MARCEL DEKKER, INC. • 270 MADISON AVENUE • NEW YORK, NY 10016

SYNTHETIC COMMUNICATIONS®
Vol. 33, No. 16, pp. 2829–2842, 2003

Acetonyltriphenylphosphonium Bromide and Its Polymer-Supported Analogues as Catalysts for the Protection of Carbonyl Compounds as Acetals or Thioacetals

Yung-Son Hon,[1,2,*] Chia-Fu Lee,[1] Rong-Jiunn Chen,[1] and Yi-Fen Huang[1]

[1]Department of Chemistry and Biochemistry, National Chung Cheng University, Chia-Yi, Taiwan, R.O.C.
[2]Institute of Chemistry, Academia Sinica, Nankang, Taipei, Taiwan, R.O.C.

ABSTRACT

Both acetonyltriphenylphosphonium bromide (ATPB) and poly-*p*-styryldiphenylacetonylphosphonium bromide (PATPB) are excellent catalysts in the protection of aldehydes as acetals or thioacetals. In general, ATPB is highly selective as ketones do not give good yields of ketals with this catalyst.

*Correspondence: Yung-Son Hon, Department of Chemistry and Biochemistry, National Chung Cheng University, Chia-Yi, Taiwan, 621, R.O.C.; Institute of Chemistry, Academia Sinica, Nankang, Taipei, Taiwan 115, R.O.C.; Fax: 886-5-2721040; E-mail: cheysh@ccu.edu.tw.

DOI: 10.1081/SCC-120022172 0039-7911 (Print); 1532-2432 (Online)

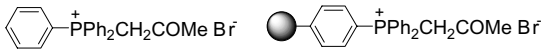
MARCEL DEKKER, INC. • 270 MADISON AVENUE • NEW YORK, NY 10016

Key Words: Acetonyltriphenylphosphonium bromide; Poly-*p*-styryldiphenylacetonylphosphonium bromide; Acetals; Thioacetals.

INTRODUCTION

The most useful protective groups for carbonyl groups are acetals and thioacetals. The synthesis of acetals or thioacetal from aldehydes and ketones is carried out by different methods depending on the case.[1] In the study of this reaction, particular attention was given to the selection of catalysts, ranging from conventional acids (sulfuric acid, ethanolic hydrochloric acid, *p*-toluenesulfonic acid, pyridinium *p*-toluenesulfonate, ferric chloride, etc.), to acidic resins such as, amberlyst-15 or acidic Montmorillonite clay K-10,[2,3] and finally to solid superacids, Nafion-H type.[4] Recently, many heterogeneous catalytic systems such as $SOCl_2$-SiO_2,[5] HY zeolite,[6] Mg-ZnTf,[7] natural kaolinitic clay[8] and modified clays such as Mont-KSH[9] and Ce-Mont[10] have been developed for such synthetic transformations.

We have reported the catalytic activity of acetonyltriphenylphosphonium bromide (ATPB) in the protection of alcohols with alkyl vinyl ethers and their deprotection.[11] It can also be employed to induce the cyclotrimerization of the aliphatic aldehydes.[12] ATPB can be easily prepared from triphenylphosphine and bromoacetone in benzene at room temperature in excellent yield.[11–13] It is crystalline ($C_{21}H_{20}BrOP$, FW 399.27, m.p. 221–223°C), nonhydroscopic, and soluble in CH_2Cl_2, $CHCl_3$, MeOH, EtOH, CH_3CN but not in THF, Et_2O, benzene, and EtOAc.



ATPB PATPB

Intrigued by ATPB's peculiar catalytic activity described above, we anchored the ATPB moiety on the cross-linked polystyrene backbone for practical purposes. This is primarily because insoluble polymeric reagents, among other features, expand the range of applicable solvents, increase the ease of work-up and product purification, lower the environmental hazards, and in most cases provide for recovery and regeneration of the supported reagents. We found that the poly-*p*-styryldiphenylacetonylphosphonium bromide (PATPB) is also a very efficient and excellent catalyst for the above mentioned reactions.[14]

In continuation of our efforts to explore its synthetic applications further, herein we report the catalytic activities of ATPB and PATPB in the formation of acetals and thioacetals from the corresponding carbonyl compounds.

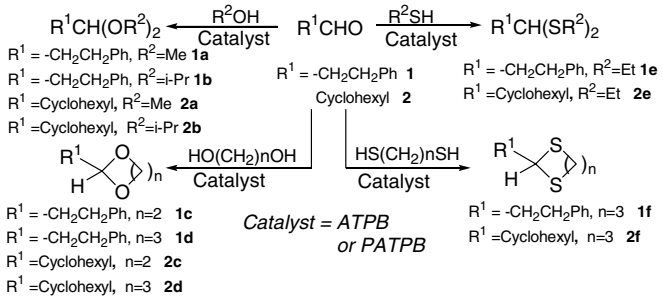
RESULTS AND DISCUSSION

ATPB as a Catalyst in the Protection of Aldehydes as Acetal or Thioacetal

We have investigated the protection of aldehydes with alcohol in the presence of ATPB. To a solution of 3-phenylpropanal (**1**) (287 mg, 2.14 mmol) in 2 mL of methanol was added ATPB (85 mg, 0.21 mmol) and the solution was stirred at RT. The reaction was complete in 20 min. The desired product **1a** was obtained in 93% yield (Sch. 1; Entry 1, Table 1). Under similar condition, 3-phenylpropanal (**1**) reacted with isopropanol to give the corresponding acetals in 65% yield after stirring at room temperature for 24 h (Entry 3). The lower yield and longer reaction time observed in the case of isopropanol shows that there is a steric problem associated with the bulky isopropoxy group in the protection of aldehyde. It is not surprising that 3-phenylpropanal (**1**) does not react with *tert*-butanol at all.

