

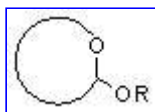
## Organic Chemistry Portal

## Reactions &gt; Organic Synthesis Search

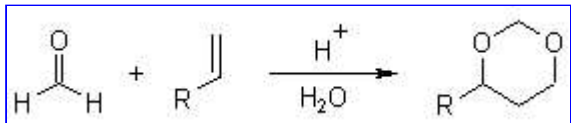
Categories: C-O Bond Formation, Synthesis of O-Heterocycles &gt;

## Synthesis of acetals

Related:

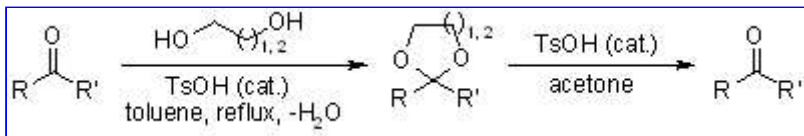


## Name Reactions

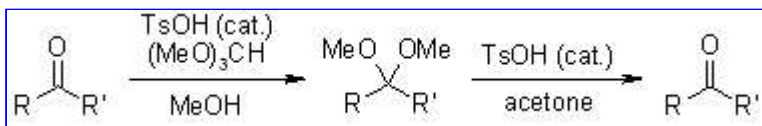


Prins Reaction

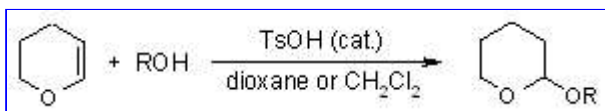
## Protecting Groups



Cyclic Acetals

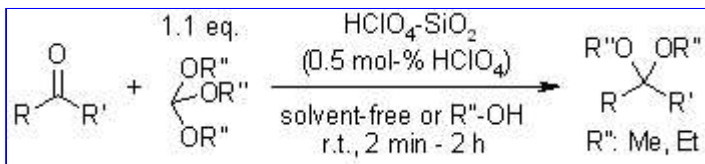


Dimethyl Acetals



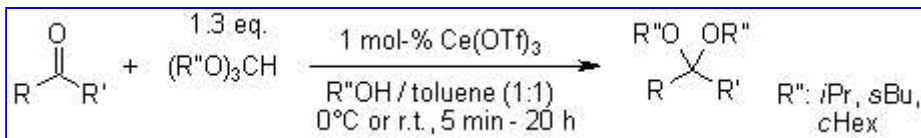
Tetrahydropyranyl Ethers

## Recent Literature



Perchloric acid adsorbed on silica gel is an extremely efficient, inexpensive, and reusable catalyst for the protection of aldehydes and ketones and the subsequent deprotection. Acetalization was mostly carried out under solvent-free conditions with trialkyl orthoformates, but weakly electrophilic carbonyl compounds and substrates that can coordinate with the catalyst, required the corresponding alcohol as solvent.

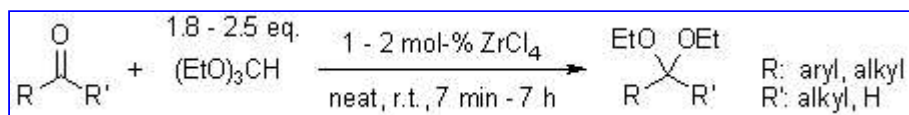
R. Kumar, D. Kumar, A. K. Chakraborti, *Synthesis*, **2007**, 299-303.



Ketone di-sec-alkyl acetals are obtained in very good yields by treatment of ketones with tri-sec-alkyl orthoformate and the

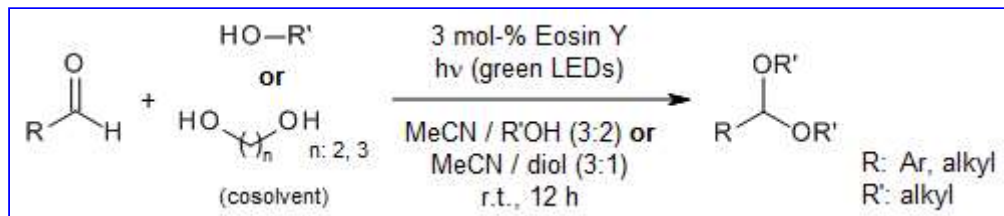
corresponding alcohol in the presence of a catalytic amount of cerium(III) trifluoromethanesulfonate.

