despite the oversimplifications inherent in it, this simple model based upon the difference in C–E bond lengths and 1,4 E···E interactions accounts for observations and provides a basis for design of crown-type ligands.

Conclusions

Analysis of the structures of 12S4, 15S5, and 18S6 shows a marked preference for gauche placement at the C–E bonds. This preference is expressed by crown thioethers generally and is diametrically opposite that shown by crown ethers. The difference in 1,4-interactions at the C–C–E–C and E–C–C–E bonds parallels the difference in conformational preference between oxa- and thia-crowns, and it can be used to rationalize the following experimentally observed order of gauche preference: C–S ≫ C–C > C–O. Prediction of conformation in $-(C-C-E)_n-$ crown-type ligands can be accomplished by the following: (1) maximizing the number of C–S bonds in gauche placement; (2) minimizing the number of C–O (or secondary C–N) bonds in gauche placement; (3) minimizing the number of C–C bonds in gauche placement. The application of these considerations to design of macrocyclic ligands is apparent.

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Supplementary Material Available: Listings of anisotropic thermal parameters, hydrogen atom positional and thermal parameters, and interatomic distances and angles for tetrathia-12-crown-4, pentathia-15-crown-5, and hexathia-18-crown-6 (4 pages); listing of observed and calculated structure factors (29 pages). Ordering information is given on any current masthead page.

Palladium-Catalyzed Reactions in the Synthesis of 3- and 4-Substituted Indoles. 2.[1] Total Synthesis of the *N*-Acetyl Methyl Ester of (±)-Clavicipitic Acids

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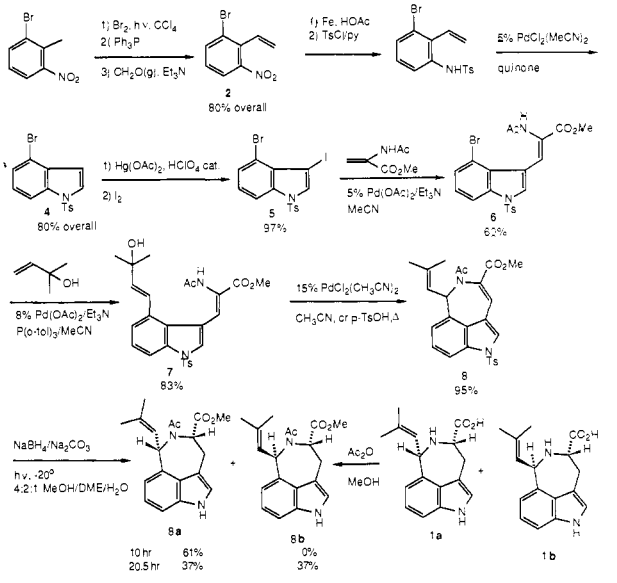
Abstract: The *N*-acetyl methyl esters of the (±)-claviciptic acids **9** were synthesized in 12 steps in overall 18% yield from commercially available 2-bromo-6-nitrotoluene. The synthesis involved, as key steps, Pd(II)-catalyzed formation of the indole and the seven-membered nitrogen-containing C-ring and Pd(0)-catalyzed introduction of both C-ring side-chain precursors.

The unusual ergot alkaloid biosynthesis derailment product clavicipitic acid (**1**) occurs in nature as a mixture of cis (**1a**) and trans (**1b**) diastereoisomers, the proportions of which depend on the specific microorganism from which it is isolated.[1] Clavicipitic acid has been the recent target of two multistep total syntheses (18[3] and 26[4] steps, respectively). These gave the desired product as mixtures of cis and trans isomers in approximately 0.5% overall yield from commercially available starting materials and involved many classical synthetic procedures, including extensive protection, deprotection, and functional group modification. Both the isolated and synthetic clavicipitic acids were converted to the *N*-acetyl methyl esters **9a,b** for ease in handling. We have been developing palladium-catalyzed approaches to the ergot alkaloids,[1,5] primarily to demonstrate the efficacy of the use of transition metals in organic synthesis. Herein we report an unconventional approach to these *N*-acetyl methyl esters (**9a,b**) of the clavicipitic acids utilizing palladium catalysis in four key carbon–carbon and carbon–nitrogen bond-forming steps.

