Efficient Assembly of 2,5,6-Substituted Pyrimidines via MgI_2-Mediated Morita−Baylis−Hillman Reaction

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A mild and efficient protocol for the synthesis of a 2,6-disubstituted pyrimidine-5-carboxylate library via a Morita−Baylis−Hillman (MBH) adduct is described. Herein, the three step methodology involves the use of substituted α-iodomethylene *β*-keto ester intermediates obtained after oxidation of the MBH adducts, which are condensed with various types of amidine or guanidine derivatives, to generate the 2, 6-disubstituted pyrimidines-5-carboxylate libraries.

Introduction

Structurally diverse small molecules serve as selective agents to dissect complex cellular signaling pathways dysregulated in disease.[1,2] With the rapid development of high throughput screening programs to identify potential drug candidates, the current challenge is to feed and sustain the screening efforts with diverse small molecule scaffolds. This process largely depends on new leads discovered via a rationally designed synthesis or screening of libraries generated via combinatorial synthesis. N-containing heterocycles are commonly occurring structural motifs in natural products, as well as pharmacophores in top-selling drugs.[3,4] Not surprisingly, they continue to be the inspiration for core scaffolds for library synthesis in modern day drug discovery.

Pyrimidines and their derivatives are valued for their pharmacological properties, such as anti-inflammatory properties,[5] antiallergic properties,[5] antidepressant properties,[6] Ca-sensing receptor antagonists,[7] and also as fungicides and pesticides.[8,9] They have been utilized by several drug discovery programs as core scaffolds for library development. 2,5,6-Trisubstituted pyrimidines, especially 5-amide, ester, and carboxylate derivatives, have gained importance as PGDS inhibitors, PPAR activators and cardiovascular agents (Figure 1).[5,10,11] A wide variety of synthetic routes are known for efficient construction of the pyrimidine ring. The condensation of a *β*-oxoester or related synthons with amidine derivatives is the most commonly utilized method.[12]

Not many *β*-oxoesters are commercially available, thus, efforts toward convenient library synthesis are hampered. In addition, the desired substitution pattern can only be accessed via multistep methods utilizing expensive or toxic metal-mediated reactions.

Our interest in the synthesis of heterocyclic libraries with potential pharmaceutical activities led us to investigate an alternative route to synthesize 2,6-disubstituted pyrimidines-5-carboxylates from α-iodomethylene *β*-keto esters, **8** (Scheme 1) and amidine or guanidine derivatives suitable for library development. The Morita−Baylis−Hillman (MBH) reaction provides a rapid method for generation of α-iodomethylene *β*-keto esters after a simple oxidation of the MBH adduct. We were especially interested in utilizing the MBH reaction because of the wide substrate tolerance, commercial availability, and ease of synthesis of the starting materials.[13−15] The Lewis acid activated MBH-type coupling of aldehyde with propiolic esters to produce substituted α-(hydroxym-

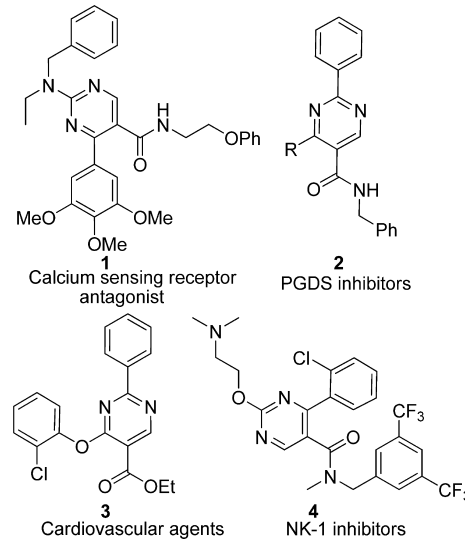

Figure 1. Pyrimidine-5-carboxylates and carboxamides with known biological activity.

