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Tetrahedron Letters 48 (2007) 7706–7708

Tetrahedron Letters

An efficient and chemoselective deprotection of aryl- and styrenyldithioketals (acetals)

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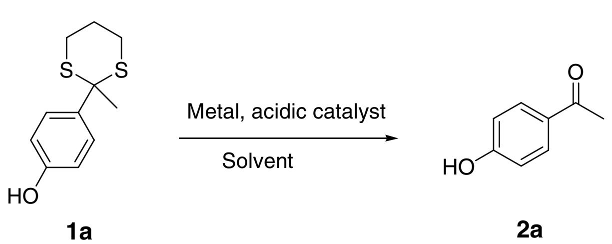
Received 21 May 2007; revised 6 August 2007; accepted 14 August 2007
Available online 19 August 2007

Abstract—In this Letter, an efficient and chemoselective deprotection of aryl- and styrenyldithioketals (acetals) is described. After being carefully examined, 10% Pd/C and Amberlite 120 in refluxing methanol was found to be an excellent condition for the chemoselective deprotection of aryl- and styrenyldithioketals (acetals) in good yields. Under this condition, no deprotection and no reduction of alkyldithioketals (acetals) was observed.

Dithioketals (acetals), while treated with sodium hydride or *n*-butyl lithium, as a carbanion source[1] or as protecting group for ketones and aldehydes have been widely employed in organic synthesis.[2] The deprotection of dithioketals (acetals) to corresponding ketones (aldehydes) also played an important role in organic synthesis.[3] Researches concerning about deprotecting of dithioketals (acetals) were variously documented in the literatures. For example, metal salts like silver(I) salt,[4] copper salt,[5] mercuric(II) salt;[6] and so on[7] were reported for deprotecting purposes. Up to date chemoselective deprotection of aryldithioketals and allyldithioketals is paid little attention. Only few procedures such as $Tl(NO_3)_2{\cdot}3H_2O$,[8a] *tert*-butyl hydroperoxide (TBHP),[8b] and *o*-iodoxybenzoic acid (IBX) in DMSO[9] as reagents were employed to unmask aryldithioketals and allyldithioketals with selectivity. However, some disadvantages, such as low yield, toxicity to earth, and tedious work-up procedures, commonly existed in those reported methods. For chemistry interesting, herein, we like to disclose an easy, efficient and chemoselective deprotection method for aryl-, and styrenyldithioketals (acetals), which has no effect on alkyldithioketals (acetals). Various metals like Pd–C, Pt–C, and Ni powder; catalytic acids like acetic acid, toluenesulfonic acid, BF_3·etherate, and Amberlite IR-120; solvents like methanol, ethanol, dioxane, and THF are, respectively, examined for this study. The deprotection of *p*-hydroxyacetophenone-1,3-dithiane used as model reaction toward various conditions was investigated (Scheme 1). The results are compiled in Table 1.

From the results obtained in Table 1, the condition of 10% Pd–C and $TsOH{\cdot}H_2O$ in refluxing methanol is the best one from the evaluation of percentage yield and reaction time. However, from the environmental concern, instead of 10% Pd/C and $TsOH{\cdot}H_2O$, the condition of 10% Pd/C and Amberlite IR-120 which has good deprotection results, is environmentally friendly and



Scheme 1.

Keywords: Deprotection; Aryldithioketals; Palladium on charcoal; Amberlite IR-120.

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doi:10.1016/j.tetlet.2007.08.054

Table 1. The results obtained from the deprotection of **1a** (0.17 mmol) with various conditions

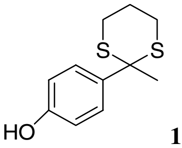
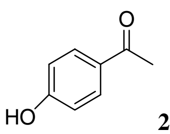
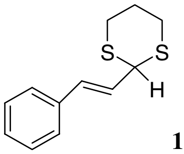
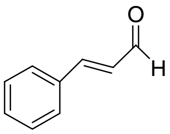
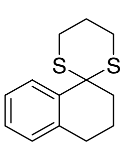
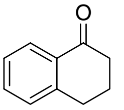
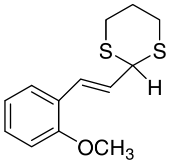
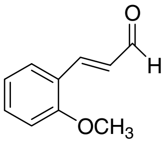
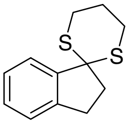
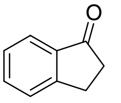
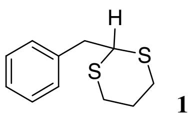
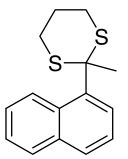
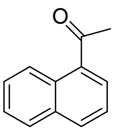
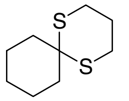
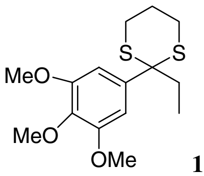
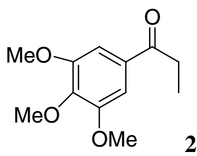
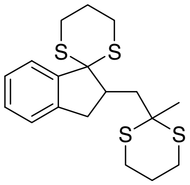
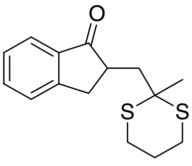
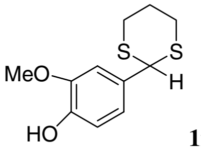
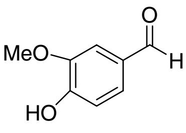
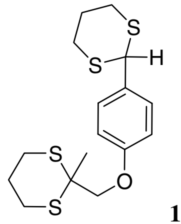
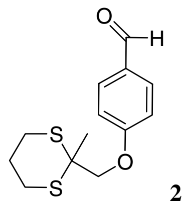
Entry	Metal[a]	Catalyst[b]	Solvent[c]	Reaction temperature	Reaction time (h)	Yield (%)
1	10% Pd–C	$TsOH{\cdot}H_2O$	Dioxane	Reflux	6	89
			EtOH	Reflux	7	90
			MeOH	Reflux	4	92
			THF	Reflux	39	82
		Amberlite IR-120	MeOH	Reflux	8	88
		HOAc			8	88
		$BF_3{\cdot}$ether	MeOH	Reflux	23	81
			MeOH	Reflux	12	84
2	10% Pt–C	$TsOH{\cdot}H_2O$	MeOH	Reflux	144	72
3	Ni	Amberlite IR-120	MeOH	Reflux	36	60

