



Fast, efficient and chemoselective method for thioacetalization and transthoacetalization using catalytic amount of P_2O_5/Al_2O_3 under microwave irradiation

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ABSTRACT

In this work, we have reported a mild, fast and efficient method for the preparation of 1,3-dithiolanes using catalytic amount of P_2O_5/Al_2O_3 under solvent-free conditions (MW). A wide variety of aldehydes and ketones can be easily protected to their corresponding 1,3-dithiolanes using 1,2-ethanedithiol in the presence of catalytic amount of P_2O_5/Al_2O_3 under microwave irradiation. Using this method, transthoacetalization of acetals and acylals into their corresponding 1,3-dithiolanes was also carried out in good yields and short reaction times.

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1. Introduction

Protection and deprotection of reactive functional groups are essential steps in the synthesis of natural products and polyfunctional compounds [1]. The protection of carbonyl compounds as thioacetals is an important protocol in organic synthesis due to their stability under both acidic and basic conditions [1], also a wide range of reagents is available to deprotect thioacetals [2]. In addition, thioacetals are also utilized as masked acyl anions or masked methylene functions in carbon–carbon bond forming reactions [3,4]. Generally, they are prepared by condensation of carbonyl compounds with thiols or dithiols using strong protic acid catalysts such as Nafion-H [5], Amberlyst-15 [6], silica sulfuric acid [7], or Lewis acids such as $BF_3 \cdot OEt_2$ [8], $AlCl_3$ [9], $InCl_3$ [10], WCl_6 [11], $H_3PW_{12}O_{40}$ [12] and 5 M $LiClO_4$ [13]. Recently, some solid supported reagents have been used for thioacetalization of carbonyl compounds, e.g. $Cu(OTf)_2-SiO_2$ [14], $TaCl_5-SiO_2$

[15], $ZrCl_4-SiO_2$ [16], $NaHSO_4-SiO_2$ [17] and $HClO_4-SiO_2$ [18]. Most recently, some methods employing $LiBF_4$ [19], I_2 [20,21], $In(OTf)_3$ [22], NBS [23], $Sc(OTf)_3$ [24], $NiCl_2$ [25], $CoCl_2$ [26], $ScCl_3$ [27], $Nd(OTf)_3$ [28], $Y(OTf)_3$ [29], $Lu(OTf)_3$ [30], $Pr(OTf)_3$ [31], $VO(OTf)_2$ [32], DBSA [33], silica functionalized sulfonic acid [34] have been reported. Although some of these methods have convenient protocols with good to high yields, the majority of these methods have certain disadvantages such as long reaction times, reflux conditions, stoichiometric amount of catalyst, tedious work-up, moisture sensitivity of the used reagent and the use of expensive and toxic catalyst. Interestingly, only a few of these methods are chemoselective for the protection of aldehydes in the presence of ketones. Therefore, there is still a need to develop a simple, mild and efficient method for the chemoselective protection of aldehydes.

2. Experimental

2.1. General remarks

All reagents were purchased from Merck and Aldrich and used without further purification. All yields refer to isolated products after purification. The products were characterized by comparison with authentic samples and by spectroscopic data (IR, 1H NMR spec-

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tra and MS). ^1H NMR spectra were recorded at 500 MHz. The spectra were measured in CDCl_3 using tetramethylsilane as the internal standard. Microwave irradiation was used by a Samsung microwave oven, Model-M9G45.

2.2. Preparation of $\text{P}_2\text{O}_5/\text{Al}_2\text{O}_3$

The reagent was prepared by combination of phosphorus pentoxide (3 g) and 3 g of aluminium oxide (90 active acidic, 0.063–0.200 mm) were mixed for 10 min in a round bottomed flask until a fine and homogenous powder was obtained. This reagent was heated in an oven at 120°C for 1 h and then stored in a sealed flask for later using.

2.3. Preparation of $\text{H}_3\text{PO}_4/\text{Al}_2\text{O}_3$

The reagent was prepared by combination of phosphoric acid 85% (3 g) and 3 g of aluminium oxide (90 active acidic, 0.063–0.200 mm) were mixed for 10 min in a round bottomed flask until a fine and homogenous powder was obtained. This reagent was heated in an oven at 120°C for 1 h and then stored in a sealed flask for later using.

2.4. Typical procedure for the preparation of 2-methyl-2-(4-nitrophenyl)-1,3-dithiolane under microwave irradiation

A mixture of 4'-nitroacetophenone (0.33 g, 2 mmol), 1,2-ethane dithiol (0.20 mL, 2.4 mmol) and $\text{P}_2\text{O}_5/\text{Al}_2\text{O}_3$ (0.13 g, 20 mol%) was taken in a sealed Teflon vessel and irradiated (900 W) for 4 min with 30 s/min intervals. After cooling, the reaction mixture was diluted with dichloromethane and filtered. The organic layer was washed with 10% Na_2CO_3 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 (hexane:EtOAc, 80:20) to obtain the pure product in 82% yield (0.39 g).