Results and Discussion

Scheme I summarizes the *successful* approach to the total synthesis of **9a,b**. The conversion of commercially available 2-bromo-6-nitrotoluene to 1-tosyl-3-iodo-4-bromoindole (**5**) has been presented in detail[1] and requires no further comment. Palladium(0)-catalyzed oxidative addition/olefin insertion ("Heck arylation"[6]) with the α-acetamidoacrylate fortuitously produced the *Z* isomer exclusively of **6** in 60% isolated yield. In addition 15–20% of deiodinated product **4** was recovered and could be recycled through the mercuration/iodination steps. Introduction of the tertiary allylic alcohol sidechain in the 4-position under similar palladium(0)-catalyzed conditions produced compound

Scheme I



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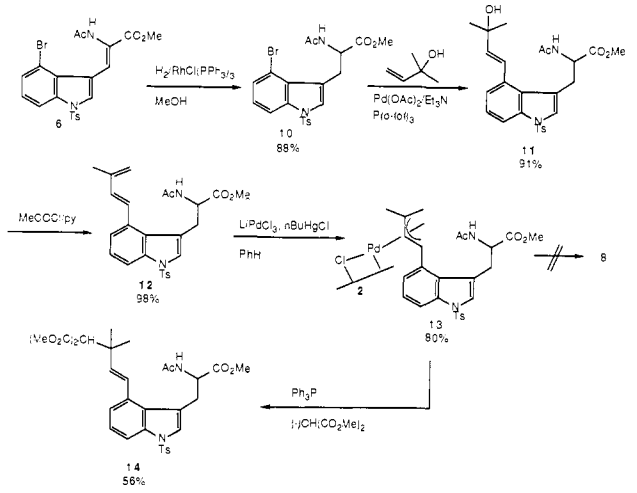
Scheme II



7, having all the requisite atoms of clavicipitic acid, in excellent yield.

Ring closure of this unsaturated precursor proved remarkably easy. Treatment of **7** with an equivalent amount of $PdCl_2(MeCN)_2$ and sodium carbonate[7] resulted in the formation of a stable palladium complex which upon hydrogenolysis produced modest yields of **8**, accompanied by several byproducts. In contrast, heating **7** at reflux in acetonitrile with 15% $PdCl_2(MeCN)_2$ as catalyst produced almost quantitative yields of **8** in less than 2 h. Note that although this is apparently a palladium(II)-catalyzed process, no reoxidation of palladium was required for catalysis, since palladium(II) hydroxide (or oxide) rather than palladium hydride was the ostensible elimination product.[8]

Similarly, *p*-toluenesulfonic acid catalyzed this same cyclization in acetonitrile at reflux. Even heating in the absence of any catalyst converted **7** to **8**, but this uncatalyzed cyclization was slow and less efficient. As will be seen below, the facility of this cyclization was due to the amide functional group being held rigidly in position for closure by the *Z* geometry of the acetamidoacrylate side chain.

Photochemical reduction of **8** with sodium borohydride also removed the tosyl group,[4,9] providing **9** as a mixture of diastereomers. Shorter reaction times (10 h) gave almost exclusively the cis derivative **9a** in 61% yield, having identical physical properties (mp, MS, IR, ^{1}H NMR, 270 MHz) with those previously reported for this compound prepared from both natural and synthetic[4] clavicipitic acid. Longer reaction times (20.5 h) gave approximately a 1:1 mixture of the *cis*-**9a** and *trans*-**9b** derivatives in 74% yield.

As is common with organic synthesis, the successful approach was not the initially planned approach, shown here in Scheme II. Ring closure using palladium(0)-catalyzed nucleophilic attack on an allylacetate[10] was to be the key step in this synthesis. Thus, acetamidoacrylate **6** was reduced in excellent yield using Wilkinson's catalyst to give **10**, which was efficiently alkylated with the appropriate tertiary allylic alcohol as above to give **11**. Conversion of **11** to its acetate proved problematic. A wide variety of acid or base-catalyzed O-acetylation resulted in elimination of water from the sensitive tertiary allylic/benzylic alcohol **11** to produce diene **12**, rather than in acetylation. Ketene failed to react in the absence of acid catalysts and produced diene **12** in the presence of acid. In contrast, diphenyl- and (trimethylsilyl)ketene formed the corresponding substituted acetates, but these failed to react with palladium(0) catalysts under mild conditions and decomposed to diene **12** under more severe conditions. In striking contrast to unsaturated compound **7** (Scheme I), saturated compounds **11** and **12** also failed to cyclize under acidic conditions or in the presence of stoichiometric or catalytic quantities of $PdCl_2(MeCN)_2$.

