Pyridinium Ylide-Assisted One-Pot Two-Step Tandem Synthesis of Polysubstituted Cyclopropanes

Qi-Fang Wang, Xiao-Kai Song, Jiao Chen, and Chao-Guo Yan*

College of Chemistry & Chemical Engineering, Yangzhou University, Yangzhou 225002, China

Received January 10, 2009

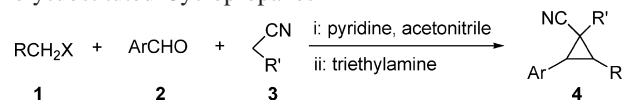
A sequential one-pot two-step tandem reaction for efficient synthesis of polysubstituted cyclopropanes has been developed. The three-component reaction of α-halogenated methylene compounds, aromatic aldehydes, and acetonitrile derivatives produced first the intermediates pyridinium salts and electron-deficient olefins, followed by cyclopropanation of pyridinium ylide with electron-deficient olefins in situ to afford polysubstituted cyclopropanes. Target compounds were obtained in high yields and were diastereomerically pure after recrystallization.

Introduction

The cyclopropane subunit plays a prominent role in organic chemistry. Its strained structure, interesting bonding characteristics, and value as an internal mechanistic probe have attracted the attention of the organic community.[1,2] It is also found as a basic structural unit in a wide variety of naturally occurring compounds and rationally designed pharmaceutical agents for its biological activity.[3] As a result, the development of efficient methods for the synthesis of cyclopropanes has attracted intensive research interest.[4,5] The most important and useful methods for the preparation of cyclopropanes include Simmons−Smith cyclopropanation,[6] transition-metal-mediated carbene transfer from aliphatic diazo compounds to carbon−carbon double bonds,[7] Michael-initiated ring closure of ylides with electron-deficient olefins,[8] and base-catalyzed cyclopropanation reaction between α-halogenated compounds with electron-deficient olefins.[9]

The combination of ylides and electron-deficient olefins with the Michael-initiated ring closure (MIRC) strategy is the most useful methodology for preparing highly substituted or functionalized cyclopropanes. Various ylides, including sulfonium,[10] telluronium,[11] arsonium,[12] and even ammonium ylides,[13] have been successfully applied in the enantioselective cyclopropanation of electron-deficient olefins. As one of special ammonium ylides, pyridinium ylides also can react with alkenes substituted with electron-withdrawing groups to give the corresponding cyclopropanes in good yields.[14] The synthetic significance of cyclopropanes has prompted investigations into better methods of synthesis by using simple and feasible approaches. In recent years, most of the synthetic efforts involving cyclopropanes have focused on the enantioselective synthesis of these compounds. The one-pot multicomponent approach or domino procedure for the preparation of the cyclopropane core is nearly neglected or not explored thoroughly.[15] As a part of our ongoing efforts in developing multicomponent syntheses to access potentially bioactive scaffolds,[16] we envisaged a novel one-pot two-step tandem reaction for the synthesis of cyclopropanes from suitable α-halomethyl compounds, aromatic aldehydes, and acetonitrile derivatives (Scheme 1). This method should be applicable to synthesis of cyclopropane libraries with high diversity. We expect this method to find extensive application in the fields of combinatorial chemistry and drug discovery.

Scheme 1. One-Pot Two-Step Tandem Synthesis of Polysubstituted Cyclopropanes[a]

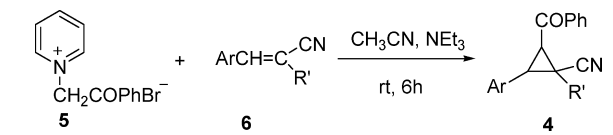


[a] R = PhCO, CO_2Et, *p*-$NO_2C_6H_4$, $CONEt_2$, etc.; X = Cl, Br; R′ = CN, CO_2Et, $CONH_2$.

