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Antonio L. Braga [a], Claudio C. Silveira [a], Luciano Dornelles [a], Gilson Zeni [a], Flavia A. D. Galarza [a] & Ludger A. Wessjohann [b]

[a] Departamento de Quimica, Universidade Federal de Santa Maria, BR-97119-900, Santa Maria, RS, Brazil

[b] Institut für Organische Chemie, Ludwig-Maximilians-Universität München, Karlstr. 23, D-80333, München, Germany

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CATALYST-DEPENDENT SELECTIVE SYNTHESIS OF O/S- AND S/S-ACETALS FROM ENOL ETHERS

Antonio L. Braga[a)*], Claudio C. Silveira[a)], Luciano Dornelles[a)], Gilson Zeni[a)], Flavia A. D. Galarza[a)], Ludger A. Wessjohann[b)*]

a) Departamento de Quimica, Universidade Federal de Santa Maria, BR-97119-900 Santa Maria - RS, Brazil

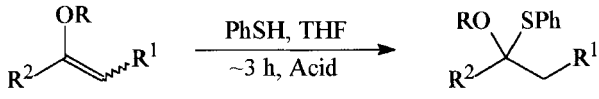
b) Institut für Organische Chemie, Ludwig-Maximilians-Universität München, Karlstr. 23, D-80333 München, Germany

Enol ethers are reacted with mercaptanes to give the corresponding O/S- or S/S-acetals in medium to high yield. Either product can be formed selectively depending on the acid catalyst and the reaction time applied.

S/S-Acetals[1)] are well established as protected forms of keto groups as well as acyl anion equivalents[2-4)]. Less common but increasingly important in organic syntheses are O/S-acetals[3a,5,6)]. S/S-Acetals are usually prepared from the corresponding aldehydes or ketones[2,4)], whereas O/S-acetals are usually obtained from O/O-acetals[6)]. Other methods are often not general or

* To whom correspondence should be addressed.

Table 1: Selective Formation of O/S-Acetals with Thiophenol

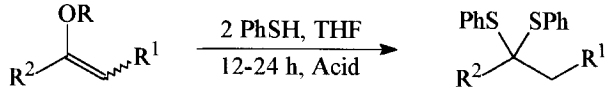


Entry #	R	R^1	R^2	Acid	Yield (%)
1	Et	H	H	none	69
2	Me	H	Me	none	70
3	Me	$-(CH_2)_4-$		none	69
4a	$-(CH_2)_2-$		H	BF_3xOMe_2	84
4b	$-(CH_2)_2-$		H	HCl (g)	78
5a	$-(CH_2)_3-$		H	BF_3xOMe_2	85
5b	$-(CH_2)_3-$		H	HCl (g)	81

require more then one step, e.g. those involving α-halo sulfides[7], lactols and sugar derivatives[8] or other compounds[9].

Quite unexpectedly we found only few instances of enol ethers used as starting materials for the title compounds. In most cases the intermediate formation of already known precursers was involved. Acylated S/S-acetals, i.e. 2-acyl-1,3-dithiolanes, were prepared from 2-(1-hydroxyalkyl)-5,6-dihydro-1,4-dioxines by an acetalization/rearrangement route[10]. Direct Lewis acid catalyzed reactions of silyl enol ethers with thiophenol yielded the corresponding phenyl vinyl sulfides[11]. For terminal phenyl vinyl sulfides (i.e. masked aldehydes) a method for the formation of S/S-acetals is reported[12]. With the exception of thiol additions to dihydropyrane[13], direct preparations of O/S-acetals from enol ethers also follow two step procedures with the intermediate formation of an O/O-acetal[14] or an α-halo ether[15].