Scheme 1. General Scheme for the Synthesis of 2,6-Disubstituted Pyrimidine-5-carboxylates from Aldehydes

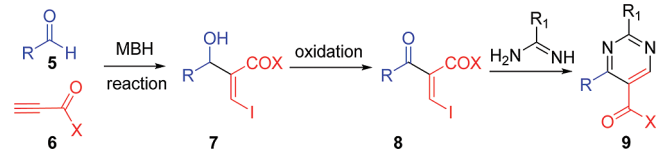

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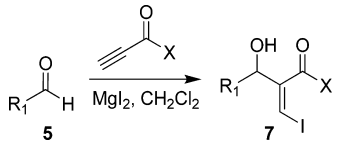
Table 1. MBH Reaction of Methyl Propiolate/Propiolamides



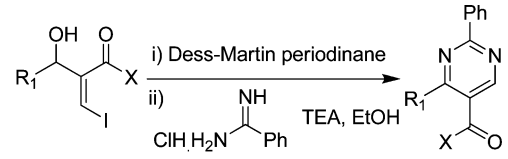
entry	compound	R_1	X	**7** yield, %
1	**7a**	Ph	OMe	60
2	**7b**	4-methoxyphenyl	OMe	69
3	**7c**	4-nitrophenyl	OMe	49
4	**7d**	naphthyl	OMe	94
5	**7e**	biphenyl	OMe	67
6	**7f**	4-(*N*,*N*-dimethylamino) phenyl	OMe	no reaction
7	**7g**	2,4-dichlorophenyl	OMe	85
8	**7h**	Me	OMe	82
9	**7i**	Bn	OMe	69
10	**7j**	propenyl	OMe	87
11	**7k**	*i*Bu	OMe	96
12	**7l**	*t*Bu	OMe	95
13	**7m**	*t*-Bu	NH_2	98
14	**7n**	Me	NHBn	27

ethyl)-iodoacrylates, **7** (Scheme 1) has been well documented in recent years.[16−28] Various groups have reported isolation of E or Z-selective synthetic methodologies toward substituted α-(hydroxymethyl)-iodoacrylates. Among the various Lewis acids that have been used: $TiCl_4/Me_2S$,[20] $BF_3 \cdot Et_2O$/TMSI,[21] $ZrCl_4/(n\text{-}Bu)_4NI$,[22] $TiCl_4/(n\text{-}Bu)_4NI$,[23] Et_2AlI,[17,24] and MgI_2;[25−28] MgI_2 is readily available, nontoxic and less sensitive to moisture. We herein report a new three step method involving the MgI_2 mediated MBH type reaction, Dess-Martin periodinane oxidation of the MBH adduct and subsequent condensation with amidine or guanidine derivatives to produce a diverse 2, 6-disubstituted pyrimidines-5-carboxylate library.

We synthesized a small library of substituted α-(hydroxymethyl)-iodoacrylates via MgI_2-promoted MBH reaction using a modified procedure of Paré et al.[25−28] This method predominantly generates Z-olefin as the major product. Our initial studies also involved the use of various Lewis acids including $MgBr_2$ and Zn(II) halides. No reaction was observed with Zn(II) halides even after 5 days; however, $MgBr_2$ formed the desired product albeit in low yield relative to MgI_2.

We investigated the scope of the MgI_2-mediated MBH reaction by examining a variety of electrophiles (Table 1). The system proved efficient for both alkyl and aryl aldehydes (49−98%, Table 1). For electron-deficient aldehydes, the MBH adduct of *p*-nitrobenzaldehyde and methyl propiolate was obtained after only 8 h in 49% yield (Table 1, entry 3). Modest to good yields were obtained for electron rich aldehydes such as *p*-methoxybenzaldehyde (Table 1, entry 2) despite incomplete conversion even after longer reaction times. However, the highly electron rich *N*,*N*-dimethyl benzaldehyde did not afford any product even after 7 days. The MBH adducts from aromatic aldehydes were obtained in 60−94% yield (Table 1, entries 1, 4, 5, 7), and the MBH adducts from aliphatic aldehydes-acetaldehyde, trimethyl acetaldehyde and isobutyraldehyde were obtained in 82%, 95% and 96% yields, respectively (Table 1, entries 8, 11, 12). The reaction conditions could be efficiently extended to α,β-unsaturated aldehydes and resulted in 87% yield for the MBH adduct from methacrolein (Table 1, entry 10). The desired MBH adduct from reaction of aldehydes with propiolamide could be isolated by simple precipitation in high yield (Table 1, entries 13). Secondary amides of propiolic acid also afforded the desired product albeit in low yields (Table 1, entry 14).