Results and Discussion

The first substrate we examined was phenacyl bromide. The Knoevenagel condensation of aromatic aldehydes and malononitrile can easily produce arylidenemalononitrile **6** (R′ = CN), and the reaction of pyridine with phenacyl bromide in refluxing toluene for about one hour afforded corresponding *N*-phenacylpyridinium bromide **5** in nearly quantitative yield. After decanting toluene, arylidenemalononitrile **6** (R′ = CN), triethylamine and acetonitrile as solvent were added and the mixture was stirred at room temperature for about six hours affording cyclopropanes **4**{*1a*−*1d*} in high yields (72−91%) (Scheme 2). *N*-Phenacylpyridinium bromide **5** can also be prepared more conveniently by reaction of pyridine with phenacyl bromide **1** in acetonitrile at room temperature for about 2−3 h. Then ethyl arylidenecyanoacetate **6** (R′ = COOEt) and triethylamine

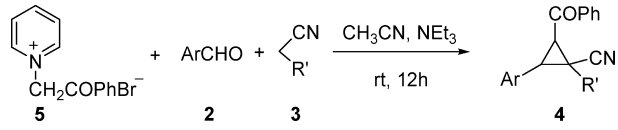
Scheme 2. Two-Step Synthesis of Polysubstituted Cyclopropanes



* To whom correspondence should be addressed. E-mail: cgyan@yzu.edu.cn.

10.1021/cc900005v CCC: $40.75
Published on Web 07/15/2009

Scheme 3. One-Pot Synthesis of Polysubstituted Cyclopropanes



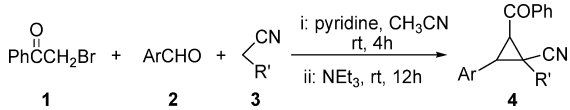
5 2 3 4

were added to give cyclopropanes **4**{*2a*−*2c*} in excellent yields (75−82%). This process is advantageous as no heating or solvent change is necessary.

In attempt to enhance the efficiency of this reaction, we investigated the development of stoichiometric one-pot three-component reaction process, in which the ethyl arylidenecyanoacetate **6** (R′ = COOEt) could be generated in situ from corresponding aromatic aldehydes and ethyl cyanoacetate. Addition of aromatic aldehyde and ethyl cyanoacetate to the *N*-phenacylpyridinium bromide in acetonitrile, followed by triethylamine and stirring overnight at room temperature, afforded cyclopropane derivatives **4**{*2d*−*2e*} in similar yields (Scheme 3). On the other hand ethyl α-bromoacetate also can react with pyridine in acetonitrile at room temperature to yield *N*-ethoxycarbonylmethylpyridinium bromide. Addition of aromatic aldehyde and malononitrile to the pyridinium salts in acetonitrile, followed by triethylamine and stirring at room temperature for six hours, produced cyclopropane derivatives **4**{*3a*−*3c*} in 65−75% yields. This modified process offers significant advantages as it precludes the necessity to generate and isolate arylidenemalononitrile in a separate step.

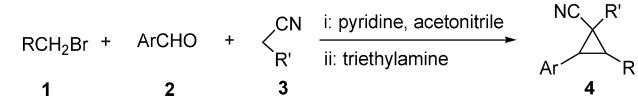
We realized that the required starting pyridinium salt can be formed in situ from the substitution reaction of α-halomethyl compounds to pyridine,[17] and arylidenemalononitrile could be formed in situ by the Knoevenagel condensation of aromatic aldehyde with malononitrile catalyzed by pyridine. Thus a three-component reaction including phenacyl bromide, aromatic aldehyde and malononitrile in the presence of pyridine in acetonitrile was carried out at room temperature. Unfortunately the reaction mostly stopped at the step of formation of arylidenemalononitrile and *N*-phenacylpyridinium bromide and could not go further to finish the formation of cyclopropane efficiently. This result indicates that pyridine can only catalyze Knoevenagel condensation but cannot catalyze cyclopropanation reaction because of its weaker basicity. After adding triethylamine to the reaction mixture, the cyclopropanation finished very quickly and cyclopropanes **4**{*1e*, *1f*} can be formed in satisfied yields (Scheme 4). This methodology is also applicable to ethyl cyanoacetate. When a mixture of phenacyl bromide, aromatic aldehyde, ethyl cyanoacetate, pyridine and acetonitrile as solvent was stirred for about 4−12 h at room temperature and then triethylamine was added to the mixture, the substituted cyclopropanes **4**{*2f*} can be formed. These facts provide a great chance for us to develop a sequential one-pot two-step tandem reaction for the efficient preparation of cyclopropanes.

