SYNTHESIS ALERTS

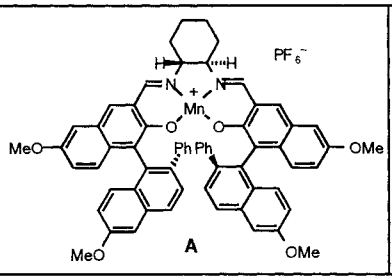
Synthesis Alerts is a new monthly feature to help readers of Synthesis keep abreast of new reagents, catalysts, ligands, chiral auxiliaries, and protecting groups which have appeared in the recent literature. Emphasis is placed on new developments but established reagents, catalysts etc are also covered if they are used in novel and useful reactions. In each abstract, a specific example of a transformation is given in a concise format designed to aid visual retrieval of information.

Synthesis Alerts is a personal selection by Paul Blakemore, Brian Dymock, Philip Hall, Philip Kocienski, J.-Y. Le Brazidec and Alessandro Pontiroli of the University of Glasgow. The journals regularly covered by the abstractors are: Angewandte Chemie International Edition, Bulletin de la Societe Chimie de France, Bulletin of the Chemical Society of Japan, Chemische Berichte, Chemistry Letters, Helvetica Chimica Acta, Journal of Organic Chemistry, Journal of Organometallic Chemistry, Journal of the American Chemical Society, Liebigs Annalen, Tetrahedron Letters.

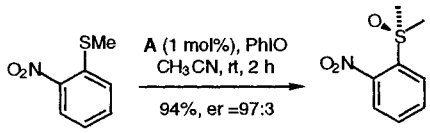
Georg Thieme Verlag does not accept responsibility for the accuracy, content, or selection of the data.

(Salen)manganese(III) Complex — ***Catalyst***

High enantioselectivity (up to 94%) was achieved in the catalytic asymmetric oxidation of sulfides to sulfoxides using the title Mn-Salen complex.



A



8 examples, 24-98% yield; ee 39-94%.

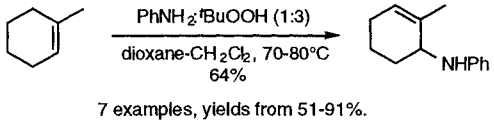
C. Kokubo, T. Katsuki *Tetrahedron* **1996**, *52*, 13895.

(Pyridine-2,6-dicarboxylate)(HMPA)Mo(O)O_2 — ***Catalyst***

The title molybdenum peroxo complex catalyses the regioselective allylic amination of alkenes by aryl amines with *tert*-butyl hydroperoxide as oxidant.

(dipic)(HMPA)Mo(O)O_2

A

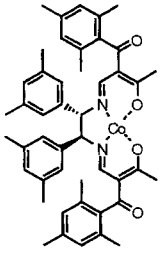


7 examples, yields from 51-91%.

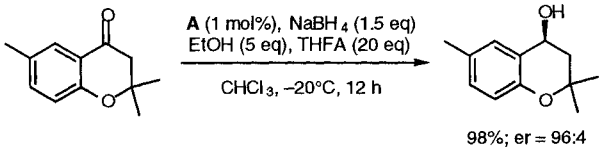
R. S. Sricastava, K. M. Nicholas *Chem. Commun.* **1996**, 2335.

Homochiral Cobalt Catalyst — ***Catalyst***

The title catalyst together with sodium borohydride and a tetrahydrofurfuryl alcohol enantioselectively reduces aromatic ketones.



A



98%; er = 96:4

7 examples: yields >98%; ee 90-97%. Alcohol additives such as tetrahydrofurfuryl alcohol (THFA) have a profound effect on the outcome of these reactions.

K. D. Sugi, T. Nagata, T. Yamada, T. Mukaiyama *Chem. Lett.* **1996**, 737.

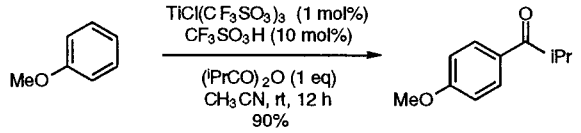
This document was downloaded for personal use only. Unauthorized distribution is strictly prohibited.

Titanium(IV) Chloride Tris(trifluoromethanesulfonate) — ***Catalyst***

Catalytic Friedel-Crafts acylation of aromatic compounds with carboxylic anhydrides may be achieved with the title compound together with triflic acid.