F. Ono, H. Takenaka, Y. Eguchi, M. Endo, T. Sato, *Synlett*, **2009**, 487-489.



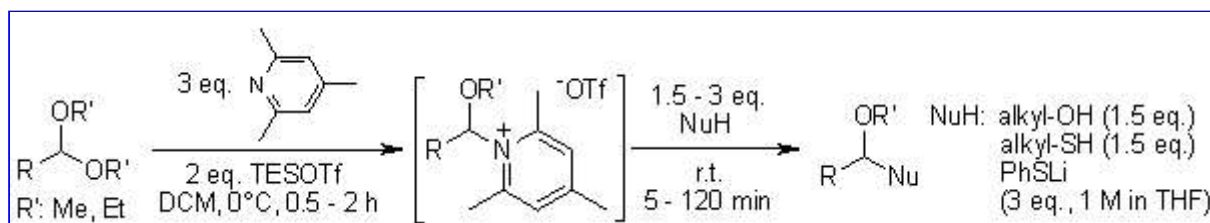
Zirconium tetrachloride (ZrCl<sub>4</sub>) is a highly efficient and chemoselective catalyst for the acetalization, and *in situ* transacetalization of carbonyl compounds under mild reaction conditions.

H. Firouzabadi, N. Iranpoor, B. Karimi, *Synlett*, **1999**, 321-323.



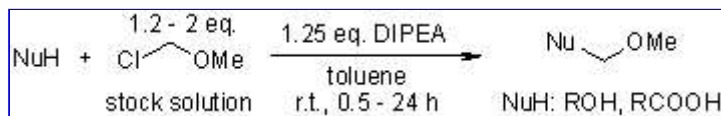
Using a photochemical method for acetalization of aldehydes under low-energy visible light irradiation, a broad range of aromatic, heteroaromatic, and aliphatic aldehydes have been protected under neutral conditions in good to excellent yields using a catalytic amount of Eosin Y as the photocatalyst. Even challenging acid-sensitive aldehydes and sterically hindered aldehydes can be converted, while ketones remain intact.

H. Yi, L. Niu, S. Wang, T. Liu, A. K. Singh, A. Lei, *Org. Lett.*, **2017**, 19, 122-125.



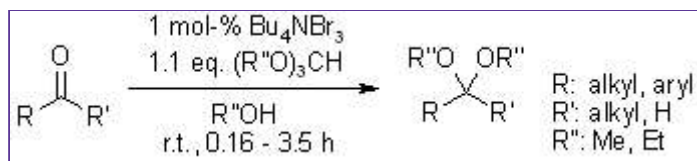
Treatment of symmetrical O,O-acetals with TESOTf and 2,4,6-collidine formed weakly electrophilic collidinium salts. Subsequent addition of nucleophiles, such as alcohols, lithium thioxide, and sodium azide, to the salts afforded the corresponding O,O-mixed, O,S- and N,O-acetals in good yields.

H. Fujioka, T. Okitsu, T. Ohnaka, R. Li, O. Kubo, K. Okamoto, Y. Sawama, Y. Kita, *J. Org. Chem.*, **2007**, 72, 7898-7902.



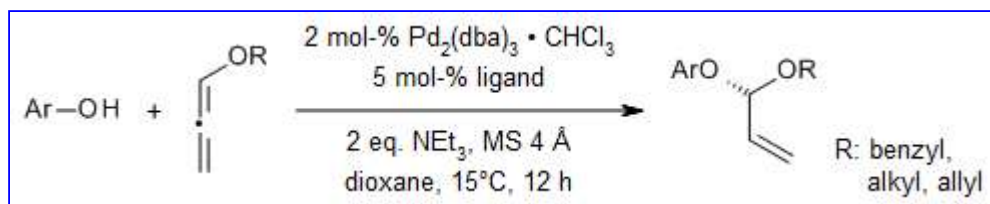
0.01 mol-% Zinc(II) salts catalyze the reaction between acetals and acid halides to provide haloalkyl ethers in near-quantitative yield in 1-4 h. The solutions of haloalkyl ethers can be utilized directly in reactions in which the presence of the ester byproduct does not interfere. Excess carcinogenic haloalkyl ether is destroyed on workup.

