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An Entry to Functionalized 2,8-Ethanonoradamantane Derivatives

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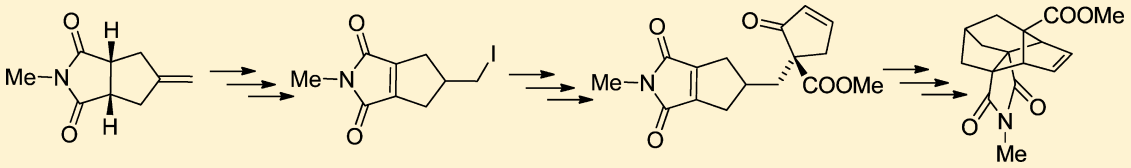
Supporting Information



ABSTRACT: The synthesis of a functionalized derivative containing the 2,8-ethanonoradamantane carbocyclic skeleton, whose key-step consists of an intramolecular Diels–Alder reaction, is described. Chemoselective reduction of an intermediate enone required protection of the maleimide function through their Diels–Alder adducts with furan.

INTRODUCTION

Compounds containing carbocyclic cage structures, such as adamantyl groups, are of significant interest in medicinal chemistry. At present, seven drugs containing the adamantane skeleton are being used clinically (Figure 1): Amantadine, rimantadine and tromantadine as antiviral agents, amantadine for the treatment of Parkinson's disease, memantine for the treatment of Alzheimer's disease, adapalene for the treatment of acne vulgaris, and vildagliptin and saxagliptin for the treatment of type 2 diabetes. Also, many other adamantane derivatives are under study at different levels, as neuroactive, anticancer, anti-infective, antihypertensive and anti-inflammatory agents.[1]

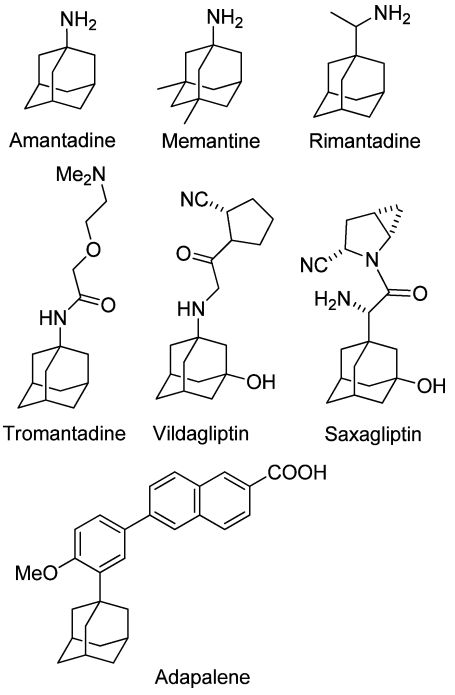


Figure 1. Drugs in clinical use, containing the adamantane skeleton.

Drugs containing other cage structures are very limited, probably due to the lack of readily available cage precursors. However, several compounds containing cage structures different from adamantane have been studied as neuroprotective agents,[2−5] HIV-1 protease inhibitors[6,7] and antivirals[8−10] (Figure 2).

In connection with the preparation of novel cage compounds with potential biological activity, we were interested in the synthesis of functionalized 2,8-ethanonoradamantane derivatives as key synthetic intermediates. Literature about 2,8-ethanonoradamantane or tetracyclo[6.2.1.0^{2,6}.0^{5,10}]undecane derivatives is very limited, and so far only three type of synthetic approaches have been described, in all cases from very specific precursors and leading to a limited number of functionalized derivatives, namely, (1) by intramolecular keto carbene insertion,[11] (2) by formic acid induced rearrangement,[12] and (3) by BF_3·Et_2O catalyzed transannular cyclization[13] (Figure 3).

Herein we report a rationally designed entry into a polyfunctionalized compound containing this carbocyclic skeleton, based on the retrosynthetic analysis shown in Scheme 1, whose key-step consists of an intramolecular Diels–Alder reaction.

RESULTS AND DISCUSSION

The starting compound **4** was recently described by our group.[14] To transform compound **4** into alkylating agent **3**, we first submitted **4** to hydroboration with 9-borabicyclo[3.3.1]-nonane (9-BBN) followed by oxidation with aqueous 35% H_2O_2 under basic conditions. Although we obtained the desired alcohol **5** as a mixture of stereoisomers, we could not separate it from the *cis*-cyclooctane-1,5-diol, formed as a byproduct.

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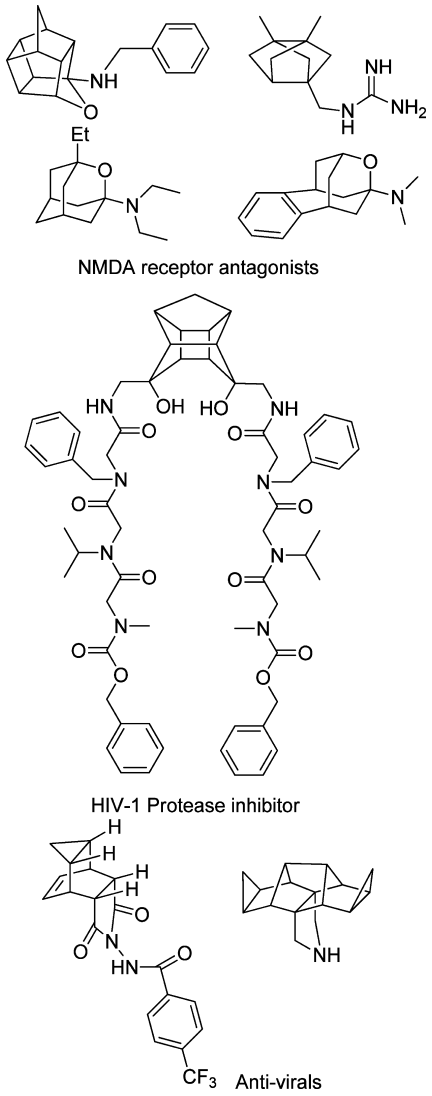


Figure 2. Biologically active cage derivatives.

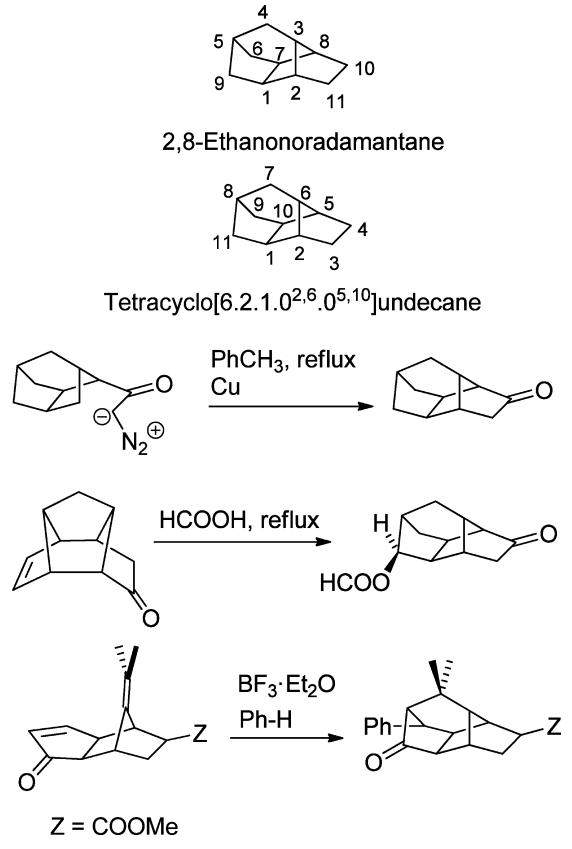
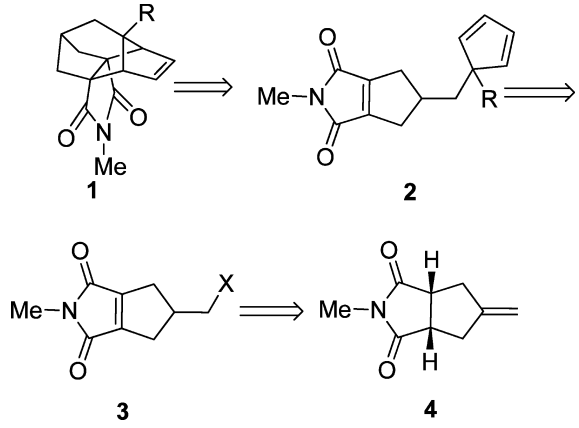


Figure 3. Structure of 2,8-noradamantane or tetracyclo[6.2.1.0^{2,6}.0^{5,10}]-undecane and known procedures to prepare compounds containing this carbocyclic skeleton.

Scheme 1. Retrosynthetic Analysis of 2,8-Noradamantane Derivative 1



Hydroboration of **4** with BH_3·THF complex followed by H_2O_2 oxidation gave an essentially 1:1 mixture of alcohol **5** plus its C5 epimer in 55% yield. Although both stereoisomers of **5** might be converted into **3**, for analytical reasons we preferred to carry out first this transformation by working with one stereoisomer. To this end, we carried out the hydroboration with dicyclohexylborane, generated in situ by reaction of the BH_3·THF complex with cyclohexene (Scheme 2). The method of Brown et al.[15] was followed, except for the use of BH_3·THF complex instead of BH_3·SMe_2. By using this reagent, after H_2O_2 oxidation of the reaction mixture and column chromatography of the crude product, we obtained pure alcohol **5** and mixtures of **5** and its C5 epimer. Altogether we obtained both alcohols in 55% yield with a calculated ratio of about 88:12 (^{1}H NMR). The configuration of the main stereoisomer was established to be that shown for **5** with the hydroxymethyl group in an exo arrangement on the basis of the ^{1}H NMR and NOESY data. This compound seems to exist preferentially with the cyclopentane ring in the shown envelope conformation with the hydroxymethyl group in a pseudoequatorial position, as shown by the observed coupling constants ($J_{3aH/4\text{-}Hn}$ ~ 0 Hz; $J_{3aH/4\text{-}Hx}$ ~ 9.6 Hz; $J_{4\text{-}Hx/4\text{-}Hn}$ = 13.2 Hz; $J_{4\text{-}Hx/5\text{-}H}$ = 12.0 Hz; $J_{4\text{-}Hn/5\text{-}H}$ = 5.7 Hz), the fourth one suggesting dihedral angles H−C5−C4−H_x and H−C5−C6−H_x close to 180°. Also, a stronger NOE among the 3a-H/4-H_x and 6a-H/6-H_x than among the 3a-H/4-H_n and 6a-H/6-H_n pairs of protons was observed in the NOESY experiment.

Protection of the hydroxyl group of the stereoisomerically pure **5** as *t*-butyldimethylsilyl ether was performed in high yield using a standard procedure.[16] For the introduction of the unsaturation at the C3a−C6a position, we decided to use the benzeneselenenylation/H_2O_2 oxidation procedure, which is well established for the introduction of a C=C bond in the α,β-position of carbonyl compounds, such as ketones, esters, nitriles, amides or lactams,[17] although we only find application