J. Izumi, T. Mukaiyama *Chem. Lett.* **1996**, 739.

$TiCl(CF_3SO_3)_3$



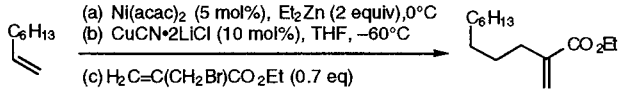
14 examples: 5 aromatics, 4 anhydrides, yields 60-98%

Nickel(II) Acetylacetonate — ***Catalyst***

Catalyses the hydrozincation of terminal olefins to afford functionalised organozinc reagents. The nickel reagent also catalyses halogen-zinc exchange with primary alkyl halides.

S. Vettel, A. Vaupel, P. Knochel *J. Org. Chem.* **1996**, *61*, 7473.

$Ni(acac)_2$



74%

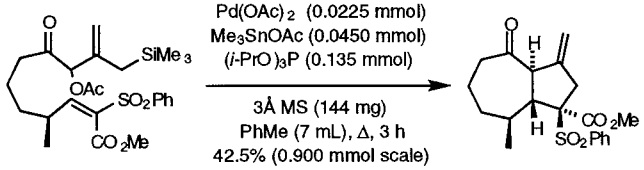
Over 20 examples documented.

Trimethyltin Acetate — ***Catalyst***

The title compound acts as a co-catalyst in intramolecular Pd-catalysed trimethylene-methane cycloadditions to electron deficient alkenes.

B. M. Trost, Higuchi, R. I. *J. Am. Chem. Soc.* **1996**, *118*, 10094.

Me_3SnOAc

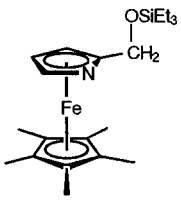


(+40% yield of two isomers)

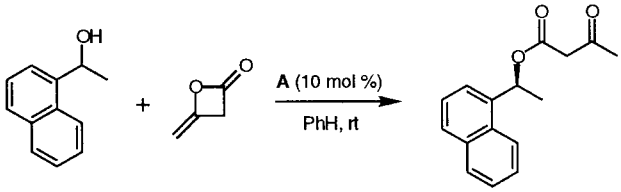
η^5-Pentamethylcyclopentadienyl-η^5-2-[(triethylsilyloxy)methyl]pyrrolyliron — ***Catalyst***

The title compound was one of 4 new chiral (π-heterocycle)FeCp* complexes evaluated as catalysts in the kinetic resolution of secondary alcohols and in cyanohydrin formation form aldehydes.

J. C. Ruble, G. C. Fu *J. Org. Chem.* **1996**, *61*, 7230.



A

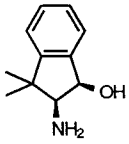


er = 94:6 at 67% conversion

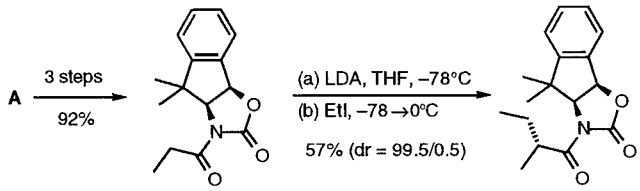
(1*R*,2*S*)-2-Amino-3,3-dimethylindan-1-ol — ***Chiral Auxiliary***

Oxazolidinones prepared from the title compound are efficient chiral auxiliaries.

A. Sudo, K. Saigo *Tetrahedron: Asymmetry* **1996**, *7*, 2939.



A



This chiral auxiliary also undergoes efficient asymmetric alkylation (4 examples), acylation (2 examples), hydroxylation (1 example) and bromination (1 example).

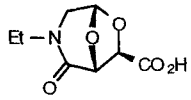
This document was downloaded for personal use only. Unauthorized distribution is strictly prohibited.

(1*S*,5 *R*,7 *S*)-3-Ethyl-2-oxo-6,8-dioxa-3-azabicyclo[3.2.1]octane-7-*exo*-carboxylic Acid — *Chiral Auxiliary*

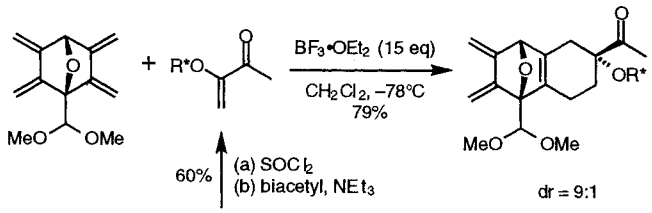
1-Acetylvinyl esters prepared from the title compound undergo regio- and diastereoselective Diels-Alder reactions promoted by $BF_3 \cdot OEt_2$.