2.5. Typical procedure for the transthioacetalization of 1,1-diacetoxy-1-(3-nitrophenyl)methane under microwave irradiation

A mixture of 1,1-diacetoxy-1-(3-nitrophenyl)methane (0.50 g, 2 mmol), 1,2-ethanedithiol (0.20 mL, 2.4 mmol) and $\text{P}_2\text{O}_5/\text{Al}_2\text{O}_3$ (0.13 g, 20 mol %) was taken in a sealed Teflon vessel and irradiated (900 W) for 2 min with 30 s/min intervals. After cooling, the reaction mixture was diluted with dichloromethane and filtered. The organic layer was washed with 10% Na_2CO_3 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 (hexane:EtOAc, 80:20) to obtain the pure product in 73% yield (0.33 g).

2.6. Typical procedure for the competitive dithioacetalization of benzaldehyde in the presence of 1,1-diacetoxy-1-(4-nitrophenyl)methane under microwave irradiation

A mixture of benzaldehyde (0.1 mL, 1 mmol), 1,1-diacetoxy-1-(4-nitrophenyl)methane (0.25 g, 1 mmol), 1,2-ethanedithiol (0.08 mL, 1 mmol) and $\text{P}_2\text{O}_5/\text{Al}_2\text{O}_3$ (0.065 g, 20 mol%) was taken in a sealed Teflon vessel and irradiated (900 W) for 1 min. After cooling, the reaction mixture was diluted with dichloromethane and filtered. The organic layer was washed with 10% Na_2CO_3 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 (hexane:EtOAc, 80:20) to obtain

2-phenyl-1,3-dithiolane in 75% yield. In this reaction 1,1-diacetoxy-1-(4-nitrophenyl)methane was intact.

3. The spectral data of some representative products

2-phenyl-1,3-dithiolane (Table 3, entry 1). IR (KBr) cm^{-1} : 3043, 2935, 1580, 1500, 1490, 1420, 1380, 700. δ_{H} (500 MHz, CDCl_3) 7.58–7.53 (2 H, m), 7.38–7.29 (3 H, m), 5.69 (1 H, s), 3.58–3.52 (2 H, m), 3.43–3.37 (2 H, m).

2-(4-Bromophenyl)-1,3-dithiolane (Table 3, entry 2). IR (KBr) cm^{-1} : 3055, 2930, 1599, 1570, 1472, 1420, 1375, 1075, 880, 795, 750, 690. MS (EI), m/z (relative intensity): 262 ($\text{M}^+ + 2$, 40), 260 (M^+ , 35), 234 (31), 232 (30), 201 (56), 199 (42), 153 (100), 120 (22), 77 (17), 45 (32). δ_{H} (500 MHz, CDCl_3) 7.50 (2 H, d, $J = 5.00$ Hz), 7.20 (2 H, d, $J = 5.00$ Hz), 5.55 (1 H, s), 3.47–3.39 (2 H, m), 3.34–3.28 (2 H, m).

2-(3-Chlorophenyl)-1,3-dithiolane (Table 3, entry 3). IR (KBr) cm^{-1} : 3060, 2925, 1597, 1574, 1470, 1425, 1276, 1190, 1075, 888, 798, 753, 694. δ_{H} (500 MHz, CDCl_3) 7.58 (1 H, s), 7.43–7.37 (1 H, m), 7.28–7.21 (2 H, d, $J = 7.58$ Hz), 5.62 (1 H, s), 3.56–3.48 (2 H, m), 3.42–3.36 (2 H, m).

2-(4-Chlorophenyl)-1,3-dithiolane (Table 3, entry 4). IR (KBr) cm^{-1} : 3080, 2920, 1600, 1470, 1440, 1375, 1050, 850, 745. δ_{H} (500 MHz, CDCl_3) 7.70 (2 H, d, $J = 6.55$ Hz), 7.25 (2 H, d, $J = 6.55$ Hz), 5.60 (1 H, s), 3.51–3.41 (2 H, m), 3.36–3.29 (2 H, m).

2-(3-Nitrophenyl)-1,3-dithiolane (Table 3, entry 5). IR (KBr) cm^{-1} : 3086, 2922, 1579, 1534, 1344, 1275, 1076, 822, 722. δ_{H} (500 MHz, CDCl_3) 8.44 (1 H, s), 8.16 (1 H, d, $J = 7.03$ Hz), 7.87 (1 H, d, $J = 7.73$ Hz), 7.52 (1 H, t, $J = 7.46$ Hz), 5.71 (1 H, s), 3.59–3.54 (2 H, m), 3.48–3.43 (2 H, m).

2-(4-Methoxyphenyl)-1,3-dithiolane (Table 3, entry 7). IR (KBr) cm^{-1} : 3065, 2900, 1600, 1580, 1470, 1300, 1250, 1220, 1180, 1025, 830, 750. MS (EI), m/z (relative intensity): 214 ($\text{M}^+ + 2$, 11), 212 (M^+ , 71), 184 (40), 183 (35), 153 (58), 151 (100), 136 (16), 108 (22), 77 (12), 45 (20). δ_{H} (500 MHz, CDCl_3) 7.46 (2 H, d, $J = 8.47$ Hz), 6.82 (2 H, d, $J = 8.47$ Hz), 5.63 (1 H, s), 3.78 (3 H, s), 3.53–3.46 (2 H, m), 3.39–3.29 (2 H, m).

2-(3-Methoxyphenyl)-1,3-dithiolane (Table 3, entry 8). IR (KBr) cm^{-1} : 3060, 2930, 2830, 1598, 1475, 1430, 1240, 1170, 1030, 880, 785, 690. δ_{H} (500 MHz, CDCl_3) 7.28 (1 H, t, $J = 7.56$ Hz), 7.16 (2 H, s), 6.85 (1 H, d, $J = 7.57$ Hz), 5.67 (1 H, s), 3.85 (3 H, s), 3.52–3.51 (2 H, m), 3.37–3.36 (2 H, m).