Scheme 4. One-Pot Two-Step Synthesis of Polysubstituted Cyclopropanes

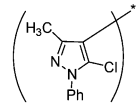
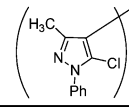


1 2 3 4

Table 1. Synthesis of Substituted Cyclopropanes

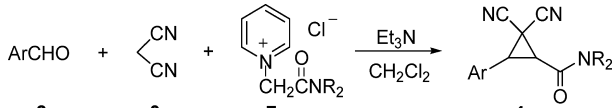


1 2 3 4

entry	R	Ar	R'	yield(%)	mp(°C)[Lit.]
4{*1a*}	C_6H_5CO	C_6H_5	CN	88	120–121[8b]
4{*1b*}	C_6H_5CO	*p*-MeC_6H_4	CN	72	161–162[8d]
4{*1c*}	C_6H_5CO	*p*-ClC_6H_4	CN	91	175–176[8b]
4{*1d*}	C_6H_5CO	*p*-BrC_6H_4	CN	76	169–170[8d]
4{*1e*}	C_6H_5CO	*p*-FC_6H_4	CN	61	156[8c]
4{*1f*}	C_6H_5CO	*m*-ClC_6H_4	CN	54	170-171
4{*2a*}	C_6H_5CO	*p*-ClC_6H_4	COOEt	82	91-92
4{*2b*}	C_6H_5CO	*p*-BrC_6H_4	COOEt	79	95-96
4{*2c*}	C_6H_5CO	*m*-BrC_6H_4	COOEt	75	146-147
4{*2d*}	C_6H_5CO	C_6H_5	COOEt	64	78
4{*2e*}	C_6H_5CO	*p*-FC_6H_4	COOEt	70	99
4{*2f*}	C_6H_5CO	*m*-ClC_6H_4	COOEt	58	138
4{*3a*}	COOEt	*o*-BrC_6H_4	CN	75	191-193[16]
4{*3b*}	COOEt	2, 4-$Cl_2C_6H_3$	CN	62	201-203
4{*3c*}	COOEt	*p*-*t*-BuC_6H_4	CN	70	173-175
4{*4a*}	*p*-$NO_2C_6H_4$	C_6H_5	CN	90	169-170
4{*4b*}	*p*-$NO_2C_6H_4$	*p*-MeC_6H_4	CN	81	161-162
4{*4c*}	*p*-$NO_2C_6H_4$	*p*-EtC_6H_4	CN	79	122
4{*4d*}	*p*-$NO_2C_6H_4$	*p*-*i*-PrC_6H_4	CN	93	122
4{*4e*}	*p*-$NO_2C_6H_4$	*p*- $(CH_3)_2NC_6H_4$	CN	48	164-165
4{*4f*}	*p*-$NO_2C_6H_4$	*p*-$MeOC_6H_4$	CN	82	130-131
4{*4g*}	*p*-$NO_2C_6H_4$	*p*-FC_6H_4	CN	90	167
4{*4h*}	*p*-$NO_2C_6H_4$	*p*-ClC_6H_4	CN	94	201
4{*4i*}	*p*-$NO_2C_6H_4$	*p*-BrC_6H_4	CN	91	208
4{*4j*}	*p*-$NO_2C_6H_4$	*m*-MeC_6H_4	CN	87	130
4{*4k*}	*p*-$NO_2C_6H_4$	*m*-$PhOC_6H_4$	CN	93	116
4{*4l*}	*p*-$NO_2C_6H_4$		CN	82	161-162
4{*5a*}	*p*-$NO_2C_6H_4$	C_6H_5	COOEt	85	110
4{*5b*}	*p*-$NO_2C_6H_4$	*p*-MeC_6H_4	COOEt	75	111
4{*5c*}	*p*-$NO_2C_6H_4$	*p*-EtC_6H_4	COOEt	85	103
4{*5d*}	*p*-$NO_2C_6H_4$	*p*-*i*-PrC_6H_4	COOEt	87	103
4{*5e*}	*p*-$NO_2C_6H_4$	*p*-$MeOC_6H_4$	COOEt	80	125
4{*5f*}	*p*-$NO_2C_6H_4$	*p*-FC_6H_4	COOEt	90	119
4{*5g*}	*p*-$NO_2C_6H_4$	*p*-ClC_6H_4	COOEt	93	162
4{*5h*}	*p*-$NO_2C_6H_4$	*p*-BrC_6H_4	COOEt	88	170
4{*5i*}	*p*-$NO_2C_6H_4$	*m*-MeC_6H_4	COOEt	81	114-115
4{*5j*}	*p*-$NO_2C_6H_4$	*m*-$PhOC_6H_4$	COOEt	85	145-146
4{*5k*}	*p*-$NO_2C_6H_4$	*m*-$NO_2C_6H_4$	COOEt	85	105
4{*6a*}	*p*-$NO_2C_6H_4$	C_6H_5	$CONH_2$	66	175
4{*6b*}	*p*-$NO_2C_6H_4$	*p*-MeC_6H_4	$CONH_2$	52	198-199
4{*6c*}	*p*-$NO_2C_6H_4$	*p*-EtC_6H_4	$CONH_2$	50	153-154
4{*6d*}	*p*-$NO_2C_6H_4$	*p*-*i*-PrC_6H_4	$CONH_2$	52	159
4{*6e*}	*p*-$NO_2C_6H_4$	*p*-FC_6H_4	$CONH_2$	55	190
4{*6f*}	*p*-$NO_2C_6H_4$	*p*-ClC_6H_4	$CONH_2$	75	206
4{*6g*}	*p*-$NO_2C_6H_4$	*p*-BrC_6H_4	$CONH_2$	68	202-203
4{*6h*}	*p*-$NO_2C_6H_4$	*m*-MeC_6H_4	$CONH_2$	55	174
4{*6i*}	*p*-$NO_2C_6H_4$	*m*-$PhOC_6H_4$	$CONH_2$	69	166-167
4{*6j*}	*p*-$NO_2C_6H_4$	*m*-NO_2Ph	$CONH_2$	53	156
4{*6k*}	*p*-$NO_2C_6H_4$		$CONH_2$	62	223-224