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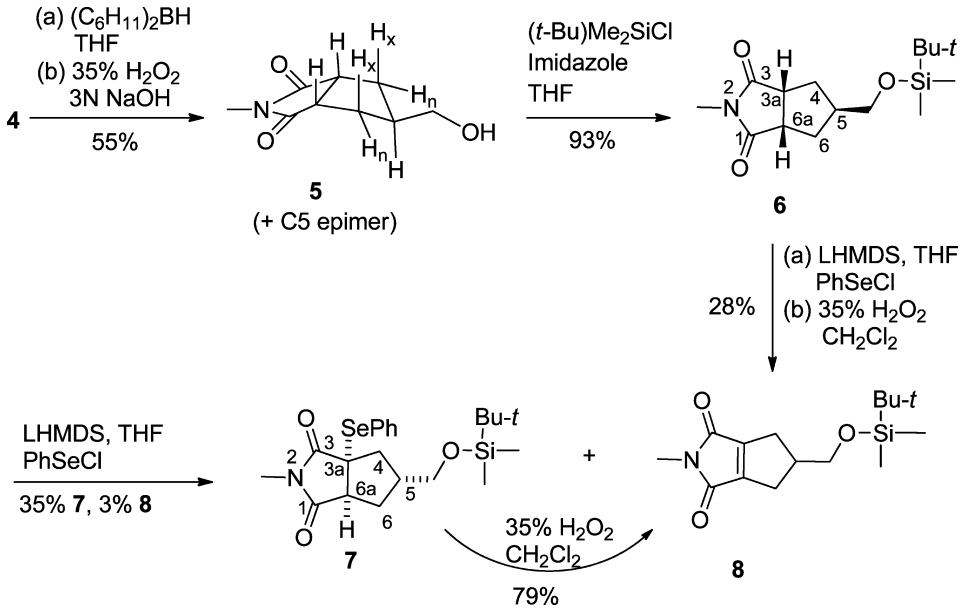
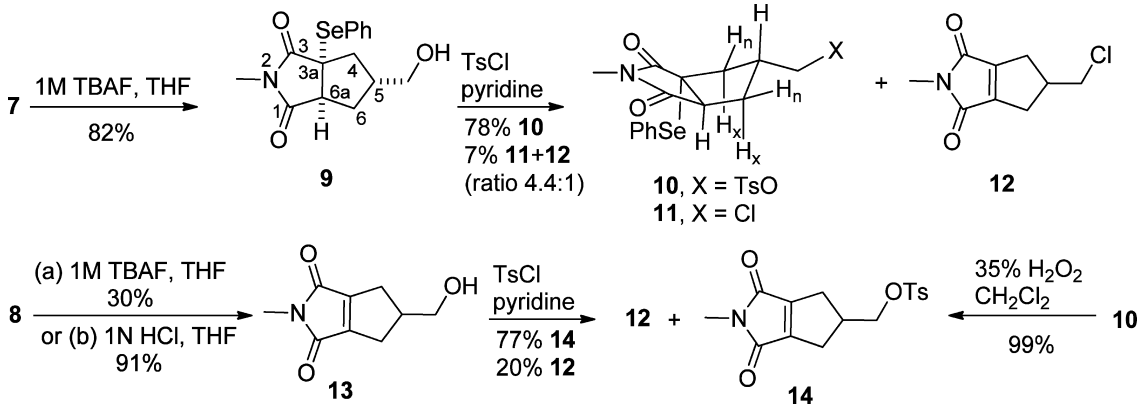
Scheme 2. Preparation of Compounds 7 and 8 from the Starting Imide 4



Scheme 3. Preparation of Tosylates 10 and 14



of this procedure to transform succinimide derivatives to the corresponding maleimides, in the case of α-acylsuccinimides.[18] Benzeneselenenylation of succinimide **6** was carried out by reaction with lithium hexamethyldisilazide (LHMDS), prepared in situ by reaction of hexamethyldisilazane (HMDS) with *n*-BuLi in hexanes, followed by reaction with benzeneselenenyl chloride.[17] The benzeneselenenylated product **7** was obtained in only 35% yield, the elimination product **8** was also isolated in 3% yield, and much starting compound **6** was recovered (37%), in spite of using an excess of base. Formation of **8** might take place by base-induced elimination of benzeneselenol from **7**. Hydrogen peroxide oxidation of **7** gave in good yield maleimide **8**. More conveniently, oxidation of the crude mixture from the benzeneselenenylation of **6** gave compound **8** in 28% yield. The relative configuration of **7** and its derivatives was established as before on the basis of the ^{1}H NMR and NOESY data for its derived tosylate **10** (Scheme 3). The cis relationship among the benzeneselenenyl group at C3a and 6a-H is required to allow the syn-elimination of phenylselenenic acid from the intermediate selenoxide during the transformation of **7** to **8**. Compound **7** and its derivatives (**9**, **10**, **11**, **15**, **16**, **23** and **24**) are racemic compounds, and the configurations shown for them correspond to the first enantiomer described by their IUPAC names (see the Experimental Section).

Reaction of **7** with tetrabutylammonium fluoride (TBAF)[16] gave in good yield the corresponding alcohol **9**, which on reaction with tosyl chloride gave tosylate **10** (Scheme 3). Column chromatography of the crude tosylate allowed us to isolate pure tosylate **10** in 78% yield and a mixture of chlorides **11** and **12** in a ratio about 4.4:1 (by ^{1}H NMR) in 7% yield. From the ^{1}H NMR spectrum of tosylate **10**, the following coupling constants were obtained: $J_{4\text{-Hx}/4\text{-Hn}}$ = 13.2 Hz, $J_{4\text{-Hx}/5\text{-H}}$ ~ 11.8 Hz, $J_{4\text{-Hn}/5\text{-H}}$ ~ 6.0 Hz, $J_{5\text{-H}/CH2OTs}$ = 6.0 Hz, $J_{4\text{-Hn}/6\text{-Hn}}$ ~ 1.2 Hz, $J_{5\text{-H}/6\text{-Hx}}$ ~ 10.4 Hz, $J_{5\text{-H}/6\text{-Hn}}$ ~ 6.0 Hz, $J_{6\text{-Hx}/6\text{-Hn}}$ = 12.6 Hz, $J_{6\text{-Hx}/6a\text{-H}}$ ~ 10.4 Hz, $J_{6\text{-Hn}/6a\text{-H}}$ ~ 0 Hz). Also, a NOE among 6a-H/6-H_x stronger than among 6a-H/6-H_n was observed. All these data suggest that the configuration and the preferred conformation of **10** is that shown, in which the cyclopentane ring is in an envelope conformation with the tosyloxymethyl group in a pseudoequatorial arrangement. Although chloride **12** (1.3% yield) might be formed from chloride **11** by pyridine-induced elimination of phenylselenol, we cannot discard the possibility that the starting alcohol **9** contained a small amount of alcohol **13**.

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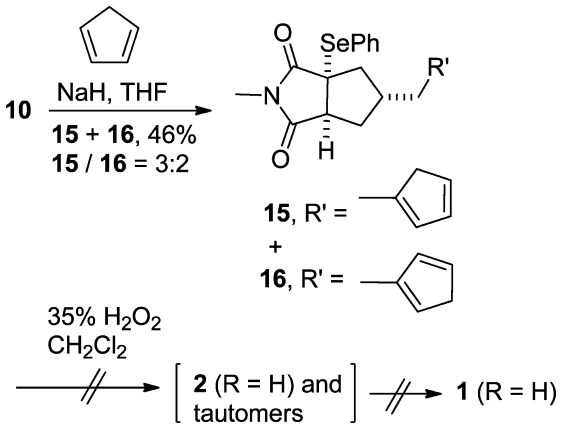
Surprisingly, reaction of **8** with TBAF gave the expected alcohol **13** in only 30% yield. Hydrolysis of the imide function was observed when deprotection of **8** was attempted with 1 M HCl in a mixture of THF and MeOH at room temperature for 3 d.[19] Fortunately treatment of **8** with 1 M HCl in THF gave alcohol **13** in high yield. Tosylation of **13** gave mainly tosylate **14**, chloride **12** being also formed in low yield. Both compounds could be separated by column chromatography and fully characterized. Alternatively, tosylate **14** was obtained in high yield from tosylate **10** by oxidation with H_2O_2 and elimination of the benzeneselenenyl group.

Reaction of tosylate **14** with sodium cyclopentadienide in THF at low temperature (−40 °C or from 0 °C to room temperature) gave a mixture of products in which neither the expected substitution product **2** (R = H) or tautomers nor the desired intramolecular Diels−Alder adduct **1** (R = H) were detected by ^{1}H NMR. Alternatively, reaction of tosylate **10** with sodium cyclopentadienide in THF at −40 °C gave in 46% yield a mixture of the substitution products **15** and **16** in a ratio about 3:2, established by integration of the fully differentiated signals corresponding to the cyclopentadienyl group of both tautomers (Scheme 4).[20] However, oxidation of this mixture

Scheme 4. Attempted Preparation of Tetracycle 1 (R = H)



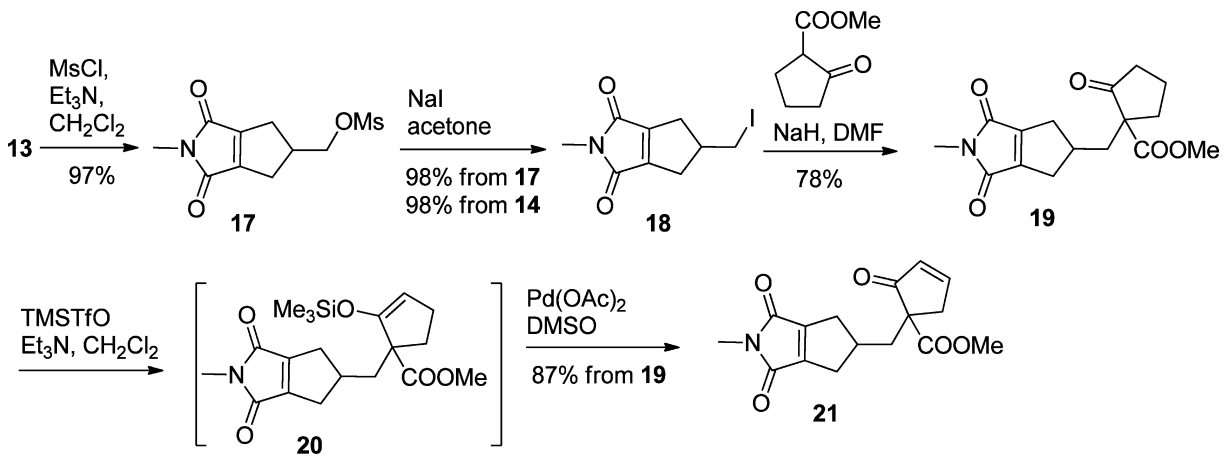
with H_2O_2 gave a complex mixture of products not containing (^{1}H NMR) the expected compound **1** (R = H) or its precursor **2** (R = H) or its tautomers. The last products might have polymerized through intermolecular Diels−Alder reactions.

To favor the intramolecular cycloaddition in compound **2**, we then planned the preparation of **2** (R = COOMe) using a methodology we had previously used to prepare methyl 1-benzylcyclopenta-2,4-diene-1-carboxylate.[21] Reaction of alcohol **13** with mesyl chloride in CH_2Cl_2 in the presence of Et_3N[22] gave mesylate **17** in 97% yield (Scheme 5). In this case, formation of the corresponding chloride **12** was not observed. To favor C-alkylation in the alkylation step leading to compound **19**, mesylate **17** and tosylate **14** were transformed in high yield into iodide **18** by reaction with NaI in acetone under reflux.[23] Reaction of iodide **18** with the sodium salt of methyl 2-oxocyclopentane-1-carboxylate in DMF at 0 °C for 4 h gave product **19** in 78% yield, after purification by column chromatography. Reaction of **19** with trimethylsilyl triflate (TMSOTf) in CH_2Cl_2 in the presence of Et_3N gave the corresponding trimethylsilyl enol ether **20**, which was used as such in the next step. Oxidation of **20** with $Pd(OAc)_2$ in DMSO at room temperature for 16 h gave enone **21** in 87% global yield from ketone **19**, after purification by column chromatography (Scheme 5).[24] Worthy of note and contrarily to our previous experience,[21] oxidation of **20** by using a catalytic amount of $Pd(OAc)_2$ (5−10%) and oxygen,[25,26] or by using $Pd(OAc)_2$ (0.5 equiv) plus benzoquinone (0.5 equiv) as in the original method of Saegusa,[27,28] gave a low yield of **21** (25 and 53% yield, respectively).

Reduction of the ketone function of **21** with $NaBH_4$ in the presence of $CeCl_3{\cdot}7H_2O$ (Luche conditions),[29] under similar conditions to those used for the preparation of a related compound,[21,26] gave a stereoisomeric mixture **22**, derived from the reduction not only of the ketone but also of the imide functions (Scheme 6). To study the possibility of carrying out a chemoselective reduction of **21**, we performed this transformation under different conditions, using an excess of $CeCl_3{\cdot}7H_2O$, taking into account the possible preferential coordination of the imide function, and reducing the amount of $NaBH_4$ until 0.5 mol $NaBH_4$/mol **21**, always working at −40 °C for 15 min. When the molar ratio $NaBH_4$/**21** was 1.0 or 0.5, mixtures of all possible products derived from the reduction of the enone, the imide or both functions of **21** plus starting compound were obtained in different ratio.