Preparation of the title compound from (*R*,*R*)-tartaric acid: L. H. Hurley, *J. Med. Chem.* **1989**, *9*, 2027.

Z. Dienes, P. Vogel *J. Org. Chem.* **1996**, *61*, 6958.



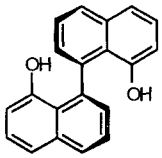
A



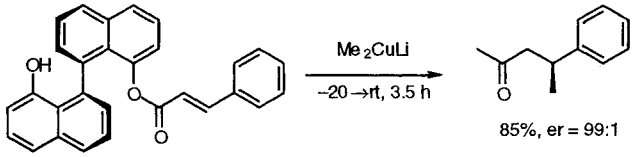
1,1′-Binaphthalene-8,8′-diol — *Chiral Auxiliary*

α,β-Unsaturated monoesters of **A** undergo conjugate addition of simple lithium dialkyl cuprates with high diastereoselectivity.

K. Fuji, X. Yang, K. Tanaka, N. Asakawa *Tetrahedron Lett.* **1996**, *37*, 7373.



A

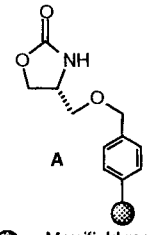


Following 1,4-addition, a formal 1,2-addition of the nucleophile occurs to yield the corresponding ketone. 11 examples illustrating reaction of various α,β-unsaturated monoesters of **A** with dimethyl or dibutyl cuprates (yields 54-91%, ee 96-100%).

Polymer Bound Oxazolidinone — *Chiral Auxiliary*

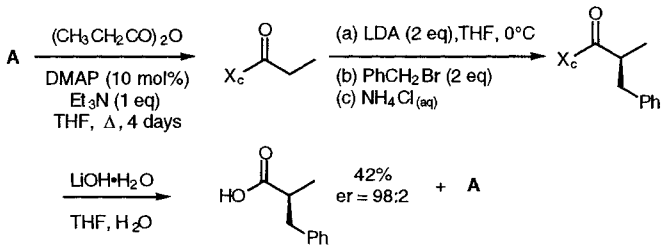
An oxazolidinone bound to Merrifield resin provides a chiral auxiliary for solid phase asymmetric alkylation of carbonyl compounds.

S. M. Allin, S. J. Shuttleworth *Tetrahedron Lett.* **1996**, *37*, 8023.



A

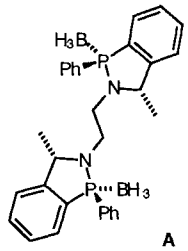
● = Merrifield resin



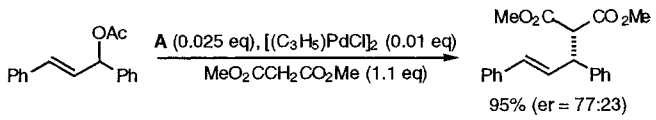
Azaphosphole Borane Complex — *Ligand*

Synthesis and applications of a new class of C2 symmetric phosphorus donor ligand for asymmetric catalysis.

G. Brenchley, M. Fedouloff, E. Merifield, M. Wills *Tetrahedron: Asymmetry* **1996**, *7*, 2809.



A

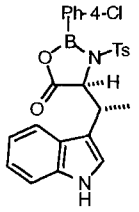


The title ligand can be in asymmetric hydrogenation (1 example) and hydrosilylation (3 examples).

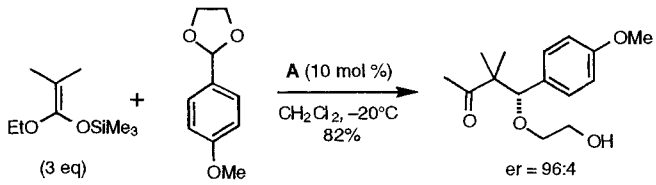
N-Tosyl-(αS,βR)-β-methyltryptophan — *Ligand*

Arylboron complex **A** prepared from the title compound and dichloro-(4-chlorophenyl)borane catalyse enantioselective cleavage of 2-aryl-1,3-dioxolanes with ketene acetals.