Table 2. Oxidation of MBH Adducts **9a**−**m** Followed by Condensation with Benzamidine



7a-m **9a-m**

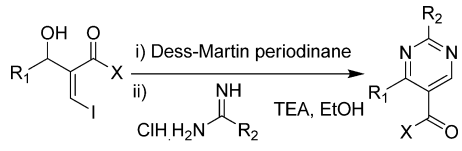
Entry	Compound	R_1	X	**9**[a] Yield, %
1	9a	Ph	OMe	80
2	9b	4-methoxyphenyl	OMe	71
3	9c	4-nitrophenyl	OMe	51
4	9d	naphthyl	OMe	63
5	9e	biphenyl	OMe	45
6	9g	2,4-dichlorophenyl	OMe	66
7	9h	Me	OMe	82
8	9i	Bn	OMe	75
9	9j	Propenyl	OMe	35
10	9k	*i*Bu	OMe	66
11	9l	*t*-Bu	OMe	85
12*	9m	*t*-Bu	NH_2	10

*isolated yields low due to highly polar nature of the starting material
[a] Yield over two steps.

The Dess−Martin periodinane is often used when a mild, selective oxidant is required.[29−34] We were able to cleanly oxidize the MBH adducts with Dess−Martin periodinane to generate the α-iodomethylene β-keto esters, **8** (Scheme 1). Other oxidizing agents, such as PCC and Jones reagent,[35] did not afford the products in similar purity and yields. The α-iodomethylene β-keto esters, **8** were used immediately and condensed with benzamidine under basic conditions to generate the 2, 5, 6-trisubstituted pyrimidines in good to excellent yields (**9a**−**m**, Table 2). In general, esters afforded the products in better yield than the primary amide probably due to the high polarity of the amides which led to problems in product isolation (Table 2, entry 12). Among the aryl substituted MBH adducts, substitutions on the phenyl ring somewhat lowered the yield of the resulting pyrimidines possibly because of steric effects (Table 2, entries 1, 4, 5, 6). All alkyl substituted starting materials, afforded good yields of substituted pyrimidines. The oxidation product when R_1 was propenyl group was light sensitive and showed some deterioration while handling, leading to lowering in yield of the final product (Table 2, entry 9).

To further examine the scope and utility of this sequence additional amidine and guanidine derivatives were treated with the aliphatic α-iodomethylene β-keto ester, **8h** and **8l**, under the same reaction system conditions (Table 3). In all cases, the reaction proceeded smoothly in modest to high yields. Notable examples from Table 3 include reactions with benzamidine, guanidine, and a guanidylated amino acid

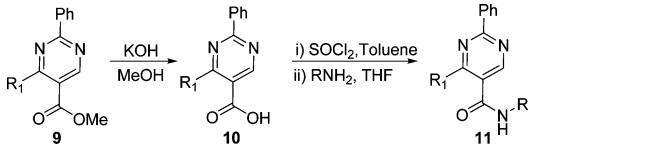
Table 3. Pyrimidine Synthesis-Variation of the R_2 Group



7 9

Entry	Compound	R_1	R_2	X	9 Yield, %
1	9l	*t*-Bu	Ph	OMe	85
2	9n	*t*-Bu	H	OMe	21
3	9o	*t*-Bu	Me	OMe	48
4	9p	Me	NH_2	OMe	95
5	9q	*t*-Bu	SMe	OMe	60
6	9r	*t*-Bu		OMe	80

Scheme 2. Synthesis of 2,6-Disubstituted Pyrimidine-5-carboxamides



10h, R_1=Me, nearly quant.
10k, R_1=*i*Bu, 96%

11h1, R= Bn, R_1=Me, 86%
11k1, R= Bn, R_1=*i*Bu, 89%
11k2, R=Phe-OMe, R_1=*i*Bu, 91%

(Table 3, entries 1, 4, 6), which gave 85%, 95% and 80% yields, respectively, after condensation.