2-(2-Methoxyphenyl)-1,3-dithiolane (Table 3, entry 9). IR (KBr) cm^{-1} : 3060, 2945, 2840, 1600, 1470, 1370, 1245, 1175, 1035, 850, 750. δ_{H} (500 MHz, CDCl_3) 7.78 (1 H, d, $J = 7.66$ Hz), 7.29–7.26 (1 H, m), 6.99 (1 H, t, $J = 7.50$ Hz), 6.89 (1 H, d, $J = 8.19$ Hz), 6.10 (1 H, s), 3.90 (3 H, s), 3.49–3.45 (2 H, m), 3.38–3.35 (2 H, m).

2-(4-Methylphenyl)-1,3-dithiolane (Table 3, entry 10). IR (KBr) cm^{-1} : 3060, 2971, 2925, 1604, 1500, 1455, 1291, 1059, 842, 700. MS (EI), m/z (relative intensity): 198 ($\text{M}^+ + 2$, 6), 196 (M^+ , 70), 168 (20), 167 (20), 153 (90), 135 (100), 91 (39), 77 (12), 45 (22). δ_{H} (500 MHz, CDCl_3) 7.42 (2 H, d, $J = 7.54$ Hz), 7.10 (2 H, d, $J = 7.54$ Hz), 5.61 (1 H, s), 3.52–3.35 (2 H, m), 3.31–3.28 (2 H, m), 2.32 (3 H, s).

2-(2-Hydroxyphenyl)-1,3-dithiolane (Table 3, entry 12). IR (KBr) cm^{-1} : 3380, 2960, 1590, 1490, 1460, 1350, 1270, 1225, 1080, 1050, 855, 750. δ_{H} (500 MHz, CDCl_3) 7.34 (1 H, d, $J = 7.00$ Hz), 7.26 (1 H, t, $J = 8.02$ Hz), 6.93–6.88 (2 H, m), 6.77 (OH, s), 5.85 (1 H, s), 3.62–3.56 (2 H, m), 3.45–3.38 (2 H, m).

2-(1,3-dithiolan-2-yl)-5-methylfuran (Table 3, entry 14). IR (KBr) cm^{-1} : 3100, 2920, 1580, 1505, 1415, 1365, 1250, 1010, 930, 849. δ_{H} (500 MHz, CDCl_3) 6.21 (1 H, d, $J = 2.92$ Hz), 5.89 (1 H, d, $J = 2.92$), 5.63 (1 H, s), 3.49–3.43 (2 H, m), 3.36–3.30 (2 H, m), 2.31 (3 H, s).

2-(2-phenylethenyl)-1,3-dithiolane (Table 3, entry 15). IR (KBr) cm^{-1} : 3027, 2923, 1597, 1447, 1419, 1345, 1278, 1069, 968, 735. δ_{H} (500 MHz, CDCl_3) 7.48–7.20 (5 H, m), 6.48 (1 H, d, $J = 15.5$ Hz), 6.12

(1 H, dd, $J_1 = 15.5, J_2 = 8.8$ Hz), 5.20 (1 H, d, $J = 8.8$ Hz), 3.60–3.25 (4 H, m).

2-Methyl-2-pentyl-1,3-dithiolane (Table 3, entry 17). IR (KBr) cm^{-1} : 2940, 2865, 1462, 1373, 1268. δ_{H} (500 MHz, CDCl_3) 3.40–3.30 (4 H, m), 1.96–1.93 (2 H, m), 1.77 (3 H, s), 1.56–1.51 (2 H, m), 1.39–1.28 (4 H, m), 0.92 (3 H, t, $J = 6.82$ Hz).

1,4-dithia-spiro[4.6]undecane (Table 3, entry 19). IR (KBr) cm^{-1} : 2870, 1475, 1450, 1425, 1375, 960. δ_{H} (500 MHz, CDCl_3) 3.30 (4 H, m), 2.24–2.19 (4 H, m), 1.64–1.62 (8 H, m).

2-Methyl-2-phenyl-1,3-dithiolane (Table 3, entry 20). IR (KBr) cm^{-1} : 3020, 2901, 1609, 1509, 1410, 1275, 1105, 850, 829, 687. δ_{H} (500 MHz, CDCl_3) 7.82–7.81 (2 H, dd, $J_1 = 8.55, J_2 = 1.13$), 7.39–7.35 (2 H, t, $J = 8.05$ Hz), 7.30–7.27 (1 H, m), 3.54–3.50 (2 H, m), 3.46–3.40 (2 H, m), 2.21 (1 H, s).

2-Methyl-2-(4-methoxyphenyl)-1,3-dithiolane (Table 3, entry 21). IR (KBr) cm^{-1} : 3050, 2950, 2835, 1595, 1485, 1430, 1370, 1272, 1166, 1045, 886, 800, 742, 700. δ_{H} (500 MHz, CDCl_3) 7.72 (2 H, d, $J = 8.81$ Hz), 6.88 (2 H, d, $J = 8.81$ Hz), 3.80 (3 H, s), 3.51–3.48 (2 H, m), 3.42–3.39 (2 H, m), 2.20 (3 H, s).

