91–98 °C (17 mm); IR (CCl_4) 3313, 2130, 1672, 891 cm^{-1}; ^1H NMR (CCl_4) δ 0.79 (t, 3 H, J = 8 Hz), 0.86 (t, 3 H, J = 8 Hz), 1.15–1.64 (m, 4 H), 2.20 (t, 1 H, J = 2 Hz), 4.09–4.20 (m, 2 H), 4.30–4.39 (m, 2 H), 4.68 (t, 1 H, J = 2 Hz), 4.80–4.91 (m, 2 H). Anal. Calcd for $C_{12}H_{18}O_2$: C, 74.19; H, 9.34. Found: C, 73.85; H, 9.28.

All other oxolanes **3** were prepared in the same manner.

3a: bp 52–57 °C (1.4 mm); IR (CCl_4) 3311, 2130, 1672, 888 cm^{-1}; ^1H NMR (CCl_4) δ 0.83–0.98 (m, 3 H), 1.04 (s, 3 H), 1.10–1.45 (m, 4 H), 2.22 (t, 1 H, J = 2 Hz), 4.02–4.18 (m, 2 H), 4.26–4.39 (m, 2 H), 4.69–4.83 (m, 3 H). Anal. Calcd for $C_{12}H_{18}O_2$: C, 74.19; H, 9.34. Found: C, 74.23; H, 9.14.

3c: bp 58–64 °C (0.25 mm); IR (CCl_4) 3312, 2133, 1671, 891 cm^{-1}; ^1H NMR (CCl_4) δ 0.70–1.70 (m, 14 H), 2.23 (t, 1 H, J = 2 Hz), 4.06–4.18 (m, 2 H), 4.28–4.37 (m, 2 H), 4.68 (t, 1 H, J = 2 Hz), 4.80 (s, 1 H), 4.85 (t, 1 H, J = 2 Hz). Anal. Calcd for $C_{14}H_{22}O_2$: C, 75.63; H, 9.97. Found: C, 75.35; H, 9.88.

3d: bp 69–72 °C (0.4 mm); IR (CCl_4) 3315, 2130, 1665, 884 cm^{-1}; ^1H NMR (CCl_4) δ 1.05–1.90 (m, 10 H), 2.24 (t, 1 H, J = 2 Hz), 4.07–4.18 (m, 2 H), 4.26–4.36 (m, 2 H), 4.70–4.81 (m, 2 H), 5.11 (s, 1 H). Anal. Calcd for $C_{13}H_{18}O_2$: C, 75.69; H, 8.80. Found: C, 75.75; H, 8.70.

Typical Procedure for the Preparation of β-Methylene-γ-butyrolactones (4). To a solution of oxolane **6b** (1.94 g, 10 mmol) in 30 mL of acetone was added dropwise a solution of chromium trioxide (7.0 g, 70 mmol) in 40 mL of 10% aqueous H_2SO_4 over a period of 1 h under ice–water cooling. After the mixture was stirred for 2 h at 0 °C and overnight at room temperature, 100 mL of water was added, and the product was extracted with ether (4 × 20 mL). The combined ethereal extracts were washed with saturated aqueous $NaHCO_3$ (2 × 20 mL) and dried over anhydrous sodium sulfate. After the removal of the solvent, the distillation gave 1.21 g of α,α-diethyl-β-methylene-γ-butyrolactone (**4b**); bp 105–109 °C (20 mm); IR (CCl_4) 1787, 1678, 900 cm^{-1}; ^1H NMR (CCl_4) δ 0.82 (t, 6 H, J = 8 Hz), 1.35–1.92 (m, 4 H), 4.65 (t, 2 H, J = 2 Hz), 4.94 (t, 1 H, J = 2 Hz), 5.19 (t, 1 H, J = 2 Hz). Anal. Calcd for $C_9H_{14}O_2$: C, 70.10; H, 9.15. Found: C, 70.24; H, 9.45.

All other lactones **4** were obtained in the same manner.

4a: bp 97–103 °C (20 mm); IR (CCl_4) 1783, 1680, 900 cm^{-1}; ^1H NMR (CCl_4) δ 0.90 (t, 3 H, J = 7 Hz), 1.25 (s, 3 H), 1.10–1.78 (m, 4 H), 4.71 (t, 2 H, J = 2 Hz), 4.99 (t, 1 H, J = 2 Hz), 5.10 (t, 1 H, J = 2 Hz). Anal. Calcd for $C_9H_{14}O_2$: C, 70.10; H, 9.15. Found: C, 69.77; H, 9.13.

