JOURNAL OF THE AMERICAN CHEMICAL SOCIETY
J. Am. Chem. Soc., 1997, 119(25), 5982-5983, DOI:10.1021/ja9710316

Free Radical-Mediated Ketone Synthesis from Alkyl Iodides via Sequential Radical Acylation Approach

Sunggak Kim* and Joo-Yong Yoon

Department of Chemistry, Korea Advanced Institute of Science and Technology, Taejon 305-701, Korea

Supporting Information

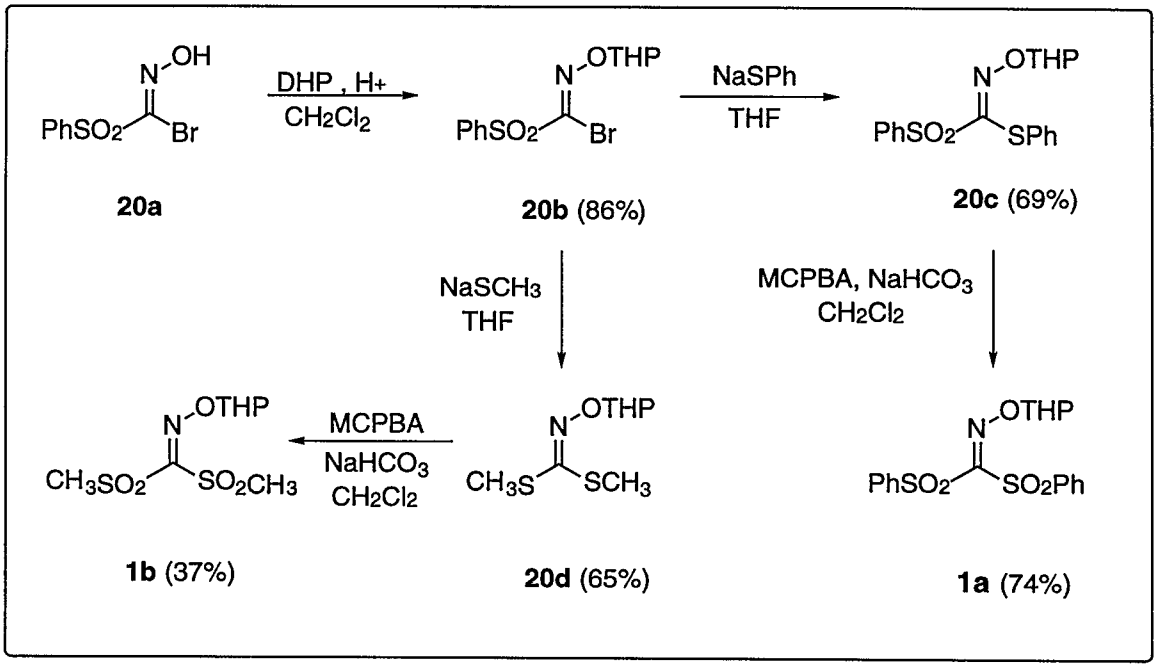
General. All reagents were of commercial quality. All dry solvents were freshly distilled under nitrogen from the appropriate drying agent before use. Diethyl ether was distilled over lithium aluminum hydride and tetrahydrofuran was distilled over sodium-benzophenone. Methylene chloride was distilled over calcium hydride. *N,N*-Dimethyl formamide was distilled over P_2O_5. Ethanol was purified by distillation from calcium oxide. ^1H and ^{13}C NMR spectra were recorded on Bruker AC-200 spectrometer. The chemical shifts in $CDCl_3$ or benzene-d_6 reported in δ (ppm) relative to $CDCl_3$ or Me_4Si as an internal reference. IR spectra were measured on a BOMEM MB-100 Fourier Transform spectrometer. High resolution mass spectra were obtained on a VG AUTOSPEC Ultma GC/MS system using direct insertion probe (DIP) and electron impact (EI) (70 eV) method. Melting point (mp) was determined on a Thomas-Hoover electrothermal capillary apparatus and was uncorrected. Flash chromatography was carried out on Merck silica 60, 230-400 mesh ASTM; eluents are given in parentheses. Analytical thin-layer chromatography (TLC) was performed on E. Merck precoated silica gel 60 F_{254} plates.

Preparation of the reagents (1a, 1b, 1c)

Benzenesulfonyl-bromo-methanone *O*-(tetrahydropyran-2-yl)-oxime (20b).

To a solution of benzenesulfonyl-bromo-methanone oxime[1] (**20a**) (660 mg, 2.5 mmol) in dichloromethane (7 mL) was added 3,4-dihydro-2*H*-pyran (275 mL, 3.0

(1) Wade, P. A.; Hinney, H. R. *J. Am. Chem. Soc.* **1979**, *101*, 1319.



mmol) and *p*-toluenesulfonic acid monohydrate (24 mg, 0.12 mmol). After being stirred at 0 °C for 30 min, the reaction mixture was diluted with dichloromethane (20 mL), washed with water (20 mL) and brine (20 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product was purified by flash silica gel column chromatography (eluted with ethyl acetate/n-hexane (1 : 3)) to give 749 mg (86%) of **20b** as a colorless oil: ^1H NMR (200 MHz, benzene-d_6) δ 1.32-1.66 (m, 6H), 3.14-3.85 (m, 2H), 5.24 (bs, 1H), 7.31-7.45 (m, 3H), 7.82-7.87 (m, 2H); ^{13}C NMR (50 MHz, benzene-d_6) δ 18.7, 25.2, 28.4, 62.0, 102.8, 129.3, 129.5, 130.0, 134.7, 138.1; IR (NaCl) 2946, 1570, 1449, 1347, 1167 cm^{-1}. HRMS (M^+) calcd for $C_{12}H_{14}BrNO_4S$: 346.9827, found 346.9803.

Benzenesulfonyl-phenylsulfanyl-methanone*O*-(tetrahydropyran-2-yl)-oxime (20c).

To a solution of **20b** (749 mg, 2.2 mmol) in tetrahydrofuran (6 mL) was added thiophenol sodium salt (345 mg, 2.6 mmol) at 0 °C. After being stirred at room temperature for 1 h, the reaction mixture was diluted with diethyl ether (20 mL), washed with water (20 mL) and brine (20 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product was purified by flash silica gel column chromatography (eluted with ethyl acetate/n-hexane (1 : 3)) to give 560 mg (69%) of **20c** as a white solid: (mp = 73 °C).

^{1}H NMR (200 MHz, $CDCl_3$) δ 1.22-1.58 (m, 6H), 3.07-3.22 (m, 1H), 3.36-3.43 (m, 1H), 5.24 (bs, 1H), 7.24 (s, 5H), 7.49-7.65 (m, 3H), 7.95-7.99 (m, 2H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 17.7, 24.6, 27.9, 61.6, 102.7, 128.6, 128.8, 129.0, 129.1, 129.4, 132.6, 134.2, 137.6, 152.3; IR (NaCl) 2950, 1445, 1333, 1207, 1162, 1121 cm^{-1}. HRMS (M^+) calcd for $C_{18}H_{19}NO_4S_2$: 377.0756, found 377.0753.