M. Kinugasa, T. Harada, A. Oku *J. Org. Chem.* **1996**, *61*, 6772.



A



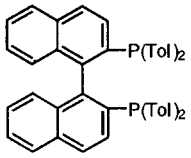
8 examples, 62-89%v yield; er = 92:8 - 96:4

This document was downloaded for personal use only. Unauthorized distribution is strictly prohibited.

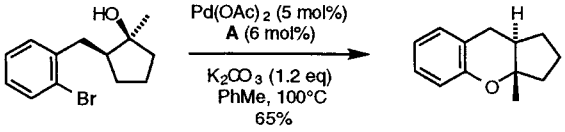
(*S*)-(–)-2,2′-Bis(di-*p*-tolylphosphino)-1,1′-binaphthyl (Tol-BINAP) — *Ligand*

The title compound is a ligand in the intramolecular Pd-catalysed ipso substitution of an aryl halide with an alcohol to generate benzo-fused oxacycles.

M. Palucki, J. P. Wolfe, S. L. Buchwald *J. Am. Chem. Soc.* **1996**, *118*, 10333.



A

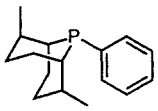


7 examples using the conditions described above (60-90% yield). A further 5 examples use 1,1′-bis(diphenylphosphino)ferrocene as ligand and sodium *tert*-butoxide as base (32-73% yield).

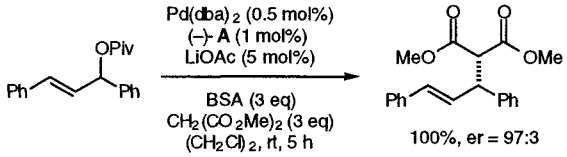
2,6-Dimethyl-9-phenyl-9-phosphabicyclo[3.3.1]nonane (9-PBN) — *Ligand*

The preparation of the monodentate phosphine ligand **A** is descibed together with its application in a palladium catalysed asymmetric allylic substitution reaction.

Y. Hamada, N. Seto, H. Ohmori, K. Hatano *Tetrahedron Lett.* **1996**, *37*, 7565.



A



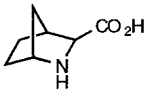
11 examples utilising predominantly the illustrated substrate with a range of malonate nucleophiles (yields 35-100%, ee 65-97%).

BSA = bis(trimethylsilyl)acetamide

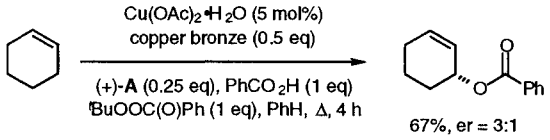
exo-2-Azabicyclo[2.2.1]heptane-3-carboxylic Acid — *Ligand*

A chiral ligand for the copper catalysed asymmetric allylic oxidation of olefins by *tert*-butyl perbenzoate.

M. J. Södergren, P. G. Andersson *Tetrahedron Lett.* **1996**, *37*, 7577.



A

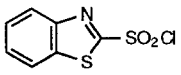


10 examples of oxidation of cyclopentene and cyclohexene under varying conditions. Proline and the analogous bicyclo[2.2.2]octane ligand were also tested (yields 25-67%, ee 11, 15, 44-65%).

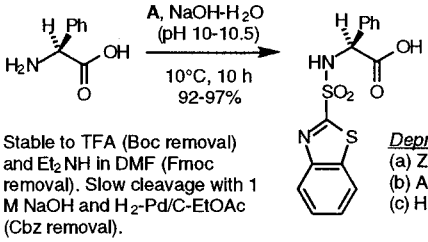
Benzothiazole-2-sulfonyl Chloride — *Protecting Group*

The title compound is prepared by reaction of the 2-mercaptobenzothiazole with chlorine in aqueous HOAc. It is stable at <0°C indefinitely but gradually decomposes at rt. The sulfonamides prepared from **A** are useful amino protecting groups in peptide coupling reactions.

E. Vedejs, S. Lin, A. Klapars, J. Wang *J. Am. Chem. Soc.* **1996**, *118*, 9796.



A



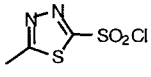
Stable to TFA (Boc removal) and Et_2NH in DMF (Fmoc removal). Slow cleavage with 1 M NaOH and H_2-Pd/C-EtOAc (Cbz removal).

