

## Convenient Reduction of Nitrobenzenes to Anilines Using Electrochemically Generated Nickel

Akito Yasuhara,\* Atsushi Kasano, and Takao Sakamoto\*

Faculty of Pharmaceutical Sciences, Tohoku University, Aobaku, Sendai 980-8578, Japan

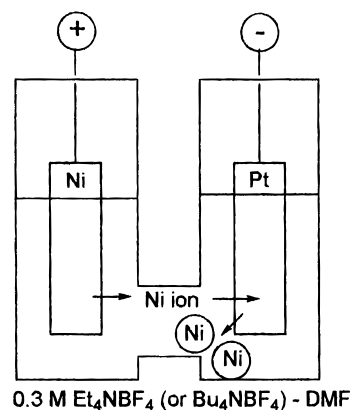
Received September 23, 1998

The reduction of nitrobenzenes with electrogenerated nickel in DMF gave anilines without affecting the alkenyl, alkynyl, halo, acetyl, methoxy, cyano, ethoxycarbonyl, formyl, benzyloxy, and phenylsulfonylamino groups at room temperature in a short time. The nickel was easily prepared by electrolysis in 0.3 M  $\text{Et}_4\text{NBF}_4$ –DMF solution under an argon atmosphere at a constant current (10 mA/cm<sup>2</sup>) and can be stored under argon at  $-20^\circ\text{C}$  for at least a week.

### Introduction

Selective reduction of nitrobenzenes to the corresponding anilines is of importance in synthetic organic chemistry. Generally, catalytic reductions with some metals (e.g., Raney nickel,<sup>1a,d</sup> Pd–C,<sup>1d</sup> PtO<sub>2</sub><sup>1a</sup>) and a mixture of metal (e.g., Fe,<sup>1b</sup> Sn,<sup>1a,b</sup> and SnCl<sub>2</sub><sup>1b,c</sup>) and HCl have been used. However, these methods are not selective and may affect functional groups such as iodo, benzyloxy, and formyl. Therefore, many other methods have been reported.<sup>2</sup> For example, the combination of hydrazine and metal (e.g., Raney nickel,<sup>3</sup> Pd–C,<sup>1d</sup> graphite<sup>4</sup>), NaBH<sub>4</sub> and metal (e.g., Pd–C,<sup>5</sup> Pt–C,<sup>6</sup> and CoCl<sub>2</sub>–C<sup>7</sup>), and RuCl<sub>2</sub>–(PPh<sub>3</sub>)<sub>2</sub>–H<sub>2</sub>.<sup>8</sup> Each method has its own advantages and disadvantages. The reductions with hydrazine or NaBH<sub>4</sub> and metal do not require the use of hydrogen gas. However, a significant disadvantage is that the reaction with hydrazine also reduces carbonyl groups substituted on nitrobenzenes while the reduction with the combination of NaBH<sub>4</sub><sup>5–7</sup> and metal often involves dehalogenation. Also, the reduction with RuCl<sub>2</sub>(PPh<sub>3</sub>)<sub>2</sub>–H<sub>2</sub> requires a high temperature and pressure.<sup>8</sup> Recently, Fischer and co-workers reported that diethyl chlorophosphite could reduce aromatic nitrobenzenes.<sup>9</sup> However, the reduction of nitrobenzenes having a cyano or methoxy group produced only low yields.

On the other hand, we reported the easy preparation of a highly reactive nickel by an electrochemical method.<sup>10</sup>



**Figure 1.** The apparatus of electrolysis for generation of active nickel.

Electrolysis was carried out in a DMF solution containing 0.3 M  $\text{Bu}_4\text{NBF}_4$  using an undivided cell with a platinum cathode and a nickel anode at constant current under an argon atmosphere to give a highly reactive nickel–DMF suspension without massive deposition (Figure 1).

We report here the reduction of nitrobenzenes to anilines by electrogenerated nickel at room temperature in a short time without affecting various functional groups.