We observed that tosylate **10**, which contains a succinimide function instead of the maleimide function, was not reduced with $NaBH_4/CeCl_3{\cdot}7H_2O$ at −40 °C for 15 min. Consequently, we planned the transformations shown in Scheme

Scheme 5. Preparation of Enone 21



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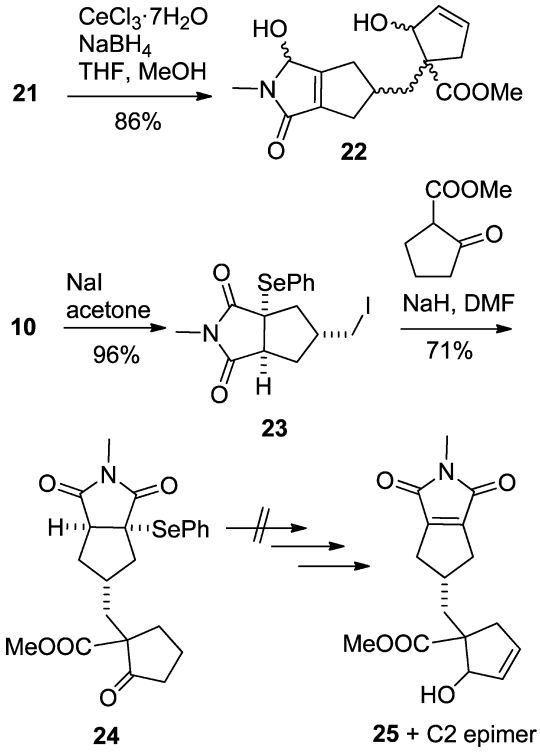
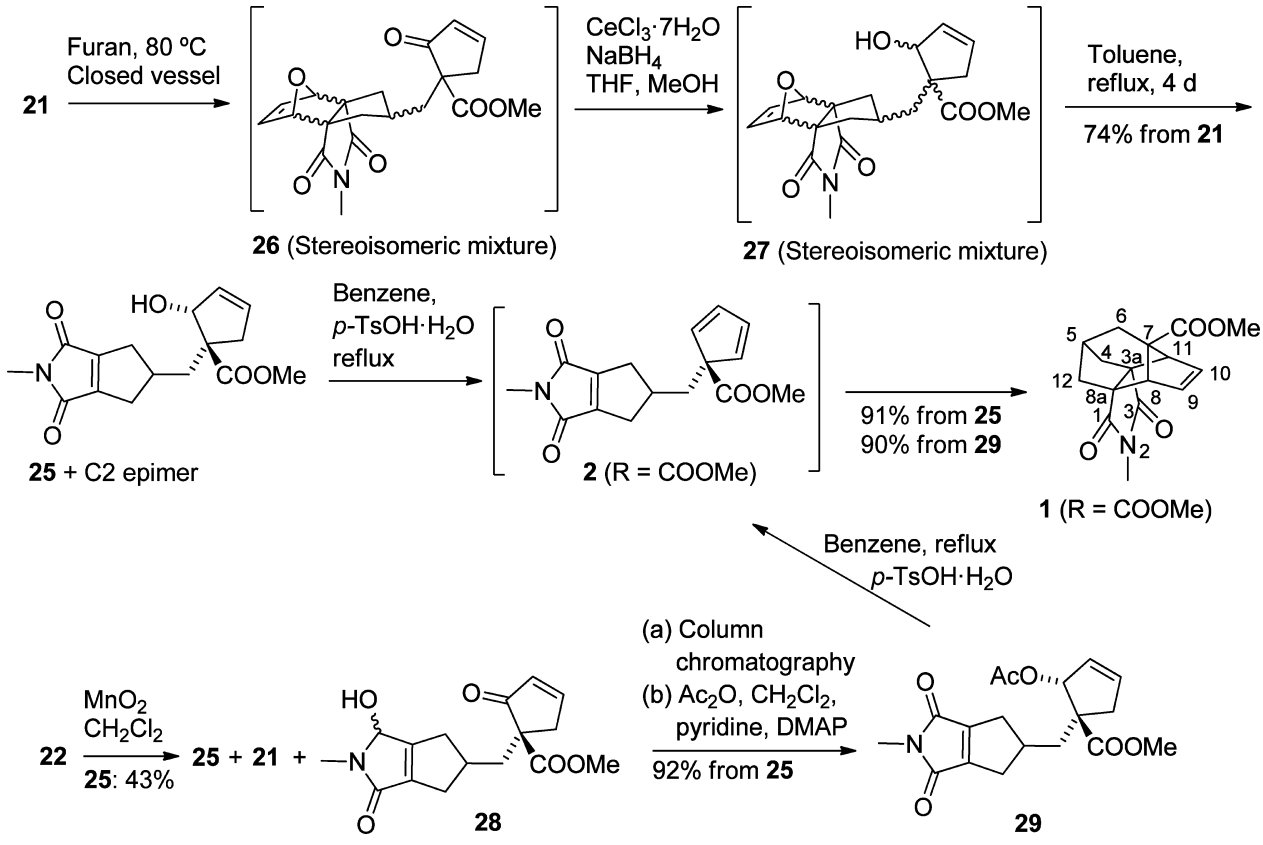
Scheme 6. Thwarted Attempts to Prepare Compound 25



6 from tosylate **10**, which was transformed as before into the corresponding iodide **23** and reacted with the sodium salt of methyl 2-oxocyclopentanecarboxylate to give **24** in good yield, as a mixture of two diastereoisomeric racemic pairs. However, reaction of **24** with TMSOTf did not give the corresponding silyl enol ether, from which allylic alcohol **25** might have been prepared (Scheme 6).

Alternatively, we could prepare alcohol **25** as shown in Scheme 7, by protecting the imide function of **21** as a Diels–Alder adduct with furan. Reaction of **21** with an excess of furan in a closed glass vessel at 80 °C for 24 h gave quantitatively a stereoisomeric mixture of four possible racemic pairs in different ratio (^{1}H NMR). From the ^{1}H NMR data (δ 6.13–6.18 and 7.72–7.80 ppm, cyclopentenone 3-H and 4-H, respectively), it was clear that the cyclopentenone moiety was present, and thus, this moiety had not reacted with furan. Reduction of the stereoisomeric mixture **26** with $NaBH_4$/$CeCl_3·7H_2O$ at −40 °C for 1 h gave a stereoisomeric mixture of allylic alcohols **27**. From the ^{1}H NMR data (δ 5.75–5.79 and 5.87–5.95 ppm, cyclopentenol 4-H and 3-H, respectively, and 4.85–5.09 ppm, cyclopentenol 2-H plus allylic H from the dihydrofuran moiety), it was clear that the enone function had been reduced, while the absence of signals around δ 4.4–4.8 ppm (MeN-C*H*OH- type of proton) was indicative that the imide function had not been reduced. Upon heating the stereoisomeric mixture **27** in an open vessel in toluene under reflux, after 4 days, most of the Diels–Alder adducts had experienced a retro-Diels–Alder reaction. When working in xylene under reflux, much degradation of the product was observed. Worthy of note, the more abundant stereoisomers **27** experienced this retro-Diels–Alder process faster than the less abundant ones, so that they became the main starting stereoisomers **27** remaining in the reaction mixture when the retrocycloaddition was stopped. From the reaction mixture, the

Scheme 7. Alternative Preparations of Compound 25 and Conversions to Polycycle 1 (R = COOMe)



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main alcohol **25** plus mixtures of **25** and its C2 epimer were isolated in 74% yield by column chromatography. By analogy with previous results,[21] the main stereoisomer must be the one shown, in which the hydroxyl function is trans with respect to the methoxycarbonyl group. This three-step transformation is worthy of note, since the retro Diels−Alder reaction leading to the maleimide product **25** takes place in toluene under reflux. The protection of 2,3-unsubstituted maleimides as furan adducts and its deprotection in refluxing anisole has been described.[30] However, to the best of our knowledge, a similar deprotection of 2,3-disubstituted maleimides[31] or maleic anhydrides[32,33] from their Diels−Alder adducts has usually been effected under flash vacuum pyrolysis (FVP) conditions at temperatures close to 400 °C.

p-Toluenesulfonic acid catalyzed dehydration of alcohol **25** in refluxing benzene, under similar conditions to those used for the preparation of methyl 1-benzylcyclopenta-2,4-dienecarboxylate,[21] led in good yield to the desired product **1** (R = COOMe), reasonably formed by intramolecular Diels−Alder reaction from cyclopentadiene maleimide **2** (R = COOMe).

This product was also obtained in an alternative less convenient way from the stereoisomeric mixture **22** by controlled oxidation with MnO_2 in CH_2Cl_2.[34] This oxidation is not chemoselective, and using a limited amount of MnO_2 led to a mixture of products, which on column chromatography gave mixtures of the two less polar products **21** and **25** and of the two more polar starting compound **22** and a product containing the enone function, whose probable structure corresponds to hydroxylactam **28**. From the integral of the olefinic and C*H*−OH protons of the different products in these fractions and their weight, the following yields of formed products could be calculated: alcohol **25** (43%), enone **21** (12%), hydroxylactam **28** (13%), recovered **22** (10%). Acetylation of a mixture of the main stereoisomer of allylic alcohol **25** and enone **21** (ratio alcohol **25**/enone **21** = 3:1) with acetic anhydride in CH_2Cl_2 in the presence of pyridine and a catalytic amount of 4-dimethylaminopyridine (DMAP) gave a mixture of acetate **29** and enone **21**, which could be easily separated by column chromatography yielding stereoisomerically pure acetate **29** in 92% global yield from the amount of alcohol **25** in the starting mixture. Acid catalyzed elimination of acetic acid from acetate **29** as described before for the dehydration of alcohol **25** led in high yield to the same polycyclic product **1** (R = COOMe).

CONCLUSION

In conclusion, we have developed a synthetic entry to a highly functionalized 2,8-ethanonoradamantane derivative, whose key step consists of an intramolecular Diels−Alder reaction. Protection of a maleimide function during the $NaBH_4$/$CeCl_3{\cdot}7H_2O$ reduction of an enone has been nicely achieved by selective cycloaddition of the maleimide with furan, deprotection after enone reduction being effected in refluxing toluene. This polycyclic compound might be a new scaffold for the preparation of compounds with potential biological activity.

EXPERIMENTAL SECTION

General Methods. Melting points were determined in open capillary tubes. Chemical shifts (δ) are reported in ppm related to internal TMS or $CDCl_3$. Multiplicities are reported using the following abbreviations: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad or their combinations. Assignments given for the NMR spectra are based on DEPT, $^1H/^{13}C$ single quantum correlation (gHSQC sequence) and $^1H/^{13}C$ multiple bond correlation (gHMBC sequence) experiments and also, for certain compounds, on NOESY spectra information. Infrared spectra were obtained by using the attenuated total reflectance (ATR) technique. Absorption values are given as wavenumbers (cm^{-1}), and the intensities of the absorptions are given as strong (s), medium (m) or weak (w). High-resolution mass spectra (HRMS) were obtained with electrospray ionization using a TOF mass analyzer (ESI-MS) and are reported as m/z (relative ratio). Flash column chromatography was performed on silica gel 60 A C.C (35−70 mesh). The eluents employed are reported as volume/volume percentages. For the thin layer chromatography (TLC), aluminum-backed sheets with silica gel 60 F_{254} were used, and spots were visualized with UV light and/or 1% aq $KMnO_4$.

(3a*R*,5*s*,6a*S*)-2-Methyl-5-(hydroxymethyl)-4,5,6,6a-tetrahydrocyclopenta[c]pyrrole-1,3(2*H*,3a*H*)-dione, 5. To a cold (0 °C, ice−water bath) solution of cyclohexene (3.7 mL, 3.0 g, 36.5 mmol) in anhydrous THF (15 mL), a solution of the $BH_3{\cdot}$THF complex in THF (1M, 17.7 mL, 17.7 mmol) was added dropwise. Then, the reaction mixture was stirred for 15 min at 0 °C and for 2 h at room temperature. After cooling again to 0 °C, a solution of **4** (1.01 g, 6.10 mmol) in THF (67 mL) was added dropwise, and the reaction mixture was stirred for 4 h at this temperature. Absolute EtOH (12 mL) was added dropwise, and the mixture was stirred for 10 min at room temperature, until no more hydrogen evolution was observed. The mixture was cooled to 0 °C, and aqueous solutions of H_2O_2 (35%, 8 mL) and NaOH (3N, 10.6 mL) were simultaneously added dropwise, keeping the temperature at around 0 °C. The reaction mixture was concentrated, the residue was treated with water (40 mL) and EtOAc (50 mL), the organic phase was separated, and the aqueous one was extracted with EtOAc (2 × 50 mL). The combined organic phases were dried (anhydrous Na_2SO_4) and concentrated in vacuo. The oily residue (3.63 g) was subjected to column chromatography (silica gel, 90 g, hexane/EtOAc mixtures). On elution with EtOAc, in order of elution **5** (253 mg) and mixtures of **5** and its C5 epimer 10:2 (271 mg) and 10:4 (91 mg) were obtained as light yellow oils. Total 614 mg, 55% yield of **5** plus its C5 epimer, **5**/C5 epimer ratio 88:12 (by ^1H NMR). Analytical and spectroscopic data of **5**: R_f = 0.27 (silica gel, 4.9 cm, EtOAc); IR (ATR) ν 3600−3200 (max. at 3432, m), 2949 (m), 2922 (m), 2853 (m), 1771 (w), 1686 (s), 1678 (s), 1432 (m), 1381 (m), 1307 (m), 1281 (m), 1160 (w), 1087 (m), 1026 (m), 996 (m), 972 (m), 603 (m) cm^{-1}; ^1H NMR δ 1.62−1.77 [m, 2H, 4(6)-H_x], 1.87 (ttt, J = 12.0 Hz, J' = 5.7 Hz, J'' = 5.7 Hz, 1H, 5-H), 1.90−2.05 (br s, 1H, OH), 2.19 [dd, J' = 13.2 Hz, J'' = 6.0 Hz, 2H, 4(6)-H_n], 2.94 (s, 3H, *N*-CH_3), 3.16−3.22 [m, 2H, 3a(6a)-H], 3.57 (d, J' = 5.6 Hz, 2H, CH_2OH); ^{13}C NMR δ 25.0 (CH_3, *N*-CH_3), 32.9 [CH_2, C4(6)], 40.6 (CH, C5), 44.8 [CH, C3a(6a)], 64.5 (CH_2, CH_2OH), 180.3 [C, C1(3)]. HRMS (ESI) (m/z) calcd for $[C_9H_{13}NO_3 + H]^+$: 184.0968. Found: 184.0968. Anal. Calcd for $C_9H_{13}NO_3{\cdot}0.1H_2O$ (185.01): C, 58.43; H, 7.19; N, 7.57. Found: C, 58.36; H, 7.41; N, 7.29.

