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A new $InCl_3$-catalyzed reduction of anthrones and anthraquinones by using aluminum powder in aqueous media

Chunyan Wang,[a] Jieping Wan,[a] Zhiguo Zheng[b] and Yuanjiang Pan[a,*]

[a] *Department of Chemistry, Zhejiang University, Hangzhou 310027, PR China*
[b] *Zhejiang Hisoar Pharm. Co., Ltd, Taizhou 318000, PR China*

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Abstract—$InCl_3$-catalyzed reduction of anthrones and anthraquinones was investigated under different conditions. A new synthetic method for anthracenes in aqueous media under mild conditions is described.

1. Introduction

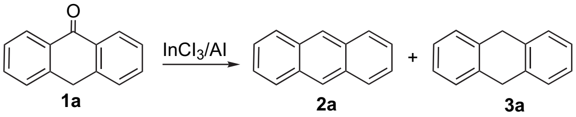
Because of its good properties, such as compatibility with water and air, high efficiency and good selectivity in catalysis, the chemistry of indium is of current interest from the viewpoint of organic synthesis.[1] Indium chloride has attracted considerable attention due to its diverse applications as a catalyst in organic synthesis under mild conditions.[2,3] Recently, the combination of indium chloride and aluminum powder generating activated indium in situ has been applied to some reductions, in which good and interesting results were obtained.[4] To our knowledge, however, indium chloride catalyzed reduction of anthrones and anthraquinones has not been reported to date.

Generally, there are two methods to reduce anthrones: zinc reductions and $NaBH_4$ reductions. The former, which are fairly useful for the reduction of anthraquinone, leads mainly to the coupled products when applied to anthrones under either acidic[5] or alkaline[6] conditions. In addition, zinc reductions are incompatible with halogenated anthrones. $NaBH_4$ reductions have proven to be a general method.[7] However, nitrogen atmosphere and mixed organic solvents are required, which is usually a troublesome process. Therefore, it is worthwhile to develop a simple, efficient, and environmentally friendly method for the reduction of anthrones. In this paper, $InCl_3$-catalyzed reductions of anthrones and 9,10-anthraquinones by Al powder were investigated. A new green method to generate anthracenes was described in this paper.

2. Results and discussion

2.1. Optimization of $InCl_3$-catalyzed reduction of anthrones

Initially, the reduction of anthrone as an example was optimized under different conditions, including the amounts of indium chloride and Al powder, the reaction temperature, and the additive (Scheme 1). When only Al powder (4 mmol) and NH_4Cl (1 g) were added to anthrone (1 mmol) in 50% aqueous alcohol solution, the mixture was stirred for 11 h at reflux (Table 1, entry 1). A small polar spot with purple fluorescence was detected by TLC. Purification by silica gel column chromatography gave **2a** and **3a** (**2a**/**3a**=20:1) in a poor yield, which were determined by NMR and HRMS. Change of the solvents did not improve the results (entries 2 and 3). Substitution of AcOH for NH_4Cl resulted in a better yield (entry 4). However, excessive AcOH (2 mL) led to failure of the reduction (entry 5). When 1 mmol indium chloride was added to the mixture the reaction was significantly accelerated, stirring the mixture for only 3.5 h resulted in 87% yield (entry 6). Larger amounts of product **3a** were obtained. Lowering the reaction temperature or using NH_4Cl did not avoid further reduction of anthrone to 9,10-dihydroanthracene with **3a** appearing before anthrone was completely consumed (entries 7 and 8). Finally, the reduction in the presence



Scheme 1.

Keywords: $InCl_3$/Al; Anthrones; Anthraquinones; Reduction.

* Corresponding author. Tel.: +86 571 8795 1264; fax: +86 571 8795 1629; e-mail: cheyjpan@zju.edu.cn

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Table 1. Study of the reduction of anthrone under different conditions[a]