Deprotection conditions:
(a) Zn/HOAc-EtOH, rt
(b) Al(Hg)/Et_2O-H_2O, rt
(c) H_3PO_2/DMF or THF, rt-reflux

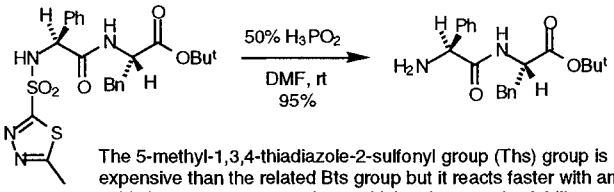
5-Methyl-1,3,4-thiazole-2-sulfonyl Chloride — *Protecting Group*

The preparation and reactions of the title compound are very similar to benzothiazole-2-sulfonyl chloride (see accompanying abstract). The corresponding sulfonamides also have similar stability and are deprotected under the same conditions as the benzothiazole-2-sulfonyl (Bts) group.

E. Vedejs, S. Lin, A. Klapars, J. Wang *J. Am. Chem. Soc.* **1996**, *118*, 9796.



A

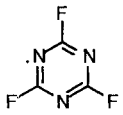


The 5-methyl-1,3,4-thiadiazole-2-sulfonyl group (Ths) group is more expensive than the related Bts group but it reacts faster with amino acids in aqueous suspension and it has improved solubility and crystallinity in some cases. The reductive deprotection conditions shown above do not affect *N*-tosylsulfonamides.

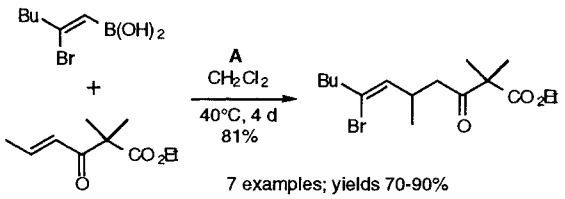
This document was downloaded for personal use only. Unauthorized distribution is strictly prohibited.

Cyanuric Fluoride — *Reagent*

The title compound induces 1,4-addition of alkenylboronic acids with α,β-unsaturated ketones to give γ,δ-unsaturated ketones.



A



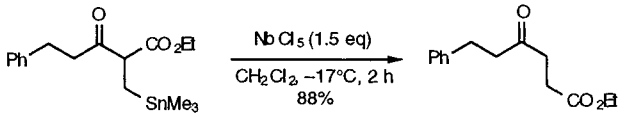
7 examples; yields 70-90%

S. Hara, S. Ishimura, A. Suzuki *Synlett* **1996**, 993.

Niobium Pentachloride — *Reagent*

α-[(Trialkylstannyl)methyl]-β-oxo esters may be homologated to the corresponding γ-oxo esters with the title reagent.

$NbCl_5$

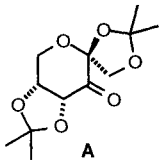


6 examples, yields from 34-88%

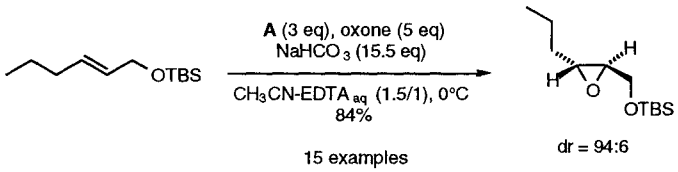
M. Yamamoto, M. Nakazawa, K. Kishikawa, S. Kohmato *Chem. Commun.* **1996**, 2353.

1,2:4,5-Di-*O*-isopropylidene-D-*erythro*-2,3-hexodiuro-2,6-pyranose — *Reagent*

An efficient asymmetric epoxidation of *trans*-olefins using oxone as the oxidant is mediated by the title ketone.



A



15 examples

dr = 94:6

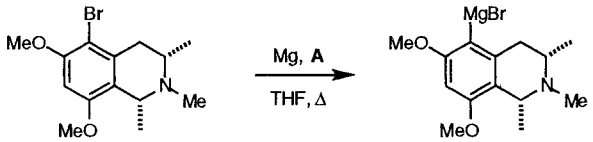
Y. Tu, Z. -X. Wang, Y. Shi *J. Am. Chem. Soc.* **1996**, *118*, 9806.

1,2-Dibromotetrafluoroethane — *Reagent*

The title compound can be used as an entrainer to activate magnesium for the formation of Grignard reagents in substrates containing amine functionality.