The protection of aldehydes with diols was also investigated. In the presence 0.1 mol equiv. of ATPB, 3-phenylpropanal (**1**) reacted with ethylene glycol and 1,3-propanediol, respectively, to give the corresponding acetals in excellent yields in 1 h (Entries 5, 7).

Under the catalysis of ATPB, the α,α-disubstituted aldehyde such as cyclohexanecarboxaldehyde (**2**) could react with methanol, ethylene glycol, and 1,3-propanediol, respectively, to give the corresponding



Scheme 1.

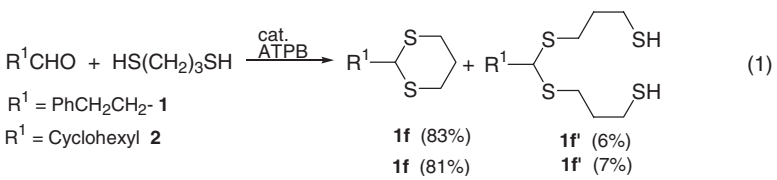
Table 1. The reaction of aldehyde with alcohol or thiol in the presence of ATPB catalysts at room temperature.

Entry	R^1CHO $R^1=$	ATPB (mol equiv.)	Alcohol	(mol equiv.)	Time (h)	Acetal or thiacetal	Yield[b] (%)
1	$PhCH_2CH_2$- **1**	0.1	MeOH	–[a]	1/3	**1a**	93
2	Cyclohexyl **2**	0.1	MeOH	–[a]	1/6	**2a**	90
3	$PhCH_2CH_2$- **1**	0.1	i-PrOH	–[a]	24	**1b**	65
4	Cyclohexyl **2**	0.1	i-PrOH	–[a]	24	**2b**	15[c]
5	$PhCH_2CH_2$- **1**	0.1	$HO(CH_2)_2OH$	2	3/4	**1c**	92
6	Cyclohexyl **2**	0.1	$HO(CH_2)_2OH$	2	2/3	**2c**	88
7	$PhCH_2CH_2$- **1**	0.1	$HO(CH_2)_3OH$	2	1	**1d**	91
8	Cyclohexyl **2**	0.1	$HO(CH_2)_3OH$	2	5/6	**2d**	92
9	$PhCH_2CH_2$- **1**	0.1	EtSH	3	1/2	**1e**	90
10	Cyclohexyl **2**	0.1	EtSH	3	1/4	**2e**	89
11	$PhCH_2CH_2$- **1**	0.1	$HS(CH_2)_2SH$	2	1/2	**1f**	83
12	Cyclohexyl **2**	0.1	$HS(CH_2)_3SH$	2	2/3	**2f**	81

[a]Alcohol was used as solvent.
[b]Isolated yields.
[c]About 80% of the aldehyde **2** was recovered.

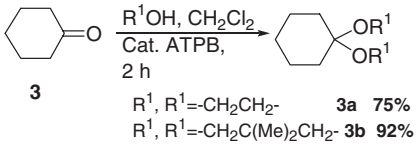
acetals in excellent yields (Entries 2, 6, 8, Table 1). All these reactions completed within 1 h at RT. However, aldehyde **2** reacted sluggishly with isopropanol to afford the corresponding acetal in only about 15% yield. We recovered most of the aldehyde **2** (Entry 4).

ATPB is also effective in the protection of aldehydes with mercaptans. In the presence 0.1 mol equiv. of ATPB, both aldehydes **1** and **2** reacted with ethanethiol (5 mol equiv.) to give the corresponding dithioacetals **1e** and **2e**, respectively in excellent yields (Entries 9 and 10, Table 1). Similarly, both aldehydes **1** and **2** reacted with 1,3-propanedithiol to give the corresponding dithioacetals **1f** and **2f**, respectively in excellent yields (Entries 11 and 12, Table 1; Eq. (1)). All these reactions completed within 1 h at RT. Interestingly, we isolated a small amount of dithiol **1f′** and **2f′** in each of these two reactions (Eq. (1)).



(1)

We wish to investigate the catalytic activity of ATPB in the protection of ketones. We found that when cyclohexanone (**3**) was treated with 3 mol equiv. of ethylene glycol or 2,2-dimethyl-1,3-propanediol in the presence of catalytic amount of ATPB in dichloromethane, the 1,3-dioxane **3a** and 1,3-dioxolane **3b** could be isolated in 75% and 92% yields, respectively (Eq. 2). Under similar reaction conditions, we could not form ketals from α-tetralone (**4**) with either ethylene glycol or 2,2-dimethyl-1,3-propanediol. However, acyclic ketones such as acetophenone (**5**) or 4-phenyl-2-butanone (**6**) reacted with ethylene glycol or 2,2-dimethyl-1,3-propanediol to give less than 20% conversion of the ketals. Attempts to improve the yield of the ketals by increasing the reaction temperature and prolonging the reaction time did not produce the expected results. In general, ATPB might not be a good catalyst in the protection of ketones as ketals. This is indicative of its selectivity in forming acetals from aldehydes.