4c: bp 65–69 °C (0.37 mm); IR (CCl_4) 1781, 1673, 899 cm^{-1}; ^1H NMR (CCl_4) δ 0.82 (t, 3 H, J = 8 Hz), 0.90 (t, 3 H, J = 6 Hz), 1.00–1.95 (m, 8 H), 4.63 (t, 2 H, J = 2 Hz), 4.94 (t, 1 H, J = 2 Hz), 5.16 (t, 1 H, J = 2 Hz). Anal. Calcd for $C_{11}H_{18}O_2$: C, 72.49; H, 9.96. Found: C, 72.29; H, 9.76.

4d:[2] bp 62–64 °C (0.32 mm); mp 42–43 °C; IR (CCl_4) 1785, 1672, 898 cm^{-1}; ^1H NMR (CCl_4) δ 1.20–2.10 (m, 10 H), 4.67 (t, 2 H, J = 2 Hz), 5.02 (t, 1 H, J = 2 Hz), 5.08 (t, 1 H, J = 2 Hz).

Registry No. **1a**, 123-15-9; **1b**, 97-96-1; **1c**, 123-05-7; **1d**, 2043-61-0; **2a**, 83561-19-7; **2b**, 83561-20-0; **2c**, 83561-21-1; **2d**, 83561-22-2; **3a**, 83561-23-3; **3b**, 83561-24-4; **3c**, 83561-25-5; **3d**, 83561-26-6; **4a**, 83561-27-7; **4b**, 83561-28-8; **4c**, 83561-29-9; **4d**, 63965-86-6; cobaloxime (I), 53790-02-6; triethoxymethane, 122-51-0; $HC(OCH_2C{\equiv}CH)_3$, 83561-30-2; $HOCH_2C{\equiv}CH$, 107-19-7.

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Facile Synthesis of the Enantiomers of *exo*-Brevicomin

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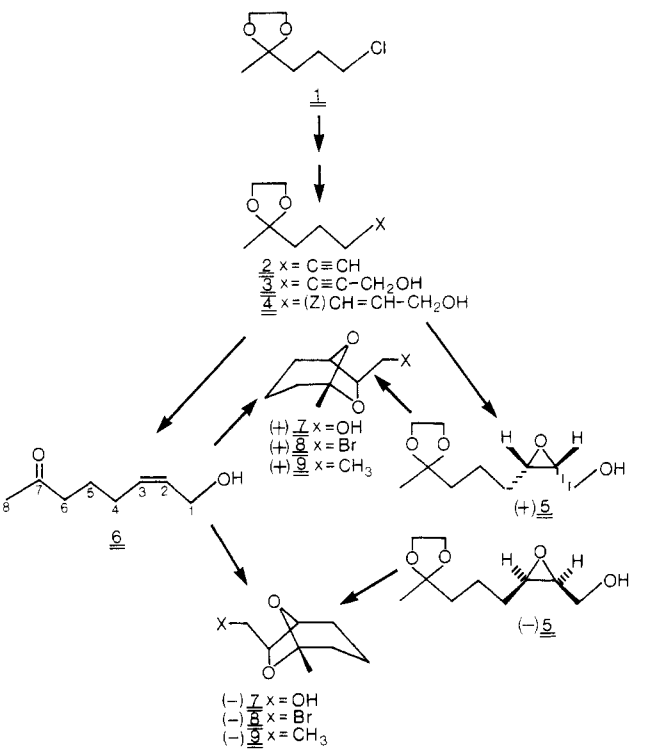
Received May 21, 1982

exo-Brevicomin (**9**) is produced by three species of *Dendroctonus* beetles as part of their pheromone complex.[1-3] Two of the species, *D. brevicomis* (western pine beetle) and *D. ponderosae* (mountain pine beetle), are of major economic importance in western North Amercia. Racemic *exo*-brevicomin is attractive in the field to *D. brevicomis* although it is known that the (1*R*,7*R*)-(+) isomer is naturally produced by these beetles. The effects of racemic *exo*-brevicomin on *D. ponderosae* vary from antiaggregation to attraction, apparently depending on the release rate of the pheromone, as well as on the host and location of the population being tested.[3] This variation raises the possibility that different populations of *D. ponderosae* discriminate between different chiral isomers of *exo*-brevicomin. In order to examine the field response of *D. ponderosae* to the enantiomers of *exo*-brevicomin and to determine the chirality of *exo*-brevicomin in *D. ponderosae*, we required efficient syntheses of both chiral forms of this bicyclic ketal.

