Montmorillonite K-10 Clay as an Efficient Solid Catalyst for Chemoselective Protection of Carbonyl Compounds as Oxathiolanes with 2-Mercaptoethanol

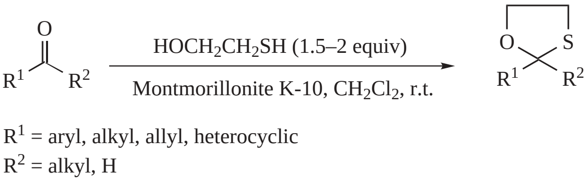
Siddhartha Gogoi, Jagat C. Borah, Nabin C. Barua*
Natural Products Chemistry Division, Regional Research Laboratory (CSIR), Jorhat-785006, Assam, India
Fax +91(376)2370011; E-mail: ncbarua2000@yahoo.co.in

Received 9 March 2004

Abstract: Montmorillonite K-10 clay has been found to be a mild and efficient solid catalyst for the protection of a variety of carbonyl compounds, such as oxathiolanes, with 2-mercaptoethanol in good to excellent yields. In addition, by using this catalyst, high chemoselective protection of aldehydes in presence of ketones has been achieved.

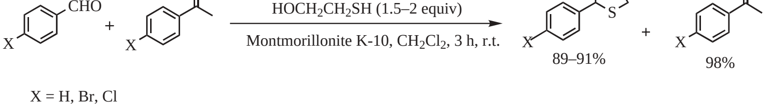
Key words: carbonyl compounds, 2-mercaptoethanol, montmorillonite K-10, chemoselective, oxathiolanes

The protection-deprotection sequence is probably the most recurrent functional group interconversion in multistep organic synthesis. Amongst the numerous protecting groups employed to protect aldehydes and ketones from nucleophilic attack, 1,3-oxathioacetals have long been used as a protective group[1] and an acyl anion[2] equivalent in C-C bond forming reactions.[3] Moreover, the use of oxathiolanes is much more convenient than the corresponding O,O-acetals or S,S-acetals because they are comparatively more stable than O,O-acetals under acidic conditions and easier to remove than the corresponding S,S-acetals. On the other hand, Eliel[4] and the others[5] have clearly established the use of chiral 1,3-oxathioacetals as chiral auxiliaries for the enantioselective synthesis of α-hydroxy acids and glycols in organic synthesis. In the literature there are several methods reported for the preparation of oxathiolanes from carbonyl compounds employing acid catalysts such as dry hydrogen chloride or HCl,[6] $HClO_4$,[7] refluxing with TsOH,[8] $BF_3{\cdot}OEt_2$,[9] Bu_4NBr_3,[10] TMSOTf,[11] i-Pr_3SiOTf,[12] SO_2,[13] $ZrCl_4$,[14] $ZnCl_2$–Na_2SO_4,[15] ion-exchange resins[16] and $Sc(OTf)_3$[17] as catalyst or as stoichiometric reagents. Unfortunately, most of the reported procedures have certain drawbacks such as long reaction times,[14] low yields of the products,[10] refluxing of the reaction mixture, formation of unwanted side products, use of expensive reagents and tedious work up procedure. Therefore, the developments in this area demand further searches for better catalysts that are superior to the existing ones especially with regard to toxicity and selectivity. In recent years, there has been a tremendous upsurge of interest in the use of different clays as heterogeneous and environment friendly catalysts for different organic transformations. In this context, we have developed a mild and efficient method for the protection of aldehydes and ketones with 2-mercaptoethanol in the presence of montmorillonite K-10 clay. Due to strong catalytic activity as Brønsted acid, montmorillonite K-10 clay has been most frequently used in fine organic synthesis. Although montmorillonite K-10 has been used extensively as a catalyst for the protection of carbonyl and hydroxyl groups with trimethylorthoformate[18] and 3,4-dihydro-2*H*-pyran,[19] as a Lewis acid in aldol condensation,[20] Diels–Alder[21] and Friedel–Crafts reaction,[22] a literature search clearly shows that there has been no investigation into the protection of carbonyl groups with 2-mercaptoethanol in the presence of this clay. Herein we report a mild and efficient method for the 1,3-oxathioacetalization of carbonyl compounds in good to high yields as well as the chemoselective protection of various aldehydes in the presence of ketones by using montmorillonite K-10 clay in CH_2Cl_2 at room temperature (Scheme 1).



