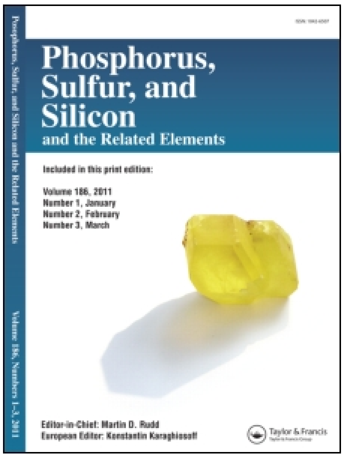


Phosphorus, Sulfur, and Silicon and the Related Elements
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713618290

Chemoselective Dithioacetalization of Carbonyl Compounds Using Magnesium Hydrogensulfate as Efficient Heterogeneous Catalyst

Hamid Reza Shaterian[a]; Asghar Hosseinian[a]; Majid Ghashang[a]; Fahimeh Khorami[a]
[a] Department of Chemistry, Faculty of Sciences, University of Sistan and Baluchestan, Zahedan, Iran

To cite this Article Shaterian, Hamid Reza , Hosseinian, Asghar , Ghashang, Majid and Khorami, Fahimeh(2008) 'Chemoselective Dithioacetalization of Carbonyl Compounds Using Magnesium Hydrogensulfate as Efficient Heterogeneous Catalyst', Phosphorus, Sulfur, and Silicon and the Related Elements, 183: 10, 2490 — 2501

To link to this Article: DOI: 10.1080/10426500801967740

URL: http://dx.doi.org/10.1080/10426500801967740

Phosphorus, Sulfur, and Silicon, 183:2490–2501, 2008
Copyright © Taylor & Francis Group, LLC
ISSN: 1042-6507 print / 1563-5325 online
DOI: 10.1080/10426500801967740

Chemoselective Dithioacetalization of Carbonyl Compounds Using Magnesium Hydrogensulfate as Efficient Heterogeneous Catalyst

Hamid Reza Shaterian, Asghar Hosseinian,
Majid Ghashang, and Fahimeh Khorami
Department of Chemistry, Faculty of Sciences, University of Sistan and Baluchestan, Zahedan, Iran

Carbonyl compounds have been successfully converted into their corresponding dithiolanes and dithianes derivatives with 1,2-ethanedithiol and 1,3-propanedithiol in excellent yield at room temperature and short reaction times using a catalytic amount of magnesium hydrogensulfate. The synthetic simple procedures reported in this paper constitute an exceptionally mild procedure for carbonyl protection in ambient conditions.

Keywords 1,3-dithiane; 1,3-dithiolane; dithioacetalization; heterogeneous catalyst; $Mg(HSO_4)_2$

INTRODUCTION

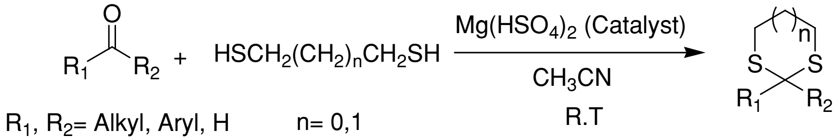
Since the introduction of 1,3-dithianes as nucleophilic acylating reagents by Corey and Seebach,[1] dithioacetals have become widely used tools for the formation of C—C bonds. In addition, the stability exhibited by 1,3-dithiolanes under acidic or basic conditions has led to their synthetic utility as carbonyl protecting groups[2] and as intermediates in the conversion of a carbonyl function to a hydrocarbon derivative.[3,4]

They are generally obtained by protic acid or Lewis acid catalyzed condensation of carbonyl compounds with thiols or dithiols. Several Brønsted and Lewis acid catalysts such as: $Sc(OTf)_3$,[5] $InCl_3$,[6] iodine supported on natural phosphate[7] $CoCl_2$,[8] $NiCl_2$,[9] NBS,[10] $In(OTf)_3$,[11] $MoO_2(acac)_2$,[12] [bmim]HSO_4,[13] *p*-dodecyl benzenesulfonic

Received 2 December 2007; accepted 4 January 2008.
We are thankful to the Sistan and Baluchestan University Research Council for the partial support of this research.