(3a*R*,5*s*,6a*S*)-2-Methyl-5-[(*t*-butyldimethylsilyloxy)methyl]-4,5,6,6a-tetrahydrocyclopenta[c]pyrrole-1,3(2*H*,3a*H*)-dione, 6. To a solution of **5** (490 mg, 2.68 mmol) in anhydrous THF (6 mL), imidazole (432 mg, 6.34 mmol) was added. After the mixture was stirred for 10 min at room temperature, *t*-butyldimethylsilyl chloride (98% content, 487 mg, 3.23 mmol) was added, and the mixture was stirred for 48 h under an Ar atmosphere. The reaction mixture was filtered through a short pad of silica gel and Celite washing the solid with EtOAc (20 mL). The combined filtrate and washings were concentrated in vacuo, and the residue was taken in EtOAc (8 mL), washed with water (3 × 4 mL) and brine (2 × 4 mL), dried (anhydrous Na_2SO_4) and concentrated in vacuo to give **6** (739 mg, 93% yield) as a yellow oil, which was used as such in the next step: R_f = 0.55 (silica gel, 8 cm, EtOAc); IR (ATR) ν 2955 (w), 2928 (w), 2886 (w), 2856 (w), 1774 (w), 1698 (s), 1431 (m), 1383 (m), 1281 (m), 1252 (m), 1117 (m), 1089 (m), 1001 (m), 977 (m), 834 (s), 774 (s) cm^{-1}; ^1H NMR δ 0.01 [s, 6H, $Si(CH_3)_2$], 0.86 [s, 9H, $SiC(CH_3)_3$], 1.70−1.77 [m, 2H, 4(6)-H_x], 1.85 (ttt, J = 11.2 Hz, J' = 5.6 Hz, J'' = 5.6 Hz, 1H, 5-H), 2.14 [dd, J = 13.2 Hz, J' = 6.0 Hz, 2H, 4(6)-H_n], 2.96 (s, 3H, *N*-CH_3), 3.15−3.21 [m, 2H, 3a(6a)-H], 3.54 (d, J = 9.2

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Hz, 2H, CH_2–O); ^{13}C NMR δ −5.5 [CH_3, $Si(CH_3)_2$], 18.3 [C, $SiC(CH_3)_3$], 25.0 (CH_3, *N*-CH_3), 25.8 [CH_3, $SiC(CH_3)_3$], 32.8 [CH_2, C4(6)], 40.7 (CH, C5), 45.0 [CH, C3a(6a)], 64.5 (CH_2, CH_2O–), 180.5 [C, C1(3)]. HRMS (ESI) (*m*/*z*) cacld for $[C_{15}H_{27}NO_3Si + H]^+$: 298.1833. Found: 298.1829. Anal. Calcd for $C_{15}H_{27}NO_3Si$ (297.47): C, 60.57; H, 9.15; N, 4.71. Found: C, 60.51; H, 9.26; N, 4.54.

(3a*RS*,5*RS*,6a*SR*)-5-(*t*-Butyldimethylsilyloxymethyl)-2-methyl-3a-(phenylselanyl)-4,5,6,6a-tetrahydrocyclopenta[c]pyrrole-1,3(2*H*,3a*H*)-dione, 7. To a cold solution (−78 °C, acetone−CO_2 bath) of hexamethyldisilazane (HMDS, 0.74 mL, 3.55 mmol) in anhydrous THF (10 mL), a solution of *n*-BuLi in hexane (2.2 M, 1.34 mL, 2.95 mmol) was added dropwise. The reaction mixture was allowed to warm to 0 °C (ice−water bath) and was stirred for 1 h at this temperature. The mixture was again cooled to −78 °C, and a solution of **6** (695 mg, 2.34 mmol) in anhydrous THF (3 mL) was added dropwise. The reaction mixture was stirred at this temperature for 15 min, allowed to warm to 0 °C, stirred for 1 h at this temperature and cooled again to −78 °C. To the above reaction mixture, a solution of benzeneselenenyl chloride (95% content, 570 mg, 2.83 mmol) in anhydrous THF (5.2 mL) was added. The mixture was stirred for 30 min at −78 °C, allowed to warm to 0 °C, stirred for 30 min at this temperature and then overnight at room temperature. The reaction mixture was quenched with saturated aqueous NH_4Cl solution (5 mL), water (5 mL) and Et_2O (5 mL) were added, the organic phase was separated, and the aqueous one was extracted with Et_2O (2 × 5 mL). The combined organic phases were washed with water, dried (anhydrous Na_2SO_4) and concentrated in vacuo. The residue (1.06 g) was subjected to column chromatography (silica gel, 42.6 g, hexane/EtOAc mixtures). On elution with hexane/EtOAc 9:1, in order of elution, compound **8** (18 mg, 3% yield, 5% yield taking into account the recovered starting compound) and **7** (368 mg, 35% yield, 56% yield taking into account the recovered starting compound) and starting compound **6** (260 mg) were isolated as light yellow oils. Analytical and spectroscopic data of **7**: R_f = 0,32 (silica gel, 5 cm, hexane/EtOAc 9:1); IR (ATR) ν 2952 (w), 2923 (w), 2886 (w), 2855 (w), 1775 (w), 1700 (s), 1429 (m), 1379 (m), 1283 (m), 1252 (m), 1088 (m), 1021 (m), 1005 (m), 834 (s), 775 (s), 742 (s), 693 (m) cm^{-1}; ^1H NMR δ 0.00 [s, 6H, $Si(CH_3)_2$], 0.86 [s, 9H, $SiC(CH_3)_3$], 1.73 (dd, J = 12.0 Hz, J' = 12.8 Hz, 1H, 4-H_x), 1.82−1.91 (complex signal, 2H, 5-H and 6-H_x), 1.98−2.11 (m, 1H, 6-H_n), 2.45−2.50 (m, 1H, 4-H_n), 2.74 (s, 3H, *N*-CH_3), 3.20 (d, J = 9.6 Hz, 1H, 6a-H), 3.52 (d, J = 4.8 Hz, 2H, CH_2–O), 7.27−7.39 [tm, J = 7.4 Hz, 2H, Ar-3(5)-H], 7.36−7.40 (tm, J = 7.4 Hz, 1H, Ar-4-H), 7.59−7.61 [dd, J = 8.2 Hz, J' = 1.2 Hz, 2H, Ar-2(6)-H]; ^{13}C NMR δ −5.5 [CH_3, $Si(CH_3)_2$], 18.3 [C, $SiC(CH_3)_3$], 25.1 (CH_3, *N*-CH_3), 25.8 [CH_3, $SiC(CH_3)_3$], 32.3 (CH_2, C4), 39.4 (CH_2, C6), 41.6 (CH, C5), 53.2 (CH, C6a), 53.9 (C, C3a), 64.0 (CH_2, CH_2–O), 125.9 (C, Ar–C1), 129.2 [CH, Ar–C3(5)], 129.8 (CH, Ar–C4), 137.3 [CH, Ar–C2(6)], 178.2 (C, C3), 179.1 (C, C1). HRMS (ESI) (*m*/*z*) calcd for $[C_{21}H_{32}NO_3{}^{80}SeSi + H]^+$: 454.1326. Found: 454.1311. Anal. Calcd for $C_{21}H_{31}NO_3SeSi$ (452.52): C, 55.74; H, 6.90; N, 3.10. Found: C, 56.21; H, 7.05; N, 3.12.

5-{[(*t*-Butyldimethylsilyl)oxy]methyl}-2-methyl-5,6-dihydrocyclopenta[c]pyrrole-1,3(2*H*,4*H*)-dione, 8. To a cold (0 °C, ice−water bath) and stirred solution of **11** (408 mg, 0.90 mmol) in CH_2Cl_2 (10 mL), a solution of H_2O_2 35% (0.63 mL) in water (1.26 mL) was added dropwise, keeping the temperature around 0 °C. The reaction mixture was allowed to warm to room temperature and stirred for 1 h at this temperature. A saturated aqueous $NaHCO_3$ solution (1.2 mL) was added. The organic phase was separated, and the aqueous one was extracted with CH_2Cl_2 (3 × 5 mL). The combined organic phases were washed with water, dried (anhydrous Na_2SO_4) and concentrated in vacuo. The residue (261 mg) was subjected to column chromatography (silica gel, 6.5 g, hexane/EtOAc mixtures). On elution with hexane/EtOAc 95:5, product **8** (210 mg, 79% yield) was isolated as light yellow oil. An analytical sample of **8** was obtained as a white solid on drying at 10^{-2} Torr: mp 38−40 °C; R_f = 0.26 (silica gel, 7.4 cm, hexane/EtOAc 9:1); IR (ATR) ν 2951 (w), 2923 (w), 2881 (w), 2852 (w), 1769 (w), 1713 (s), 1704 (s), 1470 (w), 1432 (m), 1375 (m), 1366 (m), 1246 (m), 1103 (m), 1082 (m), 1061 (m), 982 (m), 846 (s), 831 (s), 777 (s), 726 (m), 705 (m), 664 (m) cm^{-1}; ^1H NMR δ 0.03 [s, 6H, $Si(CH_3)_2$], 0.86 [s, 9H, $SiC(CH_3)_3$], 2.43−2.58 (m, 2H) and 2.67−2.77 (m, 2H) [4(6)-H_{cis} and 4(6)-H_{trans}], 2.95 (s, 3H, *N*-CH_3), 2.99−3.07 (m, 1H, 5-H), 3.59 (d, J = 6.0 Hz, 2H, CH_2O); ^{13}C NMR δ −5.5 [CH_3, $Si(CH_3)_2$], 18.2 [C, $SiC(CH_3)_3$], 23.7 (CH_3, *N*-CH_3), 25.8 [CH_3, $SiC(CH_3)_3$], 29.5 [CH_2, C4(6)], 44.8 (CH, C5), 65.6 (CH_2, CH_2O), 152.3 [C, C3a(6a)], 167.5 [C, C1(3)]. HRMS (ESI) (*m*/*z*) calcd for $[C_{15}H_{26}NO_3Si + H]^+$: 296.1676. Found: 296.1669. Anal. Calcd for $C_{15}H_{25}NO_3Si$ (295.45): C, 60.98%; H, 8.53%; N, 4.74. Found: C, 60.93; H, 8.67; N, 4.48.

One-Pot Preparation of 8 from 6. To a cold solution (−78 °C, acetone−CO_2 bath) of HMDS (2.77 mL, 13.2 mmol) in anhydrous THF (40 mL), a solution of *n*-BuLi in hexane (2.15 M, 5.1 mL, 11.0 mmol) was added dropwise. The reaction mixture was allowed to warm to 0 °C (ice−water bath) and was stirred for 1 h at this temperature. The mixture was again cooled to −78 °C, and a solution of **6** (2.60 g, 8.74 mmol) in anhydrous THF (15 mL) was added dropwise. The reaction mixture was stirred at this temperature for 15 min, allowed to warm to 0 °C, stirred for 1 h at this temperature and cooled again to −78 °C. To the above reaction mixture, a solution of benzeneselenenyl chloride (98% content, 2.07 g, 10.6 mmol) in anhydrous THF (20 mL) was added. The mixture was stirred for 30 min at −78 °C, allowed to warm to 0 °C, stirred for 30 min at this temperature and then overnight at room temperature. The reaction mixture was quenched with saturated aqueous NH_4Cl solution (18 mL), water (18 mL) and Et_2O (30 mL) were added, the organic phase was separated, and the aqueous one was extracted with Et_2O (2 × 30 mL). The combined organic phases were washed with water, dried (anhydrous Na_2SO_4) and concentrated in vacuo. The residue (4.10 g) was used as such for the next step.