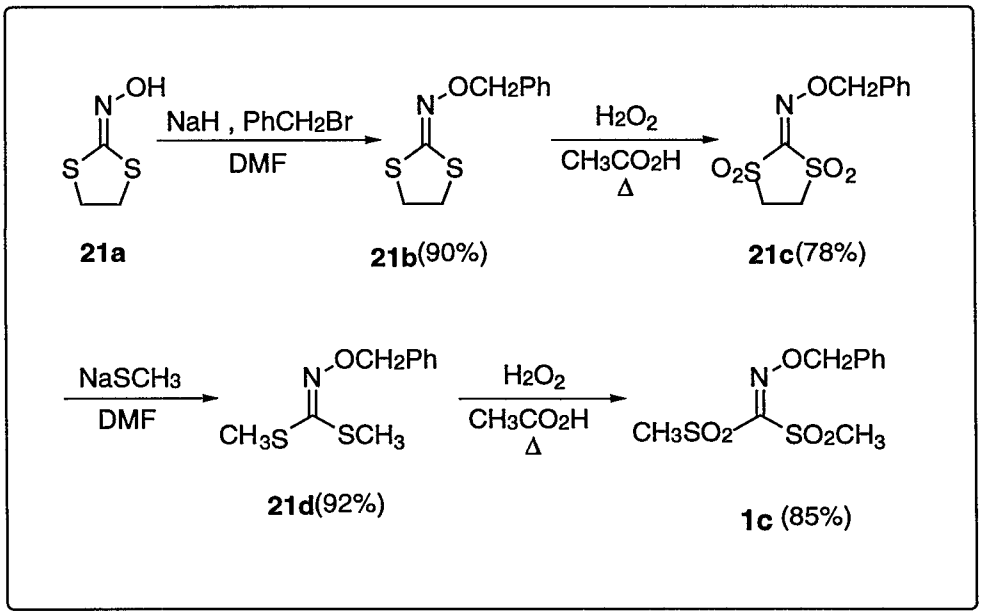
Bis-benzenesulfonyl-methanone *O*-(tetrahydropyran-2-yl)-oxime (1a).

To a solution of **20c** (560 mg, 1.48 mmol) in CH_2Cl_2 (8 mL) was added $NaHCO_3$ (995 mg, 11.8 mmol) and 3-chloroperbenzoic acid (57~86%) (1.7 g, 6.0 mmol) at 0 °C. After being stirred for 1 h at 0 °C, the reaction mixture was heated for 1 h at 40 °C, diluted with CH_2Cl_2 (15 mL) and washed with aqueous $NaHCO_3$ solution (2 x 20 mL), aqueous $Na_2S_2O_3$ solution (10 mL) and brine (10 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product was purified by flash silica gel column chromatography (eluted with ethyl acetate/n-hexane (1 : 2)) to give 448 mg (74%) of **1a** as a white solid: (mp = 104 ~ 106 °C). ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.44-1.72 (m, 6H), 3.22-3.33 (m, 1H), 3.45-3.54 (m, 1H), 5.27-5.36 (m, 1H), 7.44-8.03 (m, 10H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 17.6, 17.9, 18.1, 24.2, 24.3, 24.4, 27.3, 27.6, 27.7, 61.8, 62.0, 62.1, 103.9, 104.4, 105.0, 125.4, 125.8, 128.7, 128.8, 129.0, 129.2, 129.5, 129.7, 131.9, 132.0, 134.6, 134.7, 135.0, 135.1, 137.7, 138.7, 138.8, 140.4, 140.5, 153.7, 158.9, 159.8; IR (NaCl) 1588, 1447, 1344, 1164 cm^{-1}. HRMS (M^+) calcd for $C_{18}H_{19}NO_6S_2$: 409.0654, found 409.0649.

Bis-methylsulfanyl-methanone *O*-(tetrahydropyran-2-yl)-oxime (20d).

To a solution of **20b** (766 mg, 2.25 mmol) in *N*,*N*-dimethylformamide (6 mL) was added sodium thiomethoxide (315 mg, 4.5 mmol) at 0 °C. After being stirred at room temperature for 30 min, the reaction mixture was diluted with diethyl ether (20 mL), washed with water (20 mL) and brine (20 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by flash silica gel column chromatography (eluted with ethyl acetate/n-hexane (1 : 10)) to give 324 mg (65%) of **20d** as a colorless oil: ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.55-1.67 (m, 3H), 1.71-1.83 (m, 3H), 2.39 (s, 3H), 2.42 (s, 3H), 3.51-3.61 (m, 1H), 3.85-3.96 (m, 1H), 5.31 (bs, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 13.3, 15.0, 19.1, 25.2, 28.8, 62.1, 100.5, 154.8; IR (NaCl) 1526, 1433, 1112, 926 cm^{-1}. HRMS (M^+) calcd for $C_8H_{15}NO_2S_2$: 221.0544, found 221.0542.

Bis-methylsulfonyl-methanone *O*-(tetrahydropyran-2-yl)-oxime (1b) was similarly prepared in the same manner as **1a** in 37% yield as a white solid: (mp = 85 °C). ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.57-1.99 (m, 6H), 3.28 (s, 3H), 3.30 (s, 3H), 3.64-3.86 (m, 2H), 5.59 (bs, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 18.0, 24.5, 27.8, 42.9, 44.8, 62.7, 105.5, 153.0; IR (NaCl) 1552, 1334, 1156, 953 cm^{-1}. HRMS (M^+) calcd for $C_8H_{15}NO_6S_2$: 285.0341, found 285.0329.



[1,3]Dithiolan-2-one oxime (21a).[2]

To a solution of 1,2-dibromoethane (1.42 mL, 16.5 mmol) and potassium carbonate (2.76 g, 20.0 mmol) in ethanol (35 mL) was added isopropylammonium isopropyldithiocarbamate (3.21 g, 16.5 mmol) during 15 min at 40 °C. After being stirred at 80 °C for 10 min, the reaction mixture was cooled, filtered, diluted with diethyl ether (100 mL), and washed with water (100 mL x 2) and brine (100 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The crude product ([1,3]dithiolan-2-ylidene-isopropyl-amine) was diluted with ethanol (35 mL) and added to hydroxylamine hydrochloride (1.39 g, 20.0 mmol) in water (5 mL). After being stirred at 100 °C for 2 h, the reaction mixture was cooled, diluted with ethyl acetate (100 mL), and washed with water (100 mL x 2) and brine (100 mL). The organic layer was dried

(2) Cannon, D. S.; Addor, R. W. **U. S. 3,183,148** (CI. 167-33), May 11, 1965.

over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by passing through a short column of silica gel (eluted with ethyl acetate/n-hexane (1 : 2)) to give 1.36 g (61%) of **21a** as a white solid: (mp = 126 °C). ^{1}H NMR (200 MHz, acetone-d_6) δ 3.38-3.52 (m, 4H), 7.97 (s, 1H); ^{13}C NMR (50 MHz, acetone-d_6) δ 36.2, 37.4, 160.1; IR (NaCl) 3142, 2986, 2820, 1592, 1425, 1291, 1153 cm^{-1}.

[1,3]Dithiolan-2-one *O*-benzyl-oxime (21b).

