl-2-trifluoromethyl-1,3-butadiene with nucleophiles

Eun Joon Yang, Sung Lan Jeon, In Howa Jeong

Department of Chemistry, Yonsei University, Wonju 220-710, South Korea



► 3-Phenylsulfonyl-2-trifluoromethyl-1,3-butadiene underwent the regioselective nucleophilic addition reactions with heteroatom nucleophiles. ► The amine addition product of 3-phenylsulfonyl-2-trifluoromethyl-1,3-butadiene underwent the 5-*endo-trig* cyclization reaction to give the 4-phenylsulfonyl-3-trifluoromethylpyrrolidine derivatives. ► 4-Phenylsulfonyl-3-trifluoromethylpyrrolidine derivatives regenerated the 1,3-butadiene via amine elimination reaction.

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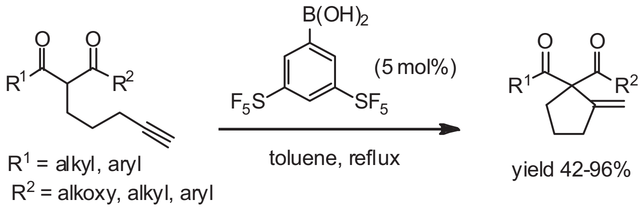
3,5-Bis(pentafluorosulfanyl)phenylboronic acid: A new organocatalyst for Conia-ene carbocyclization of 1,3-dicarbonyl compounds having terminal alkynes

Yu-Dong Yang, Xu Lu, Etsuko Tokunaga, Norio Shibata

Department of Frontier Materials, Graduate School of Engineering, Nagoya Institute of Technology, Gokiso, Showa-ku, Nagoya 466-8555, Japan



► Bis(pentafluorosulfanyl)phenylboronic acid is as an efficient organocatalyst. ► Bis(pentafluorosulfanyl)phenylboronic acid is a catalyst for Conia-ene reaction. ► Bis(pentafluorosulfanyl)phenylboronic acid is a catalyst for carbocyclization. ► SF$_5$ function is a lipophilic alternative to the NO$_2$ group. ► SF$_5$ function is a sterically demanding alternative to the NO$_2$ group.

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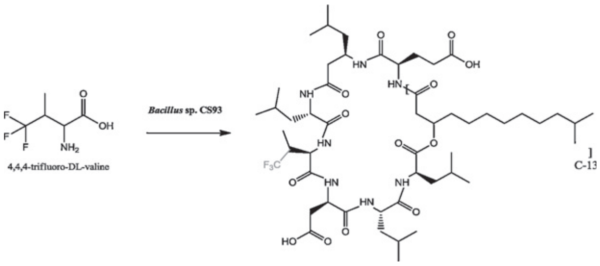
Production of the novel lipopeptide antibiotic trifluorosurfactin via precursor-directed biosynthesis

Neil K. O'Connor[a], Dilip K. Rai[b], Benjamin R. Clark[a], Cormac D. Murphy[a]

[a]*School of Biomolecular and Biomedical Science and the Centre for Synthesis and Chemical Biology, University College Dublin, Belfield, Dublin 4, Ireland*
[b]*Department of Food Biosciences, Teagasc Food Research Centre, Ashtown, Dublin 15, Ireland*



► Employed precursor-directed biosynthesis to biosynthesise fluorinated lipopeptides. ► *Bacillus* sp. CS93 produced small quantities of trifluorosurfactin when incubated with 4,4,4-trifluoro-DL-valine. ► Most of the fluorinated amino acid was converted to 4,4,4-trifluoro-2-hydroxy-3-methylbutanoic acid.

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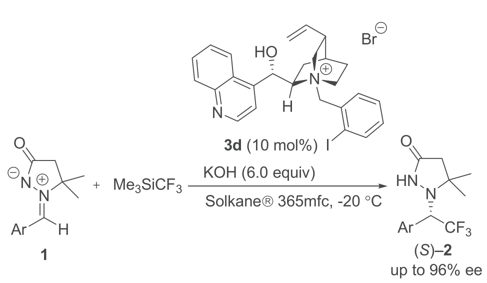
N-2-Iodobenzylcinchoninium bromide is effective for catalytic enantioselective trifluoromethylation of azomethine imines in Solkane® 365mfc

Satoshi Okusu, Hiroyuki Kawai, Xiu-Hua Xu, Etsuko Tokunaga, Norio Shibata

Department of Frontier Materials, Graduate School of Engineering, Nagoya Institute of Technology, Gokiso, Showa-ku, Nagoya 466-8555, Japan



► Solkane® 365mfc is an environmental benign solvent for the trifluoromethylation. ► Solkane® 365mfc is a solvent for the enantioselective trifluoromethylation. ► Iodobenzylcinchoninium bromide affects an asymmetric trifluoromethylation. ► Solkane® 365mfc is 1,1,1,3,3-pentafluorobutane, $CF_3CH_2CF_2CH_3$.