To a cold (0 °C, ice−water bath) and stirred solution of the above crude product (4.10 g) in CH_2Cl_2 (60 mL), a solution of H_2O_2 35% (2.8 mL) in water (5.5 mL) was added dropwise, keeping the temperature around 0 °C. The reaction mixture was allowed to warm to room temperature and stirred for 1 h at this temperature. A saturated aqueous $NaHCO_3$ solution (7 mL) was added, the organic phase was separated, and the aqueous one was extracted with CH_2Cl_2 (2 × 11 mL). The combined organic phases were washed with water, dried (anhydrous Na_2SO_4) and concentrated in vacuo. The residue (2.73 g) was subjected to column chromatography (silica gel, 82 g, hexane/EtOAc mixtures). In order of elution, product **8** (725 mg, 28% total yield from **6**, 53% yield taking into account the recovered starting **6**, hexane/EtOAc 9:1), as light yellow oil, and starting compound **6** (1.23 g, hexane/EtOAc 85:15) were isolated.

(3a*RS*,5*RS*,6a*SR*)-5-(Hydroxymethyl)-2-methyl-3a-(phenylselanyl)-4,5,6,6a-tetrahydrocyclopenta[c]pyrrole-1,3(2*H*,3a*H*)-dione, 9. To a cold (0 °C, ice−water bath) solution of **7** (234 mg, 0.52 mmol) in anhydrous THF (7 mL), a solution of tetrabutylammonium fluoride (TBAF) in THF (1M, 0.67 mL, 0.67 mmol) was added dropwise, and the mixture was stirred for 2 h at room temperature under an Ar atmosphere. Saturated aqueous NH_4Cl solution (0.4 mL) was added, the mixture was stirred for 10 min, the solvents were evaporated under reduced pressure, and the residue (450 mg) was subjected to column chromatography (silica gel, 9 g, hexane/EtOAc mixtures). On elution with hexane/EtOAc 4:6, product **9** (144 mg, 82% yield) was isolated as a brown oil: R_f = 0.25 (silica gel, 6 cm, hexane/EtOAc 4:6); IR (ATR) ν 3300−3600 (w, OH st), 2939 (w), 2872 (w), 1770 (w), 1691 (s), 1430 (m), 1379 (m), 1283 (m), 1085 (m), 1021 (m), 743 (m), 693 (m) cm^{-1}; ^1H NMR δ 1.56 (br s, 1H, OH), 1.66 (s, H_2O), 1.73 (dd, J = 13.2 Hz, J' = 11.6 Hz, 1H, 4-H_x), 1.80−1.88 (m, 1H, 6-H_x), 1.87−1.97 (m, 1H, 5-H), 2.09−2.14 (ddm, J = 12.7 Hz, J' = 5.8 Hz, 1H, 6-H_n), 2.52−2.57 (ddm, J = 13.2 Hz, J' = 4.0 Hz, 1H, 4-H_n), 2.74 (s, 3H, *N*-CH_3), 3.21−3.24 (dm, J = 9.2 Hz, 1H, 6a-H), 3.58 (d, J = 3.2 Hz, 2H, CH_2OH), 7.28−7.32 [tm, J = 7.6 Hz, 2H, Ar-3(5)-H], 7.37−7.44 (tm, J = 7.4 Hz, 1H, Ar-4-H), 7.59−7.62 [dm, J = 7.6 Hz, 2H, Ar-2(6)-H]; ^{13}C NMR δ 25.1 (CH_3, *N*-CH_3), 32.5 (CH_2, C6), 39.5 (CH_2, C4), 41.6 (CH, C5), 53.1 (CH, C6a), 53.7 (C, C3a), 64.2 (CH_2, CH_2OH), 125.8 (C, Ar–C1), 129.2 [CH, Ar–C3(5)], 129.9 (CH, Ar–C4), 137.1 [CH, Ar–C2(6)], 178.0 (C, C3), 179.0 (C, C1). HRMS (ESI) (*m*/*z*) calcd for

$[C_{15}H_{17}NO_3{}^{80}Se + H]^+$: 340.0446. Found: 340.0449. Anal. Calcd for $C_{15}H_{17}NO_3Se$ (338.26): C, 53.26; H, 5.07; N, 4.14. Found: C, 52.92; H, 5.24; N, 3.96.

(3a*RS*,5*RS*,6a*SR*)-2-Methyl-3a-(phenylselanyl)-5-(tosyloxymethyl)-4,5,6,6a-tetrahydrocyclopenta[c]pyrrole-1,3(2*H*,3a*H*)-dione, 10, and (3a*RS*,5*RS*,6a*SR*)-5-(Chloromethyl)-2-methyl-3a-(phenylselanyl)-4,5,6,6a-tetrahydrocyclopenta[c]pyrrole-1,3-(2*H*,3a*H*)-dione, 11. To a cold (0 °C, ice−water bath) solution of alcohol **9** (708 mg, 2.09 mmol) in anhydrous pyridine (7 mL), tosyl chloride (599 mg, 3.14 mmol) was slowly added in 20 min, and the reaction mixture was stirred at room temperature overnight. Aqueous HCl (2N, 50 mL) was added, and the mixture was extracted with EtOAc (3 × 50 mL). The combined organic extracts were washed with water (30 mL) and brine (30 mL), dried (anhydrous Na_2SO_4) and concentrated in vacuo. The residue (1.01 g) was subjected to column chromatography (silica gel, 30 g, hexane/EtOAc mixtures). On elution with hexane/EtOAc 7:3, a mixture of chlorides **11** and **12** as orange oil (approximate ratio by ^{1}H NMR: 4.4:1, 50 mg, 7% yield) and tosylate **10** as yellow oil (800 mg, 78% yield) were obtained.

*Analytical and Spectroscopic Data of **10**.* R_f = 0.51 (silica gel, 4.5 cm, hexane/EtOAc 1:1); IR (ATR) ν 3058 (w), 2949 (w), 2890 (w), 1772 (w), 1697 (s), 1597 (w), 1430 (m), 1379 (m), 1361 (m), 1287 (m), 1188 (m), 1174 (s), 1094 (m), 1020 (w), 963 (m), 813 (m), 743 (m), 693 (m), 665 (m) cm^{-1}; ^{1}H NMR δ 1.60 (s, H_2O), 1.65 (dd, J = 13.0 Hz, J' = 11.8 Hz, 1H, 4-H_x), 1.76 (dt, J = 12.0 Hz, J' = 10.4 Hz, 1H, 6-H_x), 1.99 (ttt, J = 11.6 Hz, J' = 6.0 Hz, J'' = 6.0 Hz, 1H, 5-H), 2.04−2.09 (ddm, J = 12.6 Hz, J' = 5.8 Hz, 1H, 6-H_n), 2.45 (s, 3H, Ar−CH_3), 2.49 (ddd, J = 13.2 Hz, J' = 5.6 Hz, J'' = 1.2 Hz, 1H, 4-H_n), 2.72 (s, 3H, *N*-CH_3), 3.17 (d, J = 10.4 Hz, 1H, 6a-H), 3.93 (d, J = 5.6 Hz, 2H, CH_2OTs), 7.28−7.32 [m, 2H, Ar-3(5)-H Ar−Se], 7.34 [d, J = 8.2 Hz, 2H, Ar-3(5)-H, Ts], 7.38−7.42 (tm, J = 7.4 Hz, 1H, Ar-4-H, Ar−Se), 7.55−7.58 [dm, J = 8.0 Hz, 2H, Ar-2(6)-H, Ar−Se], 7.75 [d, J = 8.2 Hz, 2H, Ar-2(6)-H, Ts]; ^{13}C NMR δ 21.6 (CH_3, Ar−CH_3), 25.2 (CH_3, *N*-CH_3), 32.3 (CH_2, C6), 38.4 (CH, C5), 39.2 (CH_2, C4), 52.7 (CH, C6a), 53.0 (C, C3a), 70.4 (CH_2, CH_2OTs), 125.5 (C, Ar−C1, PhSe), 127.9 [CH, Ar−C2(6), Ts], 129.3 [CH, Ar−C3(5), PhSe], 129.9 [CH, Ar−C3(5), Ts], 130.0 (CH, Ar−C4, PhSe), 132.6 (C, Ar−C1, Ts), 137.9 [CH, Ar−C2(6), PhSe], 145.1 (C, Ar−C4, Ts), 177.3 (C, C3), 178.4 (C, C1). HRMS (ESI) (m/z) calcd for $[C_{22}H_{23}NO_5S^{80}Se + H]^+$: 494.0534. Found: 494.0543. Anal. Calcd for $C_{22}H_{23}NO_5SSe$ (492.45): C, 53.66; H, 4.71; N, 2.84. Found: C, 54.06; H, 4.77; N, 2.65.

*Analytical and Spectroscopic Data of **11** from the Spectra of Its Mixture with **12**.* R_f = 0.62 (silica gel, 4,5 cm, hexane/EtOAc 1:1); IR (ATR) ν 2946 (w), 2860 (w), 1772 (w), 1696 (s), 1429 (m), 1378 (m), 1292 (m), 1278 (m), 1087 (m), 1020 (m), 741 (m), 729 (m), 693 (m) cm^{-1}; ^{1}H NMR δ 1.80 (dd, J = 12.6 Hz, J' = 11.6 Hz, 1H, 4-H_x), 1.83−1.94 (ddd, J = 12.4 Hz, J' = 12.0 Hz, J'' = 10.4 Hz, 1H, 6-H_x), 2.02−2.15 (dt, J = 12.0 Hz, J' = 6.0 Hz, 1H, 5-H), 2.15−2.20 (ddm, J = 12.8 Hz, J' = 6.0 Hz, 1H, 6-H_n), 2.49 (ddd, J = 12.8 Hz, J' = 5.6 Hz, J'' = 1.6 Hz, 1H, 4-H_n), 2.76 (s, 3H, *N*-CH_3), 3.23 (d, J = 9.6 Hz, 1H, 6a-H), 3.47 (dd, J = 12.0, J' = 6.0 Hz, 1H) and 3.49 (dd, J = 12.0, J' = 6.0 Hz, 1H) (CH_2Cl), 7.29−7.33 [m, 2H, Ar-3(5)-H Ar−Se], 7.40 (tm, J = 7.4 Hz, 1H, Ar-4-H, Ar−Se), 7.59−7.63 [dm, J = 8.0 Hz, 2H, Ar-2(6)-H, Ar−Se]; ^{13}C NMR δ 25.2 (CH_3, *N*-CH_3), 33.4 (CH_2, C6), 40.4 (CH_2, C4), 41.1 (CH, C5), 45.9 (CH_2, CH_2Cl), 52.9 (CH, C6a), 53.3 (C, C3a), 125.6 (C, Ar−C1, PhSe), 129.3 [CH, Ar−C3(5), PhSe], 130.0 (CH, Ar−C4, PhSe), 137.1 [CH, Ar−C2(6), PhSe], 177.6 (C, C1), 177.7 (C, C3). HRMS (ESI) (m/z) calcd for $[C_{15}H_{16}ClNO_2{}^{80}Se + H]^+$: 358.0113. Found: 358.0106.