Since catalytic cyclization of **11** via (π-allyl)palladium chemistry was inaccessible, the corresponding stoichiometric process was attempted. Hydropalladation of diene **12** with HPdCl, generated in situ by the reaction of *n*-butylmercuric chloride with $LiPdCl_3$,[11] produced the yellow, air-stable (π-allyl)palladium complex **13** in excellent yield. Although this complex underwent the typical intermolecular alkylation by stabilized carbanions (e.g., malonate to give **14**), it resisted *all* attempts to effect intramolecular amidation (e.g., conversion of **13** to **9**). Under a wide variety of conditions either regeneration of diene **12** (by proton abstraction from a methyl group) or allylic alcohol **11** (presumably by nucleophilic attack on the π-allyl complex by adventitious water!) was observed. (It should be noted that although amination of (π-allyl)palladium complexes is common,[10] the corresponding *amidation* is rare.[12,13])

The complete failure of this planned last step led to the revised approach (Scheme I) which ultimately resulted in a 12-step total synthesis of the *N*-acetyl methyl esters of (±)-clavicipitic acid **9** in overall 18% yield from commercially available starting materials. This represents an approximate 40-fold increase in yield over existing methods and provides an illustration of the efficacy of transition metals in organic synthesis.

Experimental Section

General Data. Melting points were taken with a Mel-temp apparatus and are uncorrected. Infrared spectra were recorded on a Beckman 4240 spectrometer. ^{1}H NMR spectra were recorded with an IBM-Bruker WP270SY (270 MHz) spectrometer or a Nicolet NTC FT 1180 (360 MHz) spectrometer with tetramethylsilane (Me_4Si) as an internal standard. Liquid chromatography was carried out under moderate pressures (20–60 psi) either by using columns of appropriate size packed with Merck Silica gel 60 (230–400 mesh) or by using a Chromatotron (Harrison Research) radial-layer chromatographic device with plates of Kiesel gel 60 PF 254 silica gel. Unless otherwise stated, all reactions were run under an argon atmosphere. Acetonitrile, dichloromethane, hexane, and ethyl acetate were distilled from calcium hydride. Tetrahydrofuran was distilled from sodium with benzophenone as an indicator. Elemental analyses were performed by M-H-W Laboratories, Phoenix, AZ.

Preparation of 4-Bromo-1-tosylindole (4). The published procedure[1] for the preparation of indole **4** was modified to allow for a more simple workup. The reaction was run as stated,[1] and the crude reaction mixture evaporated under reduced pressure. The residue was dissolved in chloroform and washed twice with 1 N aqueous sodium hydroxide solution and twice with water. The combined aqueous phase was back-extracted with chloroform and the combined organic phase dried and evaporated under reduced pressure. The residue was purified by chromatography on silica gel, with hexane as the eluent, to give an 80% yield of indole **4**.

Preparation of Indole 6. Indole **6** was prepared as published previously,[1] except the reaction mixture was heated 5 h instead of 45 h. The yield increased to 60% (from 47%[1]).

Alkylation of 6 To Give 7. A mixture of 0.219 g (0.446 mmol) of 3-(2-acetamido-2-carbomethoxyethen-1-yl)4-bromo-1-tosylindole, 0.171 g (2.0 mmol, 4.5 equiv) of 2-methyl-3-buten-2-ol, 0.008 g (8 mol %) of palladium(II) acetate, 0.027 g (20 mol %) of tri-*o*-tolylphosphine, and 0.068 g (0.67 mmol, 1.5 equiv) of triethylamine in 0.5 mL of acetonitrile was heated at 100 °C in a sealed tube for 5 h. The mixture was cooled to room temperature, dissolved in 50 mL of dichloromethane, and filtered through Celite. The filtrate was evaporated under reduced pressure, leaving 0.36 g of a yellow oil which was purified by radial chromatography on silica gel. Hexane–ethyl acetate (1:1) eluted tri-*o*-tolylphosphine. Hexane–ethyl acetate (1:2) eluted the product. Evaporation of the solvent gave 0.184 g (83%) of **7** as a white solid. Recrystallization from hexane–ethyl acetate gave the analytical sample: mp 126.5–128

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°C; ^{1}H NMR ($CDCl_3$) δ 1.42 (s, 6 H, $-CH(CH_3)_2$), 2.15 (b s, 3 H, $-NHCOCH_3$), 2.34 (s, 3 H, tosyl CH_3), 3.82 (s, 3 H, $-COOCH_3$), 6.17 (d, 1 H, J = 15.8 Hz, indole $-CH$=CH–), 7.05 (d, 1 H, J = 15.8 Hz, indole –CH=CH–), 7.15–7.30 and 7.70–7.90 (m, 11 H, aromatic –H, –NH, and –OH); IR (KBr) 3210 (br, OH, NH), 1722 ($COOCH_3$), 1660 ($NHCOCH_3$) cm^{-1}. Anal. Calcd for $C_{26}H_{28}N_2O_6S$: C, 62.89; H, 5.69; N, 5.64; S 6.46. Found: C, 63.05; H, 5.77; N, 5.72; S, 6.21.