To a suspension of sodium hydride (60% dispersion in mineral oil) (480 mg, 12.0 mmol) in *N*,*N*-dimethylformamide (20 mL), under nitrogen at 0 °C, was added [1,3]dithiolan-2-one oxime (**21a**) (1.35 g, 10.0 mmol). After being stirred for 20 min at 0 °C, benzyl bromide (1.5 mL, 12.0 mmol) was added. Over a period of 1 h at room temperature, the reaction mixture was diluted with diethyl ether (50 mL), quenched with aqueous NH_4Cl solution (30 mL), washed with water (30 mL) and brine (60 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product was purified by passing through a short column of silica gel (eluted with ethyl acetate/n-hexane (1 : 3)) to give 2.03 g (90%) of **21b** as a yellow solid: (mp = 36 °C). ^{1}H NMR (200 MHz, $CDCl_3$) δ 3.30-3.45 (m, 4H), 5.14 (s, 2H), 7.30-7.37 (m, 5H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 35.8, 37.2, 76.7, 127.8, 127.9, 128.3, 137.5, 160.6; IR (NaCl) 1553, 1453, 1049, 956 cm^{-1}. HRMS (M^+) calcd for $C_{10}H_{11}NOS_2$: 225.0282, found 225.0286.

1,1,3,3,-Tetraoxo-[1,3]dithiolan-2-one *O*-benzyl-oxime (21c).

To a solution of **21b** (2.03 g, 9.0 mmol) in glacial acetic acid (9 mL) was added hydrogen peroxide (35% solution in water) (3.7 mL, 45.0 mmol) dropwise, with external cooling (0 °C). The reaction mixture was stirred for 10 min at room temperature and heated for 30 min at 100 °C. When TLC examination showed a single new spot, the reaction mixture was cooled, diluted with dichloromethane (50 mL), and washed with aqueous $Na_2S_2O_3$ solution (50 mL), aqueous $NaHCO_3$ solution (2 x 50 mL), and brine (50 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The crude powder was recrystallized from n-hexane (20 mL) to afford 1.60 g (78%) of **21c** as a white solid: (mp = 136 °C). ^{1}H NMR (200 MHz, $CDCl_3$) δ 3.69-3.79 (m, 4H), 5.46 (s, 2H), 7.37 (bs, 5H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 49.1, 49.5, 81.6, 128.7, 128.8, 129.2,

134.1, 146.2; IR (NaCl) 1522, 1327, 1148, 1101, 843 cm^{-1}. HRMS (M^+) calcd for $C_{10}H_{11}NO_5S_2$: 289.0079, found 289.0071.

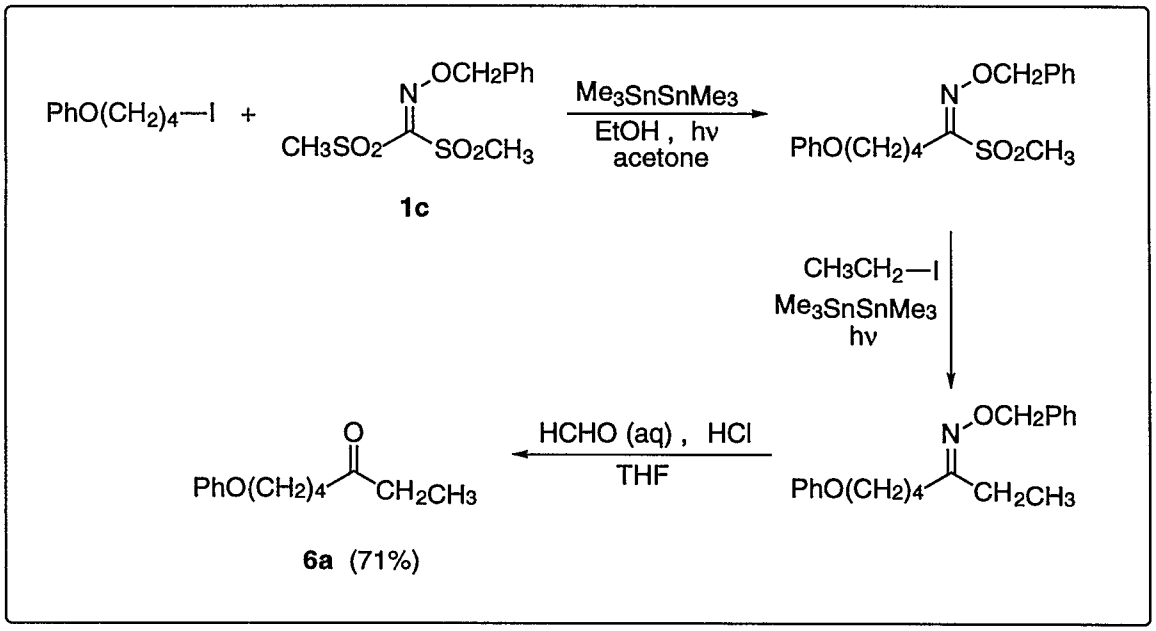
Bis-methylsulfanyl-methanone *O*-benzyl-oxime (21d).

To a solution of **21c** (1.60 g, 5.53 mmol) in *N*,*N*-dimethylformamide (10 mL) was added sodium thiomethoxide (855 mg, 12.2 mmol) at 0 °C. After being stirred at room temperature for 30 min, the reaction mixture was diluted with diethyl ether (30 mL), washed with water (40 mL) and brine (40 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by passing through a short column of silica gel (eluted with ethyl acetate/n-hexane (1 : 30)) to give 1.16 g (92%) of **21d** as a colorless oil: ^1H NMR (200 MHz, $CDCl_3$) δ 2.39 (s, 3H), 2.40 (s, 3H), 5.14 (s, 2H), 7.27-7.36 (m, 5H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 13.4, 15.1, 76.4, 127.6, 128.0, 128.2, 137.7, 152.7; IR (NaCl) 1524, 1454, 996, 944 cm^{-1}. HRMS (M^+) calcd for $C_{10}H_{13}NOS_2$: 227.0439, found 227.0446.

Bis-methylsulfonyl-methanone *O*-benzyl-oxime (1c).

To a solution of **21d** (1.16 g, 5.09 mmol) in glacial acetic acid (5 mL) was added hydrogen peroxide (35% solution in water) (2.1 mL, 25.5 mmol) dropwise, with external cooling (0 °C). The reaction mixture was stirred for 10 min at room temperature and heated for 30 min at 100 °C. When TLC examination showed a single new spot, the reaction mixture was cooled, diluted with dichloromethane (40 mL), and washed with aqueous $Na_2S_2O_3$ solution (40 mL), aqueous $NaHCO_3$ solution (2 x 40 mL), and brine (40 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product was purified by passing through a short column of silica gel (eluted with ethyl acetate/n-hexane (1 : 1)) to give 1.26 g (85%) of **1c** as a white solid: (mp = 75 °C). ^1H NMR (200 MHz, $CDCl_3$) δ 3.19 (s, 3H), 3.26 (s, 3H), 5.47 (s, 2H), 7.38 (bs, 5H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 43.1, 44.6, 81.8, 128.8, 128.9, 129.4, 133.9, 152.0; IR (NaCl) 1533, 1456, 1316, 1153, 1018, 958 cm^{-1}. HRMS (M^+) calcd for $C_{10}H_{13}NO_5S_2$: 291.0235, found 291.0226.