Address correspondence to Hamid Reza Shaterian, Department of Chemistry, Faculty of Sciences, University of Sistan and Baluchestan, P. O. Box 98135-674, Zahedan, Iran. E-mail: hrshaterian@hamoon.usb.ac.ir

acid (DBSA),[14] $TiCl_4$,[15] $LaCl_3$,[16] hydrobromic acid,[17] $ZnCl_2$,[18] $Y(OTf)_3$[19] Iron(III) fluoride,[20] and $VO(OTf)_2$[21] have been used in thioacetalization reactions. Many of these methods require long reaction times, reflux conditions, stoichiometric amounts of catalyst, unwanted side products, and show low selectivity when applied to the mixtures of aldehydes and ketones. Therefore, there is still a need to develop a simple and efficient method for dithioacetalization of carbonyl groups. Thus, in continuation of our previous work on heterogeneous catalysts,[22] we wish to report an efficient method for the dithioacetalization of carbonyl compounds in high to excellent yields by employing $Mg(HSO_4)_2$ as active heterogeneous catalyst (Scheme 1). We believe that our method is very simple, mild, rapid and new to the literature.



SCHEME 1

This catalyst is safe and easy to handle; environmentally benign; presents fewer disposal problems; and it is stable in reaction media. Magnesium hydrogensulfate has been used in some organic reactions, such as acetylation and formylation of alcohols,[23] cleavage of C=N,[24] and oxidation of thiols.[25]

RESULTS AND DISCUSSION

In the first reaction, benzaldehyde (1 mmol) was converted to its corresponding 2-phenyl-1,3-dithiane using $Mg(HSO_4)_2$ (0.05 g, 20 mol%) as catalyst in the presence of various solvents at room temperature (Table I). The results in Table I show that amongst these solvents, acetonitrile was the solvent of choice in terms of time and product yield.

To find out the optimum quantity of the catalyst, the reaction of benzaldehyde with 1,3-propandithiol was carried out using different quantities of $Mg(HSO_4)_2$ under ambient conditions in acetonitrile as solvent (Table II). As can be seen from Table II, best results were obtained when using 0.025 g (10 mol%) of the catalyst.

Next, we prepared a range of cyclic dithioacetals under the following reaction conditions: aldehydes or ketones (1 eq), 1,3-propandithiol or 1,2-ethanedithiol (1.1 eq), and acetonitrile (as solvent, 2 mL) in the presence of $Mg(HSO_4)_2$ (0.025 g, 10 mol%) (Table III).

TABLE I Conversion of Benzaldehyde (1mmol) to 2-Phenyl-1,3-dithiane Using 1,3-Propanedithiol (1.1 mmol) in the Presence of $Mg(HSO_4)_2$ (0.05 g, 20 mol%) as Catalyst Under a Variety Solvents (2 mL) at Room Temperature

Entry	Solvent	Time (min)	Yield (%)[a]
1	Chloroform	17	96
2	Dichloromethane	16	93
3	Ethylacetate	60	Incompletely
4	n-Hexane	15	91
5	EtOH	60	Incompletely
6	H_2O	60	Incompletely
7	Acetonitrile	0.5	97

[a] Yields refer to the pure isolated products.