Palladium-Catalyzed Formation of 8. A mixture of 0.212 g (0.427 mmol) of **7** and 0.017 g (15 mol %) of palladium(II) chloride–bis(acetonitrile) in 20 mL of acetonitrile was degassed, left under an argon balloon, and heated under reflux for 2 h. The mixture was cooled to room temperature and the solvent evaporated, leaving a thick yellow oil. Purification by radial chromatography on silica gel eluting with hexane–ethyl acetate (1:1) gave, after evaporation of the solvent, 0.194 g (95%) of **8** as a white solid: mp 89–95 °C; ^{1}H NMR ($CDCl_3$) δ 1.57 (s, 3 H, $-C$=CCH_3), 1.83 (s, 6 H, $-C$=$C-H_3$ and $-NHCOCH_3$), 2.38 (s, 3 H, tosyl CH_3), 3.83 (s, 3 H, $-COOCH_3$), 4.78 (b d, 1 H, J = 8.4 Hz, –NCH indole), 6.61 (d, 1 H, J = 8.4 Hz, $-C$=CHCHN–), 7.20–7.40 (m, 5 H, ArH, CH=CCO_2CH_3), 7.75–7.95 (m, 4 H, ArH); IR (KBr) 1714 ($COOCH_3$), 1650 ($NHCOCH_3$) cm^{-1}. Anal. Calcd for $C_{26}H_{26}N_2O_5S$: C, 65.25; H, 5.48; N, 5.85; S, 6.70. Found: C, 65.46; H, 5.69; N, 5.78; S, 6.55.

***p*-Toluenesulfonic Acid Catalyzed Formation of 8.** A mixture of 0.062 g (0.125 mmol) of **7** and 2.4 mg (10 mol %) of *p*-toluenesulfonic acid monohydrate in 5 mL of acetonitrile was heated under reflux for 1 h. The mixture was cooled to room temperature and the solvent evaporated, leaving a thick yellow oil.

Purification by radial chromatography on silica gel eluting with hexane–ethyl acetate (1:1) gave, after evaporation of the solvent, 0.058 g (97%) of **8** which was identical in all respects with the material isolated from the palladium-catalyzed reaction.

Photochemical $NaBH_4$ Reduction/Detosylation of 8 To Give 9a and 9b. A mixture of 0.100 g (0.209 mmol) of **8**, 0.100 g (2.65 mmol, 12.7 equiv) of sodium borohydride, and 0.100 g (0.94 mmol, 4.5 equiv) of anhydrous sodium carbonate in 5 mL of a 4:2:1 mixture of methanol–dimethoxyethane–water was cooled to −20 °C and irradiated with a 450-W bulb for 20.5 h. The solvent was evaporated under reduced pressure and the residue partitioned between dichloromethane and water. The aqueous phase was extracted again with dichloromethane and the combined organic layer dried over anhydrous magnesium sulfate and filtered. The filtrate was evaporated under reduced pressure leaving a clear oil. Chromatographic purification on a 1-mm silica gel plate using dichloromethane–methanol (99:1) as eluent gave 0.050 g (74%) of **9** as a 1:1 mixture of diastereomers (by NMR). Separation of the two diastereomers was accomplished by preparative thin-layer chromatography, using multiple elutions with 2:1 toluene–ethyl acetate as the eluent. Recrystallization of **9a** (R_f 0.22) from carbon tetrachloride–hexane gave colorless crystals: mp 118–121 °C (lit.[3] mp 117–119 °C); ^{1}H NMR ($CDCl_3$) δ 1.76 (s, 3 H, $-C$=CCH_3), 1.91 (s, 3 H, $-C$=CCH_3), 2.17 (s, 3 H, $-NHCOCH_3$), ABX system, δ_A 3.51, δ_B 3.72, δ_X = 4.42 (J_{AX} = 12.3 Hz, J_{BX} = 3.3 Hz, J_{AB} = 15.8 Hz, $-CH_2CH$–), 3.73 (s, 3 H, $COOCH_3$), 5.23 (d, 1 H, J = 6.5 Hz, $-C$=$CHCH$N–), 5.84 (d, 1 H, J = 6.5 Hz, $-C$=CHCHN), 6.84 (d, 1 H, J = 7.0 Hz, indole 2H), 7.05–7.20 (m, 2 H, ArH), 7.27 (m, 1 H, ArH), 8.48 (b s, 1 H, NH); IR (KBr) 3240 (NH), 1733 ($COOCH_3$), 1628 ($NHCOCH_3$) cm^{-1}. Physical data for this compound was identical in all respects to that reported for natural[2] and synthetic[3] material.

