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Notes

Diels–Alder Reactions of α-Substituted Styrenes with *p*-Benzoquinone

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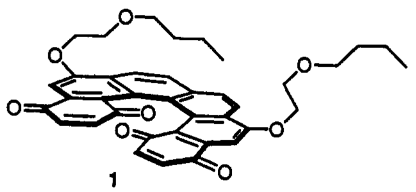
Large quantities of carbocyclic helicenes, for example **1**, can be made by a new procedure that combines divinyl aromatics with *p*-benzoquinone.[1] The key to good yields is to substitute alkoxy substituents at the α-positions of the styrenes.[2] Although the Diels–Alder reactions of styrenes with *p*-benzoquinone and other dienophiles have been extensively studied,[3] no similar transformations have been reported for the simplest examples, enol ethers of the parent compound, acetophenone.[4] In fact, the only mono(1-alkoxyvinyl)benzene reported to form a Diels–Alder adduct is the dimethylsilylidene derivative of the enol of 2-hydroxyacetophenones.[5] Accordingly, we investigated and report here the practicality of Diels–Alder syntheses employing *p*-benzoquinone and simple styrenes that have alkoxy and other electron-donating groups substituted on the α-carbons of the double bonds.



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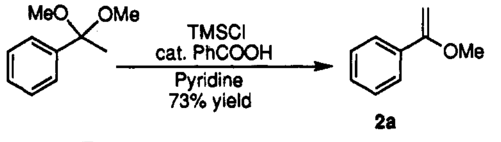
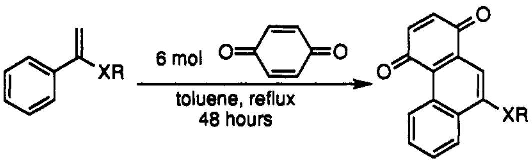
Enol ethers **2a** and **2b** were prepared (Scheme 1) using novel methods[1b] used previously to synthesize **1** and the related bis-methyl ether. These enol ethers and the methylthio analogue **2c**,[6] when combined with *p*-benzoquinone according to Scheme 2, gave 43–57% yields of 1,4-phenanthrenediones.[7] The crude products' ^{1}H NMR spectra identified only *p*-benzoquinone, hydroquinone, **3a**–**c**, and, by weak broad peaks, possibly polymers. Styrene itself (**2d**) gave a 31% yield under the same conditions.[9]

Scheme 1



Scheme 2



2a (XR = OCH_3) **3a** (57% yield)
2b (XR = $OCH_2CH_2OCH_2CH_2CH_2CH_3$) **3b** (51% yield)
2c (XR = SMe) **3c** (43% yield)
2d (XR = H) **3d** (31% yield)

We were unable to detect (by TLC analysis) any of the initial Diels–Alder adduct whose further oxidation undoubtedly leads to the 1,4-phenanthrenediones. When **2b** was combined with only 1 mol of *p*-benzoquinone, the TLC analysis of the product showed only **3b** and residual starting material.

Nitrogen-substituted styrenes **4**[10] and **5**[11] did not give Diels–Alder adducts with *p*-benzoquinone.[12] The initial dark green colors of the solutions might indicate that electrons transfer from the nitrogen compounds to the quinone. The ultimate products, however, are intractable solids.

When styrenes that have heteroatom substituents in the aromatic ring are combined with *p*-benzoquinone, they

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[1] (a) Liu, L.; Katz, T. J. *Tetrahedron Lett.* **1990**, *31*, 3983. (b) Willmore, N. D.; Liu, L.; Katz, T. J. *Angew. Chem.* **1992**, *104*, 1081. *Angew. Chem., Int. Ed. Engl.* **1992**, *31*, 1093.

[2] Similar activation of nonaromatic dienes is well known. See: (a) Fringuelli, F.; Taticchi, A. *Dienes in the Diels–Alder Reaction*; Wiley: New York, 1990. (b) Danishefsky, S. *Acc. Chem. Res.* 1981, *14*, 400, and references cited therein.

