See discussions, stats, and author profiles for this publication at: https://www.researchgate.net/publication/26687646

ChemInform Abstract: Beyond the Aza-Morita— Baylis—Hillman Reaction: Lewis Base Catalyzed Reactions of N-Boc-imines with Ethyl 2,3-Butadienoate

ARTICLE in THE JOURNAL OF ORGANIC CHEMISTRY · AUGUST 2009

Impact Factor: 4.72 · DOI: 10.1021/jo9008832 · Source: PubMed

CITATIONS READS 17

3 AUTHORS, INCLUDING:



Xiaoyang Guan University of Colorado Boulder

18 PUBLICATIONS 346 CITATIONS

SEE PROFILE



Beyond the Aza-Morita—Baylis—Hillman Reaction: Lewis Base-Catalyzed Reactions of N-Boc-imines with Ethyl 2,3-Butadienoate

Xiao-Yang Guan, Yin Wei,* and Min Shi*

State Key Laboratory of Organometallic Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, 354 Fenglin Road, Shanghai 200032, China

weiyin@mail.sioc.ac.cn; mshi@mail.sioc.ac.cn

Received April 29, 2009

Lewis base catalyzed reactions of N-Boc-imines and ethyl 2,3-butadienoate were investigated systematically. The normal aza-Morita-Bylis-Hillman products were obtained in good to excellent yields catalyzed by DABCO. When PPh₃ was used as the catalyst, novel rearrangement product (E)-ethyl 2-((Z)-(tert-butoxycarbonylimino)-(aryl)methyl)but-2-enoates could be formed in moderate yields.

The use of imines as electrophiles in the Morita-Baylis-Hillman reactions, 1 commonly referred to as the aza-Morita-Baylis-Hillman (aza-MBH) reaction, 2 is extremely fascinating because of the great potential of its products for further transformation and its superior mild reaction conditions. 3 An extension of the aza-MBH reaction comes through variation in the structure of the α , β -unsaturated carbonyl compounds such as allenoates. However, there are

very few reports about the aza-MBH reactions of imines with allenoates⁴ providing densely functionalized allenes because many kinds of imines and 2,3-butadienoates are easy to obtain via cycloaddition reactions under different Lewis bases.^{5–7} For instance, the reactions of *N*-tosylated imines and 2,3-butadienoates catalyzed by phosphine to give five-membered pyrrolidine derivatives (Scheme 1, eq 1) have been reported by Lu.⁵ For the same reaction, we previously reported that different heterocyclic products such as azetidine or dihydropyridine derivatives could be formed in the presence of 1,4-diazabicyclo[2.2.2]octane (DABCO) or *N*,*N*-4-dimethylaminopyridine (DMAP), respectively (Scheme 1, eqs 2 and 3).⁷

Lu has also reported that the normal aza-MBH adducts could be formed in moderate yield in the PPh₃-catalyzed reaction between methyl 2,3-butadienoate and *N*-(ethoxycarbonyl)benzaldimine instead of *N*-sulfonylimines (Scheme 2, eq 1).^{5b} Our DABCO-catalyzed reactions of *N*-tosylated imines with ethyl 2,3-butadienoate only afford trace normal aza-MBH adducts (Scheme 2, eq 2).^{7b} These results showed that the reactivities of both imines and catalysts influence the final products from the same starting materials.

In this paper, we report the different reactivity patterns shown by nitrogen- and phosphorus-containing Lewis bases as catalysts in the reactions of *N*-Boc-imines with ethyl 2,3-butadienoate, which are different from the previous observations in the normal aza-MBH reactions of other imines and beyond the scope of the aza-MBH reactions.