(2)

PATPB as a Catalyst in the Protection of Aldehyde as Acetal or Thioacetal

A copolymer of styrene and *p*-styryldiphenylphosphine (5:1), containing 2% divinylbenzene (**4**) as cross-linking agent was treated with excess bromoacetone to give polymeric acetonyltriphenylphosphonium bromide (PATPB) in quantitative yield. Each gram of the polymeric phosphonium salt contained ca. 1.88 mmol of phosphine estimated from the elemental analysis.[14] We employed this home-made resin in the present study. Polymer-supported triphenylphosphine (2.6–3.2 mmol/g on polystyrene, 2% crosslinked, 200–400 mesh) is also commercially available.[15] It can also be employed to prepare the corresponding polymeric acetonyltriphenylphosphonium bromide (PATPB).

We tried to find out optimal reaction condition for the acetal formation catalyzed by PATPB. To a solution of 3-phenylpropanal (**1**) (321.6 mg, 2.40 mmol) in 2.4 mL of methanol was added PATPB (127 mg, it is estimated to contain 0.24 mol equiv. of the acetonyltriphenylphosphonium bromide moiety) and the heterogeneous mixture

Table 2. The reaction of aldehyde with alcohol or thiol in the presence of PATPB catalysts at room temperature.

Entry	R^1CHO $R^1=$	PATPB (mol equiv.)	Alcohol	(mol equiv.)	Time (h)	Acetal or thiacetal	Yield[b] (%)
1	$PhCH_2CH_2$– **1**	1/10	MeOH	–[a]	0.25	**1a**	91
2	$PhCH_2CH_2$– **1**	1/30	MeOH	–[a]	1.6	**1a**	90
3	$PhCH_2CH_2$– **1**	1/50	MeOH	–[a]	10	**1a**	90
4	Cyclohexyl **2**	1/50	MeOH	–[a]	24	**2a**	87
5	$PhCH_2CH_2$– **1**	1/20	i-PrOH	–[a]	48	**1b**	82
6	$PhCH_2CH_2$– **1**	1/50	$HO(CH_2)_2OH$	5	48	**1c**	84
7	Cyclohexyl **2**	1/50	$HO(CH_2)_2OH$	5	48	**2c**	73
8	$PhCH_2CH_2$– **1**	1/50	$HO(CH_2)_3OH$	5	24	**1d**	85
9	Cyclohexyl **2**	1/50	$HO(CH_2)_3OH$	5	26	**2d**	78
10	$PhCH_2CH_2$– **1**	1/40	EtSH	3	24	**1e**	70
11	Cyclohexyl **2**	1/40	EtSH	3	24	**2e**	62
12	$PhCH_2CH_2$– **1**	1/40	$HS(CH_2)_2SH$	3	24	**1f**	50
13	Cyclohexyl **2**	1/10	$HS(CH_2)_3SH$	3	24	**2f**	67

[a]Alcohol was used as solvent.
[b]Isolated yields.

was stirred at RT for 15 min to give the dimethylacetal **1a** in 91% yield (Entry 1, Table 2). When the mole ratio of aldehyde to phosphonium bromide moiety on PATPB was changed to 1:30, the reaction took 1.6 h to give the acetal **1a** in 90% yield (Entry 2). When their mole ratio was changed to 1:50, the reaction was complete only after 10 h to give the acetal **1a** in 90% yield (Entry 3). Thus, it is inferred that the mole ratio of aldehyde to phosphonium bromide moiety on PATPB affects the reaction rate significantly, but not on chemical yields. In order to minimize the use of PATPB, we choose the reaction condition of Entry 3 for the further study. In a typical procedure, PATPB (25 mg, 0.05 mol equiv. of the catalytic moiety) was added to a solution of 3-phenylpropanal (**1**) (321.6 mg, 2.40 mmol) in 2.4 mL of methanol and the reaction mixture was stirred at RT. The reaction was complete in 10 h. The reaction mixture was diluted with ethyl acetate (5 mL) followed by filtration through a sintered glass funnel. The filtrate was concentrated to give a practically pure product. In order to get analytically pure product, the crude product was chromatographed on silica gel to give the desired product **1a** (388.8 mg, 2.16 mmol) in 90% yield (Entry 3, Table 2). Using the above procedure, 3-phenylpropanal (**1**) was reacted with isopropanol, ethylene glycol, and 1,3-propanediol, respectively, to give

the corresponding acetals in good yields at room temperature within 48 h (Entries 5, 6, 8, Table 2). Cyclohexanecarboxaldehyde (**2**) reacts with methanol, ethylene glycol, and 1,3-propanediol, respectively, to give the corresponding acetals in good yields (Entries 4, 7, 9, Table 2). All these reactions were found to be complete within 48 h at RT. When the mole ratio of aldehyde to phosphonium bromide moiety on PATPB was changed to 1:40, both aldehydes **1** and **2** reacted with ethanethiol or 1,3-propanedithiol to give the corresponding dithioacetals **1e**, **2e**, **1f**, and **2f**, respectively, in good yields (Entries 10, 11, 12, and 13).