Entry	Reductant	Additive	Solvent (mL)	Temp (°C)	Time (h)	Total yield % (**2a**/**3a**)[b]
1	Al	NH_4Cl	4 ($EtOH/H_2O$=1:1)	90	11	35 (20:1)
2	Al	NH_4Cl	4 ($MeOH/H_2O$=1:1)	90	11	0
3	Al	NH_4Cl	4 (*i*-$PrOH/H_2O$=1:1)	90	11	Trace
4	Al	AcOH	4 ($EtOH/H_2O$=1:1)	90	11	68 (20:1)
5[c]	Al	AcOH	4 ($EtOH/H_2O$=1:1)	90	11	0
6	$InCl_3$/Al	AcOH	4 ($EtOH/H_2O$=1:1)	90	3.5	87 (10:1)
7	$InCl_3$/Al	NH_4Cl	4 ($EtOH/H_2O$=1:1)	90	11	76 (20:1)
8	$InCl_3$/Al	AcOH	4 ($EtOH/H_2O$=1:1)	55	11	78 (10:1)
9	$InCl_3$/Al	NH_4Cl	4 ($EtOH/H_2O$=1:1)	rt	5	65 (100:0)
10[d]	$InCl_3$/Al	AcOH	4 ($EtOH/H_2O$=1:1)	rt	5	90 (100:0)
11	Al	AcOH	4 ($EtOH/H_2O$=1:1)	rt	32	—

[a] Reaction conditions: anthrone (1 mmol), NH_4Cl (1 g) or AcOH (1 mL), Al powder (4 mmol), and $InCl_3$ (1 mmol) except for mentioned especially.

[b] Total isolated yield of **2a** and **3a**. Determined by ^1H NMR.

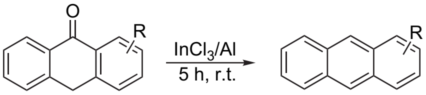
[c] AcOH (2 mL) was added.

[d] $InCl_3$ (0.2 mmol) and Al powder (1.5 mmol).

of NH_4Cl or AcOH at room temperature was investigated, in which **2a** was the single product (entries 9 and 10). At room temperature, $InCl_3$/Al along with AcOH yielded 90% **2a** in which only 0.2 mmol indium chloride and 1.5 mmol Al powder were required (entry 10). But no product was obtained after being stirred for 32 h in the absence of indium chloride (entry 11). It was clearly demonstrated that indium chloride efficiently catalyzed the reduction of anthrone to anthracene **2a** by using Al powder in aqueous media. From these results, the conditions in entry 10 were selected as the optimized conditions.

2.2. $InCl_3$-catalyzed reduction of different substituted anthrones

In order to investigate the limitation of the scope of the substrates for this reaction condition (Table 1, entry 10), the substrates were extended to some substituted anthrones (Scheme 2). In all these experiments, anthracenes **2** were obtained as single products in moderate to good yields. Furthermore, this indium chloride catalyzed reduction was compatible with halogen atom. The results are listed in Table 2.



1 **2**

Scheme 2.

Table 2. $InCl_3$/Al mediated synthesis of anthracenes from the substituted anthrones[a]

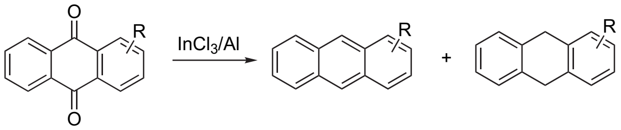
Compounds	R	Yield of **2** (%)[b]
2a	H	90
2b	2-CH_3	88
2c	2-C_2H_5	92
2d	1-CH_3, 3-CH_3	76
2e	1-CH_3, 4-CH_3	80
2f	2-Cl	72
2g	2-Br	74

[a] Reaction conditions: anthrones (1 mmol), indium chloride (0.2 mmol), Al (1.5 mmol), AcOH (1 mL), and solvent (4 mL, $EtOH/H_2O$=1:1).

[b] Isolated yields.

2.3. $InCl_3$-catalyzed reduction of 9,10-anthraquinones

However, reactions of diketo compounds appeared to be more difficult than anthrones (Scheme 3). For 9,10-anthraquinone, no desired product was obtained under the above optimized conditions (Table 3, entries 1 and 2). When the temperature of oil bath was increased to 90 °C and the mixture was stirred for 11 h, it gave **2** and **3** in 52% yield (**2**/**3**=95:5) (entry 3). 2-Ethyl anthraquinone gave the products with a ratio of **2** and **3** being 5:1 (entry 4). Reducing the amount of Al powder from 4 to 2.2 mmol resulted in the products **2c** and **3c** (entry 5) in total 44% yield, in which the ratio of **2c** and **3c** was improved. Other substituted anthraquinones were all reduced to the mixture of **2** and **3** in moderate yield (entries 6–10), but the formation of **3** could not be avoided.