[3] (a) For an extensive review see Wagner-Jauregg, T. *Synthesis* **1980**, 769. (b) Rosen, B. I.; Weber, W. P. *J. Org. Chem.* **1977**, *42*, 3463. (c) Manning, W. B.; Tomaszewski, J. E.; Muschik, G. M.; Sato, R. I. *J. Org. Chem.* **1977**, *42*, 3465. (d) Muschik, G. M.; Tomaszewski, J. E.; Sato, R. I.; Manning, W. B. *J. Org. Chem.* **1979**, *44*, 2150. (e) Manning, W. B.; Wilbur, D. J. *J. Org. Chem.* **1980**, *45*, 733. (f) Manning, W. B.; Kelly, T. P.; Muschik, G. M. *J. Org. Chem.* **1980**, *45*, 2535. (g) Manning, W. B. *Tetrahedron Lett.* **1981**, *22*, 1571. (h) Muschik, G. M.; Kelly, T. P.; Manning, W. B. *J. Org. Chem.* **1982**, *47*, 4709. (i) Padias, A. B.; Tien, T.-P.; Hall, H. K., Jr. *J. Org. Chem.* **1991**, *56*, 5540, and references therein. (j) Pindur, U.; Eitel, M. *Helv. Chim. Acta* **1988**, *71*, 1060.

[4] (1-Methoxyethenyl)benzene and dimethyl azodicarboxylate combined to give two isolable products. Although neither was a simple Diels–Alder adduct, one surely was derived from such an adduct. Alder, K.; Niklas, H. *Justus Liebig's Ann. Chem.* **1954**, *585*, 97.

[5] Kita, Y.; Yasuda, H.; Tamura, O.; Tamura, Y. *Tetrahedron Lett.* **1984**, *25*, 1813.

[6] Ikehira, H.; Tanimoto, S.; Oida, T. *Bull. Chem. Soc. Jpn.* **1983**, *56*, 2537.

[7] Toluene was used as the solvent because in it the yields of **1** were the best. Acetonitrile, which Blatter, Schlüter, and Wegner[8] found a superior solvent for reactions of 1-hexyl-1-(2-naphthyl)ethene with *p*-benzoquinone, gave lower yields of **1**, as did DMF and DMSO (unpublished work of N. D. Willmore).

[8] Blatter, K.; Schlüter, A.-D.; Wegner, G. *J. Org. Chem.* **1989**, *54*, 2396.

[9] The yield was 14.3% when styrene and 1 mol of *p*-benzoquinone were refluxed in xylene (ref 3b), 31% when they were stirred in toluene for 1–7 days at 100 °C in the presence of trichloroacetic acid (ref 3f), and 26% when they were combined in refluxing toluene with chloranil and $SnCl_4$ (Tanga, M. J.; Reist, E. J. *J. Heterocycl. Chem.* **1991**, *28*, 29).

[10] Carlson, R.; Nilsson, Å. *Acta Chem. Scand.* **1984**, *B38*, 49.

[11] (a) Cyclization of *N*-acetyl-2-phenylethylamine: Thesing, J.; Funk, F. H. *Chem. Ber.* **1958**, *91*, 1546. (b) Reaction with Ac_2O to give the enamide: Brossi, A.; Dolan, L. A.; Teitel, S. *Organic Syntheses*; Wiley: New York, 1988; Collect. Vol. 6, p 1.

[12] However with benzyne, methylene isoquinolines and related compounds do give Diels–Alder adducts. (a) Saá, C.; Guitián, E.; Castedo, L.; Saá, J. M. *Tetrahedron Lett.* **1985**, *26*, 4559. (b) Castedo, L.; Guitián, E.; Saá, C.; Suau, R.; Saá, J. M. *Tetrahedron Lett.* **1983**, *24*, 2107. (c) Castedo, L; Guitián, E.; Saá, J. M.; Suau, R. *Tetrahedron Lett.* **1982**, *23*, 457. (d) Castedo, L; Guitián, E. In *Studies in Natural Products Chemistry, Volume 3, Stereoselective Synthesis* (*Part B*); Atta-ur-Rahman, Ed.; Elsevier: New York, 1989; pp 417–454.

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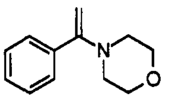

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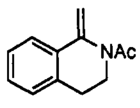

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give about the same yields as styrene itself,[3b–f,13] appreciably lower than the yields produced by styrenes that are the enol ethers of acetophenones.