The potential of several commonly used nitrogen-containing Lewis bases as catalysts has been assessed for the aza-MBH reaction of ethyl 2,3-butadienoate with *N*-Boc-imine **1a**. The results are summarized in Table 1. Notably, DABCO and pyridine are more efficient than other nitrogen-containing Lewis bases for catalysis of this reaction. As can be seen in Table 1, DABCO shows an excellent catalytic activity for the reaction of **1a** with ethyl 2,3-butadienoate in tetrahydrofuran (THF), affording product **2a** in 95% yield. Pyridine also proved as a good catalyst, forming **2a** in 66% yield (Table 1, entry 2). However, other nitrogen-containing Lewis bases *N*,*N*-4-dimethylaminopyridine (DMAP) and 1,8-diazabicyclo[5.4.0]-7-undecene (DBU) gave poor yields,

DOI: 10.1021/jo9008832

 ^{(1) (}a) Morita, K.; Suzuki, Z.; Hirose, H. Bull. Chem. Soc. Jpn. 1968, 41, 2815–2819.
(b) Baylis, A. B.; Hillman, M. E. D. German Patent 2,155,113, 1972.
(2) Perlmutter, P.; Teo, C. C. Tetrahedron Lett. 1984, 25, 5951–5952.

⁽³⁾ For reviews, see: (a) Drewes, S. E.; Roo, G. H. P. Tetrahedron 1988, 44, 4653–4670. (b) Basavaiah, D.; Rao, P. D.; Hyma, R. S. Tetrahedron 1996, 52, 8001–8062. (c) Ciganek, E. Org. React. 1997, 51, 201–350. (d) Langer, P. Angew. Chem., Int. Ed. 2000, 39, 3049–3052. (e) Basavaiah, D.; Rao, A. J.; Satyanarayana, T. Chem. Rev. 2003, 103, 811–892. (f) Masson, G.; Housseman, C.; Zhu, J. Angew. Chem., Int. Ed. 2007, 46, 4614–4628. (g) Basavaiah, D; Rao, K. V; Reddy, R. J. Chem. Soc. Rev. 2007, 36, 1581–1588. (h) Shi, Y.-L; Shi, M. Eur. J. Org. Chem. 2007, 2905–2916. (i) Singh, V; Batra, S. Tetrahedron 2008, 64, 4511–4574. (j) Declerck, V.; Martinez, J.; Lamaty, F. Chem. Rev. 2009, 109, 1–43.

⁽⁴⁾ During preparation of this manuscript, Miller published a communication about pyridylalanine (Pal)-peptide catalyzed enantioselective allenoate additions to *N*-acylimines. Cowen, B. J; Saunders, L. B; Miller, S. J. *J. Am. Chem. Soc.* **2009**, *131*, 6105–6107.

^{(5) (}a) Xu, Z.; Lu, X. Tetrahedron Lett. 1997, 38, 3461–3464. (b) Xu, Z.; Lu, X. J. Org. Chem. 1998, 63, 5031–5041. (c) Lu, X.; Zhang, C.; Xu, Z. Acc. Chem. Res. 2001, 34, 535–544.

^{(6) (}a) Zhu, X.; Lan, J.; Kwon, O. J. Am. Chem. Soc. 2003, 125, 4716–4717. (b) Tran, Y. S.; Kwon, O. Org. Lett. 2005, 7, 4289–4291. (c) Zhu, X.; Henry, C. E.; Kwon, O. Tetrahedron 2005, 61, 6276–6282. (d) Wurz, R. P.; Fu, G. C. J. Am. Chem. Soc. 2005, 127, 12234–12235. (e) Jean, L.; Marinetti, A. Tetrahedron Lett. 2006, 47, 2141–2145. (f) Scherer, A.; Gladysz, J. A. Tetrahedron Lett. 2006, 47, 6335–6337. (g) Castellano, S.; Fiji, H. D. G.; Kinderman, S. S.; Watanabe, M.; de Leon, P.; Tamanoi, F.; Kwon, O. J. Am. Chem. Soc. 2007, 129, 5843–5845. (h) Fleury-Brégeot, N.; Jean, L.; Retaileau, P.; Marinetti, A. Tetrahedron 2007, 63, 11920–11927. (i) Fang, Y.-Q.; Jacobsen, E. N. J. Am. Chem. Soc. 2008, 130, 5660–5661. (j) Panossian, A.; Fleury-Brégeot, N.; Marinetti, A. Eur. J. Org. Chem. 2008, 3826–3833. (k) Zhang, B.; He, Z.; Xu, S.; Wu, G.; He, Z. Tetrahedron 2008, 64, 9471–9479. (l) Pinto, N.; Fleury-Brégeot, N.; Marinetti, A. Eur. J. Org. Chem. 2009, 146–151