Scheme 1

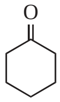
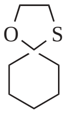
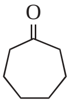
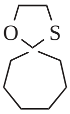
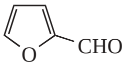
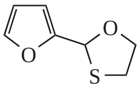
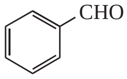
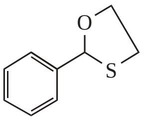
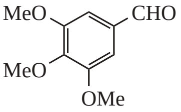
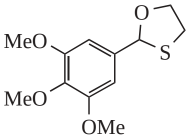
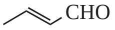
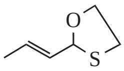
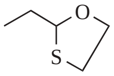
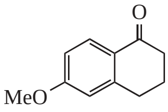
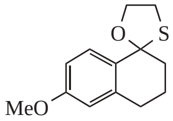
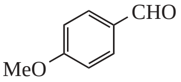
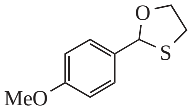
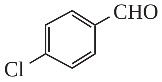
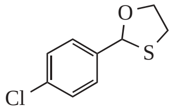
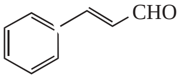
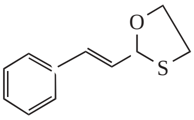
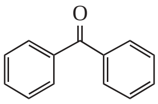
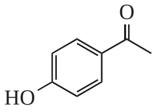
As shown in Table 1,[23] various types of aliphatic, aromatic and heterocyclic aldehydes are efficiently and rapidly converted to their corresponding 1,3-oxathiolanes in the presence of 2-mercaptoethanol (1.5–2 equiv) under the influence of montmorillonite K-10 (two times the mass of the substrate) at room temperature. It has been observed that in the case of both activated and weakly activated ar-



Scheme 2

SYNLETT 2004, No. 9, pp 1592–1594
Advanced online publication: 29.06.2004
DOI: 10.1055/s-2004-829054; Art ID: G07304ST

Table 1 Montmorillonite K-10 Catalyzed Preparation of 1,3-Oxathiolanes

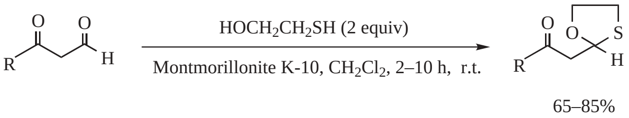
Entry	Substrates	Products[a]	Reaction time (h)	Yields (%)[b]
1			1	90
2			1	85
3			2	82
4			0.5	86
5			1.5	88
6			3	70
7			3.5	73
8			4	69
9			2	89
10			1.5	91
11			1.5	89
12		No reaction	5	–
13		No reaction	5	–

[a] All products were characterized by ^{1}H NMR, IR and mass spectroscopy.

[b] Isolated yields after purification by thin layer chromatography on silica gel.

omatic aldehydes, the yields of the products (entries 4, 5 and 10) were slightly higher than the recent protocols.[7,10] Aliphatic ketones also react efficiently to produce the corresponding oxathiolanes (entries 1, 2 and 7) in good yields. It is interesting to note that aromatic ketones did not produce the corresponding oxathiolanes under the same reaction conditions. This result indicates that the present protocol is potentially applicable for the chemoselective protection of aldehydes in the presence of ketones in multi-functional compounds. With this objective, as a representative example we have conducted some competitive protection reactions with equimolar mixtures of aldehydes and ketones (Scheme 2). It was observed that in this mixture, only aldehydes formed the oxathiolanes and ketones were almost completely recovered.

This experiment has also been extended for the intramolecular chemoselectivity between keto and aldehyde functionalities in β-ketoaldehydes (Scheme 3). It was observed that deactivated aromatic β-ketoaldehydes such as β-ketoaldehyde of p-NO$_2$-benzene when subjected to the same reaction conditions, could be converted to oxathiolanes selectively at aldehyde position after long reaction time (9–10 h) and in moderate yield (65–75%). The aldehyde group of benzylic β-ketoaldehyde also formed oxathiolane selectively in good yield (85%).



R = p-ClC$_6$H$_5$-, p-CH$_3$OC$_6$H$_5$-, CH$_3$C$_6$H$_5$-, 2-thiophene, 2-furan, C$_6$H$_5$-, PhCH$_2$-, p-NO$_2$C$_6$H$_5$-

Scheme 3 Chemoselective protection of aldehyde functionalities using clay

In conclusion, we have developed a mild and efficient method for the protection of aliphatic, heterocyclic and aromatic aldehydes as well as aliphatic ketones as the corresponding oxathiolane derivatives with 2-mercaptoethanol by using montmorillonite K-10 clay in good to excellent yields. Moreover the demonstration of the chemoselectivity between the keto and aldehyde groups makes the present method an efficient method for oxathioacetalization.

Acknowledgment

The authors gratefully acknowledge the Director, Regional Research Laboratory (CSIR), Jorhat, Assam, India for providing facilities for this work. SG thanks CSIR, New Delhi for the award of Junior Research Fellowship.

References

(1) Greene, T. W.; Wuts, P. G. M. *Protective Groups in Organic Synthesis*, 3rd ed.; Wiley: New York, **1999**, Chap. 4.

(2) (a) Lynch, J. E.; Eliel, E. L. *J. Am. Chem.Soc.* **1984**, *106*, 2943. (b) Utimoto, K.; Nakamura, A.; Molsubara, S. *J. Am. Chem. Soc.* **1990**, *112*, 8189.