The direct assembly of 2,6-disubstituted pyrimidine-5-carboxamides utilizing the MBH reaction between *N*-substituted propiolamides and aldehydes resulted in low yields (Table 1, entry 14). However, we were able to synthesize the desired 2, 6-disubstituted pyrimidine-5-carboxamides, **11** in excellent yields starting with the corresponding ester (Scheme 2). The ester was first hydrolyzed to the pyrimidine carboxylic acid under basic conditions. Treatment with $SOCl_2$ followed by quenching with the desired amine affords the desired 2, 6-disubstituted pyrimidines-5-carboxamide, **11**.

Conclusion

In summary, we have developed a new three-step methodology employing MgI_2-mediated MBH reaction of an aldehyde and propiolates or propiolamides, oxidation, followed by condensation with the appropriate amidine or guanidine derivatives. This sequence provides efficient access to a library of 2, 6 disubsituted pyrimidine-5-carboxylates. A variety of electrophiles, including electron-poor, electron-rich, aliphatic, and aromatic aldehydes were successfully employed to afford the MBH adducts. Amidine and guanidine derivatives including benzamidine and a guanidylated amino acid were used for the condensation step. These studies provide a valuable platform for the development of methodology toward other heterocycles.

Experimental Section

Materials and Methods. Starting materials, organic and inorganic reagents (ACS grade), and solvents were obtained from commercial sources and used as received unless otherwise noted. Moisture- and air-sensitive reactions were carried out under an atmosphere of argon. Thin layer chromatography (TLC) was performed on glass plates precoated with 0.25 mm thickness of silica gel (60 F-254) with fluorescent indicator (EMD or Whatman). Column chromatographic purification was performed using silica gel 60 Å, #70−230 mesh (Selecto Scientific). ^{1}H NMR and ^{13}C NMR spectra were obtained using a 400 MHz Varian Mercury plus instrument at 25 °C in chloroform-*d* ($CDCl_3$), unless otherwise indicated. Chemical shifts (δ) are reported in parts per million (ppm) relative to internal tetramethylsilane (TMS) or chloroform (δ 7.26) for ^{1}H NMR and chloroform (δ 77.0) for ^{13}C NMR. Multiplicity is expressed as (s = singlet, br = broad, d = doublet, t = triplet, q = quartet, or m = multiplet) and the values of coupling constants (J) are given in hertz (Hz). High Resolution Mass Spectrometry (HRMS) spectra were carried out on an Agilent 1100 Series in the ESI-TOF mode. Microwave reactions were performed in a closed vessel in a Biotage Initiator I microwave reactor.

General Procedure to Synthesize Substituted α-(Hydroxymethyl)*β*-iodoacrylates (7a−n). A dry flask was flushed with N_2 and loaded with MgI_2 (1.2 equiv). Aldehyde (1 mmol, 1 equiv) was added in a solution of dichloromethane (5.0 mL) at 0 °C. The reaction mixture was allowed to warm to room temperature and stirred for 30 min. Methyl propiolate (1.3 equiv) was added dropwise, and the reaction was stirred at room temperature for ∼30 h. The reaction was quenched by addition of cold 1 N HCl. The two phases were separated, and the aqueous layer was extracted with EtOAc (3×, 15 mL). The organic extracts were combined and washed with brine (1×, 15 mL). The organic layer was collected, dried over Na_2SO_4, and filtered. The solvent was removed in vacuo and the product was purified by column chromatography (20% EtOAc/hexanes) to afford the product in good to excellent yields. *Note: The reaction was found to be successful for various aldehydes at scales between 0.6−3.5 mmol.*

Methyl 3-Hydroxy-2-(iodomethylene)-4,4-dimethylpentanoate, (7l): yield 95%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.07(s, 1H), 4.24(d, J = 4 Hz, 1H), 3.83(3.79)(s, 3H), 2.59(d, J = 4 Hz, 1H), 0.89(s, 9H);^{13}C NMR (100 MHz $CDCl_3$) δ 168.2, 165.2, 145.6, 129.7, 95.4, 85.9, 82.9, 52.2, 36.3, 25.8; HRMS (ESI) calcd for $C_9H_{15}INO_3$ $[M + Na]^+$ 320.9958, found 320.9951. Spectra confirmed with previously reported results.[9]