^{(7) (}a) Zhao, G.; Huang, J.; Shi, M. *Org. Lett.* **2003**, *5*, 4737–4739. (b) Zhao, G.; Shi, M. *J. Org. Chem.* **2005**, *70*, 9975–9984. (c) Zhao, G.; Shi, M. *Org. Biomol. Chem.* **2005**, *3*, 3686–3694.

TABLE 1. Catalyst and Solvent Screen for the DABCO-Catalyzed Reactions of Ethyl 2,3-Butadienoate and N-Boc-imine 1a

entry ^a	Lewis base	solvent	yield ^b (%)
1	DABCO	THF	95
2	pyridine	THF	66
3	DMAP	THF	13
4	DBU	THF	16
5	NEt_3	THF	trace
6	imidazole	THF	trace
7	DABCO	CH_2Cl_2	99
8	DABCO	DMF	trace
9	DABCO	toluene	86
10	DABCO	CH ₃ CN	trace

^aAll reactions were carried out with **1a** (0.2 mmol) and ethyl 2,3-butadienoate (0.24 mmol) in the presence of Lewis base in solvent (1.0 mL) at room temperature. ^bIsolated yields.

SCHEME 1. Reaction of *N*-Tosylated Imines with Ethyl 2,3-Butadienoate Catalyzed by Different Lewis Bases

SCHEME 2. Normal Aza-Morita—Baylis—Hillman Reaction of Imines with 2,3-Butadienoates Catalyzed by PPh₃ or DABCO

and triethylamine (NEt₃) and imidazole could not catalyze this type of reaction (Table 1, entries 3–6). Solvent effects were also examined. The results listed in Table 1 indicated that solvent effects had a dramatic influence on the reaction. The moderately polar solvents dichloromethane and toluene were suitable for the reaction to give **2a** in excellent yields (Table 1, entries 7 and 9). However, the more polar solvents acetonitrile and *N*,*N*-dimethylformamide (DMF) retarded this reaction and led to trace products (Table 1, entries 8 and 10).

Having the identified optimal reaction conditions, we next set out to examine the scope and limitations of this reaction using various *N*-Boc-imines 1 with different substituents on the benzene rings, and the results are summarized in Table 2. As shown in Table 2, whether electron-withdrawing or electron-donating group at the *ortho-*, *meta-*, or

TABLE 2. Scope of DABCO-Catalyzed Reactions of *N*-Boc-imines 1 and Ethyl 2,3-Butadienoate

$$\begin{array}{c} H \\ CO_2Et \end{array} + \begin{array}{c} R \\ R \end{array} \begin{array}{c} DABCO \\ (20 \text{ mol}\%) \\ CH_2Cl_2, 20 \text{ h} \end{array} \begin{array}{c} NHBoc \\ CO_2Et \\ \end{array}$$

entry ^a	R	yield ^b (%)
1	<i>p</i> -MeOC ₆ H ₄ , 1b	2b , 89
2	p-MeC ₆ H ₄ , 1c	2c, 94
3	p-CF ₃ C ₆ H ₄ , 1d	2d, 77
4	p-FC ₆ H ₄ , 1e	2e , 76
5	m-MeC ₆ H ₄ , 1f	2f , 98
6	m-ClC ₆ H ₄ , 1g	2g , 84
7	$m_{1}m_{2}$, $m_{1}m_{2}$, $m_{2}m_{3}$, $m_{1}m_{2}$, $m_{2}m_{3}$	2h , 91
8	o-MeOC ₆ H ₄ , 1i	2i , 79
9	o-ClC ₆ H ₄ , 1j	2j , 87
10	2-furyl, 1k	2k, 98
11	cyclohexyl, 11	complex