9b (R_f 0.15) was isolated as a clear, colorless oil: ^{1}H NMR ($CDCl_3$) δ 1.74 (s, 3 H, $-C$=CCH_3), 1.87 (s, 3 H, $-C$=CCH_3), 2.18 (s, 3 H, $-NHCOCH_3$), ABX system, δ_A 3.41, δ_B 3.65, δ_X 3.70 (J_{AX} = 1.8 Hz, J_{BX} = 7.3 Hz, J_{AB} = 15.9 Hz, $-CH_2CH$–), 3.70 (s, 3 H, $COOCH_3$), 5.54 (b d, 1 H, J = 7.8 Hz, $-C$=$CHCH$N–), 5.67 (d, 1 H, J = 7.8 Hz, $-C$=CHCHN), 6.81 (d, 1 H, J = 6.9 Hz, indole 7H), 7.00 (b s, 1 H, indole 2H), 7.07 (t, 1 H, J = 7.7 Hz, indole 6H), 7.24 (d, 1 H, J = 8.4 Hz, indole 5H), 8.20 (b s, 1 H, indole NH); IR (neat) 3280 (NH), 1731 ($COOCH_3$), 1624 ($NHCOCH_3$) cm^{-1}. Shorter reaction time (10 h) gave exclusively the cis isomer **9a** in slightly lower yield (61%).

3-(2-Acetamido-2-carbomethoxyethyl)-4-bromo-1-tosylindole (10). A mixture of 0.404 g (0.83 mmol) of 3-(2-acetamido-2-carbomethoxyethen-1-yl)-4-bromo-1-tosylindole (**6**) and 8 mg (0.0086 mmol) of Wilkinson's catalyst in 30 mL of methanol was placed in a Fisher-Porter bottle. The suspension was hydrogenated at room temperature and 65 psi of H_2 for 21.5 h. The resulting clear, light yellow solution was evaporated under reduced pressure. The residual oil was chromatographed on silica gel. Toluene eluted trace impurities. Ethyl ether–toluene (1:1) eluted the product, giving after evaporation under reduced pressure, 0.408 g (quantitative) of **10** as a colorless solid. Recrystallization from ethyl acetate–hexane gave the analytical sample as colorless crystals: mp 118.5–119.5 °C; ^{1}H NMR (360 MHz, $CDCl_3$) δ 1.93 (s, 3 H, $NHCOCH_3$), 2.35 (s, 3 H, tosyl CH_3), ABX system, δ_A 3.33, δ_B 3.61, δ_X 5.00 (J_{AX} = 8 Hz, J_{BX} = 6 Hz, J_{AB} = 15 Hz, $-CH_2CH$–), 3.70 (s, 3 H, $COOCH_3$), 5.99 (d, J = 8 Hz, 1 H, NH), 7.13 (t, J = 8 Hz, 1 H, indole 6H), 7.24 (d, J = 8 Hz, 2 H, tosyl H adjacent to methyl), 7.39 (d, J = 8 Hz, 1 H, indole 5H), 7.47 (s, 1 H, indole 2H), 7.72 (d, J = 8 Hz, 2 H, tosyl H), 7.95 (d, J = 8 Hz, 1 H, indole 7H); IR (KBr) 3260 (NH), 1747 ($COOCH_3$), 1648 ($NHCOCH_3$), 1538 ($NHCOCH_3$) cm^{-1}. Anal. Calcd for $C_{21}H_{21}BrN_2O_5S$: C, 51.12; H, 4.29; N, 5.68. Found: C, 51.20; H, 4.49; N, 5.45.