5-(Hydroxymethyl)-2-methyl-5,6-dihydrocyclopenta[c]-pyrrole-1,3(2*H*,4*H*)-dione, 13. *a. By Reaction of Compound **8** with 1 N HCl.* To a solution of **8** (715 mg, 2.42 mmol) in THF (18 mL), HCl (1M, 24.2 mL, 24.2 mmol) was added dropwise, and the reaction mixture was stirred for 2 h at room temperature. Saturated aqueous $NaHCO_3$ solution (28 mL) was added, and the mixture was extracted with EtOAc (3 × 60 mL). The combined organic extracts were dried (anhydrous Na_2SO_4) and concentrated in vacuo. The residue (521 mg) was subjected to column chromatography (silica gel, 10.5 g, hexane/EtOAc mixtures). On elution with hexane/EtOAc 4:6, product **13** (398 mg, 91% yield) was isolated as light yellow oil: R_f = 0.15 (silica gel, 6.5 cm, hexane/EtOAc 4:6); IR (ATR) ν 3600−3150 (m, OH st), 2941 (w), 2863 (w) 1772 (w), 1688 (s), 1432 (m), 1376 (m), 1242 (m), 1067 (m), 1032 (m), 983 (m), 723 (m) cm^{-1}; ^{1}H NMR δ 2.43−2.50 (m, 2H) and 2.70−2.79 (m, 2H) [4(6)-H_{cis} and 4(6)-H_{trans}], 2.54−2.66 (br s, 1H, OH), 2.91 (s, 3H, N−CH_3), 2.99−3.09 (m, 1H, 5-H), 3.62 (d, J = 6.4 Hz, 2H, CH_2OH); ^{13}C NMR δ 23.7 (CH_3, N−CH_3), 29.4 [CH_2, C4(6)], 44.4 (CH, C5), 65.3 (CH_2, CH_2OH), 152.2 [C, C3a(6a)], 167.4 [C, C1(3)]. HRMS (ESI) (m/z) calcd for $[C_9H_{11}NO_3 + H]^+$: 182.0812. Found: 182.0815. Anal. Calcd for $C_9H_{11}NO_3{\cdot}0.4H_2O$ (188.40): C, 57.38; H, 6.31; N, 7.43. Found: C, 57.65; H, 6.42; N, 7.23.

*b. By Reaction of Compound **8** with Tetrabutylammonium Fluoride.* To a cold (0 °C, ice−water bath) solution of **8** (110 mg, 0.37 mmol) in anhydrous THF (4 mL), a solution of tetrabutylammonium fluoride (TBAF) in THF (1M, 0.48 mL, 0.48 mmol) was added dropwise, and the mixture was stirred for 2 h at room temperature under an Ar atmosphere. Saturated aqueous NH_4Cl solution (0.3 mL) was added, the mixture was stirred for 10 min, the solvents were evaporated under reduced pressure, and the residue (271 mg) was subjected to column chromatography (silica gel, 6 g, hexane/EtOAc mixtures). On elution with hexane/EtOAc 1:1, impure product **13** (20 mg, 30% yield) was isolated as a brown oil.

2-Methyl-5-(tosyloxymethyl)-5,6-dihydrocyclopenta[c]-pyrrole-1,3(2*H*,4*H*)-dione, 14, and 5-(Chloromethyl)-2-methyl-5,6-dihydrocyclopenta[c]pyrrole-1,3(2*H*,4*H*)-dione, 12. To a cold (0 °C, ice−water bath) solution of alcohol **13** (526 mg, 2.90 mmol) in anhydrous pyridine (9.1 mL), tosyl chloride (830 mg, 4.35 mmol) was slowly added in 25 min, and the reaction mixture was stirred at room temperature overnight. Aqueous HCl (1 N, 60 mL) was added, and the mixture was extracted with EtOAc (3 × 70 mL). The combined organic extracts were washed with water (60 mL) and brine (60 mL), dried (anhydrous Na_2SO_4) and concentrated in vacuo. The yellow solid residue (870 mg) was subjected to column chromatography (silica gel, hexane/EtOAc mixtures). In order of elution, chloro compound **12** (116 mg, 20% yield, hexane/EtOAc 8:2) and tosylate **14** (750 mg, 77% yield, hexane/EtOAc 7:3) were obtained as a light yellow oil and a beige solid, respectively. The analytical sample of tosylate **14** (39 mg) was obtained as a white solid by crystallization of a sample of **14** (62 mg) from EtOAc (0.6 mL): mp 134−136 °C.

*Analytical and Spectroscopic Data of **14**.* R_f = 0.36 (silica gel, 8.5 cm, hexane/EtOAc 1:1); IR (ATR) ν 2954 (w), 2911 (w), 1773 (w), 1711 (m), 1697 (s), 1596 (w), 1435 (m), 1380 (m), 1357 (s), 1307, 1187 (m), 1173 (s), 989 (m), 952 (s), 880 (m), 842 (m), 823 (m), 807 (m), 790 (m), 765 (m), 721 (m), 667 (s) cm^{-1}; ^{1}H NMR δ 2.37−2.46 (m, 2H) and 2.74−2.83 (m, 2H) [4(6)-H_{cis} and 4(6)-H_{trans}], 2.45 (s, 3H, Ar−CH_3), 2.94 (s, 3H, N−CH_3), 3.14−3.25 (m, 1H, 5-H), 4.04 (d, J = 6.4 Hz, 2H, CH_2OTs), 7.36 (d, J = 8.2 Hz, 2H, Ar-3(5)-H), 7.78 (dm, J = 8.2 Hz, 2H, Ar-2(6)-H); ^{13}C NMR δ 21.6 (CH_3, Ar−CH_3), 23.8 (CH_3, *N*-CH_3), 29.6 [CH_2, C4(6)], 41.4 (CH, C5), 71.7 (CH_2, CH_2OTs), 127.9 [CH, Ar−C2(6)], 130.0 [CH, Ar−C3(5)], 132.6 (C, Ar−C1), 145.2 (C, Ar−C4), 151.5 [C, C3a(6a)], 166.7 [C, C1(3)]. HRMS (ESI) (m/z) calcd for $[C_{16}H_{17}NO_5S + H]^+$: 336.0900. Found: 336.0908. Anal. Calcd for $C_{16}H_{17}NO_5S$ (335.37): C, 57.30; H, 5.11; N, 4.18; S, 9.56. Found: C, 57.11; H, 4.97; N, 4.17; S, 9.38.

*Analytical and Spectroscopic Data of **12**.* R_f = 0.49 (silica gel, 8.5 cm, hexane/EtOAc 1:1); IR (ATR) ν 2954 (w), 2922 (w), 2847 (w), 1773 (w), 1694 (s), 1431 (m), 1375 (m), 1243 (w), 983 (m), 728 (m) cm^{-1}; ^{1}H NMR δ 2.54−2.63 (m, 2H) and 2.83−2.92 (m, 2H) [4(6)-H_{cis} and 4(6)-H_{trans}], 2.96 (s, 3H, *N*-CH_3), 3.25−3.32 (m, 1H, 5-H), 3.63 (d, J = 6.0 Hz, 2H, CH_2Cl); ^{13}C NMR δ 23.8 [CH_3, *N*-CH_3], 30.9 [CH_2, C4(6)], 44.4 [CH, C5], 48.2 [CH_2, CH_2Cl], 151.6 [C, C3a(6a)], 167.0 [C, C1(3)]. Anal. Calcd for $C_9H_{10}ClNO_2$: C, 54.15; H, 5.05; N, 7.02; Cl, 17.76. calcd for $C_9H_{10}ClNO_2{\cdot}0.1H_2O{\cdot}0.1$hexane (210.06): C, 54.89; H, 5.57; N, 6.67; Cl, 16.88. Found: C, 54.69; H, 5.46; N, 6.62; Cl, 16.79.

Tosylate 14 from 10. To a cold (0 °C, ice−water bath) and stirred solution of **10** (190 mg, 0.39 mmol) in CH_2Cl_2 (3 mL), a

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solution of H_2O_2 35% (0.27 mL) in water (0.54 mL) was added dropwise, keeping the temperature around 0 °C. The reaction mixture was allowed to warm to room temperature and stirred for 1 h at this temperature. A saturated aqueous $NaHCO_3$ solution (0.5 mL) was added. The organic phase was separated, and the aqueous one was extracted with CH_2Cl_2 (3 × 3 mL). The combined organic phases were washed with water, dried (anhydrous Na_2SO_4) and concentrated in vacuo. The residue (132 mg) was subjected to column chromatography (silica gel, 3.3 g, hexane/EtOAc mixtures). On elution with hexane/EtOAc 8:2, product **14** (128 mg, 99% yield) was isolated as light yellow solid.

Reaction of Tosylate 14 with Sodium Cyclopentadienide. A 1.08 M THF solution of sodium cyclopentadienide was prepared by dropwise addition of freshly distilled cyclopentadiene (0.88 mL, 10.8 mmol) to a cold (0 °C, ice−water bath) mixture of NaH (275 mg, 95% content, 10.9 mmol) in anhydrous THF (10 mL). The above solution (1.05 mL, 1.1 mmol) was added dropwise under an Ar atmosphere to a cold (−41 °C, cryocool) solution of **14** (316 mg, 0.94 mmol) in anhydrous THF (4 mL), and the mixture was stirred at −41 °C for 1.5 h. The reaction mixture was concentrated in vacuo, and the residue (566 mg) was subjected to column chromatography (silica gel, 11 g, hexane/EtOAc mixtures). None of the obtained fractions showed by ^{1}H NMR the presence of the expected polycycle **1** (R = H), its precursor **2** (R = H), tautomers or other derivatives of **2** (R = H).

Mixture of (3a*RS*,5*SR*,6a*SR*)-5-[(Cyclopenta-1,3-dien-1-yl)methyl]-2-methyl-3a-(phenylselanyl)-4,5,6,6a-tetrahydrocyclopenta[c]pyrrole)-1,3(2*H*,3a*H*)-dione, 15, and (3a*RS*,5*SR*,6a*SR*)-5-[(Cyclopenta-1,4-dien-1-yl)methyl]-2-methyl-3a-(phenylselanyl)-4,5,6,6a-tetrahydrocyclopenta[c]pyrrole)-1,3-(2*H*,3a*H*)-dione, 16. A 1.08 M THF solution of sodium cyclopentadienide was prepared by dropwise addition of freshly distilled cyclopentadiene (0.88 mL, 10.8 mmol) to a cold (0 °C, ice−water bath) mixture of NaH (275 mg, 95% content, 10.9 mmol) in anhydrous THF (10 mL). The above solution (1 mL, 1.08 mmol) was added dropwise under an Ar atmosphere to a cold (−41 °C, cryocool) solution of **10** (443 mg, 0.90 mmol) in anhydrous THF (4 mL), and the mixture was stirred at −41 °C for 1.5 h and then at room temperature for 1.5 h. The reaction mixture was concentrated in vacuo, and the residue (1.1 g) was subjected to column chromatography (silica gel, 14 g, hexane/EtOAc mixtures) to give on elution with hexane/EtOAc 95:5 a mixture of products **15** and **16** in an approximate ratio of **15**/**16** = 3:2 (^{1}H NMR) (160 mg, 46% yield) as yellow oil: R_f = 0.64 (silica gel, 6.4 cm, hexane/EtOAc 1:1)

*Spectroscopic Data of the Tautomeric Mixture **15** and **16**.* IR (ATR) ν 3060 (w), 2949 (w), 1772 (w), 1697 (s), 1428 (m), 1377 (m), 1281 (m), 1086 (m), 1020 (m), 742 (m), 692 (m), 673 (m) cm^{-1}. HRMS (ESI) (m/z) calcd for $[C_{20}H_{21}NO_2{}^{80}Se + H]^+$: 388.0810. Found: 388.0812.

*NMR Data of **15** Obtained from the Spectra of Its Mixture with **16**.* ^{1}H NMR δ 1.55−1.63 (m, 1H, 4-H$_x$), 1.65−1.75 (m, 1H, 6-H$_x$), 1.79−1.93 (m, 1H, 5-H), 2.10−2.16 (m, 1H, 6-H$_n$), 2.37−2.44 (m, 2H, C*H*$_2$-C$_5$H$_5$), 2.54−2.60 (m, 1H, 4-H$_n$), 2.72 (s, 3H, *N*-CH$_3$), 2.91 (q, J = 1.5 Hz, 2H, 5′-H$_2$), 3.19 (br s, 1H, 6a-H), 5.96−5.98 (m, 1H, 2′-H), 6.29−6.32 (dq, J = 4.8 Hz, J' = 1.5 Hz, 1H, 4′-H), 6.36−6.39 (m, 1H, 3′-H), 7.27−7.31 [m, 2H, Ar-3(5)-H], 7.39 (tm, J = 7.2 Hz, 1H, Ar-4-H), 7.56−7.59 [dm, J = 8.0 Hz, 2H, Ar-2(6)-H]; ^{13}C NMR δ 25.1 (CH$_3$, *N*-CH$_3$), 33.9 (CH$_2$, C5-CH$_2$), 35.8 (CH$_2$, C6), 39.1 (CH, C5), 41.3 (CH$_2$, C5′), 42.8 (CH$_2$, C4), 53.3 (CH, C6a), 53.9 (C, C3a), 125.8 (C, Ar−C1), 127.6 (CH, C2′), 129.2 [CH, Ar−C3(5)], 129.8 (CH, Ar−C4), 134.2 (CH, C3′), 134.4 (CH, C4′), 137,1 [CH, Ar−C2(6)], 144.3 (C, C1′), 178.2 (C, C1), 179.1 (C, C3).