^aAll reactions were carried out with 1 (0.2 mmol) and ethyl 2,3-butadienoate (0.24 mmol) in the presence of DABCO in CH₂Cl₂ (1.0 mL) at room temperature. ^bIsolated yields.

para-position of the benzene ring of N-Boc-imines 1 or the furfural N-(tert-butoxycarbonyl)imine 1k were employed, the reactions proceeded smoothly to give 2 in good to excellent yields (Table 2, entries 1–10). Unfortunately, this reaction was not suitable for alkyl N-Boc imine 1l (Table 2, entry 11), yielding complexes.

In addition to nitrogen-containing Lewis bases, the catalytic potential of readily available phosphines was also explored for this reaction. The results are listed in Table 3. Interestingly, replacing DABCO by PPh₃ led to the rearrangement product 3a of normal aza-MBH adducts isolated in 63% yield with trace normal adduct 2a (Table 3, entry 1). The structure of 3a was determined by ¹H NMR, ¹³C NMR, and NOESY spectra (see the Supporting Information). We also tested several stronger nucleophilic phosphines such as tributylphosphine (PBu₃), methyldiphenylphosphine (PPh₂-Me), and dimethyl(phenyl)phosphine (PPhMe₂) and found that they could not catalyze this reaction (Table 3, entries 2-4). This implied that the nucleophilicities of phosphines had significant influence on the reaction; thus, we subsequently explored the influence of nucleophilicities of phosphines further. Three phosphines with different electronic-nature substituents on the benzene rings were chosen as catalysts to test in this reaction. We found that increasing the nucleophilicities of phosphines led to the decreased yield of 3a. The least nucleophilic phosphine tris(4-fluorophenyl)phosphine $(P(p-FC_6H_4)_3)$ could catalyze the reaction to give product **3a** in the highest yield among these three phosphines; however, the most nucleophilic tris(4-methoxyphenyl)phosphine (P(p-MeOC₆H₄)₃) just generated **3a** in 8% yield (Table 3, entries 5 and 7). The solvent effects were examined again using PPh₃ as the catalyst. Similar observations were obtained as the nitrogen base-catalyzed reactions. Dichloromethane and toluene were also optimal solvents to give 3a in 66% and 62% yield, respectively, with 2a as a byproduct (Table 3, entries 8 and 9), and the reaction could not occur in acetonitrile either (Table 3, entry 10). In order to maximize the yield of product 3a, we attempted to vary some reaction conditions. Increasing the amount of ethyl 2,3-butadienoate

TABLE 3. Catalyst and Solvent Screen for the PPh₃-Catalyzed the Reactions of Ethyl 2,3-Butadienoate and *N*-Boc-imine 1a

entrya	Lewis base	solvent	yield of $3a^b$ (%)	yield of $2a^b$ (%)
1	PPh ₃	THF	63	trace
2	PBu_3	THF	С	c
3	PPh ₂ Me	THF	c	c
4	PPhMe ₂	THF	c	c
5	$P(p-MeOC_6H_4)_3$	THF	8	trace
6	$P(p\text{-MeC}_6H_4)_3$	THF	19	trace
7	$P(p\text{-MeC}_6H_4)_3$	THF	49	30
8	PPh ₃	CH_2Cl_2	66	5
9	PPh ₃	toluene	62	11
10	PPh ₃	CH ₃ CN	trace	trace
11^{d}	PPh ₃	CH ₂ Cl ₂	39	41
12^{e}	PPh ₃	CH ₂ Cl ₂	19	49
13^{f}	PPh ₃	CH ₂ Cl ₂	22	55
14^g	PPh ₃	CH_2Cl_2	21	9