4 **2** **3**

Scheme 3.

The reaction of 1,4-disubstituted anthraquinones (**4**), in which R is H or C_2H_5, with $InCl_3$/Al gave different products.

Table 3. $InCl_3$-catalyzed reduction of anthraquinones[a]

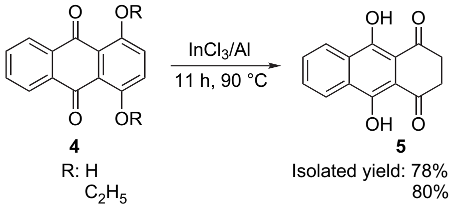
Entry	R	Reductant	Temp (°C)	Time (h)	Total yield % (**2**/**3**)[b]
1[c]	H	$InCl_3$/Al	rt	24	—
2[c]	H	Al	90	11	—
3[c]	H	$InCl_3$/Al	90	11	52 (95:5)
4[c]	2-C_2H_5	$InCl_3$/Al	90	11	68 (5:1)
5	2-C_2H_5	$InCl_3$/Al	90	11	44 (15:1)
6	2-CH_3	$InCl_3$/Al	90	11	44 (3:1)
7	1-CH_3, 3-CH_3	$InCl_3$/Al	90	11	50 (13:1)
8	1-CH_3, 4-CH_3	$InCl_3$/Al	90	11	48 (4:1)
9	2-Cl	$InCl_3$/Al	90	11	58 (3:1)
10	2-Br	$InCl_3$/Al	90	11	62 (3:1)

[a] Reaction conditions: anthraquinones (1 mmol), AcOH (1 mL), Al powder (2.2 mmol) and $InCl_3$ (1 mmol) except for mentioned especially.

[b] Total isolated yield of **2** and **3**. Determined by ^1H NMR.

[c] $InCl_3$ (1 mmol) and Al powder (4 mmol).

When the substituted anthraquinone (1 mmol), indium chloride (0.2 mmol), Al powder (4 mmol), and AcOH (1 mL) were mixed in 50% aqueous alcohol and stirred at reflux for 11 h, it gave compound **5** in good yields, which was determined by ^{1}H NMR, ^{13}C NMR, DEPT, ^{1}H–^{1}H COSY, HMQC, HMBC spectra, and HRMS. To our surprise, the new carbonyl groups in compound **5** were not reduced (Scheme 4).

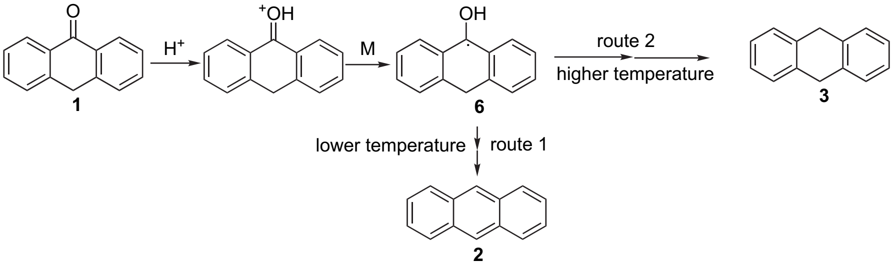


Scheme 4.

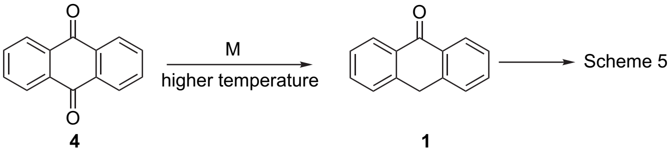
3. Proposed mechanism

Based on the results from experiments, proposed mechanisms were provided. In our experiments, it was thought that the mechanism of reduction of anthrones is similar to the reduction at metal surfaces involving ketyl radical anions (Scheme 5).[8] Protonized anthrone obtained an electron to form the intermediate **6**. Intermediate **6** could react in two directions: anthracene **2** and 9,10-dihydroanthracene **3** was obtained, respectively. In our experiments, it was found that the intermediate **6** is easy to react along route 1, which just requires room temperature. Higher temperature is required in route 2. Therefore, when the temperature was reduced from 90 °C to rt, anthracene **2** was obtained as single product in $InCl_3$-catalyzed reduction of anthrone **1**.