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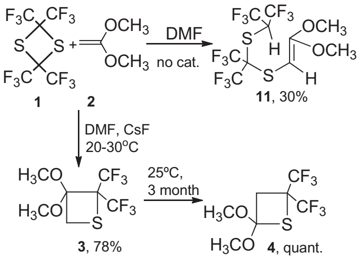
Reaction of hexafluorothioacetone dimer with ketene dimethylacetal and dimethyl thioacetal

Viacheslav A. Petrov[a], Will Marshall[b]

[a]*DuPont Central Research and Development, Experimental Station, PO Box 80500, Wilmington, DE 19880-0500, United States*
[b]*DuPont Corporate Center for Analytical Sciences, Experimental Station, PO Box 80500, Wilmington, DE 19880-0500, United States*



► Synthesis of 2,2-bis(trifluoromethyl)-3,3-bis(methoxy)thietane. ► Synthesis of 2,2-bis(trifluoromethyl)-4,4-bis(methoxy)thietane. ► Reactions of 2,2-bis(trifluoromethyl)-3,3-bis(methoxy)thietane.

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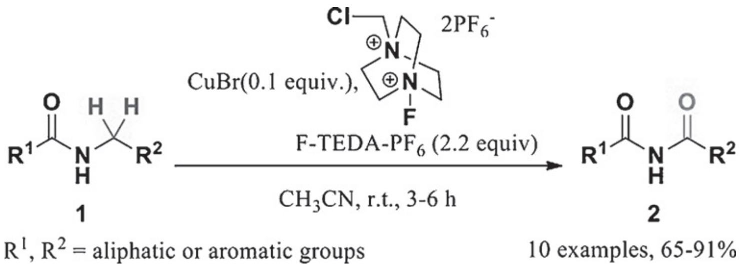
Replacement of BF_4^- by PF_6^- makes Selectfluor greener

Zhuang Jin[a], Bo Xu[a], Stephen G. DiMagno[b],
Gerald B. Hammond[a]

[a]*Department of Chemistry, University of Louisville, Louisville, KY, USA*
[b]*Department of Chemistry and Center for Materials Research and Analysis, University of Nebraska–Lincoln, Lincoln, NE, USA*



► Selectfluor®/CuBr oxidizes amides to provide imides at room temperature. ► The choice of counterion for Selectfluor® affects CuBr loading dramatically. ► A rationale for thecounterion effect is provided.

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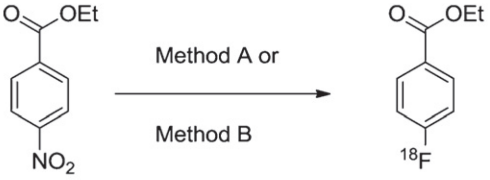
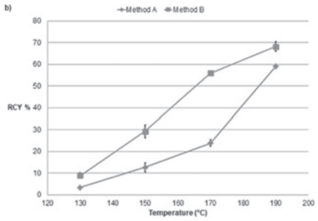
Evaluation of tetraethylammonium bicarbonate as a phase-transfer agent in the formation of [^{18}F]fluoroarenes

Christopher D. Reed, Guillaume G. Launay,
Michael A. Carroll

School of Chemistry, Bedson Building, Newcastle University, Newcastle upon Tyne NE1 7RU, UK



Method A: [^{18}F]KF/K222. Method B: [^{18}F]Et_4N.F



► We report tetraethylammonium bicarbonate, TEA·HCO_3, is a suitable phase-transfer agent for [^{18}F]radiofluorinations. ► Good yields have been achieved for a range of [^{18}F]radiofluorination methods generating [^{18}F]fluoroarenes. ► The use of TEA·HCO_3 has eliminated microreactor blockages experienced using the traditional system Kryptofix® 222/K_2CO_3.

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Fluoro-Pummerer rearrangement and analogous reactions

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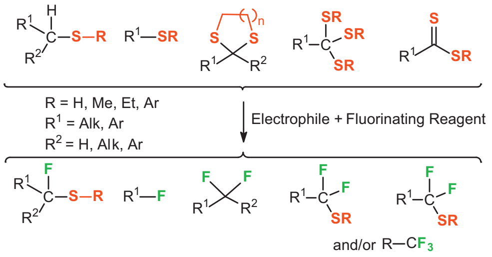

► Fluoro-Pummerer rearrangement and related reactions are reviewed. ► α-Fluorothioethers are available from sulfoxides by reaction with an electrophile in the presence of a fluoride donor. ► Desulfurization–difluorination is highlighted as a method for the preparation of *gem*-difluorides. ► Synthesis of *gem*-difluorides and trifluoromethyl derivatives by oxidative desulfurization–fluorination.