General Procedure to Synthesize the α-Iodomethylene *β*-Keto Ester (8a−m). A dry flask was flushed with N_2 and loaded with substituted α-(hydroxymethyl)-*β*-iodoacrylates (1equiv) in a solution of dichloromethane (5 mL) at 0 °C. Dess−Martin periodinane (1.1 equiv) was added dropwise, and the reaction was allowed to stir at room temperature for 1.5 h. The reaction was quenched by addition of cold 1:1 (v/v) solution of 10% $Na_2S_2O_3$ and $NaHCO_3$ (2×, 15 mL). The two phases were separated, and the aqueous layer was extracted with dichloromethane (2×, 15 mL). The organic extracts were combined and washed with cold brine (1×, 15 mL). The organic layer was collected, dried over

Na_2SO_4, and filtered. The solvent was removed in vacuo to afford the product in good to excellent yields. The product was used for further steps immediately. *Note: The reaction was found to be successful for various substituted α-(hydroxymethyl)-iodoacrylates at scales between 0.2−1.1 mmol.*

Methyl 3-Oxo-2-(iodomethylene)-4,4-dimethylpentanoate (8l): yield 96%; ^{1}H NMR (400 MHz, $CDCl_3$) 7.52(s, 1H), 3.83(s, 3H), 1.19(s, 9H);^{13}C NMR (100 MHz, $CDCl_3$) δ 205.5, 164.3, 145.7, 93.3, 52.6, 44.8, 27.0.

General Procedure to Synthesize the Pyrimidine Esters (9a−r). A solution of α-iodomethylene β-keto ester (1 equiv) in ethanol (3 mL) was mixed with TEA (2 equiv) and the amidine or guanidine derivatives as the HCl salts (1 equiv) and heated in a Biotage Initiator microwave reactor at 130 °C for 30 min. The reaction was allowed to cool, and the solvent was evaporated. The residue was washed with brine and extracted with ethyl acetate (2×, 10 mL). The organic extracts were combined, dried over Na_2SO_4, and filtered. The product was purified by column chromatography (20% EtOAc/hexanes) to provide the product in modest to excellent yields. *Note: The reaction was found to be successful for various α-iodomethylene β-keto esters at scales between 0.2−1.1 mmol.*

Methyl 4-*tert*-Butyl-2-methylpyrimidine-5-carboxylate (9l): yield 85%;^{1}H NMR (400 MHz, $CDCl_3$) δ 8.56(s, 1H), 3.92(s, 3H), 2.76(s, 3H), 1.40(s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.2, 169.3, 168.2, 156.9, 123.2, 53.0, 39.6, 29.4, 26.4; HRMS (ESI) calcd for $C_{11}H_{16}N_2O_2$ $[M + H]^+$ 209.1285, found 209.1276.

General Procedure to Generate Pyrimidine Carboxylic Acid (10). A solution of pyrimidine 5- carboxylate (1 equiv) in methanol (5 mL) was mixed with KOH (3 equiv) and stirred at room temperature overnight. The reaction was monitored by TLC at the end of 8 h, and the solvent was evaporated. The residue was taken up in EtOAc (15 mL), and the reaction was acidified with 1 M $KHSO_4$ to pH 3. The mixture was extracted with ethyl acetate (2×, 20 mL). The organic extracts were combined and washed with cold brine (1×, 15 mL). The organic layer was collected, dried over Na_2SO_4, and filtered. The solvent was evaporated in vacuo to yield a pale white solid in high to nearly quantitative yields. *Note: The reaction was found to be successful for various pyrimidine esters at scales between 0.4−1.8 mmol.*

4-Methyl-2-phenylpyrimidine-5-carboxylic acid (10h): yield nearly quant.; ^{1}H NMR (400 MHz, CD_3OD) δ 9.34(s, 1H), 8.63(d, $J = 4$ Hz, 2H), 7.79−7.72(m, 3H), 2.93(s, 3H); ^{13}C NMR (100 MHz, CD_3OD) δ 168.3, 166.1, 164.1, 159.0, 136.2, 131.6, 128.8, 128.3, 121.8, 24.5; HRMS (ESI) calcd for $C_{12}H_{10}N_2O_2$ $[M - H]^+$ 213.0670, found 213.0676.