M. A. Berliner, K. Belecki, *J. Org. Chem.*, **2005**, 70, 9618-9621.



Acyclic and cyclic acetals of various carbonyl compounds were obtained in excellent yields in the presence of trialkyl orthoformate and a catalytic amount of tetrabutylammonium tribromide in absolute alcohol. This convenient, mild, chemoselective method allows acetalization of an aldehyde in the presence of ketone, unsymmetrical acetal formation, and tolerates acid-sensitive protecting groups.

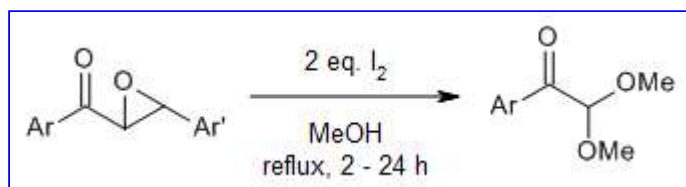
R. Gopinath, Sk. J. Haque, B. K. Patel, *J. Org. Chem.*, **2002**, 67, 5842-5845.



A Pd-catalyzed asymmetric intermolecular hydroalkoxylation of allenes with phenol as a pronucleophile gives acyclic O,O-

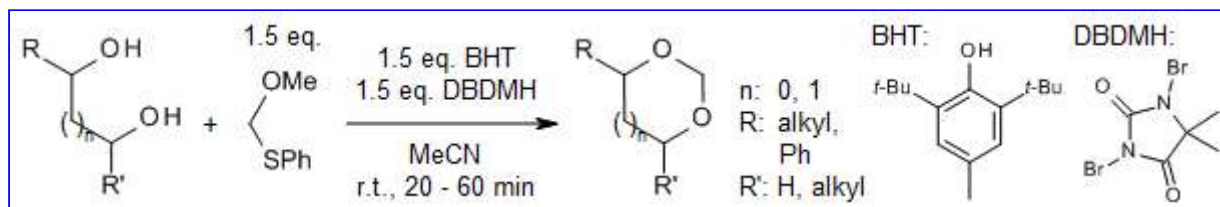
acetals in high yields with very good enantiomeric excesses.

L. Jiang, T. Jia, M. Wang, J. Liao, P. Cao, *Org. Lett.*, **2015**, 17, 1070-1073.



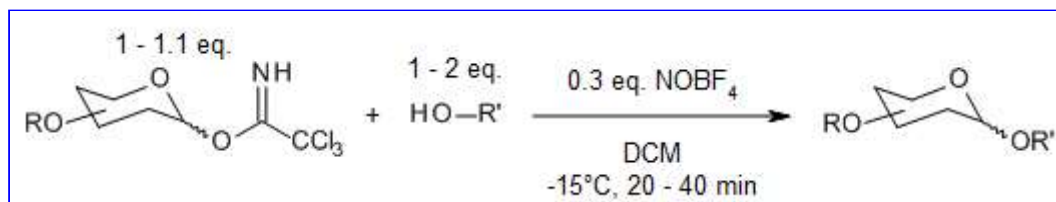
Chalcone epoxides form  $\alpha,\alpha$ -dimethoxyacetophenones on heating with iodine in methanol through C-C bond cleavage followed by acetalization of the formyl group. The process occurs through ring opening of the chalcone epoxide by methanol to form  $\beta$ -methoxy alcohol, cleavage of the C-C bond in the latter to form  $\alpha$ -ketoaldehyde, and acetalization of the formyl group to give the product.