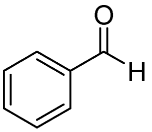
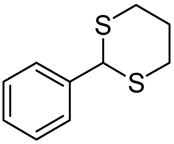
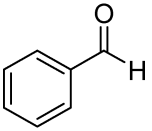
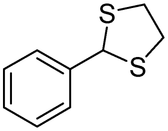
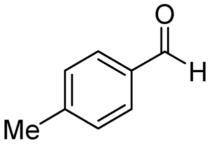
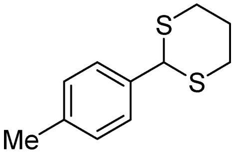
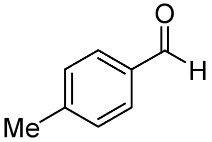
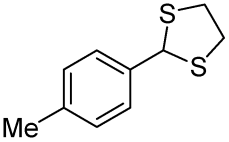
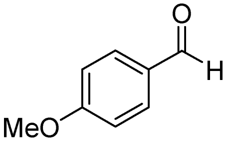
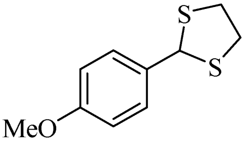
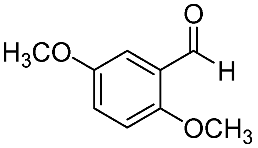
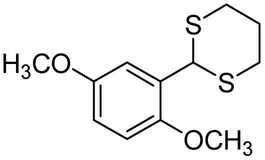
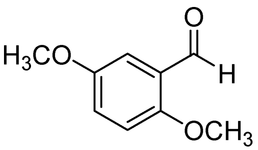
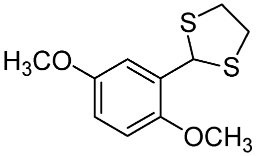
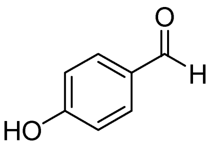
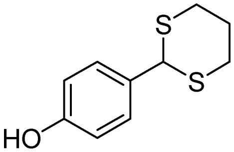
As shown in Table III, several different aliphatic and aromatic aldehydes with both electron-withdrawing and donating substituents produced corresponding cyclic dithioacetal without the formation of any side products, in high to excellent yields within a few minutes at room temperature (Table III, entries 1–29). The reaction was performed with benzaldehyde containing withdrawing as well as electron donating groups, but benzaldehydes with electron-donating groups are generally more reactive than their corresponding benzaldehydes with electron-withdrawing groups and provided the desired product at short reaction time with excellent yield (Table III, entries 3–10). As reported in the literature,[26] this observation clearly shows that the reactivity of benzaldehydes in thioacetalization reaction is more strongly affected by the electronic and steric hindrance factors. We also performed dithioacetalization reactions with aromatic and aliphatic ketones at room temperature. Benzophenone, cyclohexanone, cyclopentanone, and ethyl

TABLE II Optimization of the Amount of $Mg(HSO_4)_2$ in the Reaction of Benzaldehyde with 1,3-Propandithiol Under Ambient Conditions in Acetonitrile as Solvent

Entry	Catalyst (g)	Time (min)	Yield (%)[a]
1	0.1	Immediately	95
2	0.05	0.5	97
3	0.025	1.5	98
4	0.01	4	97
5	0.005	11	96

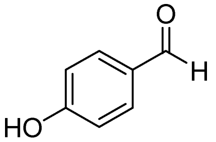
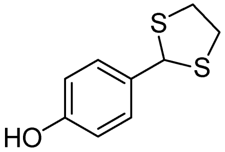
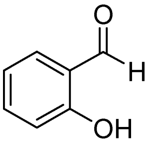
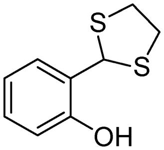
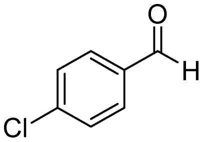
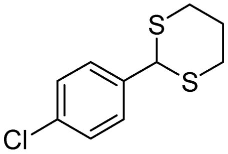
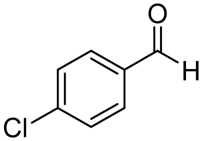
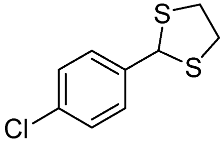
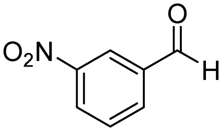
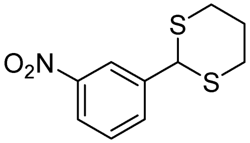
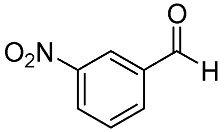
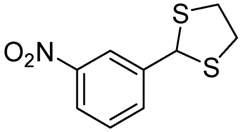
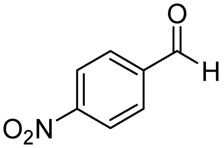
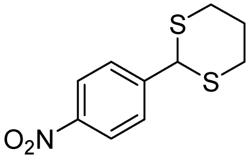
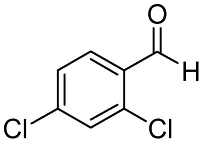
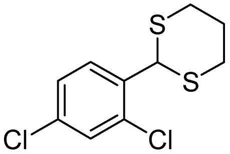
[a] Yields refer to pure isolated product.

