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Silica-supported phosphorus pentoxide: a reusable catalyst for S,S-acetalization of carbonyl groups under ambient conditions

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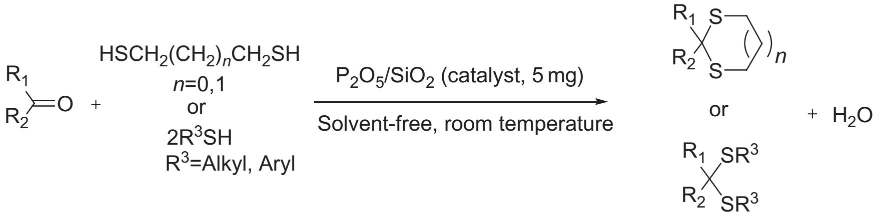
Phosphorus pentoxide supported on silica gel (P_2O_5/SiO_2) efficiently acts as a highly active and reusable catalyst for cyclic and non-cyclic S,S-acetalization of a variety of carbonyl compounds under mild, solvent-free and ambient conditions. This method offers significant advantages such as high conversion, clean work-up, short reaction times and simplicity in operation.



Keywords: P_2O_5/SiO_2; *S*,*S*-acetal; solvent-free; heterogeneous catalyst; aldehydes; ketones

1. Introduction

The protection of aldehydes and ketones to cyclic and non-cyclic *S*,*S*-acetals is a common and interesting method in organic chemistry such as multi-steps synthesis of poly-functional complex molecules (*1*). *S*,*S*-Acetals are quite stable under basic and acidic conditions (*2*). The *S*,*S*-acetals are also utilized as masked acyl anions (*3*) or masked methylene functions in carbon–carbon bond-forming reactions (*4*). Generally, they are prepared by condensation of carbonyl compounds with thiols or dithiols using strong Brønsted and Lewis acid catalysts such as HCl (*5*), $BF_3 \cdot OEt_2$(*6*), $AlCl_3$ (*7*), $TiCl_4$ (*8*), $Mg(OTf)_3$ (*9*) and $LaCl_3$ (*10*). There is still a need to develop a simple and efficient method for S,S-acetalization of carbonyl groups and chemoselective protection of aldehydes and ketones.

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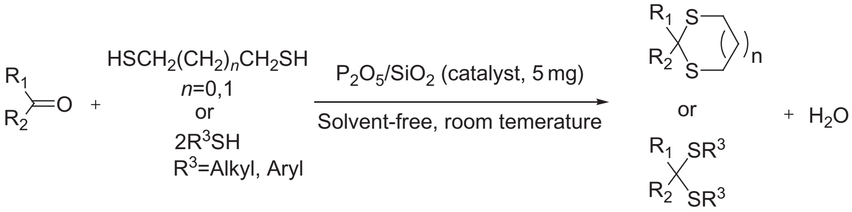


Scheme 1. The S,S-acetalization reaction of carbonyl compounds in the presence of silica supported P_2O_5 as catalyst under solvent-free and ambient conditions.

Phosphorus pentoxide is a white, flammable, dangerous, corrosive to metal and extremely deliquescent compound (*11a*). It reacts vigorously with water and water-containing substances, liberates much heat and may even cause fire (*11*). Phosphorus pentoxide-methanesulfonic acid was used for the first time as a convenient alternative to polyphosphoric acid (PPA) by Eaton *et al.* to escape the difficulties encountered with PPA (*12*). Then, P_2O_5 supported on SiO_2 as an inexpensive, heterogeneous stable, free flowing and white powder was prepared (*13*). This heterogeneous catalyst has been used in several organic reactions such as Fries rearrangement (*14*), nitration of aromatic compounds (*15*), Beckmann or Schmidt rearrangements (*16*), preparation of bisindolylmethanes (*17*), synthesis of *N*-sulfonyl imines (*18*) and Ritter reaction (*19*). In continuation of our research on the application of heterogeneous catalysts in organic reactions (*20*), we have employed silica supported P_2O_5 in S,S-acetalization of carbonyl compounds (Scheme 1).

