Pergamon

Tetrahedron Letters, Vol. 38, No. 15, pp. 2623-2624, 1997

0040-4039/97 $17.00 + 0.00

PII: S0040-4039(97)00445-0

Solid State Dethioacetalization Using Clayfen

Rajender S. Varma* and Rajesh K. Saini

Department of Chemistry and Texas Regional Institute for Environmental Studies (TRIES),
Sam Houston State University, Huntsville, TX 77341-2117, U.S.A.

Abstract: Thio acetals and ketals derived from aldehydes and ketones are readily deprotected by clayfen within seconds under solvent-free conditions. This rapid and environmentally benign method avoids the use of excess solvents and toxic oxidants usually employed in the dethioacetalization process.

Thio acetals and ketals are useful protecting groups which are routinely used in organic synthesis.[1] However the regeneration of carbonyl compounds from the corresponding thioacetals is a demanding task[2] because of the stability of these thio acetals and ketals in acidic and basic conditions. There are several processes known for the deprotection of thioacetals[3] which involve the use of toxic heavy metals such as Hg^{+2}, Ag^{+2}, Ti^{+4}, Cd^{+2} or Tl^{+3} or reagents such as benzeneseleninic anhydride.[4] Consequently, there is a need for development of newer methods which proceed under mild and environmentally benign conditions such as described recently using visible light.[5] However, alternatives utilizing photolytic[6] or electrochemical[7] techniques require expensive equipment and are not amenable to upscaling of the processes. The use of inexpensive supported reagents[8,9] appear to be an attractive option because of the selectivity and the ease of manipulation. In this context, clay-supported reagents have found widespread utility in a variety of heterogeneous reactions.[10,11] Lately, solid state organic reactions in ground state have been gaining importance.[12]

In continuation of our ongoing program to develop environmentally benign synthetic methods using solid supports and microwave activation,[13] we wish to report here a facile cleavage of thioacetals to carbonyl compounds using montmorillonite K10 clay-supported iron(III) nitrate (clayfen)[10,11] in solid state. The reaction presumably proceeds *via* the intermediacy of nitrosonium ions[10b] and no side products are formed during the deprotection reaction. The only exception being the substrates bearing free phenolic moieties where ring nitration competes e.g. the dithiolane derivative of vanillin results in the formation of 4-nitrovanillin. Consequently, the protection of phenolic groups may be required while using this method. 4-Methoxybenzaldehyde (entry 7) is regenerated rapidly in an experimental procedure that involves a simple mixing with clayfen. In some cases, a slight warming is required and we find the use of microwave irradiation[13-15] very convenient since no stirring is required. This extremely rapid, inexpensive and manipulatively simple protocol avoids the use of excess solvents and toxic oxidants and no further oxidation of ensuing carbonyl compounds is observed. Earlier use of clayfen, under heterogeneous conditions that employs a large excess of hydrocarbon solvents, requires 3-6 hours for dethioacetalization.[11] Our results for a variety of acetals and ketals are summarized in the **Table**.

Dethioacetalization of *p*-nitrobenzaldehyde dithiolane is representative of the general procedure employed: Clayfen (1.13 g, 1.2 mmol of iron(III) nitrate) is thoroughly mixed with neat thioacetal (0.227 g, 1 mmol) in the solid state. The material is transferred in a test tube and placed in an alumina bath inside the microwave oven and irradiated (40 Sec.).[14] Upon completion of the reaction, monitored on TLC (hexane:EtOAc, 8:2, v/v), the product was extracted into methylene chloride. The resulting solution is passed through a small bed of neutral alumina. Evaporation of the solvent delivers pure *p*-nitrobenzaldehyde in 97% yield. In the case of cyclic thio acetals and ketals, the liberated dithiols bind to the clay surface rather tightly and a simple washing of the clayfen affords clean products. However, for monofunctional thiol derivatives (entry 5), the thiol impurities are easily removed from the crude product by a simple washing with hexane to give pure carbonyl compounds.

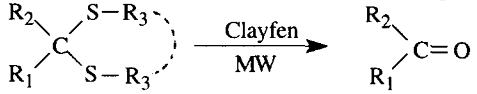
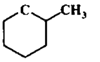
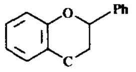


Table. Dethioacetalization of aldehydes and ketones using clayfen

Entry	R_1	R_2	R_3---R_3	Time[a] (Sec)	Yield[b] (%)
1	C_6H_5	H	-$(CH_2)_2$-	RT	95
2	*p*-NO_2-C_6H_4	H	-$(CH_2)_2$-	40	97
3	*p*-NO_2-C_6H_4	H	-$(CH_2)_3$-	RT	98
4	C_6H_5	CH_3	-$(CH_2)_2$-	RT	97
5	C_6H_5	C_6H_5	Et Et	RT	92
6	C_2H_5	C_2H_5	-$(CH_2)_2$-	RT	87
7	*p*-MeO-C_6H_4	H	-$(CH_2)_2$-	RT	97
8			-$(CH_2)_2$-	RT	94
9			-$(CH_2)_3$-	20	90

[a] RT refers to reactions that are completed on simple mixing of the substrates with clayfen at room temperature.