The important feature of this polymer-supported reagent is that the catalyst can be recovered by simple filtration during the work-up. We are able to recover most of the PATPB. The recovered PATPB was washed with benzene followed by drying in vacuo before reusing it. We have tested the reactivity of the recovered PATPB and found that it can be reused at least four times to protect 3-phenylpropanal as dimethyl acetal in excellent yields. However, we did observe a slight decay of its catalytic activity each time. It has been reported that α-bromo ketones undergo debromination with polymer-supported triphenylphosphine in refluxing methanol.[16] Presumably, the corresponding phosphonium bromide might react with methanol under refluxing conditions to give the corresponding debrominated ketone. Our protection reactions were carried out in the presence of alcohols at room temperature. This possible side reaction might occur only in small portion. Therefore, the possible reason of the decrease in reactivity of the PATPB after several times of reuse might be due to the decomposition of the polymer-supported ATPB moiety by the alcohols.

CONCLUSIONS

In summary, ATPB is a useful and economic catalyst to protect aldehydes with methanol, ethylene glycol or 1,3-propanediol as their corresponding acetals in excellent yields in a short reaction time. It is also an effective catalyst to protect aldehydes with ethanethiol, or 1,3-propanedithiol as their corresponding dithioacetals in good yields in short time. ATPB is also an effective catalyst for the protection of cyclohexanone with 1,3-propandiol or 2,2-dimethylpropanediol as their ketals in good yields. However, it is not a good catalyst for the protection of acetophenone, α-tetralone, and 4-phenyl-2-butanone as their ketals. In comparison, PATPB, its polymeric analogue, showed a good reactivity for the protection of aldehydes as their acetals or thioacetals although the

reaction time takes longer. However, it has the advantage in terms of the easy work-up and isolation of the product. Furthermore, PATPB can be recycled and reused several times, thereby making it a convenient catalyst for the protection of aldehydes as acetals or thioacetals.

EXPERIMENTAL

All reactions were carried out under nitrogen. Unless otherwise noted, materials were obtained from commercial suppliers and used without further purification. The ^{1}H and ^{13}C NMR spectra were recorded on a Bruker Avance DPX400 spectrometer, and chemical shifts were given in ppm downfield from tetramethylsilane (TMS). Infrared spectra were taken with a JASCO FT/IR 460 plus spectrophotometer and only noteworthy absorptions were listed. Mass spectra were measured on a VG Trio-2000GC/MS spectrometer by electronic impact at 70 eV (unless otherwise indicated). High Resolution Mass Spectroscopy (HRMS) was measured on a Finnigan/Thermo Quest MAT 95XL (National Chung Hsing University) or VG-11-250J Mass Spectrometer (National Chia-Tung University). The acetonyltriphenyl-phosphonium bromide (ATPB) was prepared by the reaction of bromoacetone with triphenylphosphine according to the literature procedure.[11–13] The poly-*p*-styryldiphenyl-acetonylphosphonium bromide (PATPB) was prepared by the reaction of bromoacetone with the copolymer of *p*-styryldiphenlyphosphine, styrene, and *p*-divinylbenzene according to our previous report.[14]

General procedure of the protection of aldehyde with alcohol in the presence of ATPB. To a solution of 3-phenylpropanal (**1**) (287 mg, 2.14 mmol) in 2 mL of methanol was added ATPB (85 mg, 0.21 mmol) and the solution was stirred at RT. The reaction was complete in 20 min. The solution was concentrated and the residue was chromatographed on silica gel to give the desired product **1a** (358.8 mg, 1.99 mmol) in 93% yield.

General procedure of the protection of aldehyde with diol in the presence of ATPB. To a solution of 3-phenylpropanal (**1**) (314 mg, 2.34 mmol) and ethylene glycol (160 mg, 2.58 mmol) in 2 mL of CH_2Cl_2 was added ATPB (92 mg, 0.23 mmol) and the solution was stirred at RT. The reaction was complete in 45 min, after which the solution was concentrated and chromatographed on silica gel to give the desired product **1c** (383.4 mg, 2.16 mmol) in 92% yield.

General procedure of the protection of aldehyde with thiol in the presence of ATPB. To a solution of 3-phenylpropanal (**1**) (278 mg, 2.07 mmol) and ethanethiol (270 mg, 4.36 mmol) in 2 mL of CH_2Cl_2

was added ATPB (83 mg, 0.21 mmol) and the solution was stirred at RT. The reaction was complete in 30 min. Then the solution was concentrated in well-ventilated fuming hood and chromatographed on silica gel to give the desired product **1e** (447.3 mg, 1.86 mmol) in 90% yield.

General procedure of the protection of aldehydes with alcohol in the presence of PATPB. To a solution of 3-phenylpropanal (**1**) (321.6 mg, 2.40 mmol) in 2.4 mL of methanol was added PATPB (25 mg, it is estimated to be 0.05 mol equiv. of the catalytic moiety) and the heterogeneous mixture was stirred at RT. The reaction was complete in 10 h. Then the reaction mixture was diluted with ethyl acetate and filtered through a sintered glass funnel. The solution was concentrated and the residue chromatographed on silica gel to give the desired product **1a** (388.8 mg, 2.16 mmol) in 93% yield.