### Results and Discussion

As shown in Figure 1, highly reactive nickel was prepared by electrolysis in a DMF solution containing 0.3 M tetraethylammonium tetrafluoroborate ( $\text{Et}_4\text{NBF}_4$ ) or tetrabutylammonium tetrafluoroborate ( $\text{Bu}_4\text{NBF}_4$ ) under an argon atmosphere. In this reaction,  $\text{Et}_4\text{NBF}_4$  was used as the electrolyte, because  $\text{Et}_4\text{NBF}_4$  could be more easily removed by extraction than  $\text{Bu}_4\text{NBF}_4$ . The electrolysis was carried out at a constant current of 10 mA/cm<sup>2</sup> at  $0^\circ\text{C}$  for 1158 Coulombs (ca. 4 h). The electrolysis of 1158 Coulombs prepared 2.5 mmol nickel using a platinum cathode (1 × 2 cm) and nickel anode (1 × 2 cm). After the electrolysis, the nickel–DMF suspension was transferred to a reaction flask using a syringe and was used for reduction of 0.5 mmol of nitrobenzenes. As shown in Table 1, the reduction of the nitrobenzenes

\* Corresponding author. Tel +81-22-217-6867; fax +81-22-217-6864; yasuhara@mail.pharm.tohoku.ac.jp

(1) (a) Gilman, H. *Organic Syntheses*; John Wiley & Sons: New York, 1941; Coll. Vol. 1, pp 240, 455. (b) Blatt, A. H. *Organic Syntheses*; John Wiley & Sons: New York, 1943; Coll. Vol. 2, pp 130, 160, 175, 254. (c) Horning, E. C. *Organic Syntheses*; John Wiley & Sons: New York, 1955; Coll. Vol. 3, pp 59, 63, 239, and 453. (d) Baumgarten, H. E. *Organic Syntheses*; John Wiley & Sons: New York, 1973; Coll. Vol. 5, pp 30, 346, 829, and 1130.

(2) Larock, R. C. *Comprehensive Organic Transformations*; VCH: New York, 1989; p 412.

(3) (a) Brown, R. K.; Nelson, N. A. *J. Am. Chem. Soc.* **1954**, *76*, 5149–5150. Balcom, D.; Furst, A. *J. Am. Chem. Soc.* **1953**, *75*, 4334. Kozuka, M.; Iwaizumi, M. *Bull. Chem. Soc. Jpn.* **1983**, *56*, 3165–3166.

(b) Yuste, F.; Saldana, M.; Walls, F. *Tetrahedron Lett.* **1982**, 147–148.

(4) Han, B. H.; Shin, D. H.; Cho, S. Y. *Tetrahedron Lett.* **1985**, 6233–6234.

(5) Neilson, T.; Wood, H. C. S.; Wylie, A. G. *J. Chem. Soc.* **1962**, 371–373.

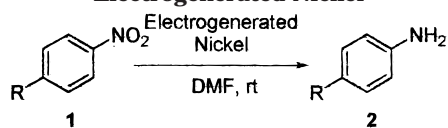
(6) Brown, H. C.; Brown, C. A. *J. Am. Chem. Soc.* **1962**, *84*, 2828–2829.

(7) Satoh, T.; Suzuki, S. *Tetrahedron Lett.* **1969**, 4555–4558.

(8) Knifton, J. F. *J. Org. Chem.* **1976**, *41*, 1200–1205.

(9) Fischer, B.; Sheihet, L. *J. Org. Chem.* **1998**, *63*, 393–395.

(10) Yasuhara, A.; Kasano, A.; Sakamoto, T. *Organometallics* **1998**, *17*, 4754–475.

**Table 1. Reduction of 4-Nitrobenzenes to Amines with Electrogenerated Nickel**

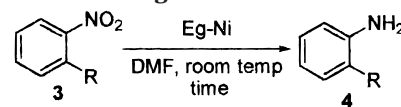
entry no	1	R	time (min)	yield (%)
1	a	I	15	76
2	b	Br	15	78
3	c	Cl	15	83
4	d	COMe	15	62
5	e	OMe	15	92
6	f	CN	15	97
7	g		15	87
8	h		15	93
9	i	CHO	15	56
10	j	OCH <sub>2</sub> Ph	18 h	22
11	j	OCH <sub>2</sub> Ph	18 h	86 <sup>a</sup>
12	k	NHSO <sub>2</sub> Ph	15	47
13	l		18 h	35 <sup>b</sup>

<sup>a</sup> Using 10 equivalents active nickel.<sup>b</sup> 4-Nitrophenol was isolated in 12% yield.