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Nickel fluoro complexes as intermediates in catalytic cross-coupling reactions

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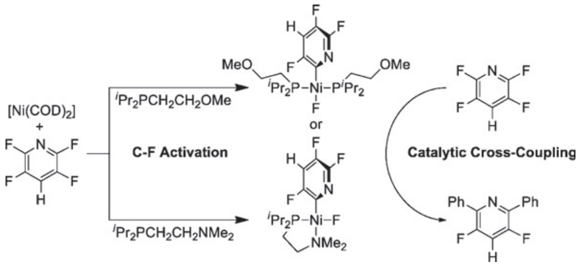

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A new synthesis of N-substituted o-trifluoroacetylanilines

Alexander F. Shidlovskii, Alexander S. Golubev, Dmitrii V. Gusev, Kyrill Yu. Suponitsky, Alexander S. Peregudov, Nikolai D. Chkanikov

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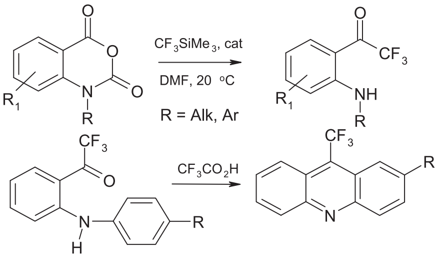
► Synthesis of N-substituted o-trifluoroacetylanilines from N-substituted isatoic anhydrides. ► Synthesis of 9-trifluoromethylacridines by cyclisation of N-aryl-o-trifluoroacetylanilines. ► Suzuki coupling in N-alkyl-*o*-trifluoroacetylbromoanilines.



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Conformational impact of pentafluorosulfanylation on acyclic aliphatic molecules

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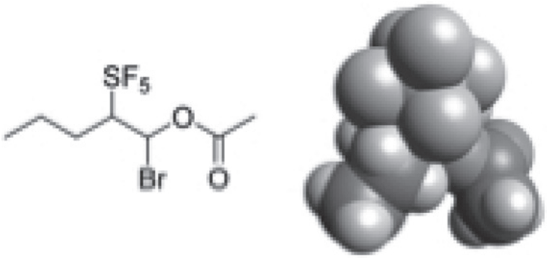
► 3D structures of select SF$_5$ compounds were determined using NMR coupling constants. ► Gamma proton wedged between equatorial fluorines in most stable conformer. ► Wedging hinders molecular rotation; gives diastereotopic signals for gamma protons.



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Halofluorination of alkenes mediated by 1,1,3,3,3-pentafluoropropene-diethylamine adduct

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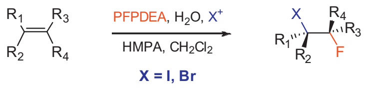
► Pentafluoropropene-diethylamine adduct is an efficient reagent in halofluorination as a source of nucleophilic fluoride. ► The halofluorination is highly regioselectivite (formation of Markovnikov products). ► The halofluorination is stereospecific in an *anti*-sence. ► The method allows introduction of fluorine into alkenes under mild conditions.



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Efficient synthesis of trifluoromethylated dihydrochalcones, aryl vinyl ketones and indanones by superelectrophilic activation of 4,4,4-trifluoro/3-(trifluoromethyl)crotonic acids

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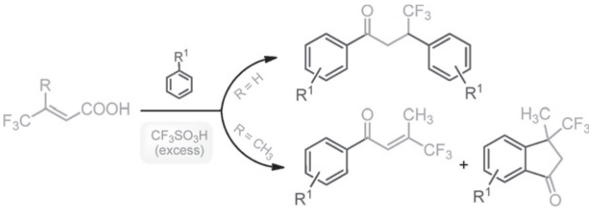
Loker Hydrocarbon Research Institute, Department of Chemistry, University of Southern California, Los Angeles, CA 90089-1661, United States



► Superacid catalyzed electrophilic substitution of arenes using 4,4,4,-trifluoro/3-trifluoromethylcrotonic acids has been investigated. ► Synthesis of various trifluoromethylated dihydrochalcones, aryl vinyl ketones and indanones has been achieved. ► Position of the trifluoromethyl group seems to have profound effect on the nature of the reaction and the products. ► Mechanistic aspects have been supported by *ab initio* calculations.