General procedure of the protection of aldehydes with diol in the presence of PATPB. To a mixture of 3-phenylpropanal (**1**) (321.6 mg, 2.40 mmol) and ethylene glycol (744.84 mg, 12.0 mmol) was added PATPB (25 mg, 0.05 mol equiv. of the catalytic moiety) and the heterogeneous mixture was stirred at RT. The reaction was complete in 48 h, after which the solution was diluted with ethyl acetate and filtered through a sintered glass funnel. The filtrate was concentrated and chromatographed on silica gel to give the desired product **1c** (358.8 mg, 2.02 mmol) in 84% yield.

General procedure of the protection of aldehydes with thiol in the presence of PATPB. To a mixture of 3-phenylpropanal (**1**) (321.6 mg, 2.40 mmol) and ethanethiol (313.1 mg, 5.04 mmol) in 2.4 mL of CH_2Cl_2 was added PATPB (25 mg, 0.05 mol equiv. of the catalytic moiety). The heterogeneous mixture was stirred at RT and the reaction was complete in 48 h. The reaction mixture was diluted with ethyl acetate and filtered through a sintered glass funnel. The filtrate was concentrated and the residue was chromatographed on silica gel to give the desired product **1e** (518.6 mg, 2.16 mmol) in 90% yield.

General procedure of the protection of aldehyde with dithiol in the presence of PATPB. To a mixture of 3-phenylpropanal (**1**) (321.6 mg, 2.40 mmol) and 1,3-propanedithiol (389.6 mg, 3.60 mmol) in 2.4 mL of CH_2Cl_2 was added PATPB (25 mg, 0.05 mol equiv. of the catalytic moiety). The heterogeneous mixture was stirred at RT and the reaction was complete in 24 h. The reaction mixture was diluted with ethyl acetate and filtered through a sintered glass funnel. The filtrate was concentrated and chromatographed on silica gel to give the desired product **1f** (268.8 mg, 2.16 mmol) in 50% yield.

3-Phenylpropionaldehyde dimethyl acetal (1a).[17] ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.90–1.95 (m, 2H, $PhCH_2C\underline{H}_2$–), 2.67 (dd, $J = 8.2$ and

6.1 Hz, 2H, $PhC\underline{H}_2$–), 3.33 (s, 6H, $-OCH_3$), 4.37 (t, $J = 5.7$ Hz, 1H, $-C\underline{H}(OCH_3)_2$), 7.18–7.28 (m, 5H, Ar-H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 30.8 ($PhCH_2\underline{C}H_2$–), 34.1 ($Ph\underline{C}H_2$–), 52.7 ($-OCH_3$), 103.8 ($-\underline{C}H(OCH_3)_2$), 125.8, 128.4, 141.6 (4°). IR (KBr) 2958, 1604, 1493, 1457, 1383 cm^{-1}. MS *m/z* (relative intensity): 180 (M^+, 4), 148 (89), 91 (100), 75 (96). HRMS calcd. for $C_{11}H_{16}O_2$: 180.1151. Found: 180.1147.

3-Phenylpropionaldehyde diisopropyl acetal (1b).[18] ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.13 (d, $J = 6.1$ Hz, 6H, $-OCH(C\underline{H}_3)_2$), 1.20 (*d*, $J = 6.2$ Hz, 6H, $-OCH(C\underline{H}_3)_2$), 1.90–1.93 (m, 2H, $PhCH_2C\underline{H}_2$–), 2.69 (t, $J = 8.2$ Hz, 2H, $PhC\underline{H}_2$–), 3.83–3.86 (m, 2H, $-OC\underline{H}(CH_3)_2$), 4.55 (1H, $-C\underline{H}(OC_3H_7)_2$), 7.18–7.26 (m, 5H, Ar-H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 22.5, 23.4, 31.0 ($PhCH_2\underline{C}H_2$–), 36.9 ($Ph\underline{C}H_2$–), 67.6 ($-O\underline{C}H(CH_3)_2$), 99.6 ($-\underline{C}H(OC_3H_7)_2$), 125.6, 128.2, 128.3, 142.0 (4°). IR (KBr) 2967, 1461, 1374 cm^{-1}. MS *m/z* (relative intensity): 235 (M^+-1, 0.2), 117 (18), 148 (31), 91 (59), 75 (100). HRMS calcd. for $C_{15}H_{24}O_2$: 236.1777. Found: 236.1770.

2-(2-Phenylethyl)-1,3-dioxolane (1c).[19] ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.03–2.08 (m, 2H, $PhCH_2C\underline{H}_2$–), 2.80–2.84 (m, 2H, $PhC\underline{H}_2$–), 3.88–3.92 (m, 2H, $-OCH_2C\underline{H}_2O$–), 4.02–4.05 (m, 2H, $-OC\underline{H}_2CH_2O$–), 4.96 (t, $J = 4.7$ Hz, 1H, $-C\underline{H}(OCH_2)_2$), 7.24–7.36 (m, 5H, Ar-H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 30.1 ($PhCH_2\underline{C}H_2$–), 35.4 ($Ph\underline{C}H_2$–), 64.8 ($-O\underline{C}H_2$–), 103.7 ($-\underline{C}H(OCH_2)_2$), 125.8, 128.3, 141.5 (4°). IR (KBr) 2949, 2875, 1599, 1493, 1457 cm^{-1}. MS *m/z* (relative intensity): 178 (49), 116 (81), 91 (95), 100 (100). HRMS calcd. for $C_{11}H_{14}O_2$: 178.0994. Found: 178.0994.