3-(2-Acetamido-2-carbomethoxyethyl)-4-(3-hydroxy-3-methyl-1-buten-1-yl)-1-tosylindole (11). A mixture of 0.493 g (1.00 mmol) of 3-(2-acetamido-2-carbomethoxyethyl)-4-bromo-1-tosylindole (**10**), 0.108 g (1.25 mmol) of 2-methyl-3-buten-2-ol, 0.127 g (1.25 mmol) of Et_3N, 11 mg (0.049 mmol) of $Pd(OAc)_2$, and 61 mg (0.20 mmol) of tri-*o*-tolylphosphine was flushed with argon and then heated in a sealed tube at 100 °C for 5 h. After being cooled to room temperature, the residue was taken up in 50 mL of CH_2Cl_2, washed with 50 mL of H_2O twice, dried (Na_2SO_4), filtered, and concentrated in vacuo to afford 0.457 g (91.9%) of colorless solid. Recrystallization from ethyl acetate–hexanes (hot filtration) afforded the analytical sample as small, shiny colorless needles: mp 148–149 °C; ^{1}H NMR (360 MHz, $CDCl_3$) δ 1.39 (s, 3 H, CH_3), 1.42 (s, 3 H, CH_3), 1.94 s, 3 H, $NHCOCH_3$), 2.34 (s, 3 H, tosyl, CH_3), ABX system, δ_A 3.20, δ_B 3.36, δ_X 4.88 (J_{AX} = 8 Hz, J_{BX} = 6 Hz, J_{AB} = 14 Hz, $-CH_2CH$–), 3.52 (s, 3 H, $COOCH_3$), 3.88 (s, 1 H, OH), 6.10 (d, 1 H, J = 8 Hz, NH), 6.30 (d, J = 16 Hz, CH=CH), 7.18–7.38 (m, 5 H, ArH), 7.73 (d, 2 H, J = 8 Hz, tosyl H), 7.87 (d, J = 7 Hz, 1 H, indole 5H). IR (KBr) 3470 (OH), 3310 (NH), 1745 ($COOCH_3$), 1675 ($NHCOCH_3$), 1539 ($NHCOCH_3$) cm^{-1}. Anal. Calcd for $C_{26}H_{30}N_2O_6S$: C, 62.63; H, 6.07; N, 5.62. Found: C, 62.54; H, 6.00; N, 5.53.

Dehydration of 11 with Acetyl Chloride/Pyridine. A mixture of 0.997 g (2.0 mmol) of **11**, 0.204 g (2.6 mmol, 1.3 equiv) of acetyl chloride, and 0.206 g (2.6 mmol, 1.3 equiv) of pyridine in 25 mL of benzene was heated under reflux for 1.5 h. The mixture was cooled to room temperature and poured into 40 mL of 5% aqueous sodium bicarbonate solution. the aqueous layer was extracted with 25 mL of benzene and the combined organic layer washed with saturated aqueous sodium chloride solution. The organic layer was dried ($MgSO_4$), filtered, and evaporated under reduced pressure, leaving 0.956 g (99%) of diene **12** as a colorless glassy solid. This compound decomposed on standing and was used without further purification: ^{1}H NMR ($CDCl_3$) δ 1.88 (s, 3 H, H_2C=CCH_3), 1.99 (s, 3 H, $-NHCOCH_3$), 2.35 (s, 3 H, tosyl CH_3), ABX system, δ_A 3.25, δ_B 3.48, δ_X 4.90 (J_{AX} = 8.3 Hz, J_{BX} = 5.6 Hz, J_{AB} = 15.8 Hz, $-CH_2CH$–), 3.72 (s, 3 H, $COOCH_3$), 5.12 (b s, 2 H, C=CH_2), 5.91 (b d, 1 H, J = 7.5 Hz, $-NHCOCH_3$), 6.68 (d, 1 H, J = 15.6 Hz, indole $-CH$=CH–), 7.06 (d, 1 H, J = 15.6 Hz, indole –CH=CH–), 7.20–7.45 (m, 5 H, ArH), 7.72 (d, 2 H, J = 7.9 Hz, tosyl H), 7.89 (d, 1 H, J = 7.5 Hz, indole 7H); IR (neat) 3280 (NH), 1732 ($COOCH_3$), 1637 ($NHCOCH_3$) cm^{-1}.