Preparation of acyclic ketones



7-Phenoxyheptan-3-one (6a)

An ethanol solution (1 mL, 0.3 M in the iodide) of 4-phenoxybutyl iodide (**2**) (83 mg, 0.3 mmol), **1c** (105 mg, 0.36 mmol) and hexamethylditin (120 mg, 0.36 mmol) was degassed for 10 min. To the reaction mixture was added acetone (110 μL, 1.5 mmol) and irradiated in a photochemical reactor[3] (300 nm). When TLC examination showed a new spot (normally 3~4 h), iodoethane (29 mL, 0.36 mmol) and hexamethylditin (119 mg, 0.36 mmol) were added. After being irradiated at 300 nm for 6 h, the reaction mixture was concentrated under reduced pressure. Ethyl acetate (10 mL), water (3~4 drops) and potassium fluoride (174 mg, 3.0 mmol) were then added and the mixture was stirred at room temperature for 1 h. After the reaction mixture was filtered through a short column of silica gel, the filterate was concentrated under reduced pressure. The crude product was diluted with tetrahydrofuran (3 mL) and then 35% aqueous formaldehyde solution (1 mL) and several drops of 10% aqueous HCl solution were added to the reaction mixture. After being stirred at room temperature for 2 h, the reaction mixture was diluted with diethyl ether (10 mL), neutralized with aqueous $NaHCO_3$ and

(3) **RAYONET** Photochemical Reactor: The Southern New England Ultraviolet Company

washed with water (10 mL) and brine (10 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product was subjected to flash silica gel column chromatography (eluted with ethyl acetate/n-hexane (1 : 5)) to give 44 mg (71%) of **6a** as a colorless oil: ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.04 (t, *J* = 7.3 Hz, 3H), 1.72-1.79 (m, 4H), 2.42 (q, *J* = 7.3 Hz, 2H), 2.47 (t, *J* = 7.4 Hz, 2H), 3.94 (t, *J* = 5.7 Hz, 2H), 6.84~6.95 (m, 3H), 7.21-7.29 (m, 2H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 7.8, 20.5, 28.8, 35.9, 41.9, 67.4, 114.5, 120.6, 129.4, 158.9, 211.3; IR (NaCl) 2938, 1715, 1601, 1498, 1247, 757 cm^{-1}. HRMS (M^+) calcd for $C_{13}H_{18}O_2$: 206.1307, found 206.1317.

1-Cyclohexyl-5-phenoxypentan-1-one (**6b**). a colorless oil: ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.18-1.41 (m, 5H), 1.61-1.83 (m, 9H), 2.25-2.36 (m, 1H), 2.49 (t, *J* = 6.6 Hz, 2H), 3.93 (t, *J* = 5.7 Hz, 2H), 6.84-6.95 (m, 3H), 7.22-7.29 (m, 2H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 20.2, 25.6,25.8, 28.4, 28.7, 40.0, 50.7, 67.4, 114.4, 120.4, 129.3, 158.9, 213.8; IR (NaCl) 2930, 1707, 1601, 1497, 1245, 755 cm^{-1}. HRMS (M^+) calcd for $C_{17}H_{24}O_2$: 260.1776, found 260.1769.

1-Phenylnonan-4-one (**6c**). a colorless oil: ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.88 (t, *J* = 6.9 Hz, 3H), 1.19- 1.32 (m, 4H), 1.55 (m, *J* = 7.2Hz, 2H), 1.89 (m, *J* = 7.5 Hz, 2H), 2.37 (q, *J* = 8.5 Hz, 4H), 2.61 (t, *J* = 7.3 Hz, 2H), 7.14-7.32 (m, 5H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 13.9, 22.4, 23.4, 25.2, 31.3, 35.0, 41.8, 42.8, 125.8, 128.3, 128.4, 141.6, 211.1; IR (NaCl) 2939, 1713, 1456, 747, 700 cm^{-1}. HRMS (M^+) calcd for $C_{15}H_{22}O$: 218.1671, found 218.1677.

2-Methyloctan-3-one (**6d**). a yellow oil: ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.82 (t, *J* = 6.9 Hz, 3H), 1.01 (d, *J* = 7.0 Hz, 6H), 1.14-1.30 (m, 4H), 1.50 (m, *J* = 7.5 Hz, 2H), 2.37 (t, *J* = 7.4 Hz, 2H), 2.53 (m, *J* = 6.9 Hz, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 13.8, 18.1, 22.4, 23.4, 31.4, 40.2, 40.7, 214.9; IR (NaCl) 2962, 2933, 1714, 1466 cm^{-1}. HRMS (M^+) calcd for $C_9H_{18}O$: 142.1358, found 142.1357.

4-[1,3]Dioxolan-2-yl-1-phenylbutan-2-one (**6e**). a colorless oil: ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.94 (td, *J* = 7.3 and 4.3 Hz, 2H), 2.57 (t, *J* = 7.3 Hz, 2H), 3.69 (s, 2H), 3.75-3.93 (m, 4H), 4.86 (t, *J* = 4.3 Hz, 1H), 7.17-7.31 (m, 5H) ; ^{13}C NMR (50 MHz, $CDCl_3$) δ 27.5, 35.8, 50.5, 64.9, 103.2, 127.0, 128.7, 129.4, 134.3. 207.3; IR (NaCl) 1715, 1558, 1455, 1139, 1034 cm^{-1}. HRMS (M^+) calcd for $C_{13}H_{16}O_3$: 220.1099, found 220.1103.

1-Hydroxy-6-phenylhexan-3-one (**6f**). a colorless oil: ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.89 (m, *J* = 7.4 Hz, 2H), 2.42 (t, *J* = 7.4 Hz, 2H), 2.57-2.64 (m, 4H), 2.81 (bs, 1H), 3.75-

3.83 (m, 2H), 7.13-7.26 (m, 5H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 24.8, 34.8, 42.3, 44.4, 57.6, 125.8, 128.2, 128.3, 141.3, 211.1; IR (NaCl) 3426, 2923, 1708, 1454, 1055, 702 cm^{-1}. HRMS (M^+) calcd for $C_{12}H_{16}O_2$: 192.1150, found 192.1153.

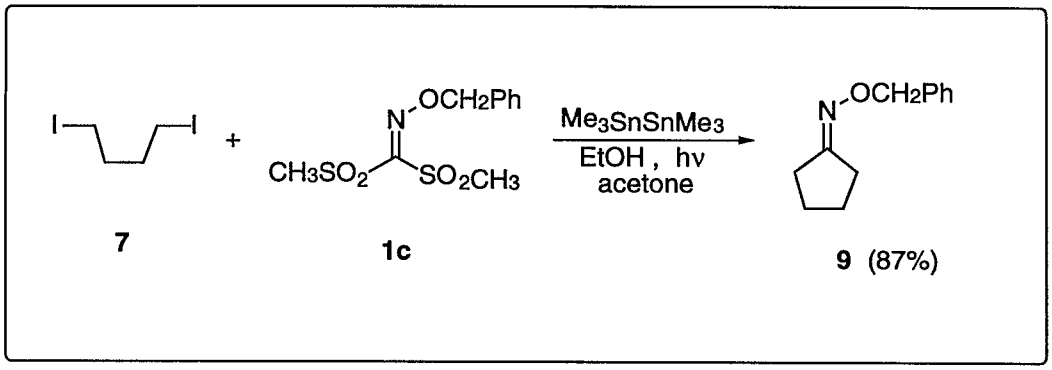
2-Methylhept-6-en-3-one (6g). a colorless oil: ^1H NMR (200 MHz, $CDCl_3$) δ 1.06 (d, *J* = 6.6 Hz, 6H), 2.23-2.34 (m, 2H), 2.47-2.64 (m, 3H), 4.90-5.05 (m, 2H), 5.68-5.88 (m, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 18.2, 27.7, 39.4, 40.8, 115.0, 137.3, 213.8; IR (NaCl) 2950, 1716, 1641, 1467 cm^{-1}. HRMS (M^+) calcd for $C_8H_{14}O$: 126.1045, found 126.1040.