2. Results and discussion

Initially, a systematic study was carried out for catalytic evaluation of P_2O_5/SiO_2 for S,S-acetalization of benzaldehyde (1 mmol) with benzyl thiol (2.2 mmol) under various conditions. The reaction is best carried out at ambient temperature under neat conditions. Next, we optimized the quantity of the catalyst for this reaction. It was observed that the use of just 5 mg (6.5 w/w%) (*18*) is sufficient to push the reaction forward immediately (Table 1, Entry 3). Larger amounts of the catalyst did not improve the results (Table 1, Entries 1 and 2). Using 2 mg of the catalyst, the reaction take place within 2 min with 90% yield.

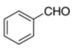
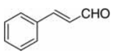
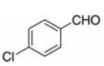
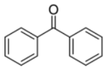
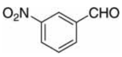
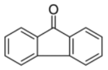
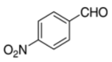
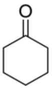
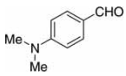
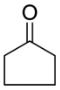
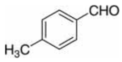
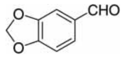
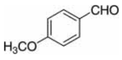
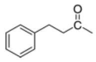
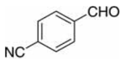
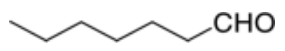
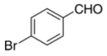
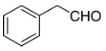
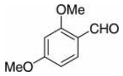
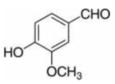
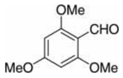
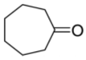
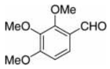
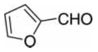
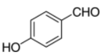
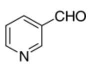
To explore the scope and limitations of this new protocol, a range of aromatic and aliphatic aldehydes and ketones with various substitution patterns were reacted with (a): 1,3-propanedithiol; (b): 1,2-ethanedithiol; (c): benzyl thiol; (d): ethyl thiol under the optimized conditions. As can be seen from Table 2, most of the substrates gave good to excellent yields of the corresponding cyclic and non-cyclic *S,S*-thioacetals immediately. Not only aldehydes but also ketones reacted immediately using P_2O_5/SiO_2 (5 mg) as the catalyst under solvent-free conditions at ambient temperature, and the desired product was obtained in satisfactory yields.

Table 1. Optimization of S,S-acetalization conditions in the model reaction of benzaldehyde and benzyl thiol in the presence of P_2O_5/SiO_2 as the catalyst under solvent-free conditions at ambient temperature.

Entry	Catalyst (mg)	Time (min)	Yield (%)[a]
1	15	Immediately	95
2	10	Immediately	96
3	5	Immediately	98
4	2	2 min	90

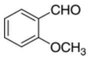
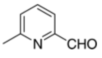
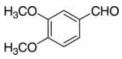
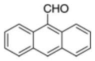
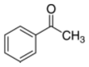
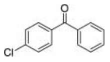
Note: [a]Yield refer to isolated pure products.

Table 2. Immediate S,S-acetalization of various aldehydes and ketones in the presence of P_2O_5/SiO_2 (5 mg) as the catalyst under solvent-free conditions at ambient temperature.