Scheme I



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exo-brevicomin have been reported. The main drawbacks to previous chiral syntheses are length,[5a] low chemical yield,[5d] synthesis of only one enantiomer,[5b,e] and uncertainty in the optical purity of the final product.

The present synthesis commences with the commercially available ketal of 5-chloro-2-pentanone (**1**) which was chain extended via a three-step sequence[6-8] to give **4** in 65% overall yield (Scheme I). A large-scale (0.2 mol) preparation of **4** without purification of intermediates gave an overall yield of 81%. The two-step chain extension to give **3** proved superior, in our hands, to the single-step reaction of **1** with either the dianion of propargyl alcohol[9] or the lithium anion of silyl- and THP-protected propargyl derivatives.[10]

Asymmetric epoxidation of **4** by the Sharpless method[11,12] followed by a nonacidic workup gave the enantiomers of **5** in high enantiomeric purity (95% ee[13]) but only moderate chemical yield (~30%). Treatment of chloroform solutions of each optical isomer of **5** with 5% aqueous hydrochloric acid gave the bicyclic alcohols **7** but in decreased optical purity (~80% ee[13]). Reasoning that the loss in enantiomeric purity was due to lack of regiochemical control during the strongly acidic conditions employed for epoxide opening, we investigated the epoxidation of an intermediate (**6**) which would produce a more easily cyclized epoxide. Accordingly, the protecting group was removed from **4**, and the keto allylic alcohol **6** was subjected to Sharpless asymmetric epoxidation for 4 days at −25 °C. Standard aqueous tartaric acid workup[11a] proved sufficiently acidic to promote cyclization of the intermediate epoxides to the enantiomers of **7** in high chemical (>70%) and optical (95% ee[13]) yields. A possibly related rearrangement during Sharpless oxidation of an allylic alcohol containing a carbonyl δ to the unsaturation has been noted by Corey.[12a]

The enantiomers of **7** were converted to (+)- and (−)-*exo*-brevicomin (**9**) by bromination to give **8** followed by methylation with lithium dimethylcuprate.[15] Attempts to displace sulfonate groups[16] from the tosylate or mesylate of **7** were unsuccessful due to competing attack of the lithium dimethylcuprate at the sulfur. Presumably the bicyclic ring system partially shields the *exo*-methylene carbon from nucleophilic attack. The overall yield of *exo*-brevicomin from (**1**) was 30–40%.

The absolute configurations and stereochemistry of the *exo*-brevicomin enantiomers are those predicted by assuming the intermediate oxirane of **6** undergoes acid-catalyzed cyclization involving inversion at C-3 and retention at C-2. An analogous mode of cyclization has been observed in previous racemic syntheses of *exo*-brevicomin.[4a]

Experimental Section

NMR spectra were recorded on Varian EM-360 and Bruker WM400 spectrometers. Mass spectra were obtained by using a Hewlett-Packard 5985B GC/MS/DS system operating at 70 eV. Elemental analyses were performed by Mr. M. Yang at Simon Fraser University. GLC analyses were performed on a 0.21 mm i.d. × 30 m SP2100 capillary column on a Hewlett-Packard 5880 gas chromatograph programmed to change the column temperature from 100 to 250 °C at 10 °C/min. Optical rotations were determined on a Perkin-Elmer P-22 spectropolarimeter (0.5-dm cell) and a Rudolph Polarimeter Model 70 (1 dm cell).

Tetrahydrofuran (THF) and ether were distilled from lithium tetrahydridoaluminate immediately prior to use. Hexamethylphosphoric triamide (HMPA) was distilled from calcium hydride and stored under argon over activated 3-Å molecular sieves. Acetylene was dried by passage through a trap (cooled to −78 °C) and a calcium chloride drying tube.