gave the corresponding anilines in a short time at room temperature. The reduction of 4-halonitrobenzene with the electrogenerated nickel proceeded in 15 min at room temperature with 76–83% yields. Especially, the electrogenerated nickel could selectively reduce the nitro group of 4-iodonitrobenzene in which the iodo group has a high reactivity for the oxidative addition of nickel in good yield without deiodination (Table 1, entry 1). The reduction of nitrobenzenes with carbonyl groups such as the acetyl (**1d**), formyl (**1i**), and ethoxycarbonyl groups (**1g**) also gave the corresponding anilines in 62, 56, and 87% yields, respectively. Also the reduction of alkene (**1g**) and alkyne (**1h**) with electrogenerated nickel proceeded in 87 and 94% yields without affecting the unsaturated carbon–carbon bonds. Although the reduction of 4-nitro-1-(phenylmethoxy)benzene (**1j**) with 5 equiv of nickel did not completely proceed and gave **2j** in 22% yield (Table 1, entry 10), the reduction with 10 equiv of nickel proceeded for 18 h at room temperature and produced **2j** in 86% yield (Table 1, entry 11). The reduction of nitrobenzenes with the phenylsulfonamino (**1k**) and allyloxy groups (**1l**) gave the corresponding anilines in low yields (47 and 35% yields). In the later case, deallylation of **1l** preceded without reduction of the nitro group to give 4-nitrophenol in 12% yield.

The reduction of 2-substituted nitrobenzenes using the electrogenerated nickel proceeded in lower yields than the reduction of the 4-substituted nitrobenzenes (Table 2). The reduction of 2-iodo- (**3a**), 2-acetyl- (**3d**), 2-methoxy- (**3e**), and 2-(phenylethynyl)nitrobenzene (**3h**) proceeded in 36–70% yields, and the yields of the corresponding 4-substituted nitrobenzenes were 62–93%.

We investigated the storage stability of the electrogenerated nickel and scaling-up the reaction (3 mmol scale of the starting material). After the electrogenerated nickel has been stored for 1 week at –20 °C under an argon atmosphere, the reduction of 4-bromonitrobenzene with the nickel gave the 4-bromoaniline in 75% yield. The reaction of the same starting material with the fresh electrogenerated nickel gave the product in 78% yield (Table 1, entry 2).

**Table 2. Reduction of 2-Nitrobenzenes into Amines with Electrogenerated Nickel**

entry no	3	R	time (min)	yield (%)
1	a	I	2 h	55
2	d	COMe	15	36
3	e	OMe	15	53 <sup>a</sup>
4	h		30	70

<sup>a</sup> Recovery yield is 16%.

The electrolysis time depended on the electrode area. Therefore, the electrogenerated nickel was prepared on a 3 mmol scale and had the same reactivity with the nickel prepared on the 0.5 mmol scale. In the case of the 3 mmol scale, the electrolysis using a nickel anode (2 × 6 cm) and platinum cathode (2 × 6 cm) was carried out for 5790 Coulombs (ca. 4 h). The reduction of 4-bromonitrobenzene (606 mg, 3 mmol) with the nickel–DMF suspension gave 4-bromoaniline (387 mg, 75%).

## Conclusion

The reduction of nitrobenzenes to anilines using electrogenerated nickel proceeds under mild conditions without affecting various functional groups on the aromatic ring. The reaction was usually performed at room temperature for 15 min. No co-reducing agents or hydrogen gas were required. Moreover, it was found that the reactive nickel can be stored for a week at –20 °C without losing its reactivity for the reduction of the nitrobenzenes. The electrogenerated nickel can be concluded to be a good reducing reagent for nitrobenzenes.

## Experimental Section

All melting points and boiling points are uncorrected. The IR spectra were measured on a JASCO IR-810 spectrophotometer. <sup>1</sup>H NMR spectra were recorded on a Varian Gemini 2000 (300 MHz). Chemical shifts are expressed in  $\delta$  (ppm) values with tetramethylsilane (TMS) as the internal reference, and coupling constants are expressed in hertz (Hz). Mass spectra (MS) and high-resolution mass spectra (HRMS) were recorded on JMS-DX303 and JMS-AX500 instruments, respectively.

**Preparation of Electrogenerated Nickel.** A platinum sheet (1 × 2 cm<sup>2</sup>) as the cathode and a nickel sheet (1 × 2 cm<sup>2</sup>) as the anode were placed in a 15 mL H-shaped undivided cell that contained 0.3 M Et<sub>4</sub>NBF<sub>4</sub>–DMF (8 mL). Electrolysis was carried out under an argon atmosphere at a constant current of 10 mA/cm<sup>2</sup> at 0 °C until 1158 coulombs of electricity had passed to produce a black suspension containing the active nickel (145 mg, 2.4 mmol).

