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An efficient and practical procedure for preparation of *gem*-diacetates from aldehydes catalysed by magnesium perchlorate

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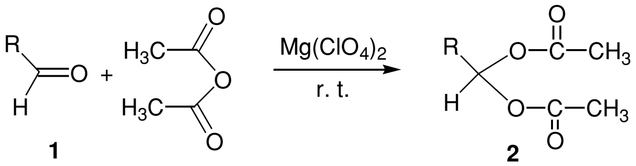
A mild and efficient method for the preparation of *gem*-diacetates from aldehydes with acetic anhydride is described using a catalytic amount of magnesium perchlorate giving excellent yields under solvent-free conditions.

Keyword: *gem*-diacetates, aldehydes, protection groups, magnesium perchlorate, solvent-free conditions

The protection of carbonyl functionalities plays an important role in multi-step organic synthesis.[1] Tremendous efforts have been made to search for suitable protective groups. Protection of aldehyde groups as *gem*-diacetates, in particular, is a more practical choice than the corresponding acetals, oxathioacetals and thioacetals. The reason for this choice is the simplicity of the protection procedure because, during acetalisation, the water formed must be removed either by physical or by chemical means.[2] In most conditions, selective formation of *gem*-diacetates of aldehydes in the presence of ketones can be achieved. In addition, acetal, oxathioacetal and thioacetal protecting groups are deprotected only under acidic conditions whereas *gem*-diacetates can be removed under either acidic or basic conditions.[3] The *gem*-diacetates of aldehydes are also useful precursors for nucleophilic substitution reactions and several are used as industrial intermediates.[4] They can be converted into compounds with other useful functional groups by reaction with appropriate reagents.[5] The synthesis of optically active aldehydes by lipase-catalysed resolution of the corresponding *gem*-diacetates has been reported.[6] Consequently, a number of catalytic methods have been developed for this transformation, which include protic acids, Lewis acids and heterogeneous catalysts.[7] 2,4,4,6-Tetrabromo-2,5-cyclohexadienone (TABCO),[8] tetrabutylammonium tribromide (TBATB),[2] Caro's acid,[9] Wells–Dawson heteropolyacid,[10] P_2O_5/montmorillonite K10,[11] $Mo/TiO_2–ZrO_2$ solid acid[12] and P_2O_5/SiO_2,[13] have also been used for this transformation. Nevertheless, the reported methodologies suffer from one or more of the following disadvantages such as long reaction times, high catalyst loading, low product yields, expensive reagents, stringent conditions, halogenated solvents, and excess of acetylating agents. Thus, there is need to develop a simple, efficient and practical method for the synthesis of *gem*-diacetates under mild conditions.

In the past few years, metal perchlorates have been widely exploited as Lewis acid promoters in various organic transformations.[14] In particular, magnesium perchlorate is inexpensive, has low toxicity and is stable to air and moisture. It has been reported as a catalyst for the formation of *t*-butyl ethers,[15] the reaction of silylated base derived from uracil, thymine and adenine with bis(epoxides),[16] the synthesis of imines and phenylhydrazones,[17] the synthesis of 1,2,3,4-tetrahydropyrimidin-2-ones,[18] the preparation of 2-substituted 1,3-alkadienes,[19] selective sulfonylation of arenes,[20] the acylation of alcohols,[21] the synthesis of 5-arylhydantoins[22] and the bromination of 1,3-dicarbonyl compounds.[23] It has been applied as a Lewis acid in enantioselective synthesis.[24] Here we report a mild and highly efficient method for the preparation of *gem*-diacetates using a catalytic amount of magnesium perchlorate under solvent-free conditions (Scheme 1).

In order to assess the potential of $Mg(ClO_4)_2$, preliminary experiments were carried out by adding 2 mmol benzaldehyde to 6 mmol of Ac_2O containing decreasing amounts of $Mg(ClO_4)_2$ at room temperature. Under these condition, 5 mol% of $Mg(ClO_4)_2$ is sufficient to afford quantitatively the *gem*-diacetate in 20 minutes. Lower catalyst loading could be used with only a marginal drop in reaction rate.