General Procedure to Synthesize Carboxamides of Pyrimidines 11. A solution of pyrimidine 5-carboxylic acid (1 equiv) in toluene (3 mL) was refluxed with $SOCl_2$ (1.5 equiv) for 2.5 h. The reaction was cooled and the solvent was removed in vacuo to afford a reddish-brown solid. The solid was dissolved in THF (5 mL) and cooled to −78 °C. TEA (3 equiv) and the amine (1 equiv) were added, and the reaction mixture was stirred for 0.5 h at −78 °C and then at room temperature for 1 h. The reaction was quenched by pouring in a mixture of $NaHCO_3$ and CH_2Cl_2 (1:1 v/v, 20 mL). The organic layer was collected. The aqueous layer was extracted with CH_2Cl_2 (2×, 15 mL). The organic layers were combined and dried over Na_2SO_4 and filtered and evaporated in vacuo. The crude product was then purified by column chromatography (20% EtOAc/hexanes) to afford the product in high yields. *Note: The reaction was found to be successful for various pyrimidine esters at scales between 0.4−1.8 mmol.*

***N*-Benzyl-4-methyl-2-phenylpyrimidine-5-carboxamide (11h1):** yield 86%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.74(s, 1H), 8.45−8.43(m, 2H), 7.50−7.48(m, 3H), 7.39−7.33(m, 5H), 6.23(br, 1H), 4.66(d, $J = 2.8$ Hz, 2H), 2.74(s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.4, 166.3, 165.1, 155.1, 137.7, 137.1, 131.5, 129.2, 128.9, 128.8, 128.2, 128.1, 126.9, 44.5, 23.6; HRMS (ESI) calcd for $C_{19}H_{17}N_3O$ $[M + H]^+$ 304.1444, found 304.1442.

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Supporting Information Available. Experimental details and spectroscopic characterization. This material is available free of charge via the Internet at http://pubs.acs.org/.

References and Notes

(1) Schreiber, S. L.; Nicolaou, K. C.; Davies, K. *Chem. Biol.* **2002**, *9*, 1–2.
(2) Webb, T. R. *Curr. Opin. Drug Discovery Dev.* **2005**, *8*, 303–308.
(3) Hassner, A.; Murthy, K. S. K.; Maurya, R.; Dehaen, W.; Friedman, O. *J. Heterocycl.Chem.* **1994**, *31*, 687–694.
(4) Butler, M. S. *J. Nat. Prod.* **2004**, *67*, 2141–2153.
(5) Aldous, S. C.; Jiang, J. Z.; Lu, J.; Ma, L.; Mu, L.; Munson, H. R.; Sabol, J. S.; Thurairatnam, S.; Vandeusen, C. L. PCT Int. Appl. WO2007041634 A1, April 12, 2007.
(6) Boes, M.; Galley, G.; Godel, T.; Hoffmann, T.; Hunkeler, W; Schnider, P.; Stadler, H. PCT Int. Appl. WO2000073279 A1, December 7, 2000.
(7) Yang, W.; Ruan, Z.; Wang, Y.; Kirk, K. V.; Ma, Z.; Arey, B. J.; Cooper, C. B.; Seethala, R.; Feyen, J. H. M.; Dickson, J. K., Jr. *J. Med. Chem.* **2009**, *52*, 1204–1208.
(8) Seitz, T.; Santel, H. J.; Luerssen K.; Schmidt, R. R.; Haenssler, G. Ger. Offen DE4224163 A1 19940127, January 27, 1994.
(9) Prisbylla, M. P. U.S. Patent 5022915 A, June 11th, 1991.
(10) Ackermann, J.; Aebi, J.; Binggeli, A.; Grether, U.; Kuhn, B.; Maerki, H.-P.; Meyer, M. U.S. Pat. Appl. Publ. US2006183754 A1, June 17th, 2006.
(11) Woltering, E.; Tuch, A.; Dittrich-Wengenroth, E.; Kretschmer, A.; Baerfacker, L.; Bauser, M.; Ellighaus, P.; Lustig, K.; Pook, E.; Weber, O. PCT Int. Appl. WO2006097220 A1, September 21, 2006.
(12) von Angerer, S. *Product Class 12:Pyrimidines. In Science of Synthesis*; Yamamoto, Y., Ed.; Thieme Publishing Group; Sttutgart, Germany, 2003; pp 379−573.
(13) Singh, V.; Batra, S. *Tetrahedron* **2008**, *64*, 4511–4574.
(14) Ciganek, E. *Org. React.* **1997**, *51*, 201–350.
(15) Basavaiah, D.; Rao, P. D.; Hyma, R. S. *Tetrahedron* **1996**, *52*, 8001–8062.
(16) Lim, H. N.; Ji, S.-H.; Lee, K.-J. *Synthesis* **2007**, *16*, 2454–2460.
(17) Li, G.; Xu, X.; Chen, D.; Timmons, C.; Carducci, M. D.; Headley, A. D. *Org. Lett.* **2003**, *5*, 329–331.
(18) Yadav, J. S.; Reddy, B. V. S.; Gupta, M. K.; Pandey, S. K. *J. Mol. Catal. A: Chemical* **2007**, *264*, 309–312.