Table 2: Selective Formation of S/S-Acetals with Thiophenol

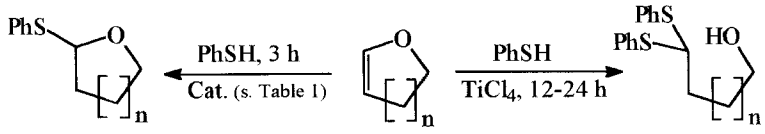


Entry #	R	R^1	R^2	Acid	Yield (%)
6	Et	H	H	BF_3xOMe_2 or HCl (g)	68
7	Me	H	Me	BF_3xOMe_2 or HCl (g)	73
8	Me	$-(CH_2)_4-$		BF_3xOMe_2 or HCl (g)	72
9	$-(CH_2)_2-$		H	$TiCl_4$	80
10	$-(CH_2)_3-$		H	$TiCl_4$	85

We now wish to report a general method for the direct and selective conversion of aliphatic, exo- and endocyclic[16] enol ethers of aldehydes and ketones to the corresponding O/S- and S/S-acetals. With thiophenol the products are formed in good yield by mixing the enol ether and the appropriate amount of thiol in THF under neutral or acidic conditions.

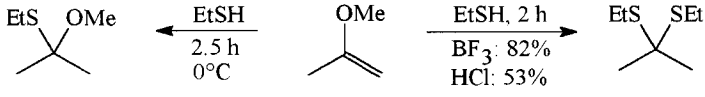
The selective formation of either the corresponding O/S- or the S/S-acetal from an enol ether is achieved by choosing an appropriate acid catalyst and/or by variation of the reaction time. Shorter reaction times and the absence of acid catalysts - or weak acid catalysts in the case of sluggish reactions - permit selective access to the O/S-acetals. Longer reaction times and the use of relatively stronger acid catalysts lead to S/S-acetals as shown in the reaction schemes and the tables.

Other solvents then THF, e.g. methylene chloride, give mixtures of products involving phenyl vinyl sulfides too. Other Lewis acids like $AlCl_3$[17]; $ZnCl_2$, $HgCl_2$ give mixtures of O/S- and S/S-acetals under the given conditions.



Endocyclic enol ethers (n = 1, 2) generally require stronger catalysts to give the products under otherwise identical conditions. The complete formation of ringopened S/S-acetals requires titanium tetrachloride. The resulting alcohol function was retained under our conditions, i.e. elimination or substitution was not observed.

Finally ethanethiol was used as an example for aliphatic mercaptanes. The reaction with methyl propenyl ether can be conducted without solvent. At 0°C and without catalyst the O/S-acetal is obtained in 42% isolated yield after 2-3 hours, whereas at room temperature and with BF_3-etherate as a catalyst 82% of the S/S-acetal can be isolated.



In summary we have presented an easy general methodology for the selective preparation of a variety of S/S- and O/S-acetals from enol ethers in one step.

General procedure for the formation of O/S-acetals from enol ethers (cf. table 1):

At 0°C, thiophenol (2 mmol) is added to a solution of the enol ether (2.2 mmol) in THF (~3 ml) under nitrogen. Addition of a mild acid catalyst (1 ml BF_3 x Me_2O; or HCl-gas bubbled through the mixture for one minute) is required for endocyclic[16] or otherwise less reactive enol ethers (see table). The mixture is reacted at room temperature for 2-3 hours. Then methylene chloride (~10 ml) is added and the solution is washed with 0.1 N aqueous sodium hydroxide (5 x 20 ml). The organic phase is dried with magnesium sulfate and the solvent is removed in a rotavapor at reduced pressure to give the O/S-acetals in 69-85% yield[18]. Further purification usually is unnecessary, but can be achieved e.g. by Kugelrohr distillation.

General procedure for the formation of S/S-acetals from enol ethers (cf. table 2):

The previous procedure is followed using thiophenol (4 mmol), an enol ether (2 mmol) and a mild acid catalyst (BF_3 x Me_2O or HCl-gas, see above) with reactive enol ethers or titanium tetrachloride (1 mmol) with the less reactive endocyclic[16] ones. The reaction time is extended to 12 (-24) hours. Yields range from 68-85%[18].

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(1) 'Acetals' according to modern nomenclature include 'Ketals'.

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(18) All compounds showed spectroscopic and analytical data consistent with the assigned structures and in accordance with the literature (cf. especially literature marked with an asterisk*).

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