(3) (a) Fuji, K.; Ueda, M.; Fujita, E. *J. Chem. Soc., Chem. Commun.* **1977**, 814. (b) Fuji, K.; Ueda, M.; Sumi, K.; Kajiwara, K.; Fujita, E.; Jwashita, T.; Miura, I. *J. Org. Chem.* **1985**, *50*, 657. (c) Fuji, K.; Ueda, M.; Fujita, E. *J. Chem. Soc., Chem. Commun.* **1983**, 49.

(4) Frye, S. V.; Eliel, E. L. *Tetrahedron Lett.* **1985**, *26*, 3907.

(5) Isobe, M.; Obeyama, J.; Funabashi, Y.; Goto, T. *Tetrahedron Lett.* **1988**, *29*, 4773.

(6) Ralls, J. W.; Dodson, R. M.; Riegel, B. *J. Am. Chem. Soc.* **1949**, *71*, 3320.

(7) Mondal, E.; Sahu, P. R.; Khan, A. T. *Synlett* **2002**, 463.

(8) Djerssi, C.; Gorman, M. *J. Am. Chem. Soc.* **1953**, *75*, 3704.

(9) Wilson, G. E. Jr.; Huang, H. G.; Schloman, W. W. Jr. *J. Org. Chem.* **1968**, *33*, 2133.

(10) Mondal, E.; Sahu, P. R.; Bose, G.; Khan, A. T. *Tetrahedron Lett.* **2002**, *43*, 2843.

(11) Ravidranathan, T.; Chavan, S. P.; Dantale, W. *Tedrahedron Lett.* **1995**, *36*, 2285.

(12) Streinz, L.; Koutek, B.; Saman, D. *Coll. Czech. Chem. Commun.* **1977**, *62*, 665.

(13) Burczyk, B.; Kortylewicz, Z. *Synthesis* **1982**, 831.

(14) Karimi, B.; Serdji, H. *Synlett* **2000**, 805.

(15) Romo, J.; Rosenkranz, G.; Djerassi, C. *J. Am. Chem. Soc.* **1951**, *73*, 4961.

(16) (a) Anteunis, M.; Beeu, C. *Synthesis* **1974**, 23. (b) Roberts, R. M.; Chang, C.-C. *J. Org. Chem.* **1958**, *23*, 783.

(17) Karimi, B.; Ma'mani, L. *Synthesis* **2003**, *16*, 2503.

(18) Taylor, E. C.; Chiang, C.-S. *Synthesis* **1977**, 467.

(19) (a) Pearson, A. J.; Roush, R. J. *Activating Agents and Protecting Groups*; John Wiley: New York, **1999**, 283. (b) Hoyer, S.; Laszlo, P.; Orlovic, M.; Polla, E. *Synthesis* **1986**, 655.

(20) Onaka, M.; Ohno, R.; Kawai, M.; Isumi, Y. *Bull. Chem. Soc. Jpn.* **1987**, *60*, 2689.

(21) Aativiela, C.; Figueras, F.; Fraile, J. M.; Gareia, J. I.; Mayoral, J. A. *Tetrahedron: Asymmetry* **1993**, *4*, 223.

(22) Chalais, S.; Cornelis, A.; Gerstmans, A.; Kolodziejski, W.; Laszlo, P.; Mathy, A.; Metra, P. *Helv. Chim. Acta* **1985**, *68*, 1196.

(23) **Typical Experimental Procedure**: To a stirred mixture of benzaldehyde (0.2 g, 1.9 mmol) and 2-mercaptoethanol (0.195 g, 2.5 mmol) in CH_2Cl_2 (5 mL) was added montmorillonite K-10 clay (0.4 g, two times the mass of the substrate). The mixture was stirred at r.t. for 0.5 h. The end of the reaction was monitored by TLC (silica gel plate; 1:12 EtOAc–hexane). After completion, the reaction mixture was filtered off and washed with CH_2Cl_2 (3×5 mL). The filtrate was dried (Na_2SO_4) and evaporation of organic solvent afforded crude product. The crude product was purified by preparative TLC over silica gel (1:12 EtOAc–hexane as a solvent system) to afford pure 2-phenyl-1,3-oxathiolane (0.271 g, 86%, entry 4 in Table 1). All the data (IR, ^{1}H NMR and mass spectra) recorded are identical with the authentic samples and the reported methods.
Spectral data for compound **4**: IR (KBr): ν_{max} = 1069 (C-O-C), 681 (C-S-C) cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.15–3.31 (m, 2 H, -S-CH_2-), 3.87–3.94 (m, 1 H, -O-CH_2-), 4.50–4.53 (m, 1 H), 6.02 (s, 1 H, -O-CH-S), 7.29–7.40 (m, 3 H), 7.44–7.48 (m, 2 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 138.99, 136.32, 129.53, 126.76, 87.17, 71.93, 34.10 ppm.