Scheme 1

To evaluate the scope of this reaction, acylation of other aldehydes was studied (Table 1). Both activated and deactivated aromatic aldehydes including acid-sensitive furfural react with acetic anhydride under such conditions to provide the corresponding *gem*-diacetate in excellent yields. It should be mentioned that electronic effects were observed, that is, aryl aldehydes with electron-rich groups (**1d**–**1i**) reacted rapidly, while substitution of electron-withdrawing groups (**1k**–**1o**) on the benzene ring decreased the reactivity, requiring longer reaction times. Cinnamaldehyde (**1r**) affords the *gem*-diacetate in 89% yield without any isomerisation of the double bond. Further, aliphatic aldehydes (**1a**–**1b**) are converted into the corresponding *gem*-diacetates in good yields. *N,N*-Diethylaminobenzaldehyde (**1w**) due to strong deactivation of the carbonyl group did not give any satisfactory yield under these conditions and mostly starting materials were recovered. It is worth noting that the hydroxy groups in 2-hydroxy- and 2-hydroxy-5-chloro- benzaldehydes (**1s** and **1u**) and vaniline (**1t**) were also acetylated to afford the corresponding triacetates under similar conditions in high yields. This reaction was further explored for the preparation of *bis*-diacetates (compound **4**) by the reaction of 1,3-di (2-formylphenoxy)propane (**3**) with 6 equiv. of acetic anhydride under similar conditions in excellent yield (Scheme 2). The tolerance of various functional groups under the present reaction conditions is also worthy of mention in that acid sensitive or oxidisable groups such as methoxy, methylenedioxy, nitro, chloro and double bonds do survive under such conditions.

Also we investigated the possible chemoselective protection of aldehydes in the presence of ketones. When a 1:1 mixture of benzaldehyde and acetophenone was allowed to react with acetic anhydride in the presence of $Mg(ClO_4)_2$ for 20 min, TLC analysis of the reaction mixture indicated complete disappearance of benzaldehyde, while acetophenone was still intact even when the reaction mixture was stirred for 24 h. This result indicates that the present protocol is highly applicable for the chemoselective protection of aldehydes in the presence of ketones.

In summary, we have demonstrated that magnesium perchlorate serves as an efficient catalyst for the preparation of *gem*-diacetates under mild reaction condition. The present

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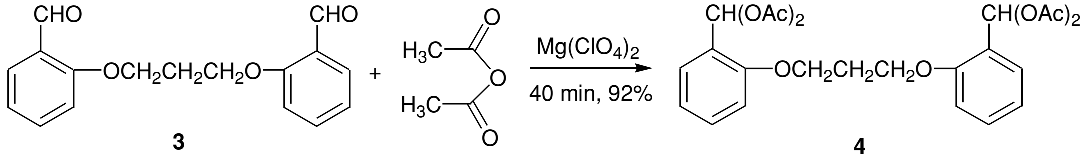