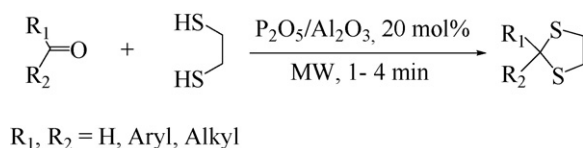
2-Methyl-2-(3-methoxyphenyl)-1,3-dithiolane (Table 3, entry 22). IR (KBr) cm^{-1} : 3059, 2962, 2925, 2835, 1604, 1488, 1432, 1238, 1171, 1044, 856, 800, 750, 677. δ_{H} (500 MHz, CDCl_3) 7.40–7.37 (2 H, m), 7.28 (1 H, t, $J = 7.93$ Hz), 6.82 (1 H, d, $J = 8.09$ Hz), 3.86 (3 H, s), 3.52–3.48 (2 H, m), 3.44–3.38 (2 H, m), 2.20 (3 H, s).

2-Methyl-2-(4-nitrophenyl)-1,3-dithiolane (Table 3, entry 23). IR (KBr) cm^{-1} : 3073, 2923, 1525, 1348, 1101, 897, 807, 687. δ_{H} (500 MHz, CDCl_3) 8.19 (2 H, d, $J = 8.88$ Hz), 7.96 (2 H, d, $J = 8.86$ Hz), 3.58–3.51 (2 H, m), 3.43–3.37 (2 H, m), 2.25 (3 H, s).

4. Results and discussion

Recently, adsorption of variety of catalysts and reagents supported on solid supports was developed because such reagents not only simplify purification processes but also help to prevent release of reaction residues into the environment. For this purpose, it is necessary to prepare stable reaction intermediates. The surface of alumina has proven to be remarkably versatile mediators of chemical reactivity. This has led to growth in the field of solid supported on alumina [35–37]. Although there are many reports using phosphorus pentoxide as a reagent in organic reactions [38–40], P_2O_5 is difficult to handle due to its moisture sensitivity at room temperature. P_2O_5 on alumina ($\text{P}_2\text{O}_5/\text{Al}_2\text{O}_3$) is easy to prepare and to handle; also it is useful reagent that could be removed from the reaction mixture by simple filtration [41,42]. Herein we wish to report a new procedure for the chemoselective thioacetalization of carbonyl compounds to their corresponding 1,3-dithiolanes in the presence of 1,2-ethanedithiol and catalytic amount of $\text{P}_2\text{O}_5/\text{Al}_2\text{O}_3$. These reactions are easily carried out under solvent-free conditions (microwave irradiation) (Scheme 1).

To optimize the reaction conditions, initially we tried to convert benzaldehyde (2 mmol) to 2-phenyl-1,3-dithiolane using $\text{P}_2\text{O}_5/\text{Al}_2\text{O}_3$ (0.13 g, 20 mol%) and 1,2-ethanedithiol (2.4 mmol) in different conditions (Table 1, entries 1–7). We also studied the conversion of acetophenone (2 mmol) to 2-methyl-2-phenyl-1,3-dithiolane using $\text{P}_2\text{O}_5/\text{Al}_2\text{O}_3$ (0.13 g, 20 mol%) and 1,2-ethanedithiol



Scheme 1. Chemoselective thioacetalization of carbonyl compounds to their corresponding 1,3-dithiolanes in the presence of 1,2-ethanedithiol and catalytic amount of $\text{P}_2\text{O}_5/\text{Al}_2\text{O}_3$ under microwave irradiation.

Table 1

Conversion of benzaldehyde and acetophenone to their corresponding 1,3-dithiolanes with $\text{P}_2\text{O}_5/\text{Al}_2\text{O}_3$ and 1,2-ethanedithiol in different conditions.

Entry	Substrate	Solvent	Yield (%) ^f	Time (min)
1 ^a	Benzaldehyde	Dichloromethane	55	180
2 ^a	Benzaldehyde	Acetonitrile	58	180
3 ^a	Benzaldehyde	Ethylacetate	48	180
4 ^a	Benzaldehyde	Diethylether	45	180
5 ^a	Benzaldehyde	Cyclohexane	50	180
6 ^b	Benzaldehyde	Solvent-free	62	180
7 ^c	Benzaldehyde	MW (900 W)	92	1
8 ^d	Acetophenone	Dichloromethane	35	60
9 ^d	Acetophenone	Acetonitrile	60	60
10 ^d	Acetophenone	Diethylether	20	60
11 ^d	Acetophenone	Cyclohexane	50	60
12 ^d	Acetophenone	1,2-dichloroethane	58	60
13 ^d	Acetophenone	Toluene	63	60
14 ^e	Acetophenone	Solvent-free	65	60
15 ^c	Acetophenone	MW (900 W)	83	4

^a The reaction was carried out in 5 mL of solvent at rt.

^b The reaction was carried out at rt.

^c The reaction was irradiated by using a Samsung microwave oven, Model-M9G45.

^d The reaction was carried out in 5 mL of solvent under reflux conditions.

^e The reaction was carried out at 80 °C.

^f The yields refer to the isolated pure products.

(2.4 mmol) in various conditions (Table 1, entries 8–15). We found that the best results were obtained when these reactions were carried out under microwave irradiation (Table 1, entries 7 and 15). Therefore, we employed the microwave irradiation for the conversion of various aldehydes and ketones to their corresponding 1,3-dithiolanes.