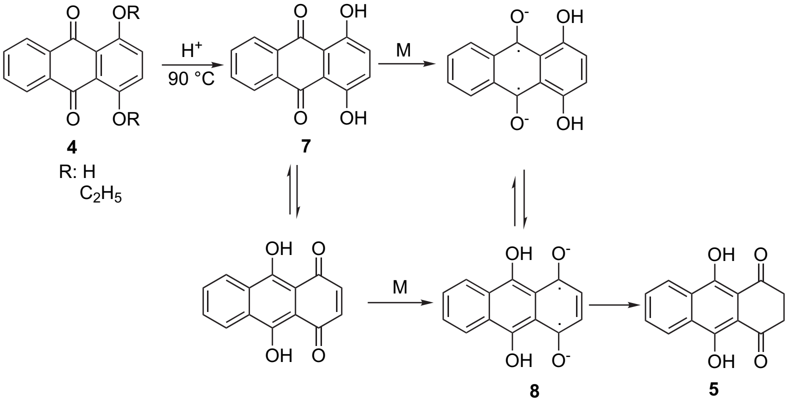
For the reduction of 9,10-anthraquinone **4**, another possible mechanism was also proposed (Scheme 6). 9,10-Anthraquinone **4** was reduced to anthrone **1** firstly. Then anthrone formed from 9,10-anthraquinone reacted in the way described in Scheme 5. Higher temperature is required during reduction of compound **4** to compound **1**, which is in agreement with experimental findings (Table 3, entry 1). At higher temperature, anthracene together with dihydroanthracene was obtained from anthrone. So anthracene could not be obtained as single product in $InCl_3$-catalyzed reduction of 9,10-anthraquinone **4**. In order to further verify the proposed mechanism, $InCl_3$-catalyzed reduction process of



Scheme 5.



Scheme 6.



Scheme 7.

9,10-anthraquinone **4** was monitored by ESI-MS. Anthrone **1** formed during the reaction (192.8 $[M-H]^-$ and 194.9 $[M+H]^+$) was found when the reaction lasted for 30 min and 2 h, but disappeared after 6 h of reaction time.

Finally, the mechanism of $InCl_3$-catalyzed reduction of 1,4-disubstituted anthraquinones (R=H, C_2H_5) (Scheme 4) was proposed (Scheme 7). Firstly, compound **4** was hydrolyzed to 1,4-dihydroxy-9,10-anthraquinone **7**. Then compound **7** was reduced to intermediate **8** by two possible routes. Finally, the product **5** was formed through the intermediate **8**.

4. Conclusion

In conclusion, indium chloride, which was applied to the reduction of anthrones and anthraquinone, showed good catalytic activity. A simple, efficient, and environmentally friendly synthetic method for anthracenes from anthrones was proposed, which was also applicable for halogenated anthrones. Although indium chloride catalyzed reductions of most anthraquinones gave two products, compound **5** was obtained as the single product in this reaction. A reasonable mechanism was proposed.

5. Experimental

5.1. General

The ^1H NMR and ^{13}C NMR spectra were obtained with a Bruker AVANCE DRX-500 NMR spectrometer (^1H, 500 MHz; ^{13}C, 125 MHz) with TMS as internal standard and $CDCl_3$ as solvent. The ESI-MS spectra were taken on a Bruker Esquire 3000 plus spectrometer. Precoated thin-layer plates of silica gel 60 GF_{254} (Qingdao Haiyang Chemical Co. Ltd., Qingdao, PR China.) were used for analytical purpose. All the benzophenones, benzaldehydes, and acetophenones were purchased from J&K chemical Co., or other commercial suppliers and were used after appropriate purification (distillation).

5.2. General procedure for $InCl_3$-catalyzed reduction of anthrones by using Al powder

Anthrone (1 mmol), Indium chloride (0.2 mmol), Al powder (1.5 mmol), and AcOH (1 mL) were added to 50% aqueous alcohol solution. The mixture was stirred for the indicated time at room temperature. Ethyl ether (10 mL) was added to the mixture, stirred for another 5 min, and then filtered. The filtrate was extracted by ethyl ether (10 mL×3). The combined organic layer was dried over anhydrous Na_2SO_4 and concentrated in vacuum. Purification by silica gel column chromatography (200–300 mesh), using petroleum ether (60–90 °C) and ethyl acetate (200:1) as eluant, afforded the corresponding product.