Scheme 2

Table 1 The preparation of *gem*-diacetates catalysed by magnesium perchlorate

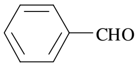
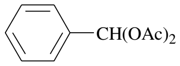
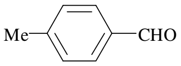
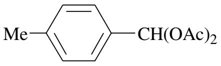
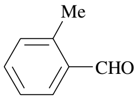
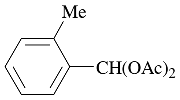
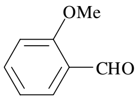
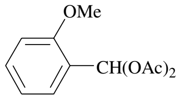
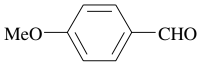
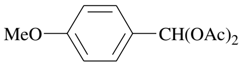
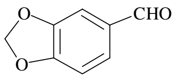
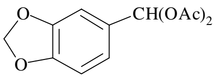
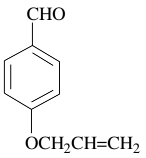
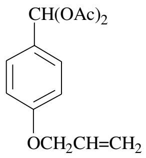
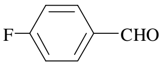
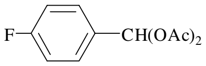
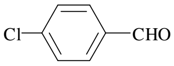
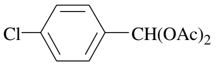
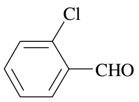
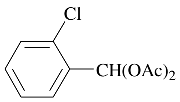
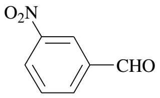
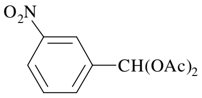
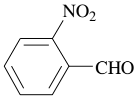
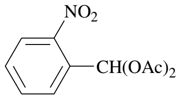
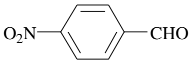
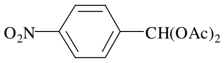
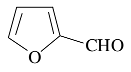
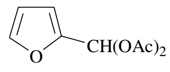
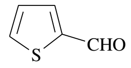
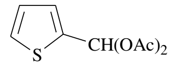
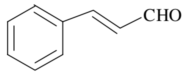
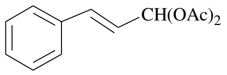
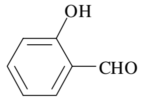
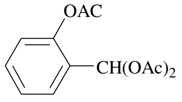
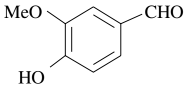
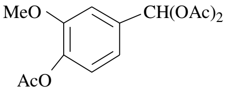
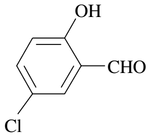
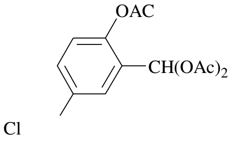
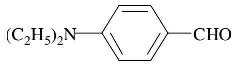
Entry	Substrate	Product	Time/min	Yield/%[a]	M.p.(T/°C) [b.p.(T/°C)/Torr]	
					Found	Reported
a	$CH_3(CH_2)_4CHO$	$CH_3(CH_2)_4CH(OAc)_2$	50	89	127–129/2	128–130/2[7]
b	$CH_3(CH_2)_8CHO$	$CH_3(CH_2)_8CH(OAc)_2$	60	91	122–124/2	141–143/10[7]
c			20	95	44–45	44–45[7]
d			40	91	80–81	82–83[7]
e			20	95	59–60	58–59[7]
f			30	93	74–75	75–76[7]
g			30	90	64–65	64–65[7]
h			20	94	78–79	78–79[7]
i			60	87	43–44	
j			40	91	51–52	50–51[7]
k			60	90	81–82	80–81[7]
l			60	95	56–57	57–58[7]
m			180	93	65–66	66–67[7]
n			180	91	85–86	86–87[7]
o			210	93[b]	126–127	127–128[7]

Table 1 *continued*

Entry	Substrate	Product	Time/min	Yield/%[a]	M.p.(T/°C) [b.p.(T/°C)/Torr	
					Found	Reported
p			30	85	51–52	50–51[7]
q			90	87	66–67	66–67[25]
r			40	89	84–85	84–85[7]
s			60	92[b]	102–104	103–104[26]
t			40	93 [b]	90–91	90–91[7]
u			90	93 [b]	81–82	63–65[27]
v			24 h	–[c]		

[a]Isolated yield. [b]6 Equiv of acetic anhydride (with respect to aldehyde) was used. [c]No reaction.

method has many obvious advantages compared to those reported in the previous literature, including the generality, the simplicity of the methodology, low loading of catalyst, excellent chemoselectivity and high yields of products.

Experimental

Melting points were recorded on X-4 apparatus and are uncorrected. IR spectra were recorded on a Bio-Rad FTS 135 spectrophotometer. ^{1}H NMR spectra were recorded with a Bruker spectrometer at 300 MHz using TMS as internal standard. Elemental analyses were performed on a Yanaca CDRDER MT-3 analyser.

General procedure for the preparation of gem-diacetates: A mixture of aldehyde (**1**, 2 mmol), freshly distilled acetic anhydride (6 mmol) and Mg(ClO$_4$)$_2$ (22 mg, 5 mol%) was stirred at room temperature. After completion of reaction (monitored by TLC), the reaction mixture was poured into sat. sodium bicarbonate solution (20 ml) and extracted with ethyl acetate (3 × 10 ml). The combined organic layers were dried over anhydrous MgSO$_4$, and the solvent was evaporated under reduced pressure. The crude product was purified by column chromatography on silica gel using EtOAc-cyclohexane (2:8) as eluent to afford as element pure *gem*-diacetates **2**.

Selective spectroscopic and analytical data

1,1-Decanediol diacetate (**2b**): IR (neat): 2921, 2861, 1760, 1370, 1241, 1200, 1005 cm^{-1}. ^{1}H NMR (CDCl$_3$) δ ppm: 0.88 (t, *J*=6.9 Hz, 3H), 1.26–1.33(m, 14H), 1.73–1.77(m, 2H), 2.07(s, 6H), 6.77 (t, *J*=5.7 Hz, 1H). Anal. Calcd for C$_{14}$H$_{26}$O$_4$: C, 65.1; H, 10.1. Found: C, 65.2; H, 10.1.