***N*-Benzyloxycarbonyl-1-aminohex-5-en-3-one (6h)**. a colorless oil: ^1H NMR (200 MHz, $CDCl_3$) δ 2.69 (t, *J* = 5.7 Hz, 2H), 3.14 (d, *J* = 6.9 Hz, 2H), 3.41 (q, *J* = 5.7 Hz, 2H), 3.82 (bs, 1H), 5.06 (s, 2H), 5.01-5.30 (m, 2H), 5.65-5.94 (m ,1H), 7.32 (s, 5H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 30.3, 35.6, 37.6, 40.4, 42.0, 47.9, 66.6, 68.3, 117.7, 119.3, 128.0, 128.1, 128.2, 128.5, 129.9, 133.8, 137.2, 140.6, 157.5, 208.2; IR (NaCl) 3363, 1711, 1541, 1256, 1057 cm^{-1}. HRMS (M^+) calcd for $C_{14}H_{17}NO_3$: 247.1208, found 247.1214.

4-Oxo-pentanoic acid ethyl ester (6i). a colorless oil: ^1H NMR (200 MHz, $CDCl_3$) δ 1.18 (t, *J* = 7.1 Hz, 3H), 2.12 (s, 3H), 2.46-2.52 (m, 2H), 2.65-2.72 (m, 2H), 4.05 (q, *J* = 7.1 Hz, 2H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 14.0, 27.9, 29.7, 37.8, 60.5, 172.6, 206.5; IR (NaCl) 2969, 1729, 1367, 1161 cm^{-1}. HRMS (M^+) calcd for $C_7H_{12}O_3$: 144.0786, found 144.0790.

***N*-Benzyloxycarbonyl-2-amino-4-oxo-pentanoic acid methyl ester (6j)**. a colorless oil: ^1H NMR (200 MHz, $CDCl_3$) δ 2.14 (s, 3H), 2.95 (dd, *J* = 18.4 and 4.3 Hz, 1H), 2.95 (dd, *J* = 18.4 and 4.3 Hz, 1H), 3.71 (s, 3H), 4.53 (td, *J* = 4.3 and 8.7 Hz, 1H), 5.10 (s, 2H), 5.72 (d, *J* = 8.7 Hz, 1H), 7.32 (s, 5H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 29.9, 45.2, 49.9, 52.7, 67.1, 128.1, 128.2, 128.5, 136.2, 157.2, 171.5, 206.4; IR (NaCl) 3369, 2937, 1725, 1520, 1233, 1057 cm^{-1}. HRMS (M^+) calcd for $C_{14}H_{17}NO_5$: 279.1107, found 279.1119.

Preparation of cyclic ketones



Cyclopentanone O-benzyl oxime (9).

An ethanol solution (1 mL, 0.3 M in the iodide) of 1,4-diiodobutane (7) (93 mg, 0.3 mmol), **1c** (105 mg, 0.36 mmol) and hexamethylditin (220 mg, 0.66 mmol) was degassed for 10 min and then acetone (110 μL, 1.5 mmol) was added. After being irradiated at 300 nm for 5 h, the reaction mixture was concentrated under reduced pressure. Ethyl acetate (10 mL), water (3~4 drop) and potassium fluoride (350 mg, 6 mmol) were then added and the mixture was stirred at room temperature for 1 h. After the reaction mixture was filtered through a short column of silica gel, the filterate was concentrated under reduced pressure. The crude product was purified by flash silica gel column chromatography (eluted with ethyl acetate/n-hexane (1 : 5)) to give 49 mg (87%) of **9** as a colorless oil: ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.69-1.78 (m, 4H), 2.34-2.49 (m, 4H), 5.09 (s, 2H), 7.30-7.38 (m, 5H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 24.6, 25.0, 27.8, 30.9, 75.3, 127.5, 127.7, 128.2, 138.5, 166.7; IR (NaCl) 2952, 1470, 1453, 1365, 1036 cm^{-1}. HRMS (M^+) calcd for $C_{12}H_{15}NO$: 189.1154, found 189.1142.

3-Benzylcyclopentanone (10a).

An ethanol solution (670 mL, 0.3M in the iodide) of 2-benzyl-1,4-diiodobutane (80 mg, 0.2 mmol), **1c** (70 mg, 0.24 mmol) and hexamethylditin (147 mg, 0.44 mmol) was degassed for 10 min and then acetone (75 μL, 1.0 mmol) was added. After being irradiated at 300 nm for 5 h, the reaction mixture was concentrated under reduced pressure. Ethyl acetate (10 mL), water (3~4 drops) and potassium fluoride (232 mg, 4.0 mmol) were then added and the mixture was stirred at room temperature for 1 h. After the reaction mixture was filtered through short silica

gel column, the filterate was concentrated under reduced pressure. After the crude product was diluted with tetrahydrofuran (2.0 mL), 35% aqueous formaldehyde solution (1 mL) and several drop of 10% aqueous HCl solution were added and the solution was stirred at room temperature for 2 h. The reaction mixture was diluted with diethyl ether (10 mL), neutralized with aqueous $NaHCO_3$ and washed with water (10 mL) and brine (10 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product was purified by flash silica gel column chromatography (eluted with ethyl acetate/n-hexane (1 : 10)) to give 30 mg (87%) of **10a** as a colorless oil: ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.83-1.96 (m, 1H), 2.03-2.13 (m, 2H), 2.17-2.29 (m, 2H), 2.36- 2.44 (m, 2H), 2.72 (d, *J* = 7.4 Hz, 2H), 7.09-7.32 (m, 5H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 19.7, 19.9, 34.2, 40.7, 42.4, 125.7, 128.2, 128.3, 139.4, 208.2; IR (NaCl) 2965, 1747, 1651, 1438 cm^{-1}. HRMS (M^+) calcd for $C_{12}H_{14}O$: 174.1045, found 174.1009.

3-Oxo-cyclopentane-1,1-dicarboxylic acid diethyl ester (10b). a colorless oil: ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.24 (t, *J* = 7.2 Hz, 6H), 2.31-2.40 (m, 2H), 2.45-2.54 (m, 2H), 2.77 (s, 2H), 4.21 (q, *J* = 7.2 Hz, 4H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 14.0, 29.9, 36.7, 45.2, 56.9, 62.0, 170.8, 214.1; IR (NaCl) 1741, 1652, 1558, 1269, 1162 cm^{-1}. HRMS (M^+) calcd for $C_{11}H_{16}O_5$: 228.0998, found 228.0998.

3-Oxo-cyclohexane-1,1-dicarboxylic acid diethyl ester (10c). a colorless oil: ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.23 (t, *J* = 7.0 Hz, 6H), 1.80-1.89 (m, 2H), 2.21-2.35 (m, 4H), 2.70 (s, 2H), 4.18 (q, *J* = 7.0 Hz, 4H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 14.0, 21.4, 29.9, 40.0, 45.5, 57.0, 61.9, 170.4, 210.7; IR (NaCl) 2954, 1713, 1652, 1507, 1456 cm^{-1}. HRMS (M^+) calcd for $C_{12}H_{18}O_5$: 242.1154, found 242.1147.