Experimental Section

Unless otherwise indicated, ^1H and ^{13}C NMR spectra were recorded at 400 and 75 MHz, respectively, used $CDCl_3$ solutions, and were referenced to the resonance of TMS. IR spectra were recorded using $CHCl_3$ solutions. Reactions were performed using dried glassware and a N_2 atmosphere that was released through an oil bubbler during Diels–Alder reactions[1b] and through a Hg bubbler during others. Toluene was distilled from potassium. *p*-Benzoquinone was recrystallized from acetone. Et_3N was stored over KOH. THF was distilled from potassium/benzophenone.

(1-Methoxyethenyl)benzene (2a). Benzoic acid (0.73 g, 6 mmol), followed by TMSCl (23 mL, 181 mmol) was added to the dimethyl acetal of acetophenone (10.0 g, 60 mmol) in pyridine (30 mL). After the mixture had been stirred at 65 °C for 20 h, Et_3N (40 mL) was added at rt. The mixture was cooled to 0 °C. Aqueous NaOH (15%, 60 mL) was added slowly, and the aqueous layer was extracted with ether (3×). Ten washings with an equal volume of dilute aqueous NaOH removed pyridine. The organic layer was washed with brine, dried ($MgSO_4$), and stripped, giving an oil. Distillation (84–85 °C, water aspirator) gave 6.31 g (78%) of **2a**: ^1H NMR (300 MHz) δ 3.74 (s, 3H), 4.21 (d, J = 2.7 Hz, 1H), 4.65 (d, J = 2.8 Hz, 1H), 7.32 (m, 3H), 7.62 (m, 2H); MS (EI) *m/z* 134 (M^+), 103, 91, 77; HRMS (EI) calcd for $C_9H_{10}O$ 134.0732, found 134.0721; ^{13}C NMR δ 55.16, 81.65, 125.29, 128.05, 128.36, 136.41, 160.80. The ^{13}C NMRs agree with those published.[14]

[1-(2-*n*-Butoxyethoxy)ethenyl]benzene (2b). NaI (49 g, 330 mmol, flame-dried in a vacuum), Et_3N (49.0 mL, 350 mmol), CH_3CN (122 mL), 2-methyl-2-phenyl-1,3-dioxolane (20 g, 121 mmol), and TMSCl (42 mL, 329 mmol) were refluxed for 1.5 h. Et_3N (50 mL) and ether (250 mL) were added, and the mixture was poured into ice/saturated aqueous $NaHCO_3$ (300 mL). The combined ether solutions from two extractions were washed with saturated $NaHCO_3$, which was back-extracted with ether. Drying with K_2CO_3 and stripping yielded 39.3 g of crude oily [1-[2-(trimethylsiloxy)ethoxy]ethenyl]benzene, which was distilled at 0.2 mmHg (bp 85 °C, 31.1g) and used for the next step even though it still contained some hexamethyldisiloxane. A pure distillation fraction was analyzed: ^1H NMR δ 0.16 (s, 9 H), 3.94 (s, 4 H), 4.21 (d, J = 2.8 Hz, 1H), 4.65 (d, J = 2.9 Hz, 1H), 7.30 (m, 3H), 7.63 (m, 2H); ^{13}C NMR δ −0.41, 61.15, 69.07, 82.61, 125.47, 128.04, 128.40, 136.49, 159.95; IR 3062, 2959, 2937, 2877, 1647, 1610, 1574, 1495, 1457, 1446, 1411, 1342, 1317, 1302, 1284, 1253, 1183, 1128, 1104, 1080, 1062, 992, 948, 845, 808, 774 cm^{-1}; MS (EI) *m/z* 237 (MH^+), 193, 117, 105, 73; HRMS (EI) calcd for ($C_{13}H_{20}O_2Si + H^+$) 237.1311, found 237.1305.