B. G. Jadhav, S. D. Samant, *Synlett*, **2014**, 25, 1591-1595.



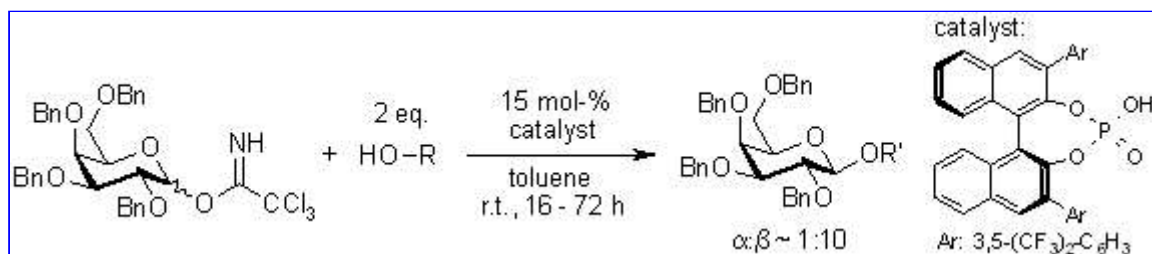
A mild and efficient method enables the formation of methylene acetals from 1,2- and 1,3-diols using methoxymethylphenylsulfide, 1,3-dibromo-5,5-dimethylhydantoin (DBDMH), and dibutylhydroxytoluene (BHT). The use of BHT suppresses side reactions and enables high-yielding formation of methylene acetals of various diols, including carbohydrate-type substrates.

T. Maegawa, Y. Koutani, K. Otake, H. Fujioka, *J. Org. Chem.*, **2013**, 78, 3384-3390.



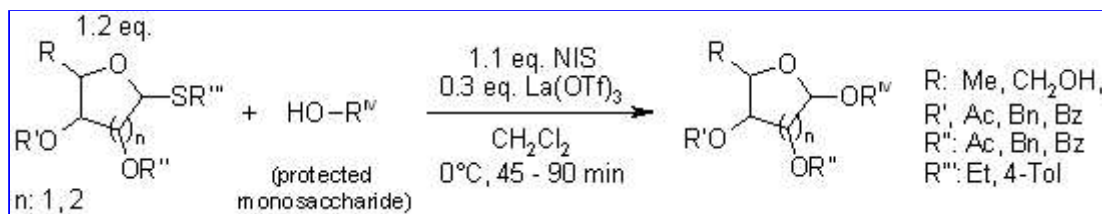
Nitrosyl tetrafluoroborate ( $\text{NOBF}_4$ ) promoted activation of glycosyl trichloroacetimidate derivatives enables an efficient stereoselective glycosylation. A series of mono- and disaccharide derivatives were synthesized in excellent yield and high stereoselectivity at the glycosylation center.

A. Sau, A. Santra, A. K. Misra, *Synlett*, **2012**, 23, 2341-2348.



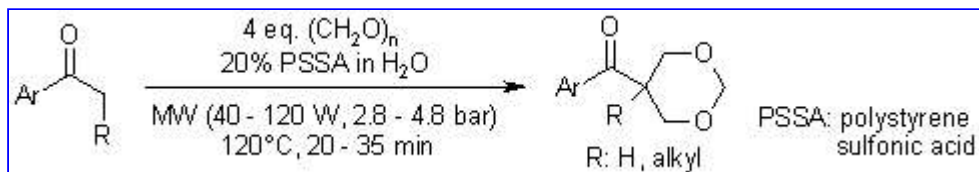
The use of a chiral Brønsted acid catalyst for the activation of trichloroacetimidate glycosyl donors influences the stereochemical outcome of glycosylation processes in toluene, hinting that perhaps diastereocontrol may become achievable through the judicious use of chiral organic catalysts.

D. J. Cox, M. D. Smith, A. J. Fairbanks, *Org. Lett.*, **2010**, 12, 1452-1455.



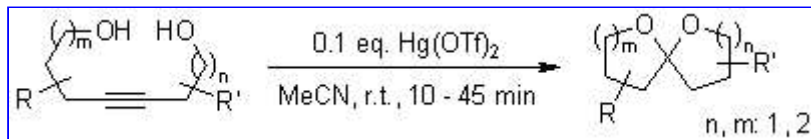
Use of  $\text{La}(\text{OTf})_3$  as a Lewis acid promoter for *N*-iodosuccinimide-mediated activation of thioglycosides enables a smooth glycosylation reaction with good to excellent yields and stereoselectivity.