TABLE III Conversion of Aldehydes and Ketones to the Corresponding 1,3-Dithiane and 1,3-Dithiolane Using $Mg(HSO_4)_2$ as Catalyst in Acetonitrile as Solvent Under Ambient Conditions

Entry	Substrate	Product	Time (min)	Yield (%)[a]
1			1.5	98
2			2	96
3			1.5	91
4			1.5	92
5			3	97
6			1.2	96
7			1.1	95
8			2	90

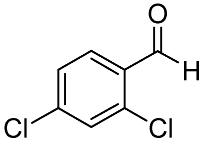
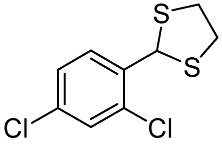
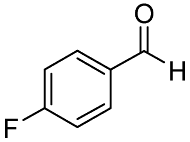
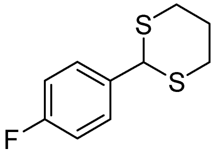
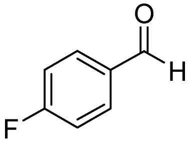
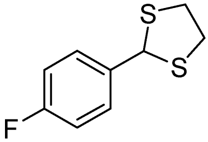
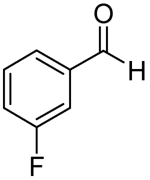
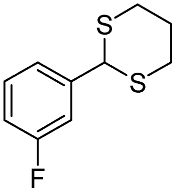
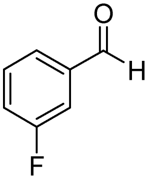
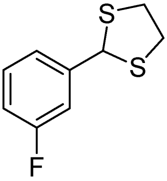
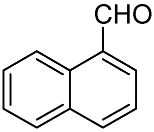
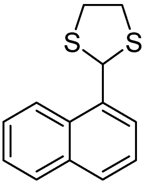
(Continued on next page)

TABLE III Conversion of Aldehydes and Ketones to the Corresponding 1,3-Dithiane and 1,3-Dithiolane Using $Mg(HSO_4)_2$ as Catalyst in Acetonitrile as Solvent Under Ambient Conditions *(Continued)*

Entry	Substrate	Product	Time (min)	Yield (%)^a
9			2	89
10			3	88
11			4	97
12			6	95
13			23	95
14			27	92
15			27	93
16			4	98

(Continued on next page)

TABLE III Conversion of Aldehydes and Ketones to the Corresponding 1,3-Dithiane and 1,3-Dithiolane Using Mg(HSO_4)$_2$ as Catalyst in Acetonitrile as Solvent Under Ambient Conditions *(Continued)*

Entry	Substrate	Product	Time (min)	Yield (%)[a]
17			11	97
18			4	95
19			5	95
20			3	96
21			5	94
22			4	98

(Continued on next page)

TABLE III Conversion of Aldehydes and Ketones to the Corresponding 1,3-Dithiane and 1,3-Dithiolane Using $Mg(HSO_4)_2$ as Catalyst in Acetonitrile as Solvent Under Ambient Conditions *(Continued)*