*NMR Data of **16** Obtained from the Spectra of Its Mixture with **15**.* ^{1}H NMR δ 1.55−1.63 (m, 1H, 4-H$_x$), 1.65−1.75 (m, 1H, 6-H$_x$), 1.79−1.93 (m, 1H, 5-H), 2.10−2.16 (m, 1H, 6-H$_n$), 2.37−2.44 (m, 2H, C*H*$_2$-C$_5$H$_5$), 2.54−2.60 (m, 1H, 4-H$_n$), 2.73 (s, 3H, *N*-CH$_3$), 2.79 (q, J = 1.5 Hz, 2H, 3′-H$_2$), 3.21 (br s, 1H, 6a-H), 6.11−6.13 (m, 1H, 2′-H), 6.22−6.24 (dq, J = 5.2 Hz, J' = 1.5 Hz, 1H, 4′-H), 6.36−6.39 (m, 1H, 5′-H), 7.27−7.31 [m, 2H, Ar-3(5)-H], 7.39 (tm, J = 7.2 Hz, 1H, Ar-4-H), 7.56−7.59 [dm, J = 8.0 Hz, 2H, Ar-2(6)-H]; ^{13}C NMR δ 25.1 (CH$_3$, *N*-CH$_3$), 34.9 (CH$_2$, C5-CH$_2$), 36.0 (CH$_2$, C6), 39.8 (CH, C5), 42.9 (CH$_2$, C4), 43.5 (CH$_2$, C3′), 53.3 (CH, C6a), 53.8 (C, C3a), 125.8 (C, Ar−C1), 128.1 (CH, C2′), 129.2 [CH, Ar−C3(5)], 129.8 (CH, Ar−C4), 131.1 (CH, C4′), 132.3 (CH, C5′), 137.1 [CH, Ar−C2(6)], 146.4 (C, C1′), 178.1 (C, C1), 179.1 (C, C3).

H_2O_2 Oxidation of the Mixture of 15 and 16. To a cold (0 °C, ice−water bath) and stirred solution of the tautomeric mixture **15** and **16** (113 mg, 0.29 mmol) in CH_2Cl_2 (20 mL), a solution of H_2O_2 35% (0.20 mL) in water (0.40 mL) was added dropwise, keeping the temperature around 0 °C. The reaction mixture was allowed to warm to room temperature and stirred for 1 h at this temperature. A saturated aqueous $NaHCO_3$ solution (0.5 mL) and water (1 mL) were added. The organic phase was separated, and the aqueous one was extracted with CH_2Cl_2 (2 × 3 mL). The combined organic phases were washed with water, dried (anhydrous Na_2SO_4) and concentrated in vacuo. The residue (90 mg) was subjected to column chromatography (silica gel, 6.5 g, hexane/EtOAc mixtures). None of the obtained fractions contained the expected product **1** (R = H) or its precursor **2** (R = H).

5-(Methanesulfonyloxymethyl)-2-methyl-5,6-dihydrocyclopenta[c]pyrrole-1,3(2*H*,4*H*)-dione, 17. To a cold (0 °C, ice−water bath) solution of alcohol **13** (205 mg, 1.13 mmol) and anhydrous Et_3N (0.36 mL, 262 mg, 2.6 mmol) in CH_2Cl_2 (12 mL), mesyl chloride (0.11 mL, 155 mg, 1.35 mmol) was added dropwise, and the reaction mixture was stirred at 0 °C for 7 h and allowed to stand at 4 °C overnight. Saturated aqueous $NaHCO_3$ solution (1.5 mL) and water (5 mL) were added. The organic phase was separated, and the aqueous one was extracted with CH_2Cl_2 (2 × 7 mL). The combined organic extracts were washed with water (10 mL) and brine (10 mL), dried (anhydrous Na_2SO_4) and concentrated in vacuo to give mesylate **17** (284 mg, 97% yield) as a thick light yellow oil that solidified on standing. On trituration of part of the above product (256 mg) with EtOAc (0.7 mL), a white solid (125 mg) was obtained: mp 104−105 °C; R_f = 0.29 (silica gel, 8.3 cm, hexane/EtOAc 2:3); IR (ATR) ν 2940 (w), 1772 (w), 1695 (s), 1432 (m), 1375 (m), 1347 (s), 1170 (s), 977 (s), 950 (s), 838 (m), 813 (m), 725 (m) cm^{-1}; ^{1}H NMR δ 2.50−2.58 (m, 2H) and 2.84−2.93 (m, 2H) [4(6)-H$_{syn}$ and 4(6)-H$_{anti}$], 2.96 (s, 3H, N−CH$_3$), 3.03 (s, 3H, CH$_3$SO$_2$), 3.25−3.35 (m, 1H, 5-H), 4.24 (d, J = 6.8 Hz, 2H, C*H*$_2$OMs); ^{13}C NMR δ 23.9 (CH$_3$, *N*-CH$_3$), 29.6 [CH$_2$, C4(6)], 37.5 (CH$_3$, CH$_3$SO$_2$), 41.6 (CH, C5), 70.9 (CH$_2$, *C*H$_2$OMs), 151.5 [C, C3a(6a)], 166.7 [C, C1(3)]. HRMS (ESI) (m/z) calcd for $[C_{10}H_{13}NO_5S + H]^+$: 260.0587. Found: 260.0582. Anal. Calcd for $C_{10}H_{13}NO_5S$ (259.28): C, 46.32; H, 5.05; N, 5.40; S, 12.37. Found: C, 45.98; H, 4.93; N, 5.31; S, 12.19.

5-(Iodomethyl)-2-methyl-5,6-dihydrocyclopenta[c]pyrrole-1,3(2*H*,4*H*)-dione, 18. *a. From Tosylate **14**.* A magnetically stirred mixture of tosylate **14** (710 mg, 2,12 mmol) and NaI (3.18 g, 21.2 mmol) in anhydrous acetone (30 mL) was heated at 56 °C for 13 h under an Ar atmosphere. The mixture was allowed to cool to room temperature, the precipitate was filtered through a pad of Celite, and the solid was washed with EtOAc (40 mL). The combined filtrate and washings were concentrated in vacuo, and the residue (3.35 g) was subjected to column chromatography (silica gel, 15 g, hexane/EtOAc mixtures) to give iodide **18** (603 mg, 98% yield), as a light yellow solid. The analytical sample of **18** (422 mg) was obtained as white solid, mp 89−90 °C, by crystallization of the above product from EtOAc (1.5 mL): R_f = 0.58 (silica gel, 9.5 cm, hexane/EtOAc 1:1); IR (ATR) ν 2952 (w), 2928 (w), 2902 (w) and 2833 (w) (C−H st), 1766 (w), 1711 (s), 1692 (s) and 1652 (m) (C═O st), 1428 (s), 1373 (s), 1237 (m), 1206 (m), 1184 (m), 984 (s), 756 (m), 725 (m), 692 (m) cm^{-1}; ^{1}H NMR δ 2.43−2.51 (m, 2H) and 2.84−2.93 (m, 2H) [4(6)-H$_{cis}$ and 4(6)-H$_{trans}$], 2.97 (s, 3H, *N*-CH$_3$), 3.07−3.18 (m, 1H, 5-H), 3.34 (d, J = 6.4 Hz, 2H, C*H*$_2$I); ^{13}C NMR δ 12.3 (CH$_2$, *C*H$_2$I), 23.9 (CH$_3$, *N*-CH$_3$), 34.1 [CH$_2$, C4(6)], 44.4 (CH, C5), 151.4 [CH, C3a(6a)], 167.1 [C, C1(3)]. HRMS (ESI) (m/z) calcd for $[C_9H_{10}INO_2 + H]^+$: 291.9829. Found: 291.9832. Anal. Calcd for $C_9H_{10}INO_2$ (291.09): C 37.14, H 3.46, N 4.81, I 43.60. Found: C 37.49, H 3.50, N 5.14, I, 43.77.

*b. From Mesylate **17**.* A magnetically stirred mixture of mesylate **17** (105 mg, 0,40 mmol) and NaI (607 mg, 4.0 mmol) in anhydrous acetone (5 mL) was heated at 56 °C for 16 h under an Ar atmosphere.

The mixture was allowed to cool to room temperature, the precipate was filtered through a pad of Celite, and the solid was washed with EtOAc (15 mL). The combined filtrate and washings were concentrated in vacuo, and the residue (664 mg) was subjected to column chromatography (silica gel, 4 g, hexane/EtOAc mixtures). On elution with hexane/EtOAc 4:1, iodide **18** (116 mg, 98% yield) was obtained as a light yellow solid.

Methyl (1*RS*)-1-[(2-methyl-1,3-dioxo-1,2,3,4,5,6-hexahydrocyclopenta[c]pyrrol-5-yl)methyl]-2-oxocyclopentanecarboxylate, 19. To a cold (0 °C, ice−water bath), magnetically stirred suspension of NaH (49 mg, 95% content, 1.93 mmol) in anhydrous DMF (2 mL), a solution of methyl 2-oxocyclopentanecarboxylate (359 mg, 0.33 mL del 95%, 2.66 mmol) was added dropwise, and the mixture was stirred for 1 h at this temperature. Then, a solution of iodide **18** (402 mg, 1.38 mmol) in anhydrous DMF (4 mL) was added dropwise, and the reaction mixture was stirred for 4 h at 0 °C. A saturated aqueous solution of NH_4Cl (2 mL) and water (1.5 mL) were added, and the mixture was extracted with EtOAc (3 × 12 mL). The combined organic extracts were dried (anhydrous Na_2SO_4) and concentrated in vacuo. The obtained residue (2.05 g) was subjected to column chromatography (silica gel, 40 g, hexane/EtOAc mixtures). On elution with hexane/EtOAc 3:1, product **19** (327 mg, 78% yield) was isolated as light yellow oil: R_f = 0.35 (silica gel, 9 cm, hexane/EtOAc 1:1); IR (ATR) ν 2951 (w), 2918 (w), 2844 (w), 1749 (m), 1707 (s) and 1696 (s), 1603 (w), 1505 (w), 1431 (m), 1377 (m), 1304 (w), 1282 (w), 1230 (m), 1175 (m), 1126 (m), 983 (m), 731 (m) cm^{-1}; ^1H NMR δ 1.78−1.85 (complex signal, 2H, 5-H_a and C5′-CH_a), 1.92−2.00 (complex signal, 2H, 4-H_a and 4-H_b), 2.19−2.36 (complex signal, 4H, 3-H_a, 4′-H_a, 6′-H_a and C5′-CH_b), 2.41 (ddt, J = 19.0 Hz, J' = 1.4 Hz, J'' = 7.0 Hz, 1H, 3-H_b), 2.61 (ddt, J = 12.6 Hz, J' = 1.4 Hz, J'' = 5.2 Hz, 1H, 5-H_b), 2.72−2.80 (m, 2H, 4′-H_b and 6′-H_b), 2.82−2.93 (m, 1H, 5′-H), 2.91 (s, 3H, *N*-CH_3), 3.70 (s, 3H, OCH_3); ^{13}C NMR δ 19.5 (CH_2, C4), 23.7 (CH_3, *N*-CH_3), 33.4 (CH_2, C5), 33.55 (CH_2) and 33.59 (CH_2) (C4′ and C6′), 37.3 (CH_2, C3), 39.7 (CH_2, C5′-CH_2), 40.6 (CH, C5′), 52.7 (CH_3, OCH_3), 60.4 (C, C1), 151.97 (C), 152.04 (C) (C3a′ and C6a′) 167.1 (C, C1′ and C3′), 170.8 (C, $COOCH_3$), 213.8 (C, C2). HRMS (ESI) (m/z) calcd. for $[C_{16}H_{19}NO_5 + H]^+$: 306.1336. Found: 306.1333. Anal. Calcd for $C_{16}H_{19}NO_5 \cdot 0.5H_2O$ (314.34): C 61.14, H 6.41, N 4.46. Found: C 61.27, H 6.27, N 4.74.