Entry	Aldehydes and ketones	Thiols or dithiols	Yield (%)[a]	Ref[b]	Entry	Aldehydes and ketones	Thiols or dithiols	Yield (%)[a]	Ref[b]
1		a b c d	94 96 98 92	(*21–25*)	17		a b c d	91 88 93 87	(*21*)
2		a b c d	92 89 86 95	(*21–25*)	18		a b c d	90 95 98 93	(*21*, *22*, *24*, *25*)
3		a b c d	88 93 94 91	(*21*, *23*)	19		a b c d	92 94 93 91	(*21*)
4		a b c d	93 91 93 87	(*21–25*)	20		a b c d	88 96 89 97	(*21*)
5		a b c d	98 92 90 88	(*21*, *22*)	21		a b c d	93 86 89 95	(*21*, *25*)
6		a b c d	95 86 96 93	(*21*, *23*, *25*)	22		a b c d	93 86 92 93	(*24*)
7		a b c d	92 94 89 94	(*21–24*)	23		a b c d	87 97 91 94	(*22*, *25*)
8		a b c d	93 90 97 92	(*22*, *23*)	24		a b c d	86 93 95 87	(*21*)
9		a b c d	91 97 93 90	(*22*, *23*)	25		a b c d	93 92 88 91	(*22*, *25*)
10		a b c d	92 91 97 93	(*22*)	26		a b c d	94 98 87 96	(*24*)
11		a b c d	93 95 91 98	(*22*)	27		a b c d	86 92 97 90	(*25*)
12		a b c d	92 94 94 92	(*22*)	28		a b c d	87 94 92 91	(*26*)
13		a b c d	95 89 91 93	(*22*)	29		a b c d	95 96 93 94	(*26*)

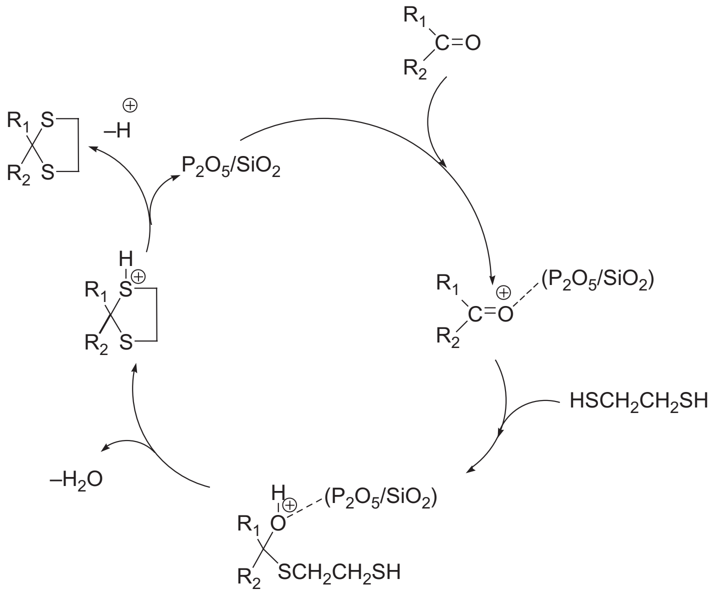
(*Continued*)

Table 2. Continued.

Entry	Aldehydes and ketones	Thiols or dithiols	Yield (%)[a]	Ref[b]	Entry	Aldehydes and ketones	Thiols or dithiols	Yield (%)[a]	Ref[b]
14		a	95	(*23*)	30		a	94	(*26*)
		b	85				b	90	
		c	96				c	89	
		d	93				d	92	
15		a	88	(*23*)	31		a	93	(*26*)
		b	96				b	93	
		c	90				c	90	
		d	89				d	89	
16		a	94	(*21, 22, 24, 25*)	32		a	96	(*21*)
		b	92				b	98	
		c	93				c	92	
		d	87				d	95	

Notes: a: 1,3-Propanedithiol; b: 1,2-ethanedithiol; c: benzyl thiol; d: ethyl thiol.