(19) Hong, W. P.; Lee, K.-J. *Synthesis* **2006**, *6*, 963–968.
(20) Kinoshita, S.; Kinoshita, H.; Iwamura, T.; Watanabe, S.-i.; Kataoka, T. *Chem.−Eur. J.* **2003**, *9*, 1496–1502.
(21) Lee, S. I.; Hwang, G.-S.; Shin, S. C.; Lee, T. G.; Jo, R. H.; Ryu, D. H. *Org. Lett.* **2007**, *9*, 5087–5089.
(22) Zhang, C.; Lu, X. *Synthesis* **1996**, 586–588.
(23) Taniguchi, M.; Hino, T.; Kishi, Y. *Tetrahedron Lett.* **1986**, *39*, 4767–4770.
(24) Wei, H.-X.; Gao, J. J.; Li, G.; Pare, P. W. *Tetrahedron Lett.* **2002**, *43*, 5677–5680.
(25) Wei, X.-H.; Jasoni, R. L.; Hu, J.; Li, G.; Paré, P. W. *Tetrahedron* **2004**, *60*, 10233–10237.
(26) Wei, X.-H.; Hu, J.; Jasoni, R. L.; Li, G.; Paré, P. W. *Helv. Chim. Acta* **2004**, *87*, 2359–2363.
(27) Deng, G.-H.; Hu, H.; Wei, H.-X.; Paré, P. W. *Helv. Chim. Acta* **2003**, *86*, 3510–3515.
(28) Senapati, B. K.; Hwang, G.-S.; Lee, S.; Ryu, D. H. *Angew. Chem., Int. Ed.* **2009**, *48*, 1–5.
(29) Dess, D. B.; Martin, J. C. *J. Org. Chem.* **1983**, *48*, 4155–4156.
(30) Dess, D. B.; Martin, J. C. *J. Am. Chem. Soc.* **1991**, *113*, 7277–7287.
(31) Boeckman, R. J., Jr.; Shao, P.; Mullins, J. J. *Org. Synth.* **2000**, *77*, 141–152.
(32) Boeckman, R. J., Jr. In *Encyclopedia of Reagents for Organic Synthesis*; Paquette, L. A., Ed.; Wiley: NewYork, 1995; pp 4982−4987.
(33) Lawrence, N. J.; Crump, J. P.; McGown, A. T.; Hadfield, J. A. *Tetrahedron Lett.* **2001**, *42*, 3939–3941.
(34) Hong, W. P.; Lee, K.-J. *Synthesis* **2006**, *6*, 0963−0968.
(35) Hoffmann, H. M. R.; Gassner, A.; Eggert, U. *Chem. Ber.* **1991**, *124*, 2475–2480.

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