To examine the substrate scope and limitation of this novel tandem reaction, a number of reactive α-halogenated methylene compounds were tested under the above-mentioned one-pot two-step reaction condition. A mixture of *p*-nitrobenzyl bromide, benzaldehyde, malononitrile, and pyridine was stirred at room temperature for 4−12 h; then triethylamine was added to the mixture, and the mixture was stirred for additional six hours. The reaction was completed by TLC analysis, and cyclopropane **4**{*4a*} was synthesized in high yield (90%) (Table 1). To achieve greater diversity,

Table 2. Two-Step Synthesis of Cyclopropane Derivatives



2 3 7 4

entry	R_2	Ar	yield (%)	mp (°C)
4{*7a*}	$(CH_2CH_2)_2O$	C_6H_5	80	199−200
4{*7b*}	$(CH_2CH_2)_2O$	*p*-MeC_6H_4	58	160
4{*7c*}	$(CH_2CH_2)_2O$	*p*-EtC_6H_4	51	170
4{*7d*}	$(CH_2CH_2)_2O$	*p*-*i*-PrC_6H_4	74	159
4{*7e*}	$(CH_2CH_2)_2O$	*p*-$MeOC_6H_4$	55	194−195
4{*7f*}	$(CH_2CH_2)_2O$	*p*-FC_6H_4	64	246−248
4{*7g*}	$(CH_2CH_2)_2O$	*p*-ClC_6H_4	79	239−240
4{*7h*}	$(CH_2CH_2)_2O$	*p*-BrC_6H_4	86	227−228
4{*7i*}	$(CH_2CH_2)_2O$	*m*-MeC_6H_4	64	157
4{*8a*}	$(CH_2)_5$	C_6H_5	66	138−139
4{*8b*}	$(CH_2)_5$	*p*-MeC_6H_4	58	153
4{*8c*}	$(CH_2)_5$	*p*-EtC_6H_4	51	128−130
4{*8d*}	$(CH_2)_5$	*p*-*i*-PrC_6H_4	57	160−161
4{*8e*}	$(CH_2)_5$	*p*-$MeOC_6H_4$	60	116
4{*8f*}	$(CH_2)_5$	*p*-FC_6H_4	84	172
4{*8g*}	$(CH_2)_5$	*p*-ClC_6H_4	88	178−180
4{*8h*}	$(CH_2)_5$	*p*-BrC_6H_4	62	190
4{*9a*}	$(Et)_2$	C_6H_5	96	123−124
4{*9b*}	$(Et)_2$	*p*-MeC_6H_4	89	122−123
4{*9c*}	$(Et)_2$	*p*-$MeOC_6H_4$	84	125−126
4{*9d*}	$(Et)_2$	*p*-ClC_6H_4	91	144−145
4{*9e*}	$(Et)_2$	*p*-BrC_6H_4	76	172−173
4{*9f*}	$(Et)_2$	*m*-BrC_6H_4	87	128−129