The distillate above (ca. 121 mmol), combined with K_2CO_3 (13.4 g, 97 mmol) in MeOH (240 mL), was stirred for 40 min and stripped. Et_2O (ca. 300 mL) was added, and the mixture was washed with saturated aqueous $NaHCO_3$ (3×), dried (K_2CO_3), and stripped in a vacuum, giving 16.5 g (83% yield from the ketal) of [1-(2-hydroxyethoxy)ethenyl]benzene. For analysis a small amount was distilled in a vacuum from bulb-to-bulb: ^1H NMR (300 MHz) δ 2.51 (s, 1H), 3.91 (s, 4H), 4.20 (d, J = 2.7 Hz, 1H), 4.65 (d, J = 2.6 Hz, 1H), 7.30 (m, 3H), 7.60 (m, 2H); ^{13}C NMR δ 61.24, 69.09, 83.05, 125.40, 128.15, 128.57, 136.29, 159.76; IR 3607, 3452, 3062, 2937, 2878, 1648, 1612, 1574, 1495, 1459, 1446, 1405, 1374, 1316, 1302, 1285, 1243, 1227, 1210, 1184, 1075, 1042, 980, 811, 724 cm^{-1}; MS (EI) *m/z* 164 (M^+), 149, 121, 105, 91, 77, 64, 46; HRMS (EI) calcd for ($C_{10}H_{12}O_2$) 164.0837, found 164.0839.

This alcohol (15.8 g, 96 mmol), combined with DMSO (96 mL), powdered KOH (21.6 g, 385 mmol), and then with BuBr (20.7 mL, 193 mmol), was stirred for 2 h. Et_3N (50 mL) was added, and after the mixture had been poured into ice/saturated aqueous $NaHCO_3$ (200 mL), it was extracted with ether (3×). Drying ($MgSO_4$) and then stripping the solvent in a vacuum gave 20.8 g (98%) of **2b**, an oil. A small amount was distilled in a vacuum from bulb-to-bulb for analysis: ^1H NMR (300 MHz) δ 0.93 (t, J = 7.4 Hz, 3H), 1.39 (sextet, J = 7.4 Hz, 2H), 1.59 (quintet, J = 7.0 Hz, 2H), 3.54 (t, J = 6.6 Hz, 2H), 3.79 (t, J = 5.0 Hz, 2 H), 4.00 (t, J = 4.9 Hz, 2 H), 4.20 (d, J = 2.6 Hz, 1H), 4.66 (d, J = 2.8 Hz, 1H), 7.30 (m, 3H), 7.63 (m, 2H); ^{13}C NMR δ 13.92, 19.30, 31.80, 67.36, 69.01, 71.30, 82.59, 125.44, 128.04, 128.40, 136.45, 159.93; IR 3061, 2961, 2934, 2874, 1646, 1610, 1600, 1574, 1495, 1458, 1447, 1381, 1363, 1316, 1302, 1286, 1240, 1127, 1080, 1063, 1049, 1028, 989, 808, 774 cm^{-1}; MS (EI) *m/z* 220 (M^+), 149, 133, 121, 120, 105, 103, 100, 91, 85, 77, 53, 52, 46; HRMS (EI) calcd for $C_{14}H_{20}O_2$ 220.1463, found 220.1468, 220.1455.

[1-(Methylthio)ethenyl]benzene (2c).[6] 2-Methyl-2-phenyl-1,3-dithiolane[15] (5.0 g, 26.0 mmol) in THF (15 mL) was added dropwise to THF (50 mL) and LDA·THF in cyclohexane solution (1.73 M, 37.5 mL, 64.9 mmol) at −78 °C, and the green solution, after being stirred for 20 min, was allowed to warm to −20 °C. The orange solution was stirred for another 30 min, cooled to −78 °C, whereupon MeI (4 mL) was added, and the mixture was allowed to warm to rt overnight. Addition of H_2O and saturated aqueous NH_4Cl and extraction with Et_2O, which was dried ($MgSO_4$) and evaporated, gave a bright yellow oil. Flash chromatography (hexanes as eluant) gave 2.5 g (65%) of **2c**, a light yellow oil. The ^1H NMR and IR spectra, the MS, and the bp agreed with those published.[6]