[4-(2-Propenyloxy)phenyl]methanediol diacetate (**2i**): IR (KBr): 3184, 3133, 1758, 1617, 1585, 1519, 1401, 1379, 1239, 1174, 1114, 1065, 995, 906, 859, 807, 672 cm^{-1}. ^{1}H NMR (CDCl$_3$) δ ppm: 2.11 (s, 6H), 4.55 (d, *J*=5.4 Hz,2H), 5.29 (dd, *J*=1.5, 16.5 Hz, 1H), 5.41 (dd, *J*=1.5, 16.5 Hz, 1H), 5.98–6.09 (m, 1H), 6.93 (d, *J*=8.7 Hz, 2H), 7.44 (d, *J*=8.7 Hz,2H), 7.62 (s, 1H). Anal. Calcd for C$_{14}$H$_{16}$O$_5$: C, 63.6; H, 6.1;. Found: C, 63.4; H, 5.9.

2-Furanylmethanediol diacetate (**2p**): IR (KBr): 3159, 3125, 2925, 1758, 1504, 1397, 1347, 1208, 1249, 1208, 1147, 1079, 1064, 1016, 971, 938, 925, 904, 882, 833, 790, 753 cm^{-1}. ^{1}H NMR (CDCl$_3$) δ ppm: 2.14 (s, 6H), 6.39–6.40 (m, 1H), 6.54 (d, *J*=3.3 Hz, 1H), 7.46 (br, s, 1H), 7.72 (s, 1H). Anal. Calcd for C$_9$H$_{10}$O$_5$: C, 54.6; H, 5.1. Found: C, 54.4; H, 5.3.

2-Thienylmethanediol diacetate (**2q**): IR (KBr): 3168, 3112, 2925, 1750, 1504, 1544, 1442, 1401, 1373, 1241, 1208, 1042, 1007, 968, 847, 764 cm^{-1}. ^{1}H NMR (CDCl$_3$) δ ppm: 2.13 (s, 6H), 7.01 (dd, *J*=4.5, 5.4 Hz, 1H), 7.25 (d, *J*=4.5 Hz, 1H), 7.38 (d, *J*=5.0 Hz, 1H), 7.92 (s, 1H). Anal. Calcd for C$_9$H$_{10}$O$_4$S: C, 50.5; H, 4.7. Found: C, 50.3; H, 4.5.

[2-(Acetyloxy)-5-chlorophenyl]methanediol diacetate (**2u**): IR (KBr): 3125, 3014, 1760, 1640, 1491, 1401, 1374, 1119, 1112, 1095, 1059, 972, 942, 909, 841, 750, 690 cm^{-1}. ^{1}H NMR (CDCl$_3$) δ ppm: 2.11 (s, 6H), 2.33 (s, 3H), 7.07 (d, *J*=8.7 Hz, 1H), 7.39 (dd, *J*=2.4, 8.7 Hz, 1H), 7.61 (d, *J*=2.4 Hz, 1H), 7.85 (s, 1H). Anal. Calcd for C$_{13}$H$_{13}$ClO$_6$: C, 51.9; H, 4.4. Found: C, 51.7; H, 4.6.

2,2′-Di(α,α-diacetoxymethanephenoxy)propane (**4**): White solid, m.p. 80–81 °C; IR (KBr): 3132, 2934, 2882, 1750, 1603, 1499, 1456, 1401, 1261, 1237, 1213, 1221, 1121, 1167, 1067, 1015, 992, 957, 755, 737 cm^{-1}. ^{1}H NMR (CDCl$_3$) δ ppm: 2.04 (s, 12H), 2.68 (t, *J*=5.7 Hz, 2H), 4.21 (t, *J*=5.7 Hz, 4H), 6.95–6.70 (m, 4H), 7.32–7.38 (m, 2H), 7.47 (d,d *J*=1.5, 7.8 Hz, 2H), 8.07 (s, 2H). Anal. Calcd for C$_{25}$H$_{28}$O$_{10}$: C, 61.5; H, 5.8. Found: C, 61.6; H, 5.9.