18 aldehydes and 3 acetonitrile derivatives such as malononitrile, ethyl cyanoacetate, and cyanoacetoamide were investigated for synthesis of cyclopropane derivatives under this condition. The protocol could be applied to the aromatic aldehydes with either electron-withdrawing groups or electron-donating groups. In the cases where cyanoacetamide was used to replace malononitrile as substrate, the yields of cyclopropanes were relatively lower. The results including yields and melting points of cyclopropane derivatives **4** were given in Table 1.

Encouraged by this success, some chloroacetoamides, such as *N*-chloroacetyldiethylamine, *N*-chloroacetylmorpholine, or *N*-chloroacetylpiperidine, were also used as substrates. Because of its relatively lower reactivity of chloride, they could not react with pyridine at room temperature to form pyridinium salts. By refluxing *N*,*N*-dialkyl chloroacetamide with pyridine in benzene at about 80 °C under conventional heating for about 2 h, the corresponding pyridinium salt was produced. After removing the solvent by evaporation and then aromatic aldehyde, malononitrile, and triethylamine were added to the reaction system, and the whole mixture was stirred in dichloromethane at the room temperature. By using this procedure a series of cyclopropylamides **4**{*7a*−*7i*, *8a*−*8h*, *9a*−*9f*} were prepared in 51−96% yields (Table 2). Thus a one-pot two step tandem reaction was developed for the efficient synthesis of polysubstituted cyclopropylamides.

The structures of all obtained cyclopropanes were fully characterized by ^{1}H and ^{13}C NMR, MS, IR spectra and were fully confirmed by single X-ray diffraction studies performed for ten representative compounds (**4**{*1c*}, **4**{*2a*}, **4**{*4a*}, **4**{*5f*}, **4**{*5g*}, **4**{*7g*}, **4**{*7h*}, **4**{*8h*}, **4**{*9b*}, and **4**{*9c*}. As an example the structure of compound **4**{*1c*} was shown in Figure 1. It should be pointed that the X-ray determination of ten cyclopropane derivatives all clearly display the two substituents at 2, 3-position of cyclopropanes are in anti

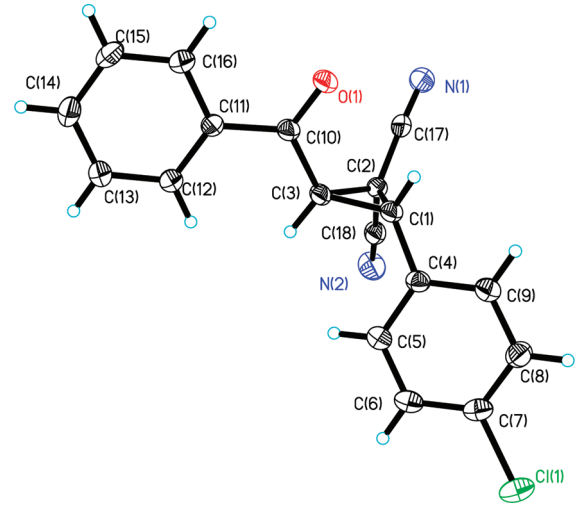
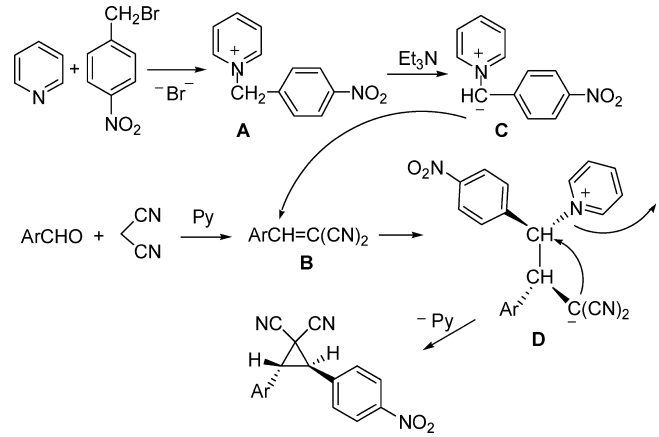