9-Methoxy-1,4-phenanthrenedione (3a). *p*-Benzoquinone (48.5 g, 447 mmol), **2a** (10.0 g, 75 mmol), and toluene (186 mL) were refluxed under N_2 for 15 h. The toluene was stripped, and *p*-benzoquinone was sublimed under vacuum from the flask heated to its neck in hot water. The solid residue was flash chromatographed on silica gel (3 in. i.d. × 5 in. height) using CH_2Cl_2 as eluant. At steam bath temperature, small amounts of *p*-benzoquinone sublimed from the eluted product under vacuum, leaving 10.2 g (57%) of **3a**, an orange solid. Recrystallized from ethanol to constant melting point, it melted at 186–192 °C dec: ^1H NMR δ 4.15 (s, 3H), 6.89 (s, 2H), 7.44 (s, 1H), 7.62 (t, J = 7.6 Hz, 1H), 7.73 (t, J = 5.8 Hz 1H), 8.33 (d, J = 8.1 Hz, 1H), 9.55 (d, J = 8.8 Hz, 1H); ^{13}C NMR δ 56.25, 99.75, 120.82, 122.30, 127.77, 127.96, 128.05, 130.40, 131.80, 134.13, 135.15, 140.92, 160.32, 186.19, 186.99; IR 1668, 1652, 1616, 1582, 1511, 1458, 1426, 1398, 1343, 1302, 1235, 1112, 1079, 1034, 1008, 843; MS (EI) *m/z* 238 (M^+), 195, 167, 156, 139, 113, 85, 83; HRMS calcd for $C_{15}H_{10}O_3$ 238.0630, found 238.0616; UV (λ_{max}, nm, log ϵ) in EtOH 201 (4.16), 293 (4.14), 364 (3.34), 447 (3.45).

9-(2-Butoxyethoxy)-1,4-phenanthrenedione (3b). *p*-Benzoquinone (5.24 g, 48.4 mmol), **2b** (1.64 g, 7.45 mmol), and toluene (12 mL) were refluxed under N_2 for 48 h. The solvent was stripped from the dark red solution, and excess *p*-benzoquinone was, as above, sublimed under vacuum. A large quantity of greenish black quinhydrone was removed by dissolving the residue in 70% CH_2Cl_2/hexanes, boiling, cooling to rt, filtering, and washing the residue with the same solvent. Evaporation and flash chromatography on silica gel (2.25 in. i.d. × 6.5 in. height) using 70% CH_2Cl_2/hexanes as eluant gave, after drying in a vacuum at 100 °C, 1.22 g (50%) of **3b**, a red solid. Recrystallized from EtOAc/hexanes, it melted at 89–90 °C. A similar experiment gave a 51% yield: ^1H NMR δ 0.94 (t, J = 7.4 Hz, 3H), 1.41 (sextet, J = 7.5 Hz, 2H), 1.62 (m, 2H), 3.61 (t, J = 6.6 Hz, 2H), 3.97 (t, J = 4.7 Hz, 2H), 4.47 (t, J = 4.7 Hz, 2H), 6.88 (s, 2H), 7.45 (s, 1H), 7.62 (ddd, J = 8.3, 7.0, and 1.3 Hz, 1H), 7.73 (ddd, J = 8.7, 6.9 and 1.6 Hz, 1H), 8.39 (dd, J = 8.4 Hz and 1.7 Hz, 1H), 9.55 (d, J = 8.7 Hz, 1H); ^{13}C NMR δ 13.90, 19.29, 31.75, 68.46, 68.77, 71.44, 100.41, 120.62, 122.43, 127.65, 127.82, 127.97, 130.34, 131.71, 133.91, 135.02, 140.79, 159.39, 185.95, 186.81; IR 3083, 2961, 2935, 2874, 1667, 1651, 1614, 1579, 1511, 1460, 1452, 1427, 1407, 1342, 1301, 1275, 1235, 1211, 1166, 1127, 1078, 1035, 1010 cm^{-1}; MS (EI) *m/z* 324 (M^+), 223, 196, 168, 151,

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[13] Liu, L. Ph.D. Dissertation, Columbia University, 1991.

[14] Taskinen, E. *J. Org. Chem.* **1978**, *43*, 2776.

[15] Kumar, V.; Dev, S. *Tetrahedron Lett.* **1983**, *24*, 1289.

139, 125, 113, 100, 85; HRMS calcd for $C_{20}H_{20}O_4$ 324.1362, found 324.1368; UV (λ_{max}, nm, log ϵ) in EtOH 294 (4.16), 364 (3.30), 452 (3.36).