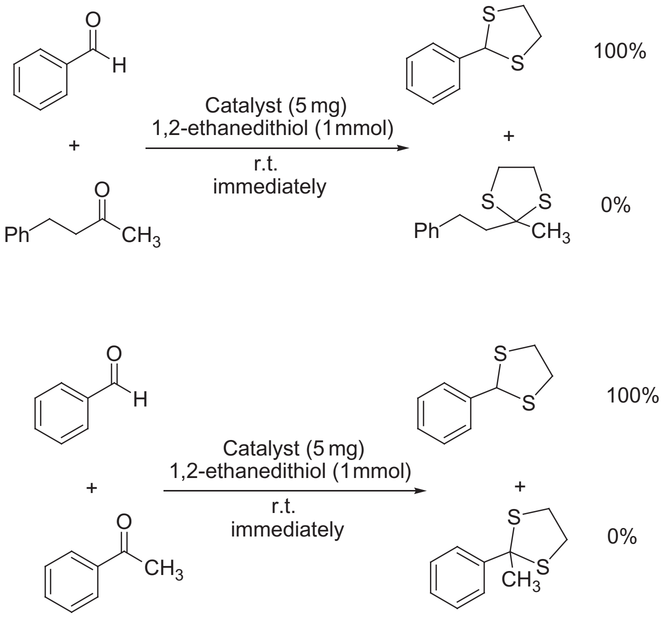
[a] Yields refer to the pure isolated products. The structure all known products were confirmed by comparison of their spectral data (FT-IR, NMR) with those of known samples (*21–26*). [b] Literature references for known products.



Scheme 2. The suggested mechanism for the conversion of carbonyl compounds to their corresponding 1,3-dithiolanes using 1,2-ethandithiol in the presence of P_2O_5/SiO_2 as catalyst.

According to the literature survey (*23*) and our results, we suggest the following mechanism for the conversion of carbonyl compounds to their corresponding 1,3-dithiolanes using 1,2-ethandithiol in the presence of P_2O_5/SiO_2 as catalyst (Scheme 2).

In order to explore the ability of P_2O_5/SiO_2 act as a selective catalyst, we carried out a competitive S,S-acetalization reaction using an equimolar mixture of benzaldehyde (1.0 mmol) and 4-phenylbutan-2-one or acetophenone (1.0 mmol) with 1,2-ethanedithiol (1 mmol) (Scheme 3). Employing this catalytic system, the highly selective conversion of benzaldehyde to 2-phenyl-1,3-dithiolane was observed, whereas ketones were intact. These observations show that the presented method is potentially applicable for the chemoselective conversion of aldehydes to corresponding *S*,*S*-acetals in the presence of ketone functions in multi-functional molecules.



Scheme 3. Chemoselective conversion of aldehydes to corresponding *S*, *S*-acetals in the presence of ketones.

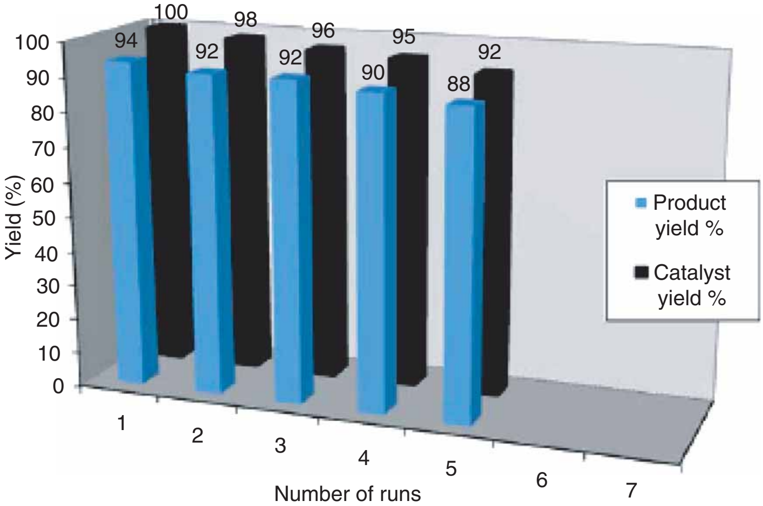


Figure 1. Recycling of the catalyst.