Figure 1. Molecular structure of **4**{*1c*} in the crystal.

Scheme 5. Proposed Mechanism for the Formation of Cyclopropanes



position. The ^{1}H NMR data of the prepared cyclopropanes all show that only one stereoisomer existed in the sample by observing signs of two couplet protons at 2, 3-positon. For examples the ^{1}H NMR spectrum of **4**{*1a*} shows two doublets at 4.03 and 3.90 ppm, respectively, with a coupling constant J = 7.8 Hz for protons at 1,2-position.[12] **4**{*7a*} displays these two protons at 3.88 and 3.24 ppm. For cyclopropanes **4**{*4a*}−**4**{*6k*}, which were derived from the reactions of *p*-nitrobenzyl bromide, the signs of the two protons at 2, 3-positon appears sometimes as AB quadruplet because of the relatively similar electronic effect of 2-*p*-nitrobenzyl and 3-aryl groups (3.74(q) ppm, J = 9.0 Hz for **4**{*4a*}). On the basis of these facts, we could conclude that cyclopropanes prepared by this procedure were in diastereomerically trans configuration, which might display that the stereochemical outcome of this reaction is thermodynamic control.

To explain the mechanism of this one-pot multicomponent tandem reaction, we propose a plausible reaction mechanism, which is illustrated in Scheme 5. The first step is the formation of the two reaction intermediates already described in the preceding paragraph, namely, *N*-*p*-nitrobenzylpyridinium salt (**A**) formed from the addition of reactive α-halogenated methylene compounds, such as *p*-nitrobenzyl bromide, to pyridine and arylidenemalononitrile (**B**) formed

by the Knoevenagel condensation of the respective aromatic aldehyde with malononitrile. The second step is a Michael addition of a pyridinium ylide (**C**), which is formed by deprotonation of the pyridinium species (**A**) by triethylamine to the arylidenemalononitrile (**B**), to afford a new carbanion intermediate (**D**). The last step is the intramolecular substitution of the carbanion to replace pyridine and formation of the cyclopropane. In the last cyclization step, The bucky aryl and *p*-nitrophenyl group would prefer anti position, which subsquently cause the formation of cycloprane with diastereomerically trans-configuration.

Conclusion

In summary, we have developed an one-pot two-step tandem reaction for the efficient synthesis of polysusbtituted cyclopropane derivatives. By using different types of α-halogenated methylene compounds, aromatic aldehydes and acetonitrile derivatives, we could obtain novel libraries of cyclopropane derivatives, which make this methodology suitable for combinatorial and parallel synthesis. The proposed reactions proceed in mild conditions and give the products in good yields with high diastereoselectivity. The separation and purification process are very simple and convenient, only needing recrystallization. Starting materials are inexpensive and commercially available.

Acknowledgment. This work was financially supported by the National Natural Science Foundation of China (Grant No. 20672091).

Supporting Information Available. Experimental details and characterization data including IR, MS, ^{1}H, and ^{13}C NMR spectra, as well as X-ray crystallography for new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

References and Notes

(1) (a) de Meijere, A.; Kozhushkov, S. I.; Khlebnivow, A. F. *Top. Curr. Chem.* **2000**, *207*, 89–147. (b) de Meijere, A.; Kozhushkov, S. I.; Hadjiarapoglou, L. P. *Top. Curr. Chem.* **2000**, *207*, 149–227.