The amount of Ni in a black suspension was confirmed by following method. After electrolysis, dry THF (30 mL) was added to the black nickel suspension, the mixture was centrifuged (3500 rpm, 1 h), and the supernatant was discarded. Dry THF was added to the precipitate, the mixture was stirred and centrifuged (3500 rpm, 10 min), and the supernatant was discarded. The precipitate was dried under reduced pressure, and the weight of precipitate was measured.

**General Procedure for Reduction of Substituted Nitrobenzenes.** The nickel–DMF suspension was added to a substituted nitrobenzene (0.5 mmol) using a syringe under an argon atmosphere. The mixture was stirred for 15 min (or 18 h) at room temperature. 2 M HCl (10 mL) was added to the reaction mixture. After the addition of Et<sub>2</sub>O (20 mL) to the solution, the mixture was filtered through a Celite pad. The

etheral layer was separated and extracted with 2 M HCl (15 mL  $\times$  3). The aqueous layers were combined, made basic with  $K_2CO_3$ , and extracted with  $Et_2O$  (20 mL  $\times$  3). The etheral layer was washed with  $H_2O$  (10 mL), dried over  $MgSO_4$ , and evaporated under reduced pressure. The residue was purified by recrystallization or distillation.

**4-Iodoaniline (2a).** Colorless needles from  $Et_2O$ -hexane; mp 59–60 °C (lit.<sup>11</sup> mp 63–65 °C);  $^1H$  NMR ( $CDCl_3/TMS$ )  $\delta$ : 3.15 (br, 2H), 6.47 (d,  $J = 8.7$  Hz, 2H), 7.41 (d,  $J = 8.7$  Hz, 2H); IR  $\nu$  (KBr)  $cm^{-1}$ : 3400, 3290.

**4-Bromoaniline (2b).** Colorless prisms from  $Et_2O$ -hexane; mp 59–61 °C (lit.<sup>11</sup> mp 62–64 °C);  $^1H$  NMR ( $CDCl_3/TMS$ )  $\delta$ : 3.65 (br, 2H), 6.57 (d,  $J = 8.8$  Hz, 2H), 7.24 (d,  $J = 8.8$  Hz, 2H); IR  $\nu$  (KBr)  $cm^{-1}$ : 3470, 3380.

**4-Chloroaniline (2c).** Colorless prisms from  $Et_2O$ -hexane; mp 67–69 (lit.<sup>11</sup> mp 68–71 °C);  $^1H$  NMR ( $CDCl_3/TMS$ )  $\delta$ : 3.65 (br, 2H), 6.61 (d,  $J = 8.8$  Hz, 2H), 7.10 (d,  $J = 8.8$  Hz, 2H); IR  $\nu$  (KBr)  $cm^{-1}$ : 3470, 3380.

**4-Aminophenyl Methyl Ketone (2d).** Colorless prisms from  $EtOAc$ -hexane; mp 104–106 °C (lit.<sup>11</sup> mp 105–107);  $^1H$  NMR ( $CDCl_3/TMS$ )  $\delta$ : 2.51 (s, 3H), 4.12 (br, 2H), 6.65 (d,  $J = 8.5$  Hz, 2H), 7.82 (d,  $J = 8.5$  Hz, 2H); MS  $m/z$ : 135 ( $M^+$ ); IR  $\nu$  (KBr)  $cm^{-1}$ : 3370, 3300, 1640.

**4-Methoxyaniline (2e).** Colorless prisms from  $Et_2O$ -hexane; mp 53–55 °C (lit.<sup>12</sup> 57–60 °C);  $^1H$  NMR ( $CDCl_3/TMS$ )  $\delta$ : 3.42 (br, 2H), 3.75 (s, 3H), 6.65 (d,  $J = 8.8$  Hz, 2H), 6.71 (d,  $J = 8.8$  Hz, 2H); IR  $\nu$  (KBr)  $cm^{-1}$ : 3420, 3345, 1230.