2-(2-Phenylethyl)-1,3-dioxane (1d).[20] ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.26–1.31 (m, 1H, $-CH_2CH_2C\underline{H}_2$–), 1.88–1.93 (m, 2H, $PhCH_2C\underline{H}_2$–), 2.04–2.08 (m, 1H, $-CH_2C\underline{H}_2CH_2$–), 2.71 (t, $J = 8.3$ Hz, 2H, $PhC\underline{H}_2$–), 3.67–3.74 (m, 2H, $-OC\underline{H}_2CH_2$–), 4.06–4.10 (m, 2H, $-OC\underline{H}_2CH_2$–) 4.49 (t, $J = 5.2$ Hz, 1H, $-C\underline{H}(OCH_2)_3$), 7.14–7.27 (m, 5H, Ar-H). ^{13}C NMR ($CDCl_3$, 100MHz) δ 25.7 ($-CH_2\underline{C}H_2CH_2$–), 30.0 ($PhCH_2\underline{C}H_2$–), 36.5 ($Ph\underline{C}H_2$–), 66.7 ($-O\underline{C}H_2$–), 101.3 ($-\underline{C}H(OCH_2)_3$), 125.7, 128.2, 128.3, 141.6 (4°). IR (KBr) 2949, 2857, 1604, 1498, 1457, 1383 cm^{-1}. MS *m/z* (relative intensity): 192 (M^+, 55), 133 (69), 114 (76), 86 (100). HRMS calcd. for $C_{12}H_{16}O_2$: 192.1151. Found: 192.1157.

3-Phenylpropanal diethyl thioacetal (1e).[21] ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.22 (t, $J = 7.5$ Hz, 1H, $-SCH_2C\underline{H}_3$), 2.10 (q, $J = 7.8$ Hz, 2H), 2.54–2.88 (m, 8H), 2.85 (t, $J = 7.9$ Hz, 2H), 3.73 (t, $J = 7.1$ Hz, 1H, $-C\underline{H}(SEt)_2$, 7.16–7.26 (m, 5H, Ar-H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 14.4 ($-SCH_2\underline{C}H_3$), 23.9 ($-S\underline{C}H_2CH_3$), 33.3 ($PhCH_2\underline{C}H_2$–), 37.5 ($Ph\underline{C}H_2$–), 50.4 ($-C\underline{H}(SEt)_2$, 125.8, 128.3, 128.4, 141.0 (4°). IR (KBr) 3022, 2921, 1595, 1489, 1452, 1378 cm^{-1}. MS *m/z* (relative intensity): 240

(M^+, 3), 178 (19), 117 (100), 91 (79). HRMS calcd. for $C_{13}H_{20}S_2$: 240.1008. Found: 240.1016.

2-(2-Phenylethyl)-1,3-dithiolane (1f).[22] ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.85–1.88 (m, 1H), 2.04–2.12 (m, 3H), 2.81–2.84 (m, 6H), 3.98 (t, $J = 7.0$ Hz, 1H), 7.17–7.30 (m, 5H, Ar-H). ^{13}C NMR ($CDCl_3$; 100MHz) δ 25.9, 30.1, 32.4, 36.8, 46.4, 125.9, 128.3, 128.4, 140.8 (4°). IR (KBr) 3032, 2930, 1609, 1493, 1420 cm^{-1}. MS m/z (relative intensity): 224 (M^+, 1), 196 (74), 131 (33), 121 (100). HRMS calcd. for $C_{12}H_{16}S_2$: 224.0695. Found: 224.0701.

3-Phenylpropionaldehyde 3-propanethiol thioacetal (1f′). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.38 (t, $J = 8.0$ Hz, 2H), 1.85–1.88 (m, 4H), 2.10–2.12 (m, 2H), 2.60–2.87 (m, 10H), 3.69 (1H, –CH(SR)$_2$), 7.19–7.29 (m, 5H, Ar-H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 23.6, 28.4, 33.2, 33.4, 37.5, 51.2, 126.1, 128.5, 140.8 (4°). IR (KBr) 3022, 2921, 2543, 1604, 1493, 1442 cm^{-1}. MS m/z (relative intensity): 332 (M^+, 50), 225 (25), 117 (100). HRMS calcd. for $C_{15}H_{24}S_4$: 332.0763. Found: 332.0771.

Cyclohexanecarboxaldehyde dimethyl acetal (2a).[17] ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.97–1.23 (m, 5H), 1.58–1.79 (m, 6H), 3.33 (s, 6H, -OCH$_3$), 3.99 (d, $J = 7.2$ Hz, 1H, –C<u>H</u>(OCH$_3$)$_2$). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 25.7, 26.4 28.0, 40.0, 53.5 (1°, –O<u>C</u>H$_3$), 108.5 (3°, –<u>C</u>H(OCH$_3$)$_2$). IR (KBr) 2912, 1452, 1378 cm^{-1}. MS m/z (relative intensity): 158 (M^+, 4), 154 (100), 136 (74), 117 (37).