***(E)*-3-Ethylidene-4-oxo-cyclopentane-1,1-dicarboxylic acid diethyl ester (10d)**. a colorless oil: ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.24 (t, *J* = 7.0 Hz, 6H), 1.81 (dt, *J* = 7.3 and 2.2 Hz, 3H), 2.89 (s, 2H), 3.14 (m, *J* = 2.2 Hz, 2H), 4.20 (q, *J* = 7.0 Hz, 4H), 6.61-6.74 (m ,1H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 10.3, 13.6, 21.6, 37.0, 42.6, 59.8, 128.5, 147.5, 176.0, 197.6; IR (NaCl) 2966, 1705, 1641, 1426, 1013 cm^{-1}. HRMS (M^+) calcd for $C_{13}H_{18}O_5$: 254.1154, found 254.1156.

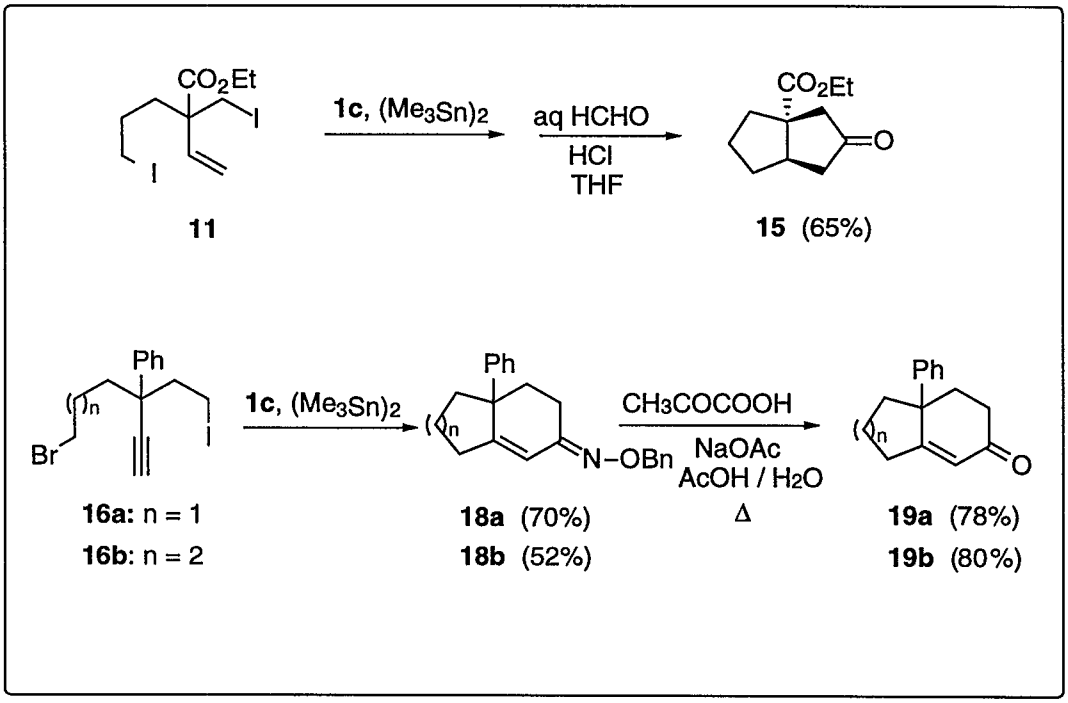
Indan-2-one (10e). a yellow solid: (mp = 55 °C). ^{1}H NMR (200 MHz, $CDCl_3$) δ 3.56 (s, 4H), 7.22-7.32 (m, 4H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 44.1, 125.0, 127.3, 137.7, 218.1; IR

(NaCl) 1749, 1387, 1182, 1144, 980 cm^{-1}. HRMS (M^+) calcd for C_9H_8O: 132.0575, found 132.0575.

Benzofuran-3-one (10f).

An ethanol solution (1 mL, 0.3 M in the iodide) of 1-iodo-2-iodomethoxy benzene (108 mg, 0.3 mmol), **1c** (105 mg, 0.36 mmol) and hexamethylditin (118 mg, 0.36 mmol) was degassed for 10 min and then acetone (110 μL, 1.5 mmol) was added. After being irradiated at 300 nm for 4 h, the reaction mixture was concentrated under reduced pressure. Ethyl acetate (10 mL), water (3~4 drops) and potassium fluoride (174 mg, 3.0 mmol) were then added and the mixture was stirred at room temperature for 1 h. After the reaction mixture was filtered through a short column of silica gel, the filterate was concentrated under reduced pressure. The crude product was diluted with benzene (6 mL), then degassed for 20 min. To a solution of the crude product in refluxing benzene (6 mL) under N_2 was added tributyltin hydride (100 μL, 0.36 mmol) and AIBN (5 mg) in benzene (6 mL) over 2 h, via a syringe pump. After being stirred in refluxing benzene for 30 min, the reaction mixture was concentrated under reduced pressure. Ethyl acetate (10 mL), water (3~4 drops) and potassium fluoride (174 mg, 3.0 mmol) were then added and the mixture was stirred at room temperature for 1 h. After the reaction mixture was filtered through a short column of silica gel, the filterate was concentrated under reduced pressure. After the crude product was treated with tetrahydrofuran (2 mL), 35% aqueous formaldehyde solution (1 mL) and several drops of 10% aqueous HCl solution at room temperature for 5 h, the reaction mixture was diluted with diethyl ether (10 mL), neutralized with aqueous $NaHCO_3$, and washed with water (10 mL) and brine (10 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product was purified by flash silica gel column chromatography (eluted with ethyl acetate/n-hexane (1 : 15)) to give 26 mg (64%) of **10f** as a white solid: (mp = 38 °C). ^1H NMR (200 MHz, $CDCl_3$) δ 5.30 (s, 2H), 7.45-7.53 (m, 2H), 7.62-7.70 (m, 1H), 7.88 (d, J = 7.6 Hz, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 81.0, 114.1, 120.0, 123.1, 129.2, 133.5, 158.9, 196.5; IR (NaCl) 1702, 1637, 1445, 1136, 1109 cm^{-1}. HRMS(M^+) calcd for $C_8H_6O_2$: 134.0368, found 134.0369.

Preparation of bicyclic ketones



2-Oxohexahydropentalene-3a-carboxylic acid methyl ester (**15**) was prepared in the same manner as **10a** in 65% yield as a colorless oil: ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.24 (t, *J* = 7.1 Hz, 3H), 1.37-1.50 (m, 1H), 1.72-1.84 (m, 3H), 1.99-2.10 (m, 1H), 2.13-2.25 (m, 2H), 2.34-2.46 (m, 1H), 2.52-2.69 (m, 1H), 2.80-2.97 (m, 2H), 4.13 (q, *J* = 7.1 Hz, 2H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 14.1, 25.4, 34.0, 37.2, 44.4, 45.2, 48.0, 56.0, 61.1, 176.6, 217.6; IR (NaCl) 1732, 1558, 1456, 1176 cm^{-1}. HRMS (M^+) calcd for $C_{11}H_{16}O_3$: 196.1099, found 196.1103.

7a-Phenyl-1,2,3,6,7,7a-hexahydro-inden-5-one *O*-benzyl oxime (**18a**) was prepared in the same manner as **9** in 70% yield as a colorless oil: ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.24-1.50 (m, 1H), 1.58-1.71 (m, 3H), 2.21-2.32 (m, 3H), 2.45-2.55 (m, 2H), 2.81-2.89 (m, 1H), 5.05 (s, 2H), 6.22 (s, 1H), 7.14-7.32 (m, 10H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 20.5, 21.5, 30.8, 36.4, 42.1, 52.0, 75.7, 118.2, 126.2, 127.1, 127.6, 127.8, 128.2, 128.3, 138.1, 144.2, 157.1, 157.4; IR (NaCl) 3029, 2941, 1644, 1599, 1451, 1037 cm^{-1}. HRMS (M^+) calcd for $C_{22}H_{23}NO$: 317.1780, found 317.1785.

4a-Phenyl-4,4a,5,6,7,8-hexahydro-3*H*-naphthalen-2-one *O*-benzyl oxime (**18b**) was prepared in the same manner as **9** in 52% yield as a colorless oil: ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.24-1.45 (m, 2H), 1.49-1.56 (m, 1H), 1.71-1.94 (m, 5H), 2.15-2.40 (m,

3H), 2.45-2.61 (m, 1H), 5.08 (s, 2H), 6.18 (s, 1H), 7.13-7.44 (m, 10H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 22.2, 27.5, 29.6, 33.4, 38.9, 39.9, 45.0, 75.7, 121.5, 126.1, 127.1, 127.3, 127.9, 128.3, 128.5, 138.1, 144.5, 157.0, 158.6; IR (NaCl) 2929, 2858, 1653, 1494, 1452, 1365, 1035 cm^{-1}. HRMS (M^+) calcd for $C_{23}H_{25}NO$: 331.1936, found 331.1926.

7a-Phenyl-1,2,3,6,7,7a-hexahydro-inden-5-one (19a)[4].

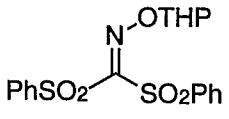
To a stirred solution of **18a** (67 mg, 0.21 mmol) in acetic acid (1 mL) and water (500 μL) was added sodium acetate (35 mg, 0.42 mmol) and pyruvic acid (22 μL, 0.32 mmol) at room temperature. After being stirred at 120 °C for 6 h, the reaction mixture was diluted with ethyl acetate (10 mL), washed with water (10 mL), aqueous $NaHCO_3$ solution (2 x 10 mL), and brine (10 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product was purified by flash silica gel column chromatography (eluted with ethyl acetate/n-hexane (1 : 7)) to give 35 mg (78%) of **19a** as a colorless liquid: ^1H NMR (200 MHz, $CDCl_3$) δ 1.39-1.51 (m, 1H), 1.65-1.82 (m, 2H), 1.86-2.22 (m, 3H), 2.32-2.41 (m, 2H), 2.52-2.68 (m, 2H), 6.12 (s, 1H), 7.14- 7.35 (m, 5H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 21.3, 31.3, 34.0, 38.0, 41.9, 52.6, 124.4, 126.8, 126.9, 128.5, 142.5, 174.4, 199.9; IR (NaCl) 2944, 1672, 1451, 1215, 1055 cm^{-1}. HRMS (M^+) calcd for $C_{15}H_{16}O$: 212.1201, found 212.1202.

4a-Phenyl-4,4a,5,6,7,8-hexahydro-3*H*-naphthalen-2-one (19b) was prepared in the same manner as **19a** in 80% yield as a colorless oil: ^1H NMR (200 MHz, $CDCl_3$) δ 1.24-1.48 (m, 2H), 1.52-1.76 (m, 2H), 1.80-1.88 (m, 1H), 1.91-2.18 (m, 4H), 2.27-2.35 (m, 2H), 2.57-2.65 (m, 1H), 6.10 (s, 1H), 7.20-7.39 (m, 5H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 22.0, 27.5, 33.7(2C), 39.8, 40.1, 45.6, 126.6, 127.1, 127.6, 128.8, 141.8, 168.8, 200.0; IR (NaCl) 2936, 1676, 1644, 1495, 1450, 1259 cm^{-1}. HRMS (M^+) calcd for $C_{16}H_{18}O$: 226.1358, found 226.1356.

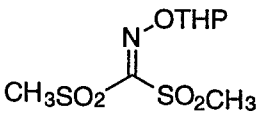
(4) Hershberg, E. B. *J. Org. Chem.* **1948**, *13*, 542.

Method of Calculations

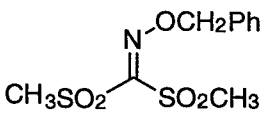
Estimates of the energies of molecular orbital for optimized structures of the species were performed by the AM1 semiempirical molecular orbital method[5] with full optimization of all geometrical variables (bond lengths, bond angles, and dihedral angles). The calculations were conducted using the MOPAC 6.3 semiempirical molecular orbital package[6] running on a SYBYL (version 6.3)[7]. Starting geometries of the molecules were generated by the BUILD option in SYBYL and geometry optimization for the ground state were carried out using EF (Eigenvector Following) routine. The computational results are shown below and include charges at iminyl carbon atoms, energies of HOMO and LUMO, and low-energy conformations of **1a**, **1b**, and **1c**.



1a

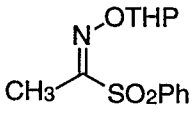


1b

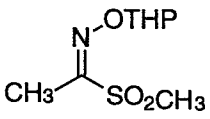


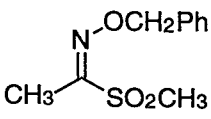
1c

C - charge	-1.417	-1.471	-1.453
HOMO energy	-10.0351	-11.2564	-9.9236
LUMO energy	**-0.7715**	**-1.0098**	**-1.1394**



3





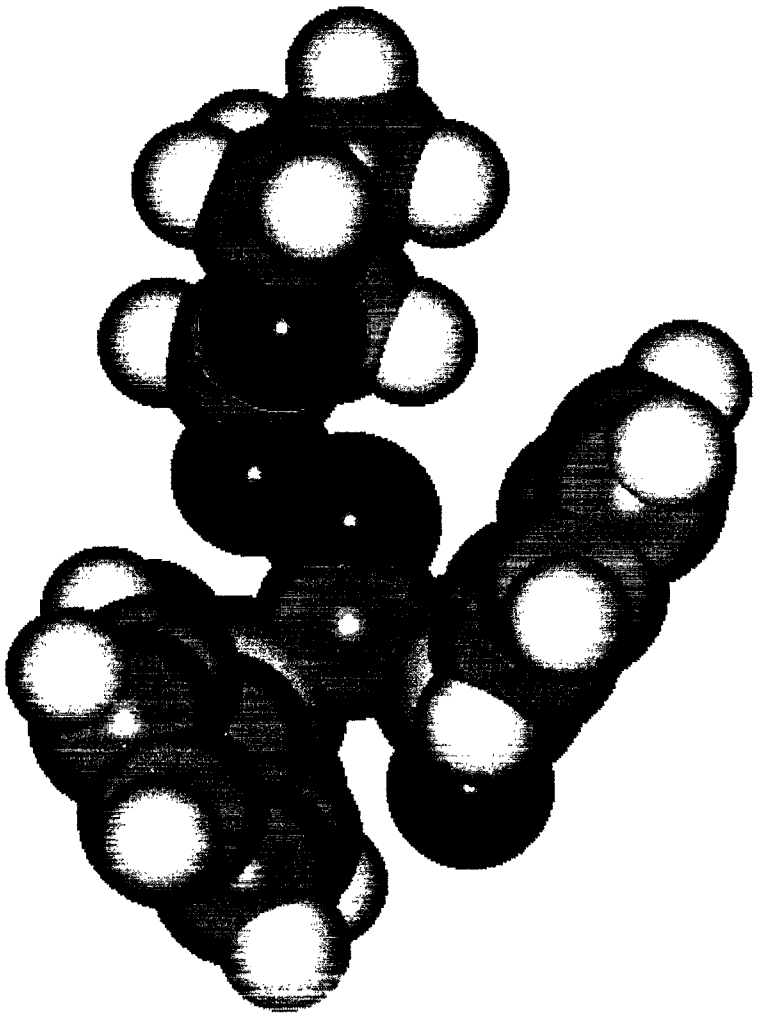
C - charge	-0.749	-0.770	-0.775
HOMO energy	-10.0451	-10.6541	-9.6313
LUMO energy	**-0.5869**	**-0.5593**	**-0.7040**

sky blue atom	carbon atom
white atom	hydrogen atom
cobalt blue atom	nitrogen atom
yellow atom	sulfur atom
red atom	oxygen atom

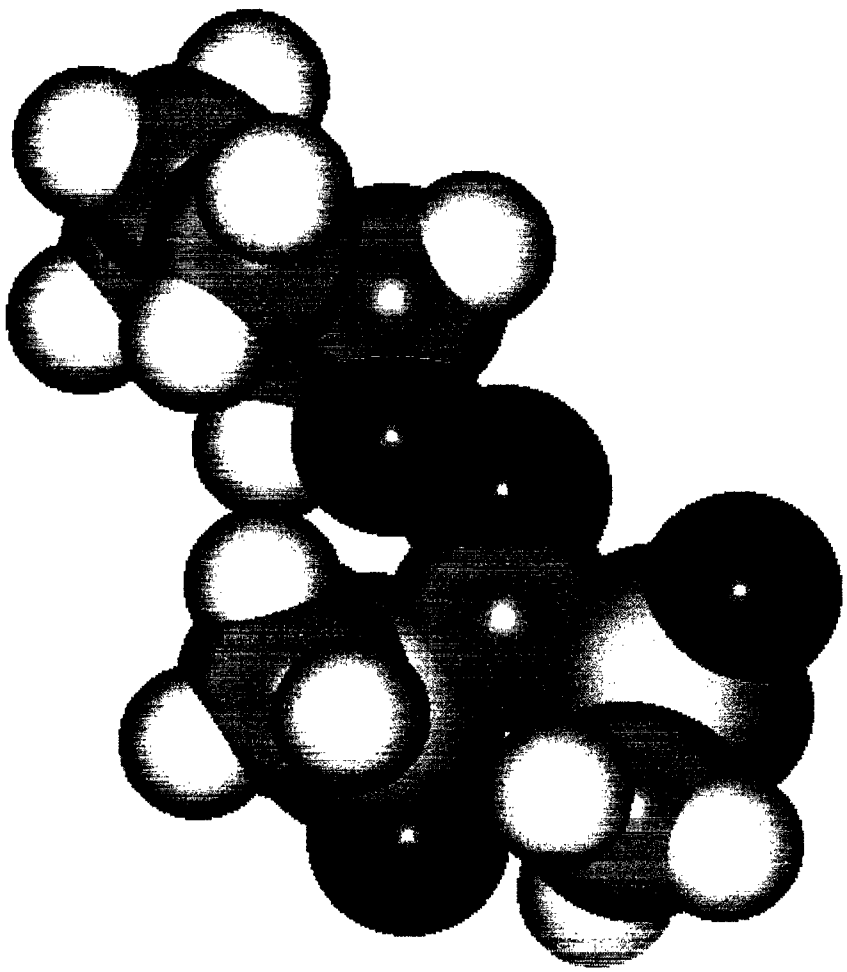
(5) Dewar, M. J. S.; Zeobisch, E. G.; Healy, E. F.; Stewart, J. J. P. *J. Am. Chem. Soc.* **1985,** *107*, 3902.

(6) Stewart, J. J. P. *QCPE* 455.

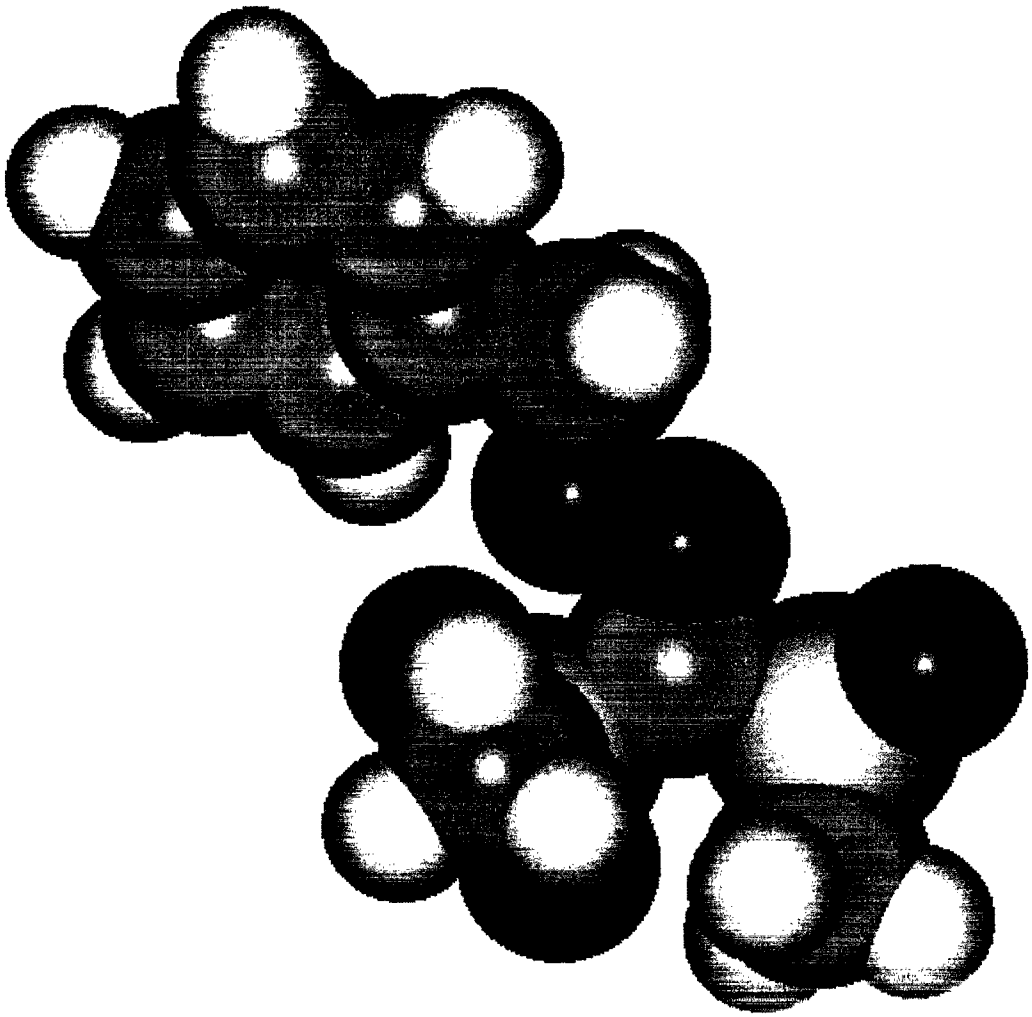
(7) Tripos Associates, 1699 S. Hanley Road, Suite 303, St. Louis, MO 63144.



1a



1b



1c