**4-Aminobenzonitrile (2f).** Colorless prisms from  $Et_2O$ -hexane; mp 83–85 °C (lit.<sup>11</sup> 83–85 °C);  $^1H$  NMR ( $CDCl_3/TMS$ )  $\delta$ : 4.15 (br, 2H), 6.65 (d,  $J = 8.8$  Hz, 2H), 7.42 (d,  $J = 8.8$  Hz, 2H); IR  $\nu$  (KBr)  $cm^{-1}$ : 3470, 3360, 2210.

**Ethyl 3-(4-Aminophenyl)propenoate (2g).** Colorless needles from  $Et_2O$ -hexane; mp 67–68 °C;  $^1H$  NMR ( $CDCl_3/TMS$ )  $\delta$ : 1.32 (t,  $J = 7.1$  Hz, 3H), 3.95 (br, 2H), 4.24 (q,  $J = 7.1$  Hz, 2H), 6.24 (d,  $J = 16.0$  Hz, 1H), 6.65 (d,  $J = 8.8$  Hz, 2H), 7.35 (d,  $J = 8.8$  Hz, 2H), 7.60 (d,  $J = 16.0$  Hz, 1H); MS  $m/z$ : 191 ( $M^+$ ); IR  $\nu$  (KBr)  $cm^{-1}$ : 3410, 3320, 1690, 1590. Anal. Calcd for  $C_{11}H_{13}NO_2$ : C, 69.09; H, 6.85; N, 7.32. Found: C, 69.16; H, 6.77; N, 7.34.

**4-(Phenylethynyl)aniline (2h).** Colorless needles from  $Et_2O$ -hexane; mp 126–128 °C (lit.<sup>13</sup> mp 128–129 °C);  $^1H$  NMR ( $CDCl_3/TMS$ )  $\delta$ : 3.81 (br, 2H), 6.64 (d,  $J = 8.8$  Hz, 2H), 7.36–7.40 (m, 5H), 7.50 (d,  $J = 8.8$  Hz, 2H); MS  $m/z$ : 193 ( $M^+$ ); IR  $\nu$  (KBr)  $cm^{-1}$ : 3470, 3380, 2210.

**4-Aminobenzaldehyde (2i).** Pale yellow solid; unstable compound;  $^1H$  NMR ( $CDCl_3/TMS$ )  $\delta$ : 4.37 (br, 2H), 6.70 (d,  $J = 8.5$  Hz, 2H), 7.68 (d,  $J = 8.5$  Hz, 2H), 9.74 (s, 1H); MS  $m/z$ : 121 ( $M^+$ ); HRMS Calcd for  $C_7H_7NO$ : 121.0527. Found: 121.0525. IR  $\nu$  (KBr)  $cm^{-1}$ : 3360, 1665.

(11) Pouchert, C. J.; Behnke J. *The Aldrich Library of  $^{13}C$  and  $^1H$  FT-NMR Spectra 2*; Aldrich Chemical Co., Inc.: New York, 1993; pp 179, 463, 481, 482, 868, 869, 1521.

(12) Budavari, S.; O'Neil, M. J.; Smith, A.; Heckelman, P. E. *The Merck Index*, 11th ed.; Merck & Co., Inc.: Rahway, NJ, 1989; p 105.

(13) Stephenes, R. D.; Castro, C. E. *J. Org. Chem.* **1963**, *28*, 3313–3315.

**4-(Phenylmethoxy)aniline (2j).** White solid; bp 145–155 °C/3 mmHg (lit.<sup>3b</sup> 201–202 °C/11 mmHg);  $^1H$  NMR ( $CDCl_3/TMS$ )  $\delta$ : 3.25 (br, 2H), 4.99 (s, 2H), 6.64 (d,  $J = 8.8$  Hz, 2H), 6.82 (d,  $J = 8.8$  Hz, 2H), 7.31–7.44 (m, 5H); MS  $m/z$ : 199 ( $M^+$ ); IR  $\nu$  (KBr)  $cm^{-1}$ : 3430, 3370.

**(4-Aminophenyl)benzenesulfonamide (2k).** Colorless needles from  $EtOAc$ -hexane; mp 170–173 °C (lit.<sup>14</sup> 171–174 °C);  $^1H$  NMR ( $CDCl_3/TMS$ )  $\delta$ : 3.62 (br, 3H), 6.54 (d,  $J = 8.8$  Hz, 2H), 6.81 (d,  $J = 8.8$  Hz, 2H), 7.43 (d,  $J = 7.4$  Hz, 2H), 7.54 (t,  $J = 7.4$  Hz, 1H), 7.69 (d,  $J = 7.4$  Hz, 2H); MS  $m/z$ : 248 ( $M^+$ ); IR  $\nu$  (KBr)  $cm^{-1}$ : 3410, 3340, 1320, 1160.