Also to optimize the amount of $\text{P}_2\text{O}_5/\text{Al}_2\text{O}_3$, we studied the conversion of 4-nitrobenzaldehyde (2 mmol) to 2-(4-nitrophenyl)-1,3-dithiolane under microwave irradiation. As shown in Table 2, the best yield of the product was obtained by using 20 mol% of $\text{P}_2\text{O}_5/\text{Al}_2\text{O}_3$. An increase of the amount of $\text{P}_2\text{O}_5/\text{Al}_2\text{O}_3$ from 20 to 25 mol% did not change the yield (Table 2, entry 3). We also studied this reaction with Al_2O_3 alone (0.065 g, 20 mol%) under the same conditions, we observed that 2-(4-nitrophenyl)-1,3-dithiolane was obtained in low yield (Table 2, entry 6). According to these results, P_2O_5 is necessary for this purpose. We also investigated this reaction using $\text{H}_3\text{PO}_4/\text{Al}_2\text{O}_3$ (0.13 g, 20 mol%) under the same conditions. We found that $\text{P}_2\text{O}_5/\text{Al}_2\text{O}_3$ is more efficient catalyst than $\text{H}_3\text{PO}_4/\text{Al}_2\text{O}_3$ under the same conditions (Table 2, entry 7).

Different kinds of aldehydes and ketones were rapidly converted to the corresponding 1,3-dithiolanes using 1,2-ethanedithiol in the presence of $\text{P}_2\text{O}_5/\text{Al}_2\text{O}_3$ (20 mol%) under microwave irradiation (Table 3). Aromatic, heteroaromatic, aliphatic, and α,β -unsaturated aldehydes were also converted to their corresponding 1,3-dithiolanes in high yields (Table 3, entries 1–16). Both cyclic and acyclic aliphatic ketones gave good yields of the desired 1,3-dithiolanes (Table 3, entries 17–19). However, aromatic ketones were slowly converted to their corresponding 1,3-dithiolanes in

Table 2

Optimization of the amount of $\text{P}_2\text{O}_5/\text{Al}_2\text{O}_3$ in the formation of 1,3-dithiolane of 4-nitrobenzaldehyde under microwave irradiation^a.

Entry	Catalyst	Mol % catalyst	Time (min)	Yield (%) ^b
1	$\text{P}_2\text{O}_5/\text{Al}_2\text{O}_3$	5	1	32
2	$\text{P}_2\text{O}_5/\text{Al}_2\text{O}_3$	10	1	65
3	$\text{P}_2\text{O}_5/\text{Al}_2\text{O}_3$	15	1	78
4	$\text{P}_2\text{O}_5/\text{Al}_2\text{O}_3$	20	1	91
5	$\text{P}_2\text{O}_5/\text{Al}_2\text{O}_3$	25	1	91
6	Al_2O_3	20	1	12
7	$\text{H}_3\text{PO}_4/\text{Al}_2\text{O}_3$	20	1	63

^a The reaction was irradiated by using a Samsung microwave oven, Model-M9G45.

^b The yields refer to the isolated pure products.

Table 3
Conversion of carbonyl compounds to their corresponding 1,3-dithiolanes with P_2O_5/Al_2O_3 and 1,2-ethanedithiol under microwave irradiation^{a,b}.

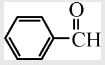
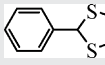
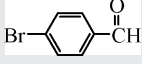
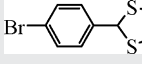
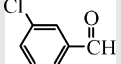
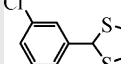
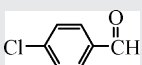
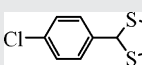
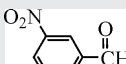
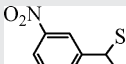
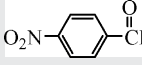
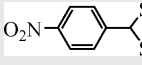
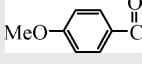
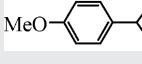
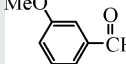
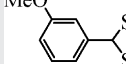
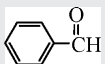
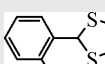

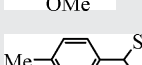
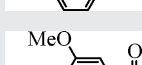
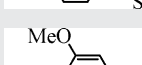
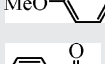
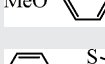
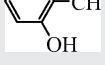
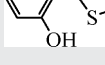
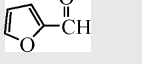
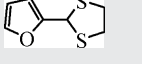
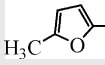
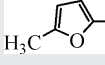
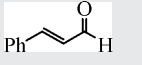
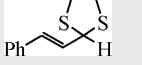
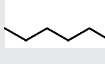
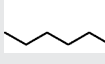
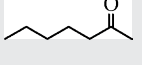
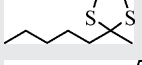
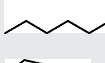
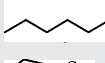
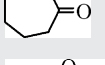
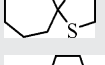
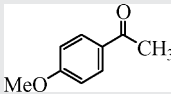
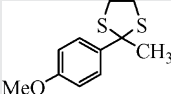
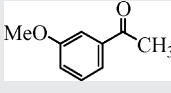
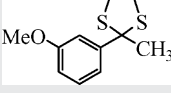
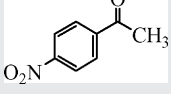
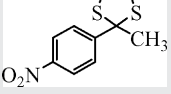
Entry	Substrates	Products	Time (min)	Yield (%)
1			1	92
2			1	94
3			1	92
4			1	93
5			1	90
6			1	91
7			1	90
8			1	92
9			1	89
10			1	91
11			1	87
12			1	88
13			1	90
14			1	92
15			1	88
16			1	89
17			2	86
18			2	85
19			2	88
20			4	83

Table 3 (Continued)

Entry	Substrates	Products	Time (min)	Yield (%)
21			4	77
22			4	80
23			4	82

^a The yields refer to the isolated pure products.