5.2.1. Anthracene (2a). ^1H NMR ($CDCl_3$, 500 MHz): δ 8.43 (s, 2H), 8.00–8.02 (m, 4H), 7.46–7.48 (m, 4H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 132.2, 128.7, 126.6, 125.9. HRMS (EI) calcd for $C_{14}H_{10}$: 178.0777 (M^+), found: 178.0782.

5.2.2. 2-Methylanthracene (2b). ^1H NMR ($CDCl_3$, 500 MHz): δ 8.36 (s, 1H), 8.31 (s, 1H), 7.90–7.99 (m, 3H), 7.75 (s, 1H), 7.42–7.44 (m, 2H), 7.32–7.35 (m, 1H), 2.55 (t, 3H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 135.1, 132.1, 132.0, 131.4, 130.5, 128.4, 128.3, 128.1, 126.5, 126.1, 125.4, 125.3, 125.1, 22.1. HRMS (EI) calcd for $C_{15}H_{12}$: 192.0934 (M^+), found: 192.0931.

5.2.3. 2-Ethylanthracene (2c). ^1H NMR ($CDCl_3$, 500 MHz): δ 8.35 (s, 1H), 8.30 (s, 1H), 7.94–7.96 (m, 3H), 7.72 (s, 1H), 7.40–7.43 (m, 2H), 7.30–7.32 (m, 1H), 2.82 (q, 2H), 1.35 (t, 3H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 141.2, 132.2, 132.0, 131.4, 130.7, 128.3, 128.2, 127.4, 126.1, 125.5, 125.3, 125.1, 125.0, 29.3, 15.3. HRMS (EI) calcd for $C_{16}H_{14}$: 206.1090 (M^+), found: 206.1088.

5.2.4. 1,3-Dimethylanthracene (2d). ^1H NMR ($CDCl_3$, 500 MHz): δ 8.46 (s, 1H), 8.28 (s, 1H), 7.94–8.02 (m, 2H), 7.60 (s, 1H), 7.41–7.44 (m, 2H), 7.14 (s, 1H), 2.84 (s, 3H), 2.56 (s, 3H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 134.7, 134.1, 132.4, 131.7, 131.3, 130.2, 128.7, 128.7, 128.0, 125.0, 122.7, 22.0, 19.7. HRMS (EI) calcd for $C_{16}H_{14}$: 206.1090 (M^+), found: 206.1090.

5.2.5. 1,4-Dimethylanthracene (2e). ^1H NMR ($CDCl_3$, 500 MHz): δ 8.55 (s, 2H), 8.03–8.05 (m, 2H), 7.47–7.49 (m, 2H), 7.20 (s, 2H), 2.79 (s, 6H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 136.4, 127.6, 127.2, 125.9, 125.0, 123.7, 121.5, 17.9. HRMS (EI) calcd for $C_{16}H_{14}$: 206.1090 (M^+), found: 206.1095.

5.2.6. 2-Chloroanthracene (2f). ^1H NMR ($CDCl_3$, 500 MHz): δ 8.39 (s, 1H), 8.31 (s, 1H), 7.92–7.99 (m, 4H), 7.46–7.50 (m, 2H), 7.36–7.38 (m, 1H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 132.3, 131.9, 131.2, 130.0, 129.8, 128.4, 128.2, 126.7, 126.5, 126.2, 125.8, 125.5. HRMS (EI) calcd for $C_{14}H_9Cl$: 212.0387 (M^+), found: 212.0385.

5.2.7. 2-Bromoanthracene (2g). ^1H NMR ($CDCl_3$, 500 MHz): δ 8.38 (s, 1H), 8.31 (s, 1H), 8.16 (s, 1H), 7.97–8.01 (m, 1H), 7.45–7.50 (m, 3H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 132.4, 132.3, 131.9, 130.0, 129.9, 129.0, 128.4, 128.3, 126.7, 126.2, 125.9, 125.5, 119.6. HRMS (EI) calcd for $C_{14}H_9Br$: 255.9882 (M^+), found: 255.9880.