Hydridopalladation of Diene 12 To Give 13. A mixture of 0.702 g (1.46 mmol) of diene **12** and 17.7 mL of 0.1 M (1.77 mmol, 1.2 equiv) lithium trichloropalladate in acetonitrile in 28 mL of benzene was stirred at room temperature for 5 min. *n*-Butylmercuric chloride (0.471 g, 1.1 equiv) was added and the mixture degassed, left under an argon balloon, and stirred at room temperature for 24 h. The mixture was filtered through Celite and the solvent evaporated under reduced pressure. The residue was purified on a 4-mm silica gel chromatotron plate, eluting with dichloromethane–methanol (9:1), to give 0.728 g (80%) of **13** as a yellow solid. Recrystallization from hexane–ethyl acetate gave the analytical sample; mp 160–165 °C. ^{1}H NMR (CD_3CN, ~2:1 mixture of diastereomers): (a) δ 1.40 (s, cis-CH_3 on π-allyl), 1.78 (s, 3 H, $NHCOCH_3$), 1.85 s, 3 H, trans-CH_3 on π-allyl), 2.32 (s, 3 H, tosyl CH_3), 3.20–3.40 and 3.55–3.75 (m, AB portion of ABX system, 2 H, $-CH_2CH$–), 3.68 (s, 3 H, $COOCH_3$), 4.65–4.80 (m, X portion of ABX system, $-CH_2CH$–), 5.22 (d, 1 H, J = 11.6 Hz, π-allyl H), 5.83 (d, 1 H, J = 11.6 Hz, π-allyl H), 6.98 (b s, 1 H, NH), 7.31 (d, 2 H, J = 7.6 Hz, tosyl H), 7.56 (s, 1 H, indole 2 H), 7.66 (t, 1 H, J = 7.6 Hz, indole 6H), 7.77 (d, 2 H, J = 7.6 Hz, tosyl H), 7.96 (d, 1 H, J = 7.6 Hz, indole 5H); (b) δ 1.35 (s, 3 H, cis-CH_3 on π-allyl), 1.45 (s, 3 H, $NHCOCH_3$), 1.92 (s, 3 H, trans-CH_3 on π-allyl), 2.32 (s, 3 H, tosyl CH_3), 3.20–3.40 and 3.55–3.75 (m, AB portion of ABX system, 2 H, $-CH_2CH$–), 3.61 (s, 3 H, $COOCH_3$), 4.65–4.80 (m, X portion of ABX system, 1 H, $-CH_2CH$–), 5.19 (d, 1 H, J = 11.6 Hz, π-allyl H), 5.72 (d, 1 H, J = 11.6 Hz, π-allyl H), 6.89 (b s, 1 H, NH), 7.25 (d, 2 H, J = 7.6 Hz, tosyl H), 7.56 (s, 1 H, indole 2H), 7.66 (t, 1 H, J = 7.6 Hz, indole 6H), 7.78 (d, 2H, J = 7.6 Hz, tosyl H), 7.98 (d, 1 H, J = 7.6 Hz, indole 5H). IR (KBr): 3360 (NH), 1745 ($COOCH_3$), 1678 ($NHCOCH_3$), 1660 ($NHCOCH_3$) cm^{-1}. Anal. Calcd for $C_{52}H_{58}Cl_2N_4O_{10}Pd_2S_2$: C, 50.09; H, 4.69; N, 4.49; S, 5.14. Found: C, 49.91; H, 4.70; N, 4.49; S, 4.92.

Alkylation of π-Allyl 13 with Dimethyl Malonate. A solution of 0.022 g (0.035 mmol) of **13** and 0.055 g (0.212 mmol, 6 equiv) of triphenyl-

phosphine in 10 mL of tetrahydrofuran was stirred under argon at room temperature for 15 min and then cooled to 0 °C. A solution of dimethyl sodiomalonate (from 0.0093 g (0.070 mmol, 2 equiv) of dimethyl malonate and 0.0017 g (0.070 mmol, 2 equiv) of sodium hydride) was added via syringe in one portion. The mixture was allowed to warm to room temperature and stirred overnight. The reaction mixture was partitioned between water and diethyl ether. The aqueous layer was extracted twice with diethyl ether, and the combined organic layer was washed with saturated aqueous sodium chloride solution. The organic layer was dried ($MgSO_4$), filtered, and evaporated under reduced pressure. Chromatographic purification (1-mm silica gel chromatotron plate, 3:1 hexane/ethyl acetate followed by preparative thin-layer chromatography, 3:1 hexane/ethyl acetate) gave 0.012 g (56%) of **14** as a clear oil: ^{1}H NMR ($CDCl_3$) δ 1.35 (s, 3 H, CH_3), 1.36 (s, 3 H, CH_3), 1.90 (s, 3 H, $-NHCOCH_3$), 2.34 (s, 3 H, tosyl CH_3), ABX system, δ_A 3.19, δ_B 3.39, δ_X 4.85 (J_{AX} = 8.3 Hz, J_{BX} = 5.3 Hz, J_{AB} = 15.5 Hz, $-CH_2CH-$), 3.48 (s, 1 H, $-CH(COOCH_3)_2$), 3.69 (s, 6 H, $-CH(COOCH_3)_2$), 3.70 (s, 3 H, $-COOCH_3$), 6.09 (d, 1 H, J = 7.8 Hz, $-NHCOCH_3$), 6.28 (d, 1 H, J = 15.8 Hz, indole $-CH=CH-$), 6.92 (d, 1 H, J = 15.8 Hz, indole $-CH=CH-$), 7.15-7.30 (m, 4 H, ArH), 7.41 (s, 1 H, indole 2*H*), 7.72 (d, 2 H, J = 8.2 Hz, ArH), 7.77 (d, 1 H, J = 7.5 Hz, indole 7*H*); IR (neat) 3300 (NH), 1745 ($COOCH_3$), 1735 ($COOCH_3$), 1645 ($NHCOCH_3$) cm^{-1}. Anal. Calcd for $C_{31}H_{36}N_2O_9S$: C, 60.77; H, 5.92; N, 4.57; S, 5.23. Found: C, 60.65; H, 6.19; N, 4.29; S, 5.41.