Cyclohexanecarbaldehyde diisopropyl acetal (2b).[23] ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.93–1.05 (m, 2H), 1.06–1.30 (m, 14H), 1.40–1.52 (m, 1H), 1.58–1.86 (m, 6H), 3.78–3.89 (m, 2H, –OC<u>H</u>(CH$_3$)$_2$), 4.23 (d, $J = 6.1$ Hz, 1H, –C<u>H</u>(OR)$_2$). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 22.6 (1°), 23.4 (1°), 26.0 (2°), 26.5 (2°), 28.2 (2°), 42.2 (3°), 68.0 (3°, –<u>C</u>H(OCH$_3$)$_2$), 103.7 (3°, –<u>C</u>H(OR)$_2$). IR (KBr) 2930, 1456, 1382 cm^{-1}. MS m/z (relative intensity): 117 (M^+−97, 4), 91 (50), 71 (43), 69 (44), 55 (100).

2-Cyclohexyl-1,3-dioxolane (2c).[24] ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.07–1.25 (m, 5H), 1.53–1.80 (m, 6H), 3.81–3.94 (m, 4H, –OCH$_2$CH$_2$O–), 4.59 (d, $J = 5.0$ Hz, 1H, –C<u>H</u>(OCH$_2$)$_2$). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 25.6, 26.3, 27.2, 41.6, 64.8 (2°, –O<u>C</u>H$_2$–), 107.5 (3°, –C<u>H</u>(OCH$_2$)$_2$). IR (KBr) 2921, 1452, 1397, 1272 cm^{-1}. MS m/z (relative intensity): 156 (M^+, 8), 155 (M^+−1, 14), 73 (100). HRMS calcd. for (M^+−H) $C_9H_{15}O_2$: 155.1073. Found: 155.1073.

2-Cyclohexyl-1,3-dioxane (2d).[20] ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.00–1.33 (m, 6H), 1.48–1.49 (m, 1H), 1.63–1.80 (m, 5H), 2.03–2.06 (m, 1H), 3.70–3.76 (m, 2H, –OC<u>H</u>$_2$CH$_2$–), 4.07–4.11 (m, 2H, –OC<u>H</u>$_2$CH$_2$–), 4.23 (d, $J = 5.3$ Hz, 1H, –C<u>H</u>(OCH$_2$)$_3$). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 25.7, 26.0, 26.4, 27.3, 42.5, 66.8 (–O<u>C</u>H$_2$–), 105.3

(–CH(OCH$_2$)$_3$). IR (KBr) 2921, 1452, 1378, 1240 cm^{-1}. MS m/z (relative intensity): 87 (M$^+$−83, 100), 83 (24), 55 (57). HRMS calcd. for $C_{10}H_{18}O_2$: 170.1307. Found: 170.1307.

Cyclohexanecarbaldehyde diethyl thioacetal (2e).[21] ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.18–1.28 (m, 11H), 1.67–1.94 (m, 6H), 2.59–2.70 (m, 4H, –SCH$_2$CH$_3$), 3.65 (d, $J = 5.6$ Hz, 1H, –CH(SEt)$_2$). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 14.6 (–SCH$_2$CH$_3$), 25.7, 26.3, 26.4, 30.7 (2°, –SCH$_2$CH$_3$), 43.4, 58.7 (3°, –CH(SEt)$_2$. IR (KBr) 2912, 1443, 1369, 1254 cm^{-1}. MS m/z (relative intensity): 218 (M$^+$, 28), 157 (84), 95 (100), 75 (75). HRMS calcd. for $C_{11}H_{22}S_2$: 218.1165. Found: 218.1165.

2-Cyclohexyl-1,3-dithioxane (2f).[22] ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.18–1.27 (m, 4H), 1.63–1.90 (m, 7H), 2.08–2.13 (m, 1H), 2.13–2.88 (m, 4H), 4.04 (d, $J = 5.4$ Hz, 1H, –CH(SR)$_2$). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 26.1, 26.2, 26.4, 30.4, 30.9, 43.1, 55.3. IR (KBr) 2921, 2847, 1452, 1268 cm^{-1}. MS m/z (relative intensity): 202 (M$^+$, 25), 119 (100), 107 (100), 95 (8.0). HRMS calcd. for $C_{10}H_{18}S_2$: 202.0851. Found: 202.0849.

Cyclohexanylcarbaldehyde 3-propanethiol thioacetal (2f′). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.27–1.44 (m, 6H), 1.78–1.96 (m, 9H), 2.64–2.82 (m, 10H), 3.64 (d, $J = 5.6$ Hz, 1H, –CH(SR)$_2$). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 23.5, 26.1, 26.2, 29.9, 30.7, 33.2, 43.1, 59.4. IR (KBr) 2921, 2838, 1447, 1347, 1263 cm^{-1}. MS m/z (relative intensity): 309 (M$^+$−1, 4), 203 (28), 107 (100), 95 (48). HRMS calcd. for $C_{13}H_{26}S_4$: 310.0920. Found: 310.0925.

1,4-Dioxaspiro[4.5]decane (3a).[25] ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.39–1.40 (br s, 2H), 1.57–1.60 (br s, 8H), 3.93 (br s, 4H, –O(CH$_2$)$_2$O–). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 23.9 (2°), 25.2 (2°), 35.2 (2°), 64.1 (2°), 109.0 (4°). IR (KBr) 2936, 1447, 1366, 1282, 1162, 1104 cm^{-1}.