5.3. General procedure for $InCl_3$-catalyzed reduction of 9,10-anthraquinones by using Al powder

9,10-Anthraquinone (1 mmol), Indium chloride (1 mmol), Al powder (indicated amount), and AcOH (1 mL) were added to 50% aqueous alcohol solution. The mixture was stirred for the indicated time under reflux. Ethyl ether (10 mL) was added to the mixture, stirred for another 5 min, and then filtered. The filtrate was extracted by ethyl ether (10 mL×3). The combined organic layer was dried over anhydrous Na_2SO_4 and concentrated in vacuum. Purification by silica gel column chromatography (200–300 mesh), using petroleum ether (60–90 °C) and ethyl acetate (200:1) as eluant, afforded the corresponding product.

5.3.1. 9,10-Dihydroxy-2,3-dihydroanthracene-1,4-dione (5). ^1H NMR ($CDCl_3$, 500 MHz): δ 13.5 (s, 2H), 8.36–8.38 (m, 2H), 7.72–7.74 (m, 2H), 3.04 (s, 4H). ^{13}C NMR

($CDCl_3$, 125 MHz): δ 201.1, 155.4, 130.6, 129.5, 124.8, 107.6, 36.0. HRMS (ESI) calcd for $C_{14}H_{10}O_4$: 242.0574 (M^+), found: 242.0571.

Acknowledgements

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References and notes

1. For review, see: Médebielle, M.; Onomura, O.; Keirouz, R.; Okada, E.; Yano, H.; Terauchi, T. *Synthesis* **2002**, 2601.
2. For review, see: Fan, X. S.; Hu, X. Y.; Zhang, Y. M. *Chin. J. Org. Chem.* **2004**, *24*, 455 and reference therein.
3. For some recent publications, see: (a) Cook, G. R.; Hayashi, R. *Org. Lett.* **2006**, *8*, 1045; (b) Weïwer, M.; Duńach, E. *Tetrahedron Lett.* **2006**, *47*, 287; (c) Duvelleroy, D.; Perrio, C.; Parisel, O.; Lasne, M.-C. *Org. Biomol. Chem.* **2005**, *20*, 3794; (d) Salavati-Niasari, M.; Hydarzadeh, S. *J. Mol. Catal. A* **2005**, *237*, 254; (e) Yasuda, M.; Yamasaki, S.; Onishi, Y.; Baba, A. *J. Am. Chem. Soc.* **2004**, *126*, 7186; (f) Tocco, G.; Begala, M.; Delogu, G.; Picciau, C.; Podda, G. *Tetrahedron Lett.* **2004**, *45*, 6909; (g) Garzya, V.; Forbes, I. T.; Lauru, S.; Maragni, P. *Tetrahedron Lett.* **2004**, *45*, 1499; (h) Miura, K.; Fujisawa, N.; Hosomi, A. *J. Org. Chem.* **2004**, *69*, 2427; (i) Rann, B. C.; Jana, R.; Samanta, S. *Adv. Synth. Catal.* **2004**, *346*, 446; (j) Chakraborti, A. K.; Gulhane, R. *Tetrahedron Lett.* **2003**, *44*, 6749; (k) Chancharunee, S.; Perlmutter, P.; Statton, M. *Tetrahedron Lett.* **2003**, *44*, 5683; (l) Yadav, J. S.; Geetha, V.; Reddy, B. V. S. *Synth. Commun.* **2002**, *32*, 3519; (m) Onishi, Y.; Ito, T.; Yasuda, M.; Baba, A. *Tetrahedron* **2002**, *58*, 8227; (n) Ranu, B. C.; Samanta, S.; Hajra, A. *Synlett* **2002**, 987; (o) Ranu, B. C.; Das, A.; Samanta, S. *Synlett* **2002**, 727.
4. Araki, S.; Kamei, T.; Hirashita, T.; Yamamura, H.; Kawai, M. *Org. Lett.* **2000**, *2*, 847.
5. (a) Talapatra, S. K.; Chakrabarti, S.; Mallik, A. K.; Talapatra, B. *Tetrahedron* **1990**, *46*, 6047; (b) Bradlaw, H. L.; Vander Werf, C. A. *J. Am. Chem. Soc.* **1947**, *69*, 1254.
6. Risinger, G. E.; Eddy, C. W. *Chem. Ind.* **1963**, 570.
7. Marquardt, D. J.; McCormick, F. *Tetrahedron Lett.* **1994**, *35*, 1131.
8. (a) Brewster, J. H. *J. Am. Chem. Soc.* **1954**, *76*, 6364; (b) Nakabayashi, T. *J. Am. Chem. Soc.* **1960**, *82*, 3900.