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Epoxidation of 3,6-Di-*tert*-butyl-2,2,7,7-tetramethyl-3,4,5-octatriene. Isolation of a Stable Methylenecyclopropanone

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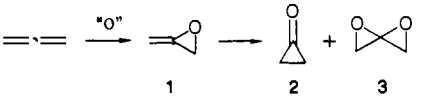
Abstract: The oxidation of 3,6-di-*tert*-butyl-2,2,7,7-tetramethyl-3,4,5-octatriene (**4**) with *m*-chloroperbenzoic acid gave the methylenecyclopropanone derivative **5** as the major product, along with the methyleneoxetanone **6** and *m*-chlorobenzoate **7**. Low-temperature ^{1}H and ^{13}C NMR studies indicate the formation of an unstable precursor to the observed products which is assigned the cumulene oxide structure **11**.

The peracid oxidation of allenes has been demonstrated to involve allene oxides (methyleneoxiranes, **1**) and cyclopropanones (**2**), as well as spirodioxides (**3**) derived from the further epoxidation of **1**.[1,2] While these species are normally reactive intermediates that evolve into stable products under the reaction conditions, examples of each have been isolated and characterized in instances where bulky substituents serve to stabilize these fragile molecules.[1] We have recently begun to extend our epoxidation studies to higher cumulenes[3] and report herein our initial results concerning the peracid oxidation of the highly hindered cumulene 3,6-di-*tert*-butyl-2,2,7,7-tetramethyl-3,4,5-octatriene (**4**).[4,5]

Reaction of **4** with 1.3 equiv of *m*-chloroperbenzoic acid (MCPBA) in CH_2Cl_2 at 0 °C with the exclusion of light gave a mixture of three products that were isolated by chromatography over silica gel, again with protection from light. These products are assigned structures **5** (84% yield), **6** (8%), and **7** (2%) on the basis of spectroscopic and chemical characterization.

Scheme I



Methylenecyclopropanone **5**[5] is a dark yellow solid, mp 56-57 °C, which analyzes for $C_{20}H_{36}O$ and shows an M + 1 peak at *m/e* 293 in its chemical-ionization mass spectrum (CH_4). Its IR spectrum (Nujol) shows a strong, high-frequency carbonyl band at 1785 cm^{-1}, as well as a strong band at 1585 cm^{-1} for the carbon-carbon double bond.[6] The 300-MHz proton NMR spectrum ($CDCl_3$) reveals sharp singlets at δ 1.14, 1.31, and 1.43 in a 2:1:1 ratio. The UV spectrum (2,2,4-trimethylpentane) manifests an unusually long wavelength $n \rightarrow \pi^*$ absorption at 435 nm (ϵ 91) in addition to a relatively weak $\pi \rightarrow \pi^*$ band at 260 nm (ϵ 6640).[6] Finally, the 75.4-MHz ^{13}C NMR spectrum ($CDCl_3$) of **5**, including a proton-coupled experiment, is fully consistent with this formulation: δ 30.9 (q), 31.3 (q), 32.2 (q), 37.3 (s), 38.5 (s), 42.5 (s), 53.9 (s), 121.4 (s), 164.5 (s), 208.4 (s).

Methylenecyclopropanone **5** is light-sensitive, decomposing essentially quantitatively to tetra-*tert*-butylallene (**8**)[8] merely upon exposure to sunlight for a few minutes.[7] A similar conversion to **8** was provoked by preparative GC of **5** with the injector port at 250 °C. Nonetheless, **5** was remarkably stable to a variety of

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