Methyl (1*RS*)-1-[(2-methyl-1,3-dioxo-1,2,3,4,5,6-hexahydrocyclopenta[c]pyrrol-5-yl)methyl]-2-(trimethylsilyloxy)cyclopent-2-enecarboxylate, 20. To a cold (0 °C, ice−water bath) solution of keto ester **19** (458 mg, 1.50 mmol) and anhydrous Et_3N (1.04 mL, 758 mg, 7.50 mmol) in anhydrous CH_2Cl_2 (4.5 mL), trimethylsilyl trifluoromethanesulfonate (0.42 mL, 98% content, 500 mg, 2.25 mmol) was added at once under an Ar atmosphere, and the mixture was stirred for 30 min at this temperature. A saturated aqueous solution of $NaHCO_3$ (1.5 mL) was added, the organic phase was separated, and the aqueous one was extracted with CH_2Cl_2 (3 mL). The combined organic phases were dried (anhydrous Na_2SO_4) and concentrated in vacuo. The residue was taken in EtOAc (6 mL); the solution was washed with water (2 × 2 mL), dried (anhydrous Na_2SO_4) and concentrated in vacuo. The red-brown oily residue corresponding to **20** (548 mg), R_f = 0.63 (silica gel, 9 cm, hexane/EtOAc 1:1), was used as such in the next step: ^1H NMR δ 0.19 [s, 9H, $Si(CH_3)_3$], 1.76−1.88 (m, 1H), 1.97 (dd, J = 14.0 Hz, J' = 7.4 Hz, 1H), 2.16−2.43 (complex signal, 6H) (4-H_a, 4-H_b, 4′-H_a, 5-H_a, 5-H_b, 6′-H_a, C5′-CH_a and C5′-CH_b), 2.75−2.83 (complex signal, 2H, 4′-H_b and 6′-H_b), 2.84−2.94 (m, 1H, 5′-H), 2.95 (s, 3H, *N*-CH_3), 3.67 (s, 3H, OCH_3), 4.71 (s, 1H, 3-H); ^{13}C NMR δ −0.2 [CH_3, $Si(CH_3)_3$], 23.7 (CH_3, *N*-CH_3), 26.4 (CH_2, C5), 32.5 (CH_2, C4), 33.7 (CH_2) and 34.2 (CH_2) (C4′ and C6′), 40.5 (CH_2, C5′-CH_2), 40.6 (CH, C5′), 51.9 (CH_3, OCH_3), 57.9 (C, C1), 103.4 (CH, C3), 152.2 (C) and 152.8 (C) (C3a′ and C6a′), 154.0 (C, C2), 167.5 (C, C1′ and C3′), 175.4 (C, $COOCH_3$).

Methyl (1*RS*)-1-[(2-methyl-1,3-dioxo-1,2,3,4,5,6-hexahydrocyclopenta[c]pyrrol-5-yl)methyl]-2-oxocyclopent-3-enecarboxylate, 21. To a solution of the above trimethylsilyl ether **20** (548 mg) in anhydrous DMSO (5.4 mL), $Pd(OAc)_2$ (344 mg, 98% content, 1.50 mmol) was added, and the mixture was stirred for 16 h at room temperature. The suspension was filtered through a pad of Celite, and the solid was washed with EtOAc. The combined filtrate and washings were concentrated in vacuo; the residue was taken in EtOAc (20 mL) and washed with water (12 mL). The organic phase was extracted with EtOAc (2 × 18 mL). The combined organic phase and washings were washed with brine (2 × 7 mL), dried (anhydrous Na_2SO_4) and concentrated in vacuo. The brown oily residue (480 mg) was subjected to column chromatography (silica gel, 24 g, hexane/EtOAc mixtures. On elution with hexane/EtOAc 3:1, keto ester **19** (47 mg) was recovered. On elution with hexane/EtOAc 7:3 to 6:4, enone **21** (396 mg, 87% yield from keto ester **19**) was obtained as a light brown solid. Crystallization of a sample (265 mg) of the above product from EtOAc (0.7 mL) and pentane (3 drops) gave the analytical sample of **21** (158 mg) as white solid: mp 87−89 °C; R_f = 0.22 (silica gel, 9 cm, hexane/EtOAc 1:1); IR (ATR) ν 3063 (w), 2948 (w), 2912 (w), 2844 (w), 1768 (w), 1744 (w), 1701 (s) and 1693 (s), 1590 (w), 1433 (m), 1374 (m), 1352 (w), 1273 (w), 1243 (m), 1205 (m), 1177 (m), 1164 (m), 982 (m), 829 (w), 753 (m), 723 (m) cm^{-1}; ^1H NMR δ 2.12 (dd, J = 14.4 Hz, J' = 7.2 Hz, 1H, C5′-CH_a), 2.28−2.38 (complex signal, 3H, 4′-H_a, 6′-H_a and C5′-CH_b, contains at 2.35, dd, J = 14.4 Hz, J' = 5.8 Hz), 2.67 (dt, J = 19.2 Hz, J' = 2.4 Hz, 1H, 5-H_a), 2.66−2.87 (complex signal, 3H, 4′-H_b, 5′-H and 6′-H_b), 2.93 (s, 3H, *N*-CH_3), 3.33 (dt, J = 19.2 Hz, J' = 2.4 Hz, 1H, 5-H_b), 3.71 (s, 3H, $COOCH_3$), 6.20 (dt, J = 10.0 Hz, J' = 5.8 Hz, 1H, 3-H), 7.80 (dt, J = 10.0 Hz, J' = 6.4 Hz, 1H, 4-H); ^{13}C NMR δ 23.7(CH_3, *N*-CH_3), 33.81 (CH_2) and 33.83 (CH_2) (C4′ and C6′), 39.4 (CH_2, C5), 39.8 (CH_2, C5′-CH_2), 40.6 (CH, C5′), 52.9 (CH_3, $COOCH_3$), 57.6 (C, C1), 132.2 (CH, C3), 151.9 (C) and 152.2 (C) (C3a′ and C6a′), 163.6 (CH, C4), 167.1 (C, C1′ and C3′), 170.8 (C, COOMe), 204.8 (C, C2). HRMS (ESI) (m/z) calcd for $[C_{16}H_{17}NO_5 + H]^+$: 304.1179. Found: 304.1174. Anal. Calcd for $C_{16}H_{17}NO_5$ (303.31): C 63.36, H 5.65, N 4.62. Found: C 63.29, H 5.80, N 4.56.

Stereoisomeric Mixture of Methyl 2-hydroxy-1-[(1-hydroxy-2-methyl-3-oxo-1,2,3,4,5,6-hexahydrocyclopenta[c]pyrrol-5-yl)methyl]cyclopent-3-enecarboxylate, 22. To a cold (0 °C, ice−water bath) of enone **21** (112 mg, 0.37 mmol) and $CeCl_3 \cdot 7H_2O$ (380 mg, 1.02 mmol) in a mixture of THF (3.3 mL) and MeOH (3.7 mL), $NaBH_4$ (54.6 mg, 1.44 mmol) was added portionwise, and the solution was stirred at room temperature for 1 h. A saturated aqueous solution of $NaHCO_3$ (1,5 mL) was added, and the mixture was extracted with CH_2Cl_2 (3 × 8 mL). The combined organic phases were dried (anhydrous Na_2SO_4) and concentrated in vacuo to give a stereoisomeric mixture of at least four diastereomeric racemic pairs of diol **22** (97.5 mg, 86% yield) as a beige solid. Crystallization of the above product from EtOAc (0.4 mL) gave an analytical sample of **22** (52 mg) as a white solid: mp 80−82 °C (EtOAc); R_f = 0.21 (silica gel, 9.5 cm, EtOAc); IR (ATR) ν 3500−3000 (max. at 3284) (m), 2920 (m), 2850 (w), 1724 (m), 1677 (s), 1653 (s), 1432 (s), 1396 (s), 1348 (m), 1316 (m), 1289 (m), 1228 (s), 1199 (m), 1166 (s), 1085 (s), 1018 (s), 980 (m), 752 (m), 729 (m), 704 (m), 661 (m) cm^{-1}; ^1H NMR δ 1.60−1.99 (complex signal, 2H, 4′-H_a and OH), 2.08−2.27 (complex signal, 3H, 4′-H_b, C5′-CH_a and 6′-H_a), 2.29−2.38 (complex signal, 1H, 5-H_a), 2.54−2.98 (complex signal, 4H, 5-H_b, 5′-H, C5′-CH_b, 6′-H_b) 2.91 (s, 3H, *N*-CH_3), 3.20−3.60 (br, 1H, OH), 3.70 (s) 3.737 (s) and 3.742 (s) (total 3H, OCH_3), 4.93 (br s), 4.95 (br s) and 4.97 (br s) (total 1H, 2-H), 5.07 (br s) and 5.11 (br s) (total 1H, 1′-H), 5.78−5.82 (complex signal, 1H, 4-H), 5.91−5.96 (complex signal, 1H, 3-H); ^{13}C NMR (the groups of signals for each carbon atom of different stereoisomers are given in order of relative intensity) δ 26.32 and 26.36 (CH_3, *N*-CH_3), 33.3, 32.9, 33.4, and 33.9 (CH_2, C6′), 35.4, 35.7, 35.1, and 34.5 (CH_2, C5′-CH_2), 39.2, 38.9, 39.1, and 38.8 (CH_2, C4′), 40.1, 39.3, 39.7, and 39.2 (CH_2, C5), 41.5, 40.9, 41.4, and 40.9 (CH, C5′), 52.2 and 52.3 (CH_3, OCH_3), 57.0, 57.5, 57.2, and 57.3 (C, C1), 79.4, 80.1, 79.9, and 80.4 (CH, C2), 81.9, 81.8, 82.01, and 81.95 (CH, C1′), 132.1, 131.82, 132.0, and 131.76 (CH, C4), 133.6, 134.0, 133.9, and 134.2 (CH, C3), 142.1, 142.29, 142.35, 142.0 (C, C3a′), 162.6, 162.8, 162.5, and 163.0 (C, C6a′), 167.44, 167.6, 167.39, 167.5 (C, C3′), 177.0 and 177.1 (C, $COOCH_3$). HRMS (ESI) (m/z) calcd for $[C_{16}H_{21}NO_5 + H]^+$ 308.1492. Found: 308.1494. Anal. Calcd for

$C_{16}H_{21}NO_5 \cdot 0.25H_2O$ (311.85): C 61.62, H 6.95, N 4.49. Found: C 61.70, H 7.11, N 4.34.

(3a*RS*,5*RS*,6a*SR*)-5-(Iodomethyl)-2-methyl-3a-(phenylselanyl)-4,5,6,6a-tetrahydrocyclopenta[c]pyrrole-1,3(2*H*,3a*H*)-dione, 23. A magnetically stirred mixture of tosylate **10** (252 mg, 0.51 mmol) and NaI (765 mg, 5.1 mmol) in anhydrous acetone (30 mL) was heated at 56 °C for 16 h under an Ar atmosphere. The mixture was allowed to cool to room temperature; the precipitate was filtered through a pad of Celite, washing the solid with EtOAc (20 mL). The combined filtrate and washings were concentrated in vacuo, and the residue (919 mg) was subjected to column chromatography (silica gel, 5 g, hexane/EtOAc mixtures). On elution with hexane/EtOAc 4:1, iodide **23** (220 mg, 96% yield) was obtained as a light yellow oil: R_f = 0.57 (silica gel, 9 cm, hexane/EtOAc 1:1); IR (ATR) ν 2928 (w), 1771 (w), 1695 (s), 1428 (m), 1377 (m), 1288 (m), 1274 (m), 1179 (m), 1086 (m), 1006 (m), 742 (m), 692 (m), 634 (m) cm^{-1}; ^1H NMR δ 1.69 (dd, J = 12.8 Hz, J' = 12.0 Hz, 1H, 4-H_x), 1.75 (dt, J = 10.4 Hz, J' = 12.0 Hz, 1H, 6-H_x), 1.80−1.90 (m, 1H, 5-H), 2.18−2.24 (ddm, J = 12.8 Hz, J' = 5.6 Hz, 1H, 6-H_n), 2.63 (ddd, J = 12.8 Hz, J' = 5.6 Hz, J'' = 1.4 Hz, 1H, 4-H_n), 2.76 (s, 3H, *N*-CH_3), 3.11 (dd, J = 10.4 Hz, J' = 6.0 Hz, 1H) and 3.16 (dd, J = 10.4 Hz, J' = 6.0 Hz, 1H) (CH_2I), 3.25 (dd, J = 10.4 Hz, J' = 1.2 Hz, 1H, 6a-H), 7.29−7.33 [m, 2H, Ar-3(5)-H], 7.41 (tm, J = 7.2 Hz, 1H, Ar-4-H), 7.61 [dm, J = 8.0 Hz, 2H, Ar-2(6)-H]; ^{13}C NMR δ 7.4 (CH_2, CH_2I), 25.2 (CH_3, *N*-CH_3), 36.3 (CH_2, C6), 41.0 (CH, C5), 43.1 (CH_2, C4), 53.1 (CH, C6a), 53.5 (C, C3a), 125.5 (C, Ar−C1), 129