3,3-Dimethyl-1,5-dioxaspiro[5.5]undecane (3b).[26] ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.96 (br s, 6H), 1.30–1.60 (m, 6H), 1.70–1.85 (m, 4H), 3.49 (br s, 4H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 22.50 (1°), 22.71 (2°), 25.70 (2°), 30.10 (4°), 32.50 (2°), 69.73 (2°), 97.62 (4°). IR (KBr) 2937, 2858, 1473, 1446, 1393, 1268 cm^{-1}. MS m/z (relative intensity): 309 (M$^+$−1, 4), 203 (28), 107 (100), 95 (48). HRMS calcd. for $C_{11}H_{20}O_2$: 184.1464. Found: 184.1466.

ACKNOWLEDGMENT

We are grateful to the National Science Council, National Chung Cheng University and Academia Sinica, Republic of China for financial support.

REFERENCES

1. (a) Maskens, A.J. Synthesis **1981**, 501; (b) Greene, T.W.; Wuts, P.G. M. *Protective Groups in Organic Synthesis*, 2nd Ed.; John Wiley & Sons, Inc.: New York, 1991; pp. 189–192; (c) Kocienski, P.J. *Protective Groups*; Enders, D., Noyori, R., Trost, B.M., Eds.; Geroge Thieme Verlag: Stutgart, New York, 1994.
2. (a) Patwardhan, S.A.; Dev, S. Synthesis **1974**, 348; (b) Lorette, N.B.; Howard, W.L.; Brown, H.J., Jr. J. Org. Chem. **1959**, *24*, 1731; (c) Dann, A.E.; Davis, J.B.; Nagler, J. J. Chem. Soc., Perkin Trans I **1979**, 158; (d) Perni, R.B. Synth. Commun. **1989**, *19*, 2383–2387.
3. Taylor, E.C.; Chiang, C.S. Synthesis **1977**, 467.
4. Olah, G.A.; Narang, S.C.; Meidar, D.; Salem, G.F. Synthesis **1981**, 282.
5. Kamitori, Y.; Hojo, M.; Masuda, R.; Kimura, J.; Yoshida, T. J. Org. Chem. **1986**, *51*, 1427–1431.
6. Kumar, P.; Reddy, R.S.; Singh, A.P.; Pandey, B. Tetrahedron Lett. **1992**, *33*, 825–826.
7. Ponde, D.E.; Deshpande, V.H.; Bulbule, V.J.; Sudalai, A.; Gajare, A.S. J. Org. Chem. **1998**, *63*, 1058.
8. Corey, E.J.; Shimoji, K. Tetrahedron Lett. **1983**, *24*, 169–172.
9. Villemin, D.; Labiad, B.; Hammadi, M. Chem. Commun. **1992**, 1192–1193.
10. Tateiwa, J.; Horiuchi, H.; Uemura, S. J. Org. Chem. **1995**, *60*, 4039–4043.
11. Hon, Y.S.; Lee, C.F. Tetrahedron Lett. **1999**, *40*, 2389–2392.
12. Hon, Y.S.; Lee, C.F. Tetrahedron **2001**, *57*, 6181–6188.
13. Ramirez, F.; Dershowitz, S. J. Org. Chem. **1957**, *22*, 41.
14. Hon, Y.S.; Lee, C.F.; Chen, R.J.; Szu, P.H. Tetrahedron **2001**, *57*, 5991–6001.
15. It is also available from Lancaster Synthesis Ltd.: Product Number 19478.
16. (a) Borowitz, I.J.; Grossmann, L.I. Tetrahedron Lett. **1962**, *11*, 471; (b) Borowitz, I.J.; Virhaus, R. J. Am. Chem. Soc. **1963**, *85*, 2183; (c) Chopard, P.A.; Hudson, R.F.; Klopman, G. J. Chem. Soc. **1965**, 1379; (d) Dhuru, S.P.; Padiya, K.J.; Salunkhe, M.M. J. Chem. Research (S) **1998**, 56.
17. (a) Hayashi, M.; Inubushi, A.; Mukaiyama, T. Bull. Chem. Soc. Jpn. **1988**, *61*, 4037–4042; (b) Hon, Y.S.; Lee, C.F. Tetrahedron **2001**, *57*, 6181–6188.
18. Ishida, A.; Mukaiyama, T. Bull. Chem. Soc. Jpn. **1977**, *50*, 1161–1168.

19. Torok, D.S.; Figueroa, J.J.; Scott, W. J. J. Org. Chem. **1993**, *58*, 7274–7276.
20. Lee, Y.S.; Valle, Luis del; Larson, G.L. Synth. Commun. **1987**, *17*, 385–392.
21. Chandrasekhar, S.; Takhi, M.; Reddy, Y.R.; Mohapatra, S.; Rao, C.R.; Reddy, K.V. Tetrahedron **1997**, *53*, 14997–15004.
22. Hon, Y.S.; Sheu, T.R.; Lee, C.F. Synth. Commun. **2000**, *30*, 97–118.
23. Ishida, A.; Mukaiyama, T. Bull. Chem. Soc. Jpn. **1977**, *50*, 1161–1168.
24. Torok, D.S.; Figueroa, J.J.; Scott, W.J. J. Org. Chem. **1993**, *58*, 7274–7276.
25. Wang, W.B.; Shi, L.L.; Huang, Y.Z. Tetrahedron **1990**, *46*, 3315–3320.
26. Lee, S.B.; Lee, S.D.; Takata, T.; Endo, T. Synthesis **1991**, 368–370.

Received in Japan November 20, 2002