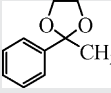
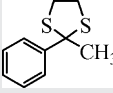
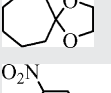
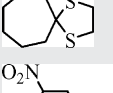
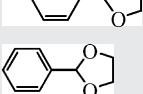
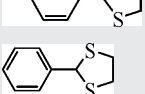
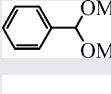
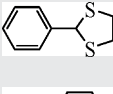
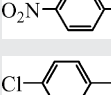
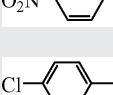
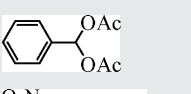
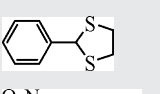
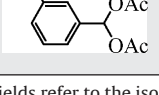
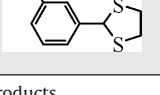
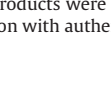
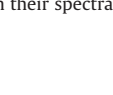


^b The products were characterized from their spectral (IR, ¹H NMR and MS) and comparison with authentic samples.

good yields (Table 3, entries 20–23). Also using this procedure, acetals and acylals were converted to their corresponding 1,3-dithiolanes in good yields (Table 4).

We also studied the role of Al₂O₃ by dithioacetalization of benzaldehyde, 4-nitrobenzaldehyde, 4-methoxybenzaldehyde and acetophenone in the absence of Al₂O₃ using P₂O₅ alone under the same conditions. We found that the yields of 1,3-dithiolanes using the combination of P₂O₅/Al₂O₃ were greater (average, 17%) than those with P₂O₅ alone. The effect of Al₂O₃ may be due to good dispersion of P₂O₅ on the surface of alumina so that it leads to significant improvements in reactivity. Also, Al₂O₃ as a support minimizes cross contamination between inorganic and organic components [43].

Table 4

Conversion of acetals and acylals to their corresponding 1,3-dithiolanes with P₂O₅/Al₂O₃ and 1,2-ethanedithiol under microwave irradiation^{a,b}.

1			4	76
2			2	82
3			2	86
4			2	83
5			2	85
6			2	82
7			2	85
8			2	70
9			2	73

^a The yields refer to the isolated pure products.

^b The products were characterized from their spectral (IR, ¹H NMR and MS) and comparison with authentic samples.

In order to evaluate the selectivity of this method, we investigated competitive reactions for the thioacetalization of benzaldehyde in the presence of 4'-nitroacetophenone, 1,1-diacetoxy-1-(4-nitrophenyl)methane, ethyl 4-nitrobenzoate and 2-(3-nitrophenyl)-1,3-dioxolane using catalytic amount of P₂O₅/Al₂O₃ under microwave irradiation. Employing this catalytic system, the highly selective conversion of benzaldehyde to 2-phenyl-1,3-dithiolane was observed (Table 5, entries 1–4). Using this method, thioacetalization of 4-acetylbenzaldehyde was carried out with high chemoselectivity (Table 5, entry 5).

To show the merit of the present work in comparison with recently reported papers, we compared our results with other reagents such as LiClO₄ [13], Cu(OTf)₂-SiO₂ [14], In(OTf)₃ [22], NBS [23], NiCl₂ [25] and CoCl₂ [26]. As shown in Table 6, the results show that the reaction yields are compatible with the reported ones and this reagent (P₂O₅/Al₂O₃) is superior to other reagents in view of the lowest reaction time.

In order to identify the structure of P₂O₅/Al₂O₃, we studied three IR spectra of Al₂O₃, H₃PO₄/Al₂O₃ and P₂O₅/Al₂O₃ (Fig. 1). In the spectrum of Al₂O₃, strong intermolecular hydrogen bonding occurs in the hydroxyl groups of Al₂O₃. Therefore, the resulting absorption at 3435.56 cm⁻¹ is broad. Infrared spectrum of H₃PO₄/Al₂O₃ show that intermolecular hydrogen bonding between hydrogen groups of Al₂O₃ and H₃PO₄ is stronger than that in Al₂O₃ alone. Therefore, the resulting absorption at 3430.74 cm⁻¹ is very broad. However, OH stretching region remains almost unchanged. Infrared spectrum of P₂O₅/Al₂O₃ show that OH stretching region shifts to 2852.2 cm⁻¹. This broad region is related to single hydroxyl group of P(O)OH [44]. As shown in Fig. 1, in structure of P₂O₅/Al₂O₃, the majority of hydroxyl groups in Al₂O₃ react with P₂O₅. Therefore, hydroxyl band in Al₂O₃ is not clearly observed. To clarify the structure of P₂O₅/Al₂O₃, we studied the other absorption bands in the infrared spectrum of P₂O₅/Al₂O₃. Two broad peaks at 2852.2 and 2291.98 cm⁻¹ are stretching bands of single hydroxyl group of P(O)OH [44]. The broad peak at 1685.48 cm⁻¹ is bending band of single hydroxyl group of P(O)OH [44]. The strong peak at 1242.9 cm⁻¹ is stretching band of P=O [44]. The strong peak at 1021.12 cm⁻¹ is related to stretching band of P–O–H [44]. Also the strong peak at 930.48 cm⁻¹ is stretching band of P–O–P [44] and the weak peak at 762.71 cm⁻¹ is related to bending band of P–O–P [44].