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References

1 T.W. Greene and P.G.M. Wuts, *Protecting Groups in Organic Chemistry*, Wiley & Sons, New York, 3rd edn, 1999.
2 V. Kavala and B.K. Patel, *Eur. J. Org. Chem.*, 2005, 441.
3 (a) K.S. Kochhar, B.S. Bal, R.P. Deshpande, S.N. Rajadhyaksha and H.W. Pinnick, *J. Org. Chem.*, 1983, **48**, 1765; (b) T.-S. Li, Z.-H. Zhang and C.-G. Fu, *Tetrahedron Lett.*, 1997, **38**, 3285; (c) G.S. Reddy, R. Radhika, P. Neelakantan and D.S. Iyengar, *Indian J. Chem.*, 2002, **41B**, 863; (d) M.A. Zolfigol, M.H. Zebarjadian, I. Mohammadpoor-Baltork and M. Shamsipur, *Synth. Commun.*, 2002, **32**, 2803; (e) M.A. Reddy, L.R. Reddy,

N. Bhanumathi and K.R. Rao, *Synth. Commun.*, 2002, **32**, 273; (f) Z-H. Zhang, L. Yin, Y.-M. Wang, J.-Y. Liu and Y. Li, *Green Chem.,* 2004, **6**, 563; (g) H. Eshghi and P. Shafieyoon, *J. Chin. Chem. Soc.,* 2005, **52**, 155; (h) H.Y. Niu, X.Y. Zhang, H.M. Guo and J.J. Wang, *J. Chem. Res., Synop.,* 2004, 764; (i) Z-H. Zhang, L. Yin, Y. Li and Y.-M. Wang, *Tetrahedron Lett.*, 2005, **46**, 889; (j) M.M Lakourj, M. Tajbakhsh, V. Khojasteh and M.H. Gholami, *Phosphorus, Sulfur Silicon Relat. Elem.*, 2004, **179**, 2645; (k) R. Hosseinzadeh, M. Tajbakhsh, A. Shakoori and M.Y. Niaki, *Monatsh. Chem.*, 2004, **135**, 1243; (l) L. Li, X.Y. Zhang, G.S. Zhang and G.R. Qu, *J. Chem. Res., Synop.,* 2004, 39; (m) Z.-H. Zhang, *J. Chem. Res., (S),* 2004, 753; (n) Z.-H. Zhang, *Monatsh. Chem.*, 2005, **136**, 1191.

4 (a) B.M. Trost and C.B. Lee, *J. Am. Chem. Soc.*, 2001, **123**, 3671; (b) M. Sandberg and L.K. Sydnes, *Org. Lett.*, 2000, **2**, 687; (c) B.M. Trost and C. Lee, *J. Am. Chem. Soc.*, 2001, **123**, 12191; (d) J.S. Yadav, B.V.S. Reddy and G.S.K.K. Reddy, *Tetrahedron Lett.*, 2000, **41**, 2695; (e) L.K. Sydnes and M. Sandberg, *Tetrahedron*, 1997, **53**, 12679; (f) T. Hirao, S. Santhitikul, H. Takeuchi, A. Ogawa and H. Sakurai, *Tetrahedron*, 2003, **59**, 10147.

5 (a) T.-S. Jin, G. Sun, Y.-W. Li and T.-S. Li, *Synth. Commun.,* 2004, **34**, 4105; (b) H. Firouzabadi, N. Iranpoor and H. Hazarkhani, *Phosphorus, Sulfur Silicon Relat. Elem.*, 2001, **176**, 165; (c) H. Firouzabadi, N. Iranpoor and H. Hazarkhani, *J. Org. Chem.,* 2001, **66**, 7527.

6 Y.S. Angelis and I. Smonou, *Tetrahedron Lett.,* 1998, **39**, 2823.

7 L. Yin, Z.-H. Zhang, Y.-M. Wang and M.-L. Pang, *Synlett*, 2004, 1727 and references cited therein.

8 H. Firouzabadi, N. Iranpoor and H.R. Shaterian, *Bull. Chem. Soc. Jpn.*, 2002, **75**, 2195.

9 M.M. Lakouraj, M. Tajbakhsh, V. Khojasteh and M.H. Gholami, *Phosphorus, Sulfur Silicon Relat. Elem.*, 2004, **179**, 2645.