We also investigated the recycling of the catalyst under solvent-free conditions using a model reaction of benzaldehyde (2 mmol) and 1,2-ethanedithiol (2.2 mmol) solvent-free at ambient temperature (Table 2, Entry 1b). After completion of reaction as checked by TLC, it was diluted with *n*-hexane and the catalyst was filtered off .The catalyst was washed twice (2 × 5 ml) with *n*-hexane. The recovered catalyst was dried in vacuum and was used for the subsequent catalytic runs. The catalytic system worked well up to five catalytic runs without loss its activities (Figure 1). Thus, this solid heterogeneous acidic catalyst is safe, easy to handle, environmentally benign, presents fewer disposal problems and is stable in reaction media. It has the advantage of being easily removed from the organic product by simple filtration and also this reagent has improved storage stability in moisture in comparison to P_2O_5, which is very sensitive to moisture and also it showed much more reactivity than unsupported P_2O_5 (*27*).

3. Conclusion

In summary, we have developed a simple and efficient method for the S,S-acetalization of carbonyl compounds using a catalytic amount of silica supported phosphorus pentoxide immediately under solvent-free conditions at ambient temperature. The catalyst can be recovered and reused for several times. This catalytic reaction show several advantages such as requirement of very low amount of catalyst, high yields, cost-effective, highly efficient, chemoselective, convenient and mild reaction conditions.

4. Experimental

All reagents were purchased from Merck and Aldrich and used without further purification. P_2O_5/SiO_2 was prepared according to the reported procedure (*18*). All yields refer to isolated products after purification. Products were characterized by comparison with authentic samples and by spectroscopy data (FT-IR, NMR spectra). The NMR spectra were recorded on a Bruker Avance 300 MHz instrument. The spectra were measured in $CDCl_3$ relative to TMS (0.00 ppm). FT-IR spectra were recorded on a Perkin-Elmer 781 spectrophotometer. TLC was performed on Silica-gel polygram SIL G/UV 254 plates.

4.1. *S,S-Thioacetalization of carbonyl compounds (general procedure)*

A mixture of carbonyl compounds (2 mmol), dithiol (2.2 mmol) or thiol (4.4 mmol) and P_2O_5/SiO_2 (5 mg) was stirred at ambient temperature. After completion of reaction as checked by TLC, it was diluted with n-hexane and the catalyst was filtered off. The filtrate solution (50 ml) was washed with aqueous 10% NaOH (2×10 ml) solution and then dried over anhydrous Na_2SO_4. The solvent was evaporated by rotary evaporator and the crude product was purified through a column of silica gel (n-hexane:EtOAc, 80:20) to obtain the pure product. All the products were characterized by comparison of their spectroscopic and physical data with the authentic samples (*21–26*).

4.2. *Spectral data of two representative products*

4.2.1. *S,S-Acetals of 28a*

FT-IR (KBr, cm^{-1}): 2925, 2925, 1675, 1415, 1232, 1158, 925, 800. ^1H NMR ($CDCl_3$, 300 MHz): δ (ppm): 8.25 (d, 2H, $J = 8.31$ Hz), 7.88 (d, 2H, $J = 8.25$ Hz), 7.81 (d, 2H, $J = 6.60$ Hz), 5.76 (s, 2H), 3.15 (t, 4H, $J = 5.56$ Hz), 2.26–2.23 (m, 4H), 2.11–2.04 (m, 4H).

4.2.2. *S,S-Acetals of 29a*

FT-IR (KBr, cm^{-1}): 2925, 1662, 1492, 1363, 1274, 1205, 1125, 983, 912, 855. ^1H NMR ($CDCl_3$, 300 MHz): δ (ppm): 9.42 (s, 1H), 8.25–8.21 (m, 1H), 8.18–8.14 (m, 1H), 7.92–7.84 (m, 2H), 3.24 (t, 2H, $J = 9.64$ Hz), 3.20 (d, 1H, $J = 6.44$ Hz), 2.86–2.77 (m, 2H), 2.20–2.08 (m, 2H).

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