S. Mukherjee, B. Mukhopadhyay, *Synlett*, **2010**, 2853-2856.



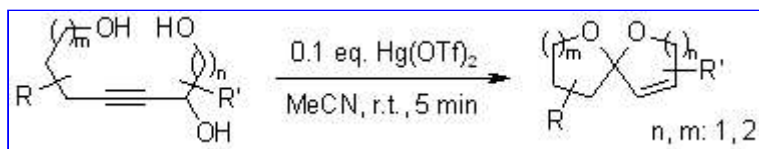
A novel microwave-assisted, operationally simple, tandem bis-aldol reaction of ketone with paraformaldehyde catalyzed by polystyrenesulfonic acid in aqueous medium delivers 1,3-dioxanes in high yield.

V. Polshettiwar, R. S. Varma, *J. Org. Chem.*, **2007**, 72, 7420-7422.

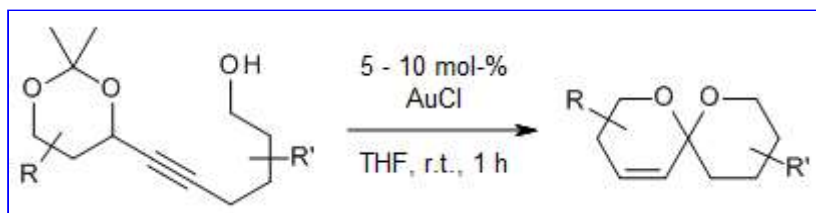


Hg(II) salts are highly efficient catalysts for a versatile construction of spiroketals in an instant reaction in high yields at ambient temperature from alkyne diols or THP-semiprotected alkyne diols in aqueous conditions. Monounsaturated spiroketals and furans were accessed with equal ease when propargylic triols (or propargylic diols) were subjected to similar conditions.

K. Ravindar, M. S. Reddy, P. Deslongchamps, *Org. Lett.*, **2011**, 13, 3178-3181.

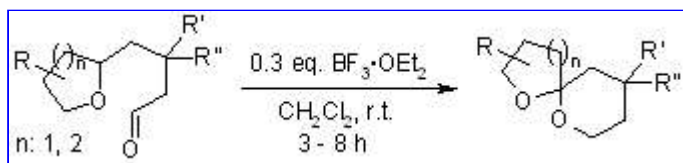


K. Ravindar, M. S. Reddy, P. Deslongchamps, *Org. Lett.*, **2011**, 13, 3178-3181.



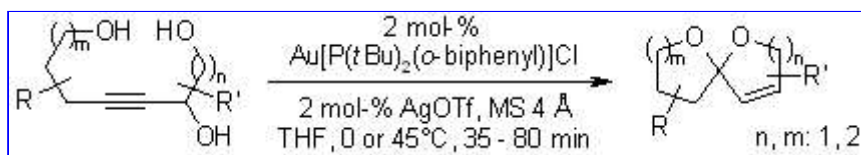
A gold-catalyzed synthesis of unsaturated spiroketals is regulated by an acetone protecting group which undergoes extrusion of acetone to deliver the desired spiroketals in good yields and diastereoselectivities. The reaction, which is carried out under very mild conditions employing AuCl as the catalyst, should be widely applicable.

P. H. S. Paioti, J. M. Ketcham, A. Aponick, *Org. Lett.*, **2014**, 16, 5320-5323.



An intramolecular hydro-O-alkylation of aldehydes leads to spiroketals, bicyclic ketals, and amins. Tertiary and sterically hindered secondary sp<sup>3</sup> C-H bonds are transformed into C-O bonds under the action of a catalytic amount of a variety of Lewis acids. The mechanism probably involves a tandem hydride transfer/cyclization sequence.

S. J. Pastine, D. Sames, *Org. Lett.*, **2005**, 7, 5429-5431.



A cyclization of monopropargylic triols to form olefin-containing spiroketals is rapid and high yielding in the presence of 2 mol % of a catalyst generated in situ from Au[P(t-Bu)<sub>2</sub>(o-biphenyl)]Cl and AgOTf. Various substituted triols lead to substituted 5- and 6-membered ring spiroketals.

A. Aponick, C.-Y. Li, J. A. Palmes, *Org. Lett.*, **2009**, 11, 121-124.