^aAll reactions were carried out with **1a** (0.2 mmol) and ethyl 2,3-butadienoate (0.24 mmol) in the presence of Lewis base in solvent (1.0 mL) at room temperature. ^bIsolated yields. ^cThese reactions gave complex product mixtures. ^dEthyl 2,3-butadienoate (0.24 mmol) in CH₂Cl₂ (3.0 mL) was added with a syringe pump for 5 h. ^eThe reaction was carried out in 2.0 mL of CH₂Cl₂. ^fThe reaction was carried out in 4.0 mL of CH₂Cl₂. ^gThe reaction was carried out with **1a** (0.3 mmol) and ethyl 2,3-butadienoate (0.2 mmol) in 1.0 mL of CH₂Cl₂.

SCHEME 3. Control Experiment

up to 3 equiv did not improve the yield.8 Based on Lu's research⁹ and our observations, we found that ethyl 2,3-butadienoate could undergo self-cycloaddition in the presence of PPh₃. In order to avoid its self-cycloaddition, we tried adding the diluted ethyl 2,3-butadienoate slowly by syringe pump, and the result showed that the yield of 3a decreased while 2a became the major product and the total yield of 2a and 3a increased (Table 3, entry 11). Interestingly, decreasing the concentration of ethyl 2,3-butadienoate also resulted in 2a becoming the major product (Table 3, entries 12 and 13). Was the formation of 3a due to the rearrangement of 2a catalyzed by PPh₃? Next, we did the control experiment in which 2a was stirred in CH₂Cl₂ in the presence of 20 mol % of PPh3 for 2 days. Compound 3a was isolated only in 14% yield with 32% of 2a being recovered (Scheme 3), and the residues were difficult to identify. It indicated that the formation of 3a was not through

TABLE 4. Scope of the PPh₃-Catalyzed Reactions of *N*-Boc-imines 1 and Ethyl 2,3-Butadienoate

entry ^a	R	Yield (%) ^{b,c}	
1	<i>p</i> -MeOC ₆ H ₄ , 1b	3b , 49	
2	p-CF ₆ C ₆ H ₄ , 1d	3c, 48	
3	<i>p</i> -FC ₃ H ₄ , 1e	3d , 61	
4	p-MeC ₆ H ₄ , 1f	3e , 66	
5	m-ClC ₆ H ₄ , 1g	3f , 48	
6	m-MeOC ₆ H ₄ , 1i	complex	
7	2-furyl, 1k	3g , 94	
8	cyclohexyl, 1 L	complex	

^aAll reactions were carried out with **1** (0.2 mmol) and ethyl 2,3-butadienoate (0.24 mmol) in the presence of PPh₃ in CH₂Cl₂ (1.0 mL) at room temperature. ^bIsolated yields. ^cTrace of **2** was also produced without isolation.

SCHEME 4. Reaction of *N*-Boc-imine 1j with Ethyl 2,3-Butadienoate Catalyzed by PPh₃

rearrangement of normal aza-MBH product 2a under the reaction conditions.

Although the yield of **3a** was not improved by variation of reaction conditions, we were still interested in the scope and limitations of the reaction catalyzed by PPh₃ (Table 4) with respect to various substrates. The reactions proceeded smoothly to afford 3 in moderate yields, using the N-Bocimines 1 with either electron-withdrawing or electron-donating substituent at the *meta*- or *para*-position of the benzene ring (Table 4, entries 1-5). In particular, the furfural N-(tertbutoxycarbonyl)imine 1k could give 3g in 94% yield (Table 4, entry 7). However, the o-methoxybenzaldehyde N-Boc-imine 1i and alkyl N-Boc-imine 1l were not suitable substrates (Table 4, entries 6 and 8). We also found that the PPh₃-catalyzed reaction of o-chlorobenzaldehyde N-Bocimine 1j and ethyl 2,3-butadienoate produced an uncommon product 3h in 24% yield, and its structure was also determined by ¹H NMR, ¹³C NMR, and NOESY spectra (Scheme 4).