Preparation of 2-Methyl-2-(4-pentynyl)-1,3-dioxolane (2). A stream of dry acetylene was used to saturate 150 mL of dry THF at ice-bath temperature. A 1.6 M hexane solution of *n*-BuLi (80 mL, 128 mmol) was added dropwise over 20 min while the temperature was maintained at 5–10 °C. After the mixture was stirred a further 0.5 h at 10 °C, 16.4 g (100 mmol) of **1** and 50 mL of dry HMPA were added. The reaction mixture was warmed to room temperature and stirred under an acetylene atmosphere for 24 h. The reaction was quenched by pouring it into ice–water (500 mL) and extracting with ether (3 × 150 mL). The combined ether extracts were washed with water (2 × 100 mL) and brine (100 mL). The extract was dried over anhydrous $MgSO_4$, concentrated in vacuo, and distilled [bp 86–87 °C (15 mmHg)] to yield 14.5 g (94%) of **2**. Analysis by GLC revealed that **2** was 98% pure: mass spectrum, *m/e* (relative intensity) 139 (40), 99 (18), 87 (100), 43 (15). Anal. Calcd for $C_9H_{14}O_2$: C, 70.10; H, 9.15. Found: C, 70.43; H, 9.37.

Preparation of 2-Methyl-2-(6-hydroxy-4-hexynyl)-1,3-dioxolane (3). A 1.6 M hexane solution of *n*-BuLi (23 mL, 37 mmol) was added dropwise over 15 min to 5.1 g (33 mmol) of **2** in 50 mL of dry THF with ice-bath cooling. After a further 10 min, anhydrous paraforaldehyde (1.3 g, 43 mmol) was added in one portion. The cooling bath was removed and the reaction mixture stirred under argon at 23 °C for 3 h. The reaction mixture was poured into ice–water (150 mL) and extracted with ether (3 × 75 mL). The combined ether extracts were washed with brine (100 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated in vacuo to yield after distillation 5.0 g (82%) of **3**: bp 115–117 °C (0.2 mmHg) [lit.[17] bp 99–107 °C (0.1 mmHg)]; 97% pure by GLC; ^1H NMR (60 MHz, $CDCl_3$) δ 4.1–4.3 (2 H, OCH_2, m), 3.9 (4 H, $O(CH_2)_2O$, s), 2.5 (1 H, OH, s), 2.1–2.4 (2 H, $CH_2C{\equiv}C$, m), 1.5–1.8 (4 H, 2 CH_2, m), 1.35 (3 H, CH_3, s). Anal. Calcd for $C_{10}H_{16}O_3$: C, 65.19; H, 8.75. Found: C, 65.54; H, 8.98.

Preparation of 2-Methyl-2-(6-hydroxy-(*Z*)-4-hexenyl)-1,3-dioxolane (4). Hydrogen was bubbled through a solution of $Ni(OAc)_2{\cdot}4H_2O$ (1.25 g, 5.0 mmol) in 50 mL of 95% ethanol while 5 mL of a solution prepared by dissolving 0.5 g of $NaBH_4$ in 12 mL of methanol containing 0.65 mL of 2 N NaOH was added. After 5 min ethylenediamine (0.8 mL) was added followed by **3** (5.6 g, 30 mmol). The reaction mixture was stirred under a H_2 atmosphere for 2 h, diluted with ether (450 mL), and filtered through Celite. The filtrate was washed with brine (100 mL), dried over anhydrous $MgSO_4$, and concentrated in vacuo. Vacuum distillation yielded 5.2 g (92%) **4**: bp 88–95 °C (0.1 mmHg); 93%

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Preparation of (*Z*)-7-Oxo-2-octen-1-ol (6). Three drops of concentrated H_2SO_4 were added to an acetone solution (350 mL) of **4** (15.0 g, 81 mmol). After the mixture was stirred for 2 h at 23 °C, anhydrous K_2CO_3 (~2 g) was added and the stirring continued for a further 0.5 h. The reaction mixture was filtered and concentrated in vacuo. Vacuum distillation yielded **6**: 10.1 g (88%); bp 100-102 °C (0.2 mmHg) [lit.[10] bp 120-125 °C (0.5 mmHg)]; 98% pure.