10 G.P. Romanelli, J.C. Autino, G. Baronetti and H.J. Thomas, *Synth. Commun.,* 2004, **34**, 3909.

11 H. Eshghi and Z. Gordi, *Phosphorus, Sulfur Silicon Relat. Elem.*, 2004, **179**, 1341.

12 B.M. Reddy, P.M. Sreekanth and A. Khan, *Synth. Commun.,* 2004, **34**, 1839.

13 B.F. Mirjalili, M.A. Zolfigol and A. Bamoniri, *Phosphorus, Sulfur Silicon Relat. Elem.*, 2004, **179**, 19.

14 (a) K.-C. Lu, S.-Y. Hsieh, L.N. Patkar, C.-T. Chen and C.-C. Liu, *Tetrahedron*, 2004, **60**, 8969; (b) G. Bartoli, J. Boeglin, M. Bosco, M. Locatelli, M. Massaccesi, P. Melchiorre and L. Sambri, *Adv. Synth. Catal.*, 2005, **347**, 33; (c) G. Bartoli, M. Bosco, E. Marcantoni, M. Massaccesi, S. Rinaldia and L. Sambri, *Tetrahedron Lett.*, 2002, **43**, 6331; (d) G. Bartoli, M. Bosco, M. Locatelli, E. Marcantoni, P. Melchiorre and L. Sambri, *Synlett*, 2004, 239; (e) G. Bartoli, M. Bosco, R. Dalpozzo, E. Marcantoni, M. Massaccesi and L. Sambri, *Eur. J. Org. Chem.,* 2003, 4611; (f) G. Bartoli, M. Bosco, M. Locatelli, E. Marcantoni, M. Massaccesi, P. Melchiorre and L. Sambri, *Synlett*, 2004, 1794; (g) S.K. Garg, R. Kumar and A.K. Chakraborti, *Synlett*, 2005, 1370.

15 G. Bartoli, M. Bosco, M. Locatelli, E. Marcantoni, P. Melchiorre and L. Sambri, *Org. Lett.*, 2005, **7**, 427.

16 R. Saladino, U. Ciambecchini and S. Hanessian, *Eur. J. Org. Chem.,* 2003, 4401.

17 A.K. Chakraborti, S. Bhagat and S. Rudrawar, *Tetrahedron Lett.*, 2004, **45**, 7641.

18 W.Y. Chen and J. Lu, *Chin. J. Org. Chem.,* 2004, **24**, 1111.

19 Y.Y. Kozyrkov and O.G. Kulinkovich, *Synlett*, 2004, 344.

20 B.P. Bandgar, V.T. Kamble and S.N. Bavikar, *J. Chem. Res., Synop.,* 2003, 287.

21 (a) G. Bartoli, M. Bosco, R. Dalpozzo, E. Marcantoni, M. Massaccesi, S. Rinaldi and L. Sambri, *Synlett*, 2003, 39; (b) A.K. Chakraborti, L. Sharma, R. Gulhane and Shivani, *Tetrahedron*, 2003, **59**, 7661.

22 C. Cativiela, J.M. Fraile, J.I. Garcia, G. Lafuente, J.A. Mayoral, R. Tahir and A. Pallares, *J. Catal.*, 2004, **226**, 192.

23 D. Yang, Y.-L. Yan and B. Lui, *J. Org. Chem.,* 2002, **67**, 7429.

24 (a) M.C. Willis, G.A. Cutting, V.J.D. Piccio, M.J. Durbin and M.P. John, *Angew. Chem. Int. Ed.*, 2005, **44**, 1543; (b) S. Kanemasa and T. Kanai, *J. Am. Chem. Soc.*, 2000, **122**, 10710; (c) M.P. Sibi, N. Prabagaran, S.G. Ghorpade and C.P. Jasperse, *J. Am. Chem. Soc.*, 2003, **125**, 11796; (d) M.P. Sibi and H. Matsunaga, *Tetrahedron Lett.*, 2004, **45**, 5925; (e) G. Desimoni, G. Faita, M. Guala and C. Pratelli, *Tetrahedron,* 2002, **58**, 2929; (f) D. Yang, M. Yang and N.-Y. Zhu, *Org. Lett.*, 2003, **5**, 3749; (g) D. Yang, Q. Gao, C.-S. Lee and K.-K. Cheung, *Org. Lett.*, 2002, **4**, 3271; (h) M.P. Sibi and M. Liu, *Org. Lett.*, 2000, **2**, 3393.

25 J.S. Yadav, B.V.S. Reddy, C. Venugopal and T. Ramalingam, *Synlett*, 2002, 604.

26 Z.-H. Zhang, T.-S. Li and C.-G. Fu, *J. Chem. Res., Synop.,* 1997, 174.