On the basis of the above results and previous literature, ⁵ a plausible mechanism for the DABCO- or PPh₃-catalyzed reaction between ethyl 2,3-butadienoate and *N*-Boc-imines 1 is proposed in Scheme 5. The Lewis base DABCO or PPh₃ as a nucleophile reacts with ethyl 2,3-butadienoate to produce the zwitterionic intermediate A1 or A2, which subsequently generates the intermediate B1 or B2 through nucleophilic addition of the *N*-Boc-imines 1. In the case of DABCO, B1 transforms to C1 through a proton transfer. The elimination of DABCO from C1 affords the product 2 and regenerates DABCO.

At the stage of the intermediate **B2**, the reaction diverges into two paths. In path **a**, the stable ylide intermediate **D** can

⁽⁸⁾ The yield using 3.0 equiv of ethyl 2,3-butadienoate is almost same as that using 1.0 equiv of ethyl 2,3-butadienoate.

⁽⁹⁾ Zhang, C.; Lu, X. J. Org. Chem. **1995**, 60, 2906–2908.

SCHEME 5. Plausible Reaction Mechanism

be formed through proton transfer and will undergo a hydrogen shift to form E when the concentration of intermediate **B2** is high. Then, the elimination of PPh₃ furnishes product 3 and regenerates the catalyst. Path b in which the intermediate **B2** follows the similar reaction path as the DABCO-catalyzed reaction to generate normal aza-MBH product 2 as the byproduct via the intermediate C2 can compete with path a and even become dominant when the concentration of B2 is low. The nature of the imine N-substituent also affects the reaction pathway. N-Acylimines with an ethoxycarbonyl substituent rather take path b to give normal aza-MBH product 2 in the presence of PPh₃ as a catalyst.4 In contrast, N-Boc-imines mainly provide product 3. Presumably, the steric hindrance of Boc group makes the proton transfer difficult to occur for formation of intermediate C2; thus, path a is more favorable with respect to N-Boc-imines.

In summary, we have presented that nitrogen- and phosphorus-containing Lewis bases show different catalytic patterns in the reactions of *N*-Boc-imines with ethyl 2,3-butadienoate. In particular, phosphorus-containing Lewis bases display a novel catalytic pattern resulting in uncommon products. Efforts are in progress to better understand the difference of the catalytic reactivity of phosphine- or

nitrogen-containing Lewis bases in these reactions. Moreover, the asymmetric version of this type of reaction is in progress in our laboratory.

Experimental Section

General Procedure for the Reaction of Ethyl 2,3-Butadienoate and N-Boc-imines. To a solution of N-Boc-imine 1 (41 mg, 0.2 mmol) and DABCO (5.5 mg, 0.04 mmol) in CH_2Cl_2 (1.0 mL) was added ethyl 2,3-butadienoate (27 mg, 0.24 mmol) in one portion. After the reaction mixture was stirred at room temperature for 20 h, the solvent was removed under reduced pressure and the residue was purified by flash column chromatography (SiO₂, eluent: EtOAc/petroleum ether = 1/10) to yield the corresponding product 2 (63 mg, 99%) as a colorless oil.

Compound 2a:. colorless oil; ${}^{1}\text{H}$ NMR (CDCl₃, 300 MHz, TMS) δ 1.19 (t, 3H, J = 7.2 Hz, CH₃), 1.44 (s, 9H, CH₃), 4.12 (q, 2H, J = 7.2 Hz, CH₂), 5.37 (s, 2H, =CH₂), 5.49 (d, 1H, J = 8.7 Hz, NH), 5.65 (d, 1H, J = 8.7 Hz, CH), 7.22–7.36 (m, 5H, Ar); ${}^{13}\text{C}$ NMR (CDCl₃, 75 MHz, TMS) δ 14.0, 28.2, 53.5, 61.1, 79.6, 81.3, 102.3, 126.6, 127.4, 128.4, 140.4, 154.7, 165.4, 212.9; IR (CH₂Cl₂) ν 3438, 3359, 2979, 2933, 1965, 1725, 1492, 1367, 1248, 1107, 1077, 1044, 1022, 886, 700 cm⁻¹; MS (ESI) m/z 340.0 (M + Na⁺, 100); HRMS (ESI) calcd for C₁₈H₂₃N₁Na₁O₄ (M + Na⁺) requires 340.15193, found 340.15176.