$Br\text{-}CF_2CF_2\text{-}Br$

A

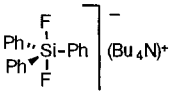


See also A. I. Meyers, R. H. Hutchings *J. Org. Chem.* **1996**, *61*, 1004.

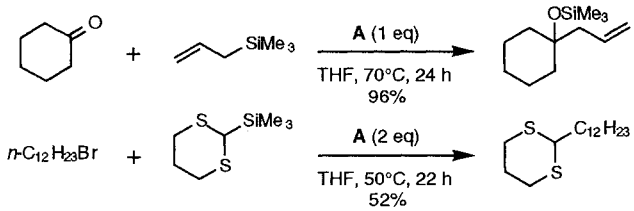
P. Chau, I. R. Czuba, M. A. Rizzacasa, G. Bringmann, K.-P. Gulden, M. Schäffer *J. Org. Chem.* **1996**, *61*, 7101.

Tetrabutylammonium Triphenyldifluorosilicate — *Reagent*

The title compound (abbreviated TBAT) is an easily handled source of anhydrous fluoride for silicon-carbon bond cleavage. It is non-hygroscopic, soluble in most organic solvents, and significantly less basic than TBAF.



A



benzyl and alkynyl silanes are also cleaved but phenyl and vinyl silanes do not react.

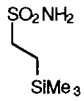
A. S. Pilcher, P. DeShong *J. Org. Chem.* **1996**, *61*, 6901.

This document was downloaded for personal use only. Unauthorized distribution is strictly prohibited.

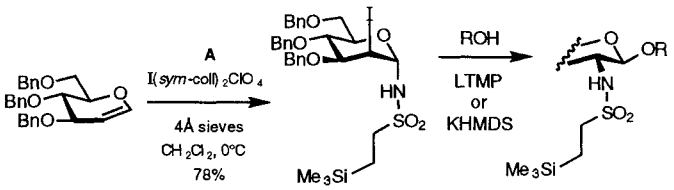
2-(Trimethylsilyl)ethanesulfonamide — *Reagent*

The title compound, together with iodonium di-*sym*-collidine perchlorate as electrophilic activator, effects sulfonamidoglycosylation of glycals. The *trans*-iodo sulfonamide adduct reacts with alcohols to give aminoglycosides in which the amine is protected as a 2-(trimethylsilyl)ethanesulfonamide.

D. A. Griffith, S. J. Danishefsky *J. Am. Chem. Soc.* **1996**, *118*, 9526.



A

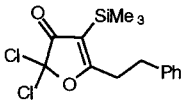


The 2-(trimethylsilyl)ethanesulfonyl protecting group is removed with CsF in hot DMF

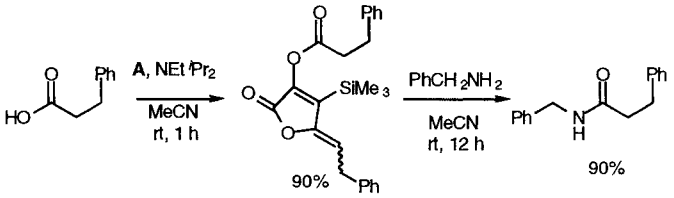
2,2-Dichloro-5-(2-phenylethyl)-4-(trimethylsilyl)furan-3-one (DPTF) — *Reagent*

A water-compatible dehydrating reagent for the synthesis of amide linkages.

M. Murakami, M. Hayashi, N. Tamura, Y. Hoshino, Y. Ito *Tetrahedron Lett.* **1996**, *37*, 7541.



A



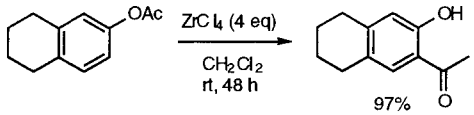
4 examples of peptide elongation.

Zirconium Tetrachloride — *Reagent*

The title compound mediates the Fries rearrangement of phenolic esters at ambient temperature.

D. C. Harrowven, R. F. Dainty *Tetrahedron Lett.* **1996**, *37*, 7659.

$ZrCl_4$



9 examples of various simple aromatic systems (yields 31-97%). In most cases an ortho-shifted adduct is the sole product with the shift being to the least sterically encumbered side. Sonication can improve the yield and lower reaction time in certain instances.

This document was downloaded for personal use only. Unauthorized distribution is strictly prohibited.