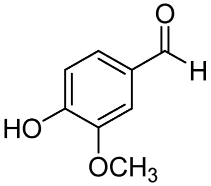
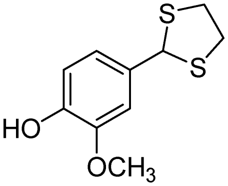
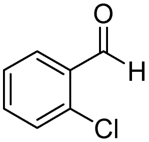
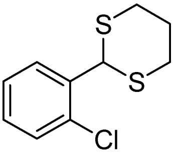
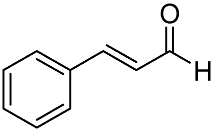
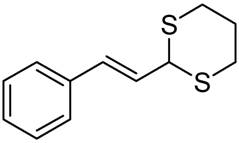
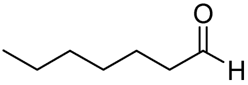
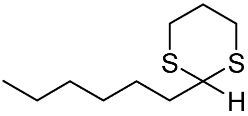
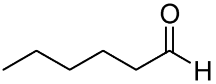
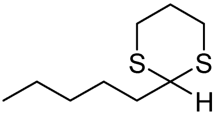
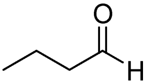
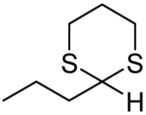
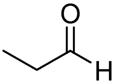
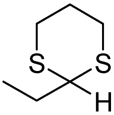
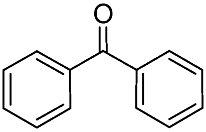
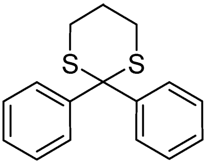
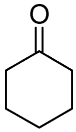
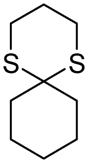
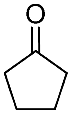
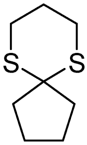
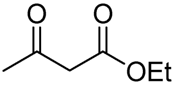
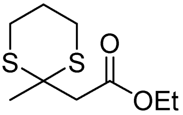
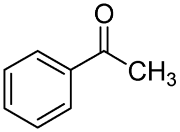
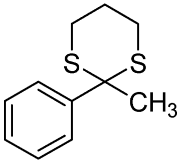
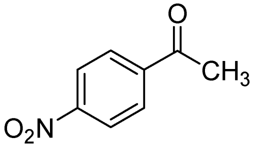
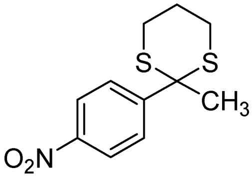
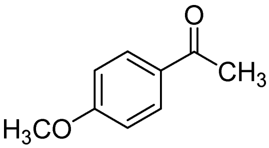
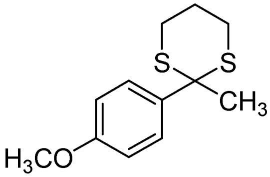
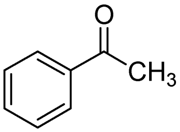
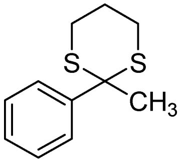
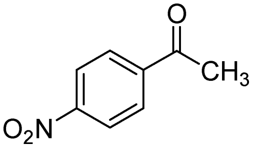
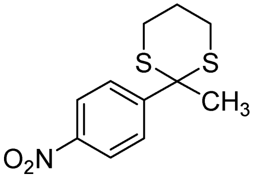
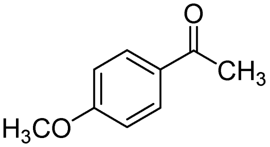
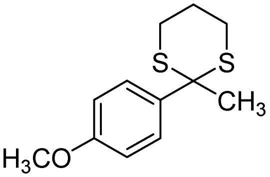
Entry	Substrate	Product	Time (min)	Yield (%)[a]
23			4	89
24			8	91
25			2	87
26			8	93
27			8	91
28			7	89
29			6	88
30			12	92

TABLE III Conversion of Aldehydes and Ketones to the Corresponding 1,3-Dithiane and 1,3-Dithiolane Using $Mg(HSO_4)_2$ as Catalyst in Acetonitrile as Solvent Under Ambient Conditions *(Continued)*

Entry	Substrate	Product	Time (min)	Yield (%)[a]
31			9	97
32			10	97
33			15	92
34			9h	40% GC Yield
35			9h	20% GC Yield
36			9h	43% GC Yield
37			9h[b]	92

(Continued on next page)

TABLE III Conversion of Aldehydes and Ketones to the Corresponding 1,3-Dithiane and 1,3-Dithiolane Using $Mg(HSO_4)_2$ as Catalyst in Acetonitrile as Solvent Under Ambient Conditions *(Continued)*

Entry	Substrate	Product	Time (min)	Yield (%)[a]
38			10h[b]	93
39			10h[b]	60% GC Yield