[a] The amount of metals used in this study is 180 mg for 10% Pd–C, 200 mg for 10% Pt–C, and 900 mg for Ni powder, respectively.

[b] The amount of acid for this study is 16 mg (0.084 mmol) for $TsOH{\cdot}H_2O$, 200 mg for Amberlite, 5.04 mg for HOAc, and five drops for $BF_3{\cdot}$ether.

[c] 8 mL for each solvent was used.

Table 2. The deprotection of 1,3-dithiaketals and 1,3-dithiaacetals by 10% Pd–C and Amberlite IR-120 in refluxing methanol[10]

Substrate[a]	Product	Time (h)	Yield (%)	Substrate[a]	Product	Time (h)	Yield (%)
 **1a**	 **2a**	8	88	 **1g**	 **2g**	36	74
 **1b**	 **2b**	5	87	 **1h**	 **2h**	30	70
 **1c**	 **2c**	5	86	 **1i**	Recovery of **1i**	48	0
 **1d**	 **2d**	18	81	 **1j**	Recovery of **1j**	48	0
 **1e**	 **2e**	32	75	 **1k**	 **2k**	6	72
 **1f**	 **2f**	8	86	 **1l**	 **2l**	8	73

[a] Each 1,3-dithiane, prepared from corresponding ketone (acetal) and 1,3-propanedithiol in the presence of $BF_3{\cdot}$etherate in CH_3Cl at 0 °C,[11c] has a satisfactory spectral data.[11]

can be recovered by simple filtration was chosen for this deprotection of aryl- and styrenyldithioketals (acetals) studies. Based on this reaction condition, various 1,3-dithiaketals and 1,3-dithiaacetals for deprotection were examined, and the results were compiled in Table 2.

From the results of Table 2, 1-aryl-1,3-dithianes (**1a**–**f**) and 2-styryl-1,3-dithianes (**1g**,**h**) can be deprotected to regenerate the corresponding aldehydes and ketones in 70–88% yields. On the other hand, 1-alkyl-1,3-dithianes (**1i**,**j**), which cannot be deprotected even after 48 h refluxing were observed. In addition, compounds (**1k** and **1l**), in which 1-aryl and 1-alkyl-1,3-dithianes co-existed in the same molecules, are subjected to chemoselective deprotection to give **2k** and **2l** in 72–73% yields, respectively. In conclusion, Amberlite IR-120 and 10% Pd–C in refluxing methanol, which is a new, simple, mild, and efficient procedure for the chemoselective deprotection of aryl-, and styrenyldithioketals (acetals) in yields of 70–88%, but has no effect to alkyldithioketals (acetals) are established.

Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2007.08.054.

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10. General procedure for the deprotection of compound **1a**–**l** to generate compound **2a**–**l**: **1a**–**l** (0.17 mmol) dissolved in methanol (8 mL) were subsequently added 10% Pd–C (180 mg) and Amberlite IR-120 (200 mg). The resulting mixture was stirred and heated to the reflux until the consumption of starting material, which was monitored by TLC. Then, the mixture was added with ethyl acetate (150 mL) and stirred for few hour. Then, the given mixture was filtered through Celite to remove Pd–C and Amberlite. The filtrate was concentrated in vacuo to give compound **2a**–**l**, respectively. The selected examples, **2k** (34 mg, 72%) was obtained as colorless oil, IR ν cm^{-1} (liquid) 3030, 2909, 1701(C$=$O), 1601, 1455, 1365, 1324, 1273, 759, 732; ^{1}H NMR (CDCl$_3$, 200 MHz) δ 1.63 (3H, s, CH$_3$), 1.82 (1H, dd, $J = 14.4$, 8.8 Hz, Ha-8), 1.82–2.09 (3H, m, Hb-8, H-2′), 2.72–3.12 (6H, m, H-2, Ha-3, H-1′, H-3′), 3.53 (1 H, dd, $J = 18.3$, 9.3 Hz, Hb-3), 7.35 (1 H, dd, $J = 7.2$, 6.9 Hz, H-5), 7.43 (1H, dd, $J = 6.9$, 1.0 Hz, H-4), 7.57 (1H, ddd, $J = 7.4$, 7.2, 1.0 Hz, H-6), 7.75 (1H, d, $J = 7.4$ Hz, H-7); EI-MS m/z (70 eV) 278 (M$^+$, 9), 204 (17), 172 (17), 161 (7), 145 (27), 133 (100), 115 (18), 91 (11), 74 (23), 59 (50).
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