9-(Methylthio)-1,4-phenanthrenedione (3c). *p*-Benzoquinone (4.48 g, 41.5 mmol), **2c** (1.04 g, 6.9 mmol), and toluene (17.3 mL) were refluxed under N_2 for 25 h. After *p*-benzoquinone had been removed by sublimation, as above, the residue was boiled with $CHCl_3/CCl_4$ (1:1, 20 mL) and, while being stirred, allowed to cool to rt. After the precipitate had been filtered and washed with $CHCl_3/CCl_4$ (1:1, 5 × 10 mL) and then $CHCl_3$ (5 × 10 mL), the solvents were stripped. The residue in warm $CHCl_3$ (required to dissolve it) was transferred by pipette to the top of a silica gel flash chromatography column (2.25 in. i.d. × 6 in. height) and **3c** was eluted with $CHCl_3$. Drying in a vacuum at 100 °C gave 750 mg (43%) of an orange crystalline solid: ^1H NMR δ 2.74 (s, 3H), 6.89 (dd, J = 15.4 and 10.1 Hz, 2H), 7.64 (ddd, J = 8.4, 6.9, and 1.4 Hz, 1H), 7.74 (ddd, J = 8.6, 7.0 and 1.4 Hz, 1H), 7.84 (s, 1H), 8.22 (d, J = 9.1 Hz, 1H), 9.56 (d, J = 9.1 Hz, 1H); IR 3155, 2956, 2901, 2259, 1816, 1794, 1665, 1655, 1614, 1562, 1504, 1468, 1420, 1384, 1356, 1318, 1294, 1248, 1217, 1189, 1168, 1085, 1080 cm^{-1}; ^{13}C NMR δ 14.80, 115.59, 123.18, 123.81, 128.44, 128.56, 129.70, 130.22, 131.30, 133.03, 135.00, 140.91, 146.98, 186.03, 187.58; MS (EI) *m/z* 254 (M^+), 239, 225, 211, 183, 172, 157, 152, 139, 113, 105, 77; HRMS calcd for $C_{15}H_{10}O_2S$ 254.0402, found 254.0403; UV (λ_{max}, nm, log ϵ) in EtOH 296 (4.99), 358 (4.27), 459 (4.21).

1,4-Phenanthrenedione (3d). Freshly distilled styrene (776 mg, 7.45 mmol) and *p*-benzoquinone (5.23 g, 48.4 mmol) in toluene (7.45 mL) were refluxed under N_2 for 5 d. The solvent was stripped, and the residue, after drying in a vacuum at 100 °C, was boiled with benzene, slowly cooled to rt while being stirred, filtered through Celite, and washed with benzene. Evaporation, dissolution in $CHCl_3$, filtration through Celite, and washing with $CHCl_3$ was followed by flash chromatography, eluting with 50% CH_2Cl_2/hexanes. Rechromatagraphy, eluting with 40% CH_2Cl_2/CCl_4, gave 482 mg (31%) of **3d**, a yellow crystalline solid. The ^{13}C NMRs observed were identical to those reported.[16]

Reaction of 4-(1-phenylethenyl)morpholine (4) with 1,4-benzoquinone. A 0.1 M solution of **4**[10] in toluene combined with 6 mol of *p*-benzoquinone either at (1) reflux overnight, (2) rt for 2 h, (3) −78 °C, with later warming to rt overnight, or (4) −78 °C overnight, afforded only intractable black solids.

Reaction of 2-Acetyl-1,2,3,4-tetrahydro-1-methyleneisoquinoline (5) with 1,4-benzoquinone. Refluxing a 1 M solution of **5**[11] in toluene for 2 h with 6.5 mol of *p*-benzoquinone gave only intractable black solids. A similar mixture after 5 h at 55 °C gave essentially no reaction (TLC analysis), while one held at 75 °C for 24 h gave a complex mixture (TLC analysis).

Acknowledgment. We thank Mr. Michael Simons for preparing **5** and the NSF (CHE 92-24634) for support. T.J.K. acknowledges support from the Kanagawa Academy of Science and Technology (KAST). N.D.W. thanks the ACS Division of Organic Chemistry for a graduate fellowship. D.A.H. thanks the NSF for support under its program "Research Experiences for Undergraduates" and the Perkin-Elmer Corp. for a Chandler Internship.

Supplementary Material Available: Spectra of all materials prepared (22 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS. See any current masthead page for ordering information.

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[16] Wilbur, D.; Manning, W. B.; Hilton, B. D.; Muschik, G. M. *Org. Magn. Reson.*, **1982**, *18*, 63.