Compound 3a:. colorless oil; 1 H NMR (CDCl₃, 300 MHz, TMS) δ 1.16 (t, 3H, J = 7.2 Hz, CH₃), 1.47 (s, 9H, CH₃), 1.80 (d, 3H, J = 7.5 Hz, CH₃), 4.17 (brs, 2H, CH₂), 7.28 (q, 1H, J = 7.5 Hz, =CH), 7.39–7.51 (m, 3H, Ar), 7.85 (d, 2H, J = 7.2 Hz, Ar); 13 C NMR (CDCl₃, 75 MHz, TMS) δ 14.0, 16.0, 27.8, 61.1, 82.1, 128.2, 128.5, 130.7, 132.1, 135.5, 143.3, 161.4, 164.1, 166.2; IR (CH₂Cl₂) ν 2979, 2933, 1723, 1625, 1578, 1449, 1368, 1253, 1233, 1151, 1064, 1034, 929, 853, 776, 693 cm⁻¹; MS (ESI) m/z 340.0 (M + Na⁺, 30); HRMS (ESI) calcd for C₁₈H₂₃N₁Na₁O₄ (M + Na⁺) requires 340.15193, found 340.15159.

Compound 3h:. colorless oil; ¹H NMR (CDCl₃, 400 MHz, TMS) δ 1.33 (s, 9H, CH₃), 1.38 (t, 3H, J = 7.2 Hz, CH₃), 4.33 (qd, 2H, J₁ = 7.2 Hz, J₂ = 2.0 Hz, CH₂), 4.90 (dd, 1H, J₁ = 12.0 Hz, J₂ = 2.0 Hz, =CH), 5.23 (dd, 1H, J₁ = 17.6 Hz, J₂ = 2.0 Hz, =CH), 5.86 (dd, 1H, J₁ = 17.6 Hz, J₂ = 12.0 Hz, =CH), 7.18 – 7.21 (m, 1H, Ar), 7.27 – 7.34 (m, 2H, Ar), 7.38 – 7.41 (m, 1H, Ar), 10.6 (s, 1H, OH); ¹³C NMR (CDCl₃, 100 MHz, TMS) δ 14.2, 27.9, 60.9, 81.1, 107.8, 116.8, 126.5, 129.2, 129.79, 129.84, 130.2, 132.8, 134.2, 148.5, 150.9, 169.1; IR (CH₂Cl₂) ν 3234, 2980, 2933, 1748, 1720, 1671, 1601, 1577, 1477, 1454, 1394, 1369, 1243, 1144, 1061, 1027, 1005, 915, 861, 802, 752 cm⁻¹; MS (ESI) m/z 374.0 (M + Na⁺, 100); HRMS (MALDI) calcd for C₁₈H₂₂Cl₁N₁Na₁O₄ (M + Na⁺) requires 374.11296, found 374.1144.

Acknowledgment. Financial support from the Shanghai Municipal Committee of Science and Technology (06XD-14005 and 08dj1400100-2), National Basic Research Program of China (973)-2009CB825300, and the National Natural Science Foundation of China (20872162, 20672127, 20732008, 20821002 and 20702013) is greatly acknowledged.

Supporting Information Available: ¹H NMR and ¹³C NMR spectroscopic and analytic data of compounds **2** and **3**. This material is available free of charge via the Internet at http://pubs.acs.org.