[b] Unoptimized yields of isolated products that exhibited physical and spectral properties in accord with the assigned structures.

In conclusion, clayfen-mediated solvent-free mixing is a convenient and environmentally benign protocol for dethioacetalization when compared to the conventional solution phase or heterogeneous reactions.

Acknowledgment: We are grateful for financial support to the Texas Advanced Research Program (ARP) in chemistry (Grant # 0036060-023) and TRIES under contract from Office of Naval Research/SERDP (Grant # N00014-96-1-1067).

REFERENCES AND NOTES

1. (a) Page, P.C.B.; Niel, M.B.V.; Prodger, J.C. *Tetrahedron* **1989**, *45*, 7643; (b) Grobel, B.-T.; Seebach, D. *Synthesis* **1977**, 357 and references cited therein.
2. (a) Cristau, H.-J.; Chabaud, B.; Labaudiniere, R.; Christol, H. *Synth. Commun.* **1981**, *11*, 423; (b) Olah, G.A.; Mehrotra, A.K.; Narang, S.C. *Synthesis* **1982**, 151; (c) Lucchetti, J.; Krief, A. *Synth. Commun.* **1983**, *13*, 1153.
3. Greene, T.W.; Wuts, P.G.M. *Protective Groups in Organic Synthesis*, John Wiley, New York, **1991**, p 201 references therein.
4. Barton, D.H.R.; Cussans, N.J.; Ley, S.V. *J. Chem. Soc., Chem. Commun.* **1977**, 751.
5. Epling, G.A.; Wang, Q. *Tetrahedron Lett.* **1992**, *33*, 5909.
6. (a) Hoshino, O.; Sawaki, S.; Umezawa, B. *Chem. Pharm. Bull.* **1979**, *27*, 538; (b) Takahashi, T.T.; Nakamura, C.Y.; Satoh, J.Y. *J. Chem. Soc., Chem. Commun.* **1977**, 680.
7. (a) Porter, Q.N.; Utley, J.H.P.; Machion, P.D.; Pardini, V.L.; Schumacher, P.R.; Viertler, H. *J. Chem. Soc., Perkin. Trans. -1* **1984**, 973; (b) Platen, M.; Steckhan, E. *Chem. Ber.* **1984**, *117*, 1679.
8. McKillop, A.; Young, D.W. *Synthesis* **1979**, 401 and 481.
9. Posner, G.H. *Angew. Chem.* **1978**, *90*, 527; *Angew. Chem. Int. Ed. Engl.* **1978**, *17*, 487.
10. (a) Delaude, L.; Laszlo, P. *J. Org. Chem.* **1996**, *61*, 6360; (b) Cornelis, A.; Laszlo, P. *Synthesis* **1985**, 909; (c) Balogh, M.; Laszlo, P. *Organic Chemistry Using Clays*, Springer-Verlag, Berlin, **1993**.
11. Balogh, M.; Cornelis, A.; Laszlo, P. *Tetrahedron Lett.* **1984**, *25*, 3313.
12. (a) Toda, F. *Synlett.* **1993**, 303; (b) Toda, F. *Acc. Chem. Res.* **1995**, *28*, 480.
13. (a) Varma, R.S.; Dahiya, R. *Tetrahedron Lett.* **1997**, *38*, in press; (b) Varma, R.S.; Dahiya, R.; Kumar, S. *Tetrahedron Lett.* **1997**, *38*, in press; (c) Varma, R.S.; Chatterjee, A.K.; Varma, M. *Tetrahedron Lett.* **1993**, *34*, 3207; (d) Varma, R.S.; Chatterjee, A.K.; Varma, M. *Tetrahedron Lett.* **1993**, *34*, 4603; (e) Varma, R.S.; Varma, M.; Chatterjee, A.K. *J. Chem. Soc., Perkin. Trans. -1* **1993**, 999; (f) Varma, R.S.; Lamture, J.B.; Varma, M. *Tetrahedron Lett.* **1993**, *34*, 3029.
14. For a critical evaluation of activation process by microwaves see: Raner, K.D.; Strauss, C.R.; Vyskoc, F.; Mokbel, L. *J. Org. Chem.* **1993**, *58*, 950. The temperature of the alumina bath (heat sink) inside a Sears Kenmore microwave oven equipped with a turntable at full power (900 Watts) found to be ~80 °C after 40 seconds of irradiation.
15. For recent reviews on microwave-assisted chemical reactions, see (a) Abramovich, R.A. *Org. Prep. Proced. Int.* **1991**, *23*, 683; (b) Whittaker, A.G.; Mingos, D.M.P. *J. Microwave Power Electromagn. Energy* **1994**, *29*, 195; (c) Majetich, G.; Hicks, R. *J. Microwave Power Electromagn. Energy* **1995**, *30*, 27; (d) Caddick, S. *Tetrahedron* **1995**, *51*, 10403; (e) Bose, A.K.; Jayaraman, M.; Okawa, A.; Bari, S.S.; Robb, E.W.; Manhas, M.S. *Tetrahedron Lett.* **1996**, *37*, 6989 and references therein.

(*Received in USA* 3 *February* 1997; *accepted* 24 *February* 1997)