**4-(Prop-2-enyloxy)aniline (2l).** According to the general procedure of the reduction of substituted nitrobenzenes, the reaction of **11** with the nickel-DMF suspension gave a crude product. The crude product was purified by column chromatography and distillation. Colorless viscous liquid; bp 55–65 °C/3 mmHg;  $^1H$  NMR ( $CDCl_3/TMS$ )  $\delta$ : 3.35 (br, 2H), 4.46 (dt,  $J = 5.5, 1.5$  Hz, 2H), 5.26 (ddd,  $J = 10.4, 2.0, 1.5$  Hz, 1H), 5.39 (ddd,  $J = 17.0, 2.0, 1.5$  Hz, 1H), 6.04 (ddd,  $J = 17.0, 10.4, 5.5$  Hz, 1H), 6.64 (d,  $J = 8.8$  Hz, 2H), 6.77 (d,  $J = 8.8$  Hz, 2H); MS  $m/z$ : 149 ( $M^+$ ); HRMS Calcd for  $C_9H_{11}NO$  149.0840. Found 149.0841; IR  $\nu$  (KBr)  $cm^{-1}$ : 3410, 3350, 1630, 1240. Anal. Calcd for  $C_9H_{11}NO$ : C, 72.46; H, 7.43; N, 9.39. Found: C, 72.40; H, 7.45; N, 9.34.

**2-Iodoaniline (4a).** Colorless needles from  $Et_2O$ -hexane; mp 52–55 °C (lit.<sup>11</sup> mp 58 °C);  $^1H$  NMR ( $CDCl_3/TMS$ )  $\delta$ : 4.09 (br, 2H), 6.48 (t,  $J = 7.9$  Hz, 1H), 6.76 (d,  $J = 7.9$  Hz, 1H), 7.14 (t,  $J = 7.9$  Hz, 1H), 7.64 (t,  $J = 7.9$  Hz, 1H); IR  $\nu$  (KBr)  $cm^{-1}$ : 3390, 3290.

**2-Aminophenyl Methyl Ketone (4d).** Pale yellow, viscous liquid; bp 95–105 °C/3 mmHg (lit.<sup>11</sup> 85–90 °C/0.5 mmHg);  $^1H$  NMR ( $CDCl_3/TMS$ )  $\delta$ : 2.56 (s, 3H), 6.29 (br, 2H), 6.61–6.66 (m, 2H), 7.25 (dt,  $J = 8.4, 1.6$  Hz, 1H), 7.70 (dd,  $J = 8.4, 1.6$  Hz, 1H); IR  $\nu$  (KBr)  $cm^{-1}$ : 3450, 3340, 1650.

**2-Methoxyaniline (4e).** Colorless liquid; bp 120–130 °C/30 mmHg (lit.<sup>11</sup> bp 225 °C/760 mmHg);  $^1H$  NMR ( $CDCl_3/TMS$ )  $\delta$ : 3.77 (br, 2H), 3.83 (s, 3H), 6.69–6.80 (m, 5H); IR  $\nu$  (KBr)  $cm^{-1}$ : 3460, 3370, 1230.

**2-(Phenylethynyl)aniline (4h).** Pale yellow prisms from hexane-acetone; mp 89–90 °C (lit.<sup>9</sup> 92 °C);  $^1H$  NMR ( $CDCl_3$ )  $\delta$ : 4.27 (br, 2H), 6.79 (t,  $J = 7.7$  Hz, 2H), 7.14 (dt,  $J = 7.9, 1.4$  Hz, 1H), 7.32–7.39 (m, 4H), 7.51–7.55 (m, 2H); MS  $m/z$ : 193 ( $M^+$ ); IR (KBr)  $cm^{-1}$  3500, 2250, 1620.

**Acknowledgment.** This research was supported by a Grant-in-Aid for Scientific Research (No 10771234) from the Ministry of Education, Science, Sports and Culture of Japan.

JO981935P

(14) Holmes, J. T., Jr.; Lawton, R. G. *J. Org. Chem.* **1983**, *48*, 3146–3150.