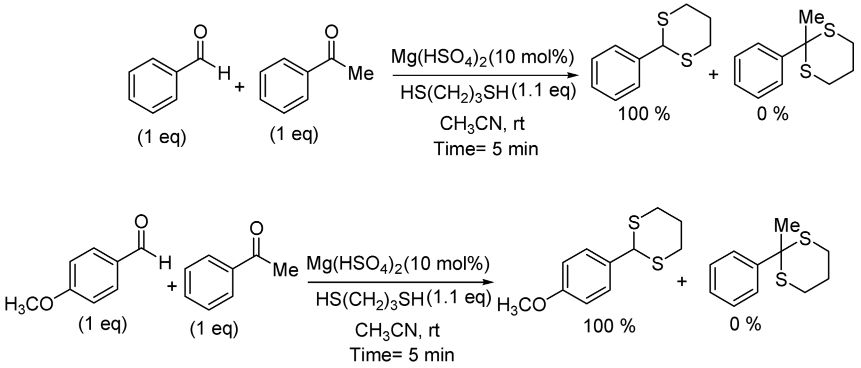
[a]Yields refer to the pure isolated products. All known products have been reported previously in the literature and were characterized by comparison of IR and ^1H NMR spectra with authentic samples.[5–21] [b]The reaction was performed at 80°C under reflux conditions.

3-oxobutanoate converted to the corresponding 1,3-dithianes at ambient conditions (Table III, Entries 30–33). But, the reaction of acetophenone and its derivatives with 1,3-propanedithiol were not completed after 9 h at room temperature (9 h, 20–43% GC yield); thus, we performed these reactions at 80°C in an oil bath (Table III, entries 36–38).

In order to show the ability of magnesium hydrogensulfate to act as chemoselective catalyst for dithioacetalization reactions, we studied dithioacetalization of benzaldehyde and 4-methoxybenzaldehyde in the presence of acetophenone. The benzaldehyde and 4-methoxybenzaldehyde were exclusively protected, whereas acetophenone was intact in the same experimental conditions (Scheme 2).

To show the merit of the present work in comparison with reported results in the literature, we compared results of magnesium hydrogensulfate with $CoCl_2$,[8] $NiCl_2$,[9] $MoO_2(acac)_2$[12], and $Y(OTf)_3$[19] in the synthesis of 2-phenyl-1,3-dithiane. As shown in Table IV, magnesium hydrogensulfate can act as effective catalyst with respect to reaction times, yields, and the obtained products.

In conclusion, we have demonstrated that magnesium hydrogensulfate is a new, efficient, mild and heterogeneous catalyst for dithioacetalization of various aldehydes and ketones at room temperature. This



SCHEME 2

simple and efficient method is a chemoselective procedure for protection of aldehydes in the presence of ketones. This synthetic mythology is important from an environmental point of view and economic considerations, because it produces little waste.

EXPERIMENTAL

All reagents were purchased from Merck and Aldrich and used without further purification. $Mg(HSO_4)_2$ was prepared via a literature procedure.[24] All yields refer to isolated products after purification. Products were characterized by comparison of spectroscopic data (IR, ^1H NMR spectra) with authentic samples. The NMR spectra were recorded on a Bruker Avance DEX 400 MHz instrument. IR spectra were recorded on a Perkin-Elmer 781 spectrophotometer. TLC was performed on Silica-gel polygram SIL G/UV 254 plates.

TABLE IV Comparison of the Efficiency of Metal Catalysts for the Synthesis of 2-Phenyl-1,3-dithiane

Entry	Catalyst	Conditions	Time	Yield (%)^{ref}
1	$CoCl_2$	CH_3CN; r.t.; Cat (5 mol%)	1 h	91[8]
2	$NiCl_2$	CH_2Cl_2-MeOH (5:1), r.t.; Cat (10 mol%)	2.5 h	94[9]
3	$MoO_2(acac)_2$	CH_3CN; r.t.; Cat (10 mol%)	3 h	94[12]
4	$Y(OTf)_3$	CH_3CN; r.t.; Cat (5 mol%)	45 min	89[19]
5	$Mg(HSO_4)_2$	CH_3CN; r.t.; Cat (10 mol%)	1.5 min	98

General Procedure for the Dithioacetalization of Carbonyl Compounds

To a mixture of a carbonyl compound (1 mmol) and 1,3-propanedithiol or 1,2-ethanedithiol (1.1 mmol) in acetonitrile (2 mL) was added 0.025 g of $Mg(HSO_4)_2$. The reaction mixture was stirred at room temperature for time indicated in Table III. The progress of the reaction was monitored by TLC or GC. After completion of the reaction acetonitrile was evaporated from the reaction mixture. The reaction mixture was combined with chloroform and filtered. The organic layer was extracted with 10% $NaHCO_3$ solution (10 ml) followed by water (10 ml) and brine solution (5 ml). Organic layer dried with anhydrous $CaCl_2$ and filtered, solvent evaporated under reduced pressure, and the pure product was obtained. The desired pure product(s) was characterized by comparison of their physical data with those of known the dithioacetals.[5–21] Spectroscopic analysis confirmed the molecular structures of the products.