Based on these results, we suggest the following structure for P₂O₅/Al₂O₃ (Scheme 2).

Based on the results, we suggest the following mechanism for the conversion of carbonyl compounds to their corresponding 1,3-dithiolanes using catalytic amount of P₂O₅/Al₂O₃ (Scheme 3). Because P–O–P bond is brittle in P₂O₅/Al₂O₃ [45],

Table 5
Competitive dithioacetal formation of benzaldehyde using 1,2-ethanedithiol in the presence of catalytic amount of P_2O_5/Al_2O_3 under microwave irradiation^a.

1	
2	
3	
4	
5	

^a The yields refer to the isolated pure products.

it can be attacked by minus oxygen in the intermediate (1). As shown in Scheme 3, after the generation of intermediate (2), the process of thioacetalization is catalyzed with intermediate (2).

Finally, to compare the efficiency of P_2O_5/Al_2O_3 with H_3PO_4/Al_2O_3 , we studied the conversion of benzoic acid to benzoic anhydride using these reagents in 1,2-dichloro ethane under reflux conditions. As shown in Scheme 4, P_2O_5/Al_2O_3 is

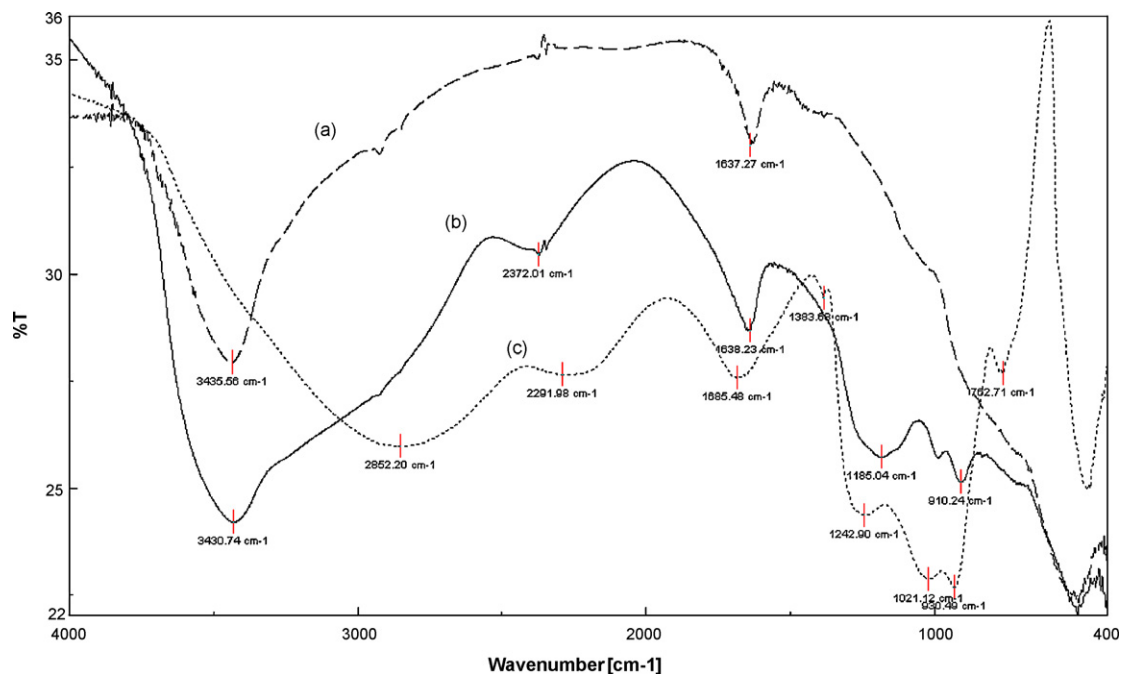
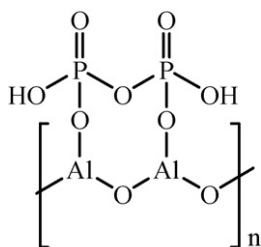
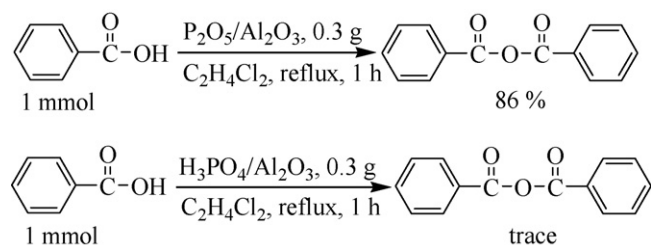
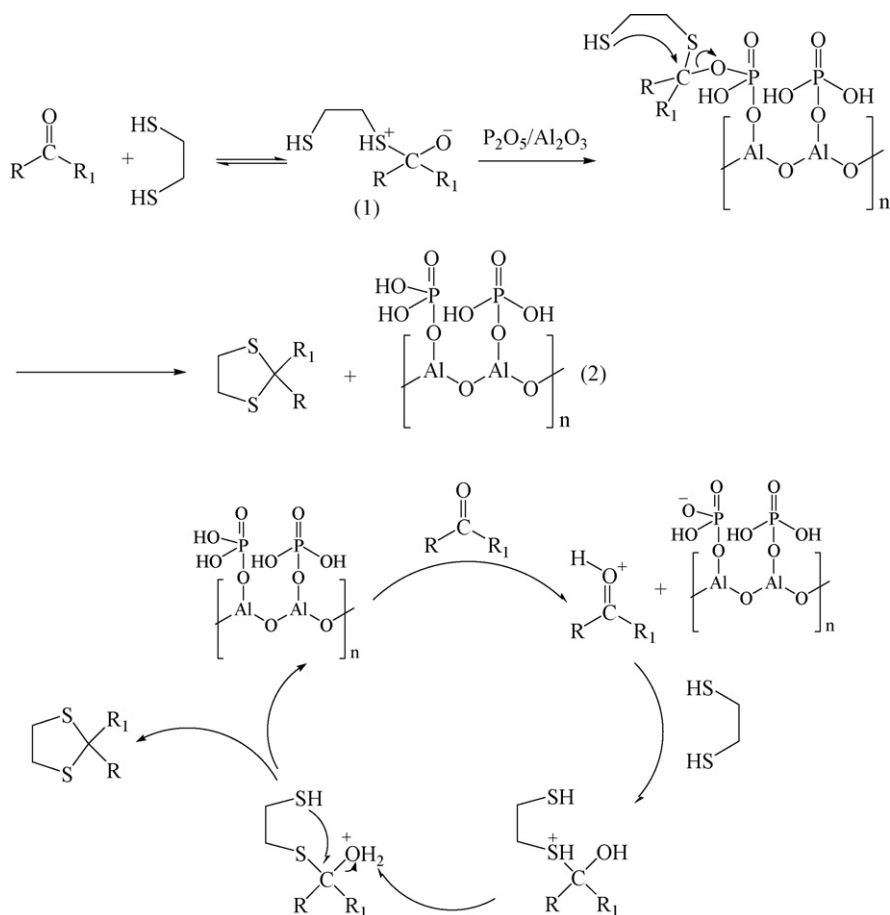