(2) Lysenko, I. L.; Lee, H. G.; Cha, J. K. *Org. Lett.* **2006**, *8*, 2671–2673.

(3) (a) Djerassi, C.; Doss, G. A. *New J. Chem.* **1990**, *14*, 713–719. (b) Salaun, J. *Curr. Med. Chem.* **1995**, *2*, 511–541. (c) Salaun, J. *Top. Curr. Chem.* **2000**, *207*, 1–67. (d) Faust, R. *Angew. Chem., Int. Ed.* **2001**, *40*, 2251–2253.

(4) (a) Lebel, H.; Marcoux, J.-F.; Molinaro, C.; Charette, A. B. *Chem. Rev.* **2003**, *103*, 977–1050. (b) Donaldson, W. A. *Tetrahedron* **2001**, *57*, 8589–8627. (c) Wessjohan, L. A.; Brandt, W.; Thiemann, T. *Chem. Rev.* **2003**, *103*, 1625–1647. (d) Reissig, H. U. *Angew. Chem., Int. Ed.* **1996**, *35*, 971–973.

(5) (a) Salaun, J. *Chem. Rev.* **1989**, *89*, 1247–1270. (b) Hartley, R. C.; Caldwell, S. T. *J. Chem. Soc., Perkin Trans.1* **2000**, 477–502. (c) Lautens, M.; Klute, W.; Tam, W. *Chem. Rev.* **1996**, *96*, 49–92.

(6) (a) Hoveyda, A. H.; Evans, D. A.; Fu, G. C. *Chem. Rev.* **1993**, *93*, 1307–1370. (b) Nicolas, I.; Le Maux, P.; Simonneaux, G. *Coord. Chem. Rev.* **2008**, *252*, 727–735.

(7) Pellissier, H. *Tetrahedron* **2008**, *64*, 7041–7095.

(8) (a) Sun, X. L.; Tang, Y. *Acc. Chem. Res.* **2008**, *41*, 937–948. (b) Peppe, C.; das Chagas, R. P.; Burrow, R. A. *J. Organomet. Chem.* **2008**, *693*, 3441–3445. (c) Ren, Z. J.; Cao, W. G.; Ding, W. Y.; Wang, Y.; Wang, L. L. *Synth. Commun.* **2004**, *34*, 3785–3792. (d) Ren, Z. J.; Cao, W. G.; Chen, J.; Wang, Y.; Ding, W. Y. *Synth. Commun.* **2005**, *35*, 3099–3104.

(9) (a) Arai, S.; Nakayama, K.; Hatano, K.; Shioiri, T. *J. Org. Chem.* **1998**, *54*, 9572–9575. (b) Arai, S.; Suzuki, Y.; Nakayarna, K.; Hatano, K.; Shioiri, T. *Tetrahedron Lett.* **1998**, *39*, 9739–9742. (c) Arai, S.; Nakayama, K.; Ishida, T.; Shioiri, T. *Tetrahedron Lett.* **1999**, *40*, 4215–4218. (d) Miyagawa, T.; Tatenuma, T.; Tadokoro, M.; Satoh, T. *Tetrahedron* **2008**, *64*, 5279–5284. (e) Elinson, M. N.; Feducovich, S. K.; Vereshchagin, A. N.; Gorbunov, S. V.; Belyakov, P. A.; Nikishin, G. I. *Tetrahedron Lett.* **2006**, *47*, 9129–9133.

(10) (a) Corey, E. J.; Chaykovsky, M. *J. Am. Chem. Soc.* **1965**, *87*, 1345–1353. (b) Aggarwal, V. K.; Thompson, A.; Jones, R. V. H.; Standen, M. C. H. *J. Org. Chem.* **1996**, *61*, 8368–8369. (c) Aggarwal, V. K.; Alsono, E.; Fang, G.; Ferrara, M.; Hynd, G.; Porcelloni, M. *Angew. Chem., Int. Ed.* **2001**, *40*, 1433–1435. (d) Shestopalov, A.; Rodinovskaya, L.; Shestopalov, A.; Zlotin, S.; Nesterov, V. *Synlett* **2003**, 2309–2312.