REFERENCES

[1] E. J. Corey and D. Seebach, *Angew. Chem., Int. Ed. Engl.*, **4,** 1075, 1077 (1965).

[2] T. W. Greene and P. G. M. Wuts, *Protective Groups in Organic Synthesis* (Wiley: New York, 1999), 3rd ed.

[3] E. J. Corey and D. Seebach, *J. Org. Chem.*, **31,** 4097 (1966).

[4] B. T. Grobel and D. Seebach, *Synthesis*, 357 (1977).

[5] A. Kamal and G. Chouhan, *Tetrahedron Lett.,* **43,** 1347 (2002).

[6] S. Muthusamy, S. A. Babu, and C. Gunanathan, *Tetrahedron Lett.,* **42,** 359 (2001).

[7] M. Zahouily, A. Mezdar, J. Rakik, A. Elmakssoudi, A. Rayadh, and S. Sebti, *J. Mol. Catal. A: Chem.,* **233,** 43 (2005).

[8] S. K. De, *Tetrahedron Lett.,* **45,** 1035 (2004).

[9] A. T. Khan, E. Mondal, P. R. Sahua, and S. Islamb, *Tetrahedron Lett.,* **44,** 919 (2003).

[10] A. Kamal, G. Chouhan, and K. Ahmed, *Tetrahedron Lett.,* **43,** 6947 (2002).

[11] S. Muthusamy, S. A. Babu, and C. Gunanathan, *Tetrahedron,* **58,** 7897 (2002).

[12] K. K. Rana, C. Guin, S. Jana, and S. C. Roy, *Tetrahedron Lett.,* **44,** 8597 (2003).

[13] N. Gupta, Sonu, G. L. Kad, and J. Singh, *Catal. Commun.,* **8,** 1323 (2007).

[14] D. Dong, Y. Ouyang, H. Yu, Q. Liu, J. Liu, M. Wang ,and J. Zhu, *J. Org. Chem.,* **70,** 4535 (2005).

[15] V. Kumar and S. Dev, *Tetrahedron Lett.,* **24,** 1289 (1983).

[16] L. Garlaschelli and G. Vidari, *Tetrahedron Lett.,* **31,** 5815 (1990).

[17] P.D. Shinde, H. B. Borate, and R. D. Wakharkar, *Arkivoc,* 110 (2004).

[18] D. A. Evans, L. K. Truesdale, K. G. Grimm, and S. L. Nesbitt, *J. Am. Chem. Soc.,* **99,** 5009 (1977).

[19] S. K. De, *Tetrahedron Lett.,* **45,** 2339 (2004).

[20] B. P. Bandgar, V. T. Kamble, and A. Kulkarni, *Aust. J. Chem.* **58,** 607 (2005).

[21] S. K. De, *J. Mole. Catal. A: Chem.,* **226,** 77 (2005).

[22] (a) H. R. Shaterian, M. Ghashang, and A. Hassankhani, *Dyes Pigm.,* 76 (2008) 564; (b) N. Iranpoor, H. Firouzabadi, and H. R. Shaterian, *Tetrahedron Lett.,* **44,** 4769 (2003).

[23] F. Shirini, M. A. Zolfigol, and B. Mallakpour, *Russ. J. Org. Chem.,* **41,** 625 (2005).

[24] F. Shirini, M. A. Zolfigol, B. Mallakpour, S. E. Mallakpour, A. R. Hajipour, and I. M. Baltork, *Tetrahedron Lett.,* **43,** 1555 (2002).

[25] F. Shirini, M. A. Zolfigol, B. Mallakpour, I. M. Altork, and A.R. Hajipour, *J. Chem. Res.*, **28** (2003).

[26] (a) R. K. Roy, V. Usha, B. K. Patel, and K. Hirao, *J. Comput. Chem.* **27,** 773 (2005); (b) R. K. Roy, P. Bagaria, S. Naik, V. Kavala, and B. K. Patel, *J. Phys. Chem. A,* **110,** 2181 (2006).