Preparation of (+)-(1*R*,7*R*)-7-(Hydroxymethyl)-5-methyl-6,8-dioxabicyclo[3.2.1]octane ((+)-7). A 0.1 M solution of titanium tetraisopropoxide (510 mL, 51 mmol) in CH_2Cl_2 at -30 °C (dry ice/CCl_4 bath) was treated with 11.3 g (55 mmol) of (-)-diethyl tartrate (Aldrich). After 10 min, alkene **6** (7.1 g, 50 mmol) was added followed by 27 mL (111 mmol) of a 4.1 M anhydrous solution of *tert*-butyl hydroperoxide in CH_2Cl_2. The reaction mixture was kept at -25 °C for 4 days under argon. An aqueous tartaric acid solution (10%, 150 mL) was added and the reaction mixture allowed to warm slowly to 0 °C. After 3 h at 0 °C and 1 h at 23 °C the CH_2Cl_2 phase was separated from the clear aqueous phase that was further extracted with CH_2Cl_2 (3 × 75 mL). The combined CH_2Cl_2 extracts were dried over anhydrous K_2CO_3, filtered, and concentrated in vacuo to yield a mixture of (+)-7 and diethyl tartrate. This mixture was taken up in ether (300 mL) and shaken for 5 min with a 1 N NaOH solution (150 mL) in order to remove the diethyl tartrate by hydrolysis. The aqueous layer was extracted with ether (2 × 100 mL), and the combined ether extracts were dried over anhydrous $MgSO_4$. Removal of the solvent in vacuo and vacuum distillation yielded (+)-7: 6.5 g (82%); bp 65-72 °C (0.1 mmHg). GLC analysis revealed (+)-7 was 90% pure and contaminated with <5% unreacted **6**. An analytical sample, purified by column chromatography (silica gel; hexane/ethyl acetate, (5:1) gave a sample that was 95% pure by GLC: $[\alpha]^{27}_D$ +53.7 ± 2.0° (*c* 0.94, $CHCl_3$); mass spectrum, *m/e* (relative intensity) 125 (25), 112 (20), 98 (15), 83 (22), 69 (31), 67 (39), 59 (92), 54 (100), 43 (57); ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.26 (1 H, C_1, br s), 4.12 (1 H, C_7, t, J = 7 Hz), 3.55 (2 H, CH_2O, overlapping dd, J = 7 Hz), 2.12 (1 H, OH, s), 1.45-2.00 (6 H, 3 CH_2, m), 1.43 (3 H, CH_3, s). Anal. Calcd for $C_8H_{14}O_3$: C, 60.74; H, 8.92. Found: C, 60.60; H, 8.99.

Preparation of (-)-7. Chiral isomer **7** was prepared in 73% yield by using the same procedure for epoxidation of **6** with the exception that (+)-diethyl tartrate was employed: $[\alpha]^{27}_D$ -58.0 ± 2.0° (*c* 1.0, $CHCl_3$). Anal. Calcd for $C_8H_{14}O_3$: C, 60.74; H, 8.92. Found: C, 60.71; H, 8.81.

Preparation of (1*R*,7*S*)-7-(Bromomethyl)-5-methyl-6,8-dioxabicyclo[3.2.1]octane ((+)-8). To a solution of (+)-7 (6.5 g, 41 mmol) in 30 mL of dry HMPA was added 11.0 g (42 mmol) of triphenylphosphine followed by 14.0 g (42 mmol) of carbon tetrabromide. An immediate exothermic reaction occurred that temporarily produced a homogeneous solution. The reaction mixture cooled to room temperature over 0.5 h and solidified. The reaction mixture was then reheated to 100 °C for 0.5 h and after cooling was triturated with pentane (5 × 100 mL). The combined pentane extracts were filtered, washed with water (100 mL) and brine (100 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated in vacuo. Vacuum distillation yielded 8.0 g (88%) of (+)-8: bp 82-85 °C (0.1 mmHg); $[\alpha]^{27}_D$ +0.9 ± 0.5° (*c* 1.3, $CHCl_3$); 99% pure by GLC; mass spectrum, *m/e* (relative intensity) 180/178 (7), 141 (95), 127 (21), 113 (17), 99 (73), 81 (48), 71 (10), 43 (100); ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.44 (1 H, C_1, br), 4.23 (1 H, C_7, dd, J = 10, 5 Hz), 3.32 (1 H, CHBr, dd, J = 10, 5 Hz), 3.22 (1 H, CHBr, J = 10 Hz), 1.40-2.00 (6 H, 3 CH_2, m), 1.42 (3 H, CH_3, s). Anal. Calcd for $C_8H_{13}O_2Br$: C, 43.46; H, 5.93. Found: C, 43.70; H, 6.08.