(11) (a) Ye, S.; Huang, Z. Z.; Xia, C. A.; Tang, Y.; Dai, L. X. *J. Am. Chem. Soc.* **2002**, *124*, 2432–2433. (b) Liao, W. W.; Li, K.; Tang, Y. *J. Am. Chem. Soc.* **2003**, *125*, 13030–13031. (c) Wang, Q. G.; Deng, X. M.; Zhu, B. H.; Ye, L. W.; Sun, X. L.; Li, C. Y.; Zhu, C. Y.; Shen, Q.; Tang, T. *J. Am. Chem. Soc.* **2008**, *130*, 5408–5409.

(12) (a) Cao, W. G.; Zhang, H.; Chen, J.; Zhou, X. H.; Shao, M.; McMills, M. C. *Tetrahedron* **2008**, *64*, 163–167. (b) Wu, X. Y.; Cao, W. G.; Zhang, H.; Chen, J.; Jiang, H. Y.; Deng, H. M.; Shao, S.; Zhang, J. P.; Chen, H. Y. *Tetrahedron* **2008**, *64*, 10331–10338. (c) Zhao, Y. H.; Zheng, C. W.; Zhao, G.; Cao, W. G. *Tetrahedron: Asymmetry* **2008**, *19*, 701–708. (d) Cao, W. G.; Zhang, H.; Chen, J.; Deng, H. M.; Shao, M.; Lei, L.; Qian, J. X.; Zhu, Y. *Tetrahedron* **2008**, *64*, 6670–6674.

(13) (a) Papageorgiou, C. D.; Ley, S. V.; Gaunt, M. J. *Angew. Chem., Int. Ed.* **2003**, *42*, 828–831. (b) Papageorgiou, C. D.; Cubillo de Dios, M. A.; Ley, S. V.; Gaunt, M. J. *Angew. Chem., Int. Ed.* **2004**, *43*, 4641–4644. (c) Vanecko, J. A.; Wan, H.; West, F. G. *Tetrahedron* **2006**, *62*, 1043–1062. (d) Bhattacharjee, S. S.; Ila, H.; Junjappa, H. *Synthesis* **1982**, 301–303. (e) Jończyk, A.; Konarska, A. *Synlett* **1999**, 1085–1087. (f) Jończyk, A.; Sucholbiak, D.; Jończyk, A. *Eur. J. Org. Chem.* **2005**, 925–933.

(14) (a) Shestopalov, A. M.; Litvinov, V. P.; Rodinovskaya, L. A.; Sharanin, Yu, A. *Zh. Org. Khim* **1991**, 146–155. (b) Vo, N. H.; Eyermann, C. J.; Hodge, C. N. *Tetrahedron Lett.* **1997**, *38*, 7951–7954. (c) Kojima, S.; Suzuki, M.; Watanabe, A.; Ohkata, K. *Tetrahedron Lett.* **2006**, *47*, 9061–9065. (d) Kojima, S.; Hiroike, K.; Ohkata, K. *Tetrahedron Lett.* **2004**, *45*, 3565–3568. (e) Kojima, S.; Fujitomo, K.; Shinohara, Y.; Shimizu, M.; Ohkata, K. *Tetrahedron Lett.* **2000**, *41*, 9847–9851. (f) Yamada, S.; Yamamoto, J.; Ohta, E. *Tetrahedron Lett.* **2007**, *48*, 855–858.

(15) Adamo, M. F. A.; Konda, V. R. *Tetrahedron Lett.* **2008**, *49*, 6224–6226.

(16) (a) Yan, C. G.; Song, X. K.; Wang, Q. F.; Sun, J.; Siemeling, U.; Bruhn, C. *Chem. Commun.* **2008**, 1440–1442. (b) Yan, C. G.; Wang, Q. F.; Song, X. K.; Sun, J. *J. Org. Chem.* **2009**, *74*, 710–718.

(17) (a) Huang, X.; Zhang, T. X. *Tetrahedron Lett.* **2009**, *50*, 208–211. (b) Bora, U.; Saikia, A.; Boruah, R. C. *Org. Lett.* **2003**, *5*, 435–438. (c) Chuang, C. P.; Tsai, A. I. *Synthesis* **2006**, 675–679.

CC900005V