Fig. 1. Infrared spectra of Al_2O_3 (a), H_3PO_4/Al_2O_3 (b) and P_2O_5/Al_2O_3 (c).

Table 6Comparison of P_2O_5/Al_2O_3 with various catalysts in the dithioacetalization of some carbonyl compounds.

Entry	Substrate	Yield % (min) [hr]						
		NBS ^a 15 mol%	NiCl ₂ ^b 10 mol%	In(OTf) ₃ ^c 10 mol%	CoCl ₂ ^d 5 mol%	Cu(OTf) ₂ -SiO ₂ ^e 5 mol%	LiClO ₄ ^f 5 equiv.	P ₂ O ₅ /Al ₂ O ₃ 20 mol%
1	C ₆ H ₅ CHO	80 (40)	96 [2.75]	89 (8)	89 [2.5]	–	77 (15)	92 (1)
2	<i>P</i> -MeOC ₆ H ₄ CHO	75 (30)	90 [0.75]	96 (6)	93 [2]	99 (30)	16 [16]	90 (1)
3	<i>P</i> -ClC ₆ H ₄ CHO	80 (30)	–	–	–	98 (30)	85 (10)	93 (1)
4	Furfural	90 (30)	–	87 (8)	–	91 [1.5]	–	90 (1)
5	cinnamaldehyde	–	–	90 (8)	–	89 [1]	80 [48]	88 (1)

^a Reaction was carried out at room temperature in CH₂Cl₂.^b Reaction was carried out at room temperature in CH₂Cl₂/MeOH.^c Reaction was carried out at room temperature in CH₂Cl₂.^d Reaction was carried out at room temperature in CH₃CN.^e Reaction was carried out at room temperature under solvent-free conditions.^f Reaction was carried out at room temperature in diethylether.**Scheme 2.** Suggested structure for P_2O_5/Al_2O_3 .**Scheme 4.** Efficiency comparison of P_2O_5/Al_2O_3 with H_3PO_4/Al_2O_3 with the conversion of benzoic acid to benzophenone.**Scheme 3.** Suggested mechanism for the conversion of carbonyl compounds to their corresponding 1,3-dithiolanes using catalytic amount of P_2O_5/Al_2O_3 .

much more efficient than $\text{H}_3\text{PO}_4/\text{Al}_2\text{O}_3$ under the same conditions.

5. Conclusion

In conclusion, $\text{P}_2\text{O}_5/\text{Al}_2\text{O}_3$ is an inexpensive, easily available, non-corrosive and environmentally benign compound. In this work, we have reported a mild, fast and efficient method for the preparation of 1,3-dithiolanes from carbonyl compounds, acetals and acylals using catalytic amount of $\text{P}_2\text{O}_5/\text{Al}_2\text{O}_3$ under solvent-free conditions (MW). These reactions were carried out in good yields and short reaction times. In contrast to other acids, this reagent does not need special precautions for handling or storage, and it can be stored at ambient temperature for weeks without losing its catalytic activity.

Acknowledgements

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