Preparation of (-)-8. The same bromination procedure applied to (-)-7 yielded (-)-8: 85% yield; 95% pure by GLC; $[\alpha]^{27}_D$ -0.6 ± 0.5° (*c* 1.4, $CHCl_3$). Anal. Calcd for $C_8H_{13}O_2Br$: C, 43.46; H, 5.93. Found: C, 43.65; H, 5.98.

Preparation of *exo*-(1*R*,7*R*)-7-Ethyl-5-methyl-6,8-dioxabicyclo[3.2.1]octane [(+)-9, (1*R*,7*R*)-*exo*-Brevicomin]. An ether solution of MeLi (1.6 M, 65 mL, 104 mmol) was added dropwise to a slurry of CuI (9.5 g, 50 mmol) in 200 mL of dry ether under argon at 10 °C. The reaction mixture was stirred for 10 min, and then a solution of (+)-8 (8.0 g, 36 mmol) in 50 mL of HMPA was added. The reaction mixture was allowed to warm to room temperature and stirred for 24 h at room temperature. The reaction mixture was poured into cold saturated NH_4Cl solution (350 mL). The ether layer was separated and the aqueous phase extracted with ether (2 × 150 mL). The combined ether extracts were washed with water (100 mL) and brine (100 mL) and dried over anhydrous $MgSO_4$. Filtration and removal of the solvent by distillation at atmospheric pressure yielded crude (+)-brevicomin that was purified by distillation to yield 3.5 g (62%) of (+)-9: bp 60-62 °C (15 mmHg) [lit.[4f] bp 70 °C (20 mmHg)]; $[\alpha]^{27}_D$ +59.0 ± 0.5° (*c* 2.5, $CHCl_3$) (lit. $[\alpha]_D$ + 84.1°,[4a] + 52°,[4b] + 70°,[4d] + 81.5°[4e]). The ^{1}NMR and mass spectra were identical with those published.[18] GLC of (+)-*exo*-brevicomin used for rotation revealed >99% chemical purity. Determination of optical purity by Profeessor F. V. Schurig by complexation chromatography revealed 95% ee. The results of the optical purity determinations are to be reported elsewhere.

Preparation of (1*S*,7*S*)-*exo*-Brevicomin ((-)-9). Reaction of lithium dimethylcuprate with (-)-8 yielded (-)-9: 69% yield; $[\alpha]^{27}_D$ -60.6 ± 0.5° (*c* 2.3, $CHCl_3$) (lit. $[\alpha]_D$ -80.6°,[4a] -67.5°,[4b] -66°[4d]).

Acknowledgment. We thank the NSERC of Canada for continued support of this work through Operating Grant A0851, a Strategic Grant (open), and a Postgraduate Fellowship (B.D.J.), the Simon Fraser University and the province of British Columbia for assistance in the acquisition of the 400-MHz NMR spectrometer, and J. H. Borden for biological advice and encouragement.

Registry No. **1**, 57558-50-6; **2**, 74066-96-9; **3**, 26330-18-7; (*Z*)-**4**, 83732-30-3; (*Z*)-**6**, 51580-48-4; (+)-**7**, 83732-31-4; (-)-**7**, 83780-99-8; (+)-**8**, 83732-32-5; (-)-**8**, 83781-00-4; (+)-**9**, 20290-99-7; (-)-**9**, 64313-75-3; acetylene, 74-86-2; formaldehyde, 50-00-0.

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Anion and Trianion Radicals of Aryl-Substituted Cyclooctatetraenes

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Received May 21, 1982

The chemistry of cyclooctatetraene (COT) and its derivatives has been the subject of extensive research for many years.[1] In particular, electronic distributions in substituted COT's have been the subject of much study.[2,3] Phenylcyclooctatetraene (PCOT) has been shown to reduce to an anion radical where significant spin density occurs in the phenyl group.[4] Other substituted PCOT's were found to follow a reasonable Hammett correlation when the phenyl substituent parameters were compared with the measured orbital splitting (ϵ) as determined by ESR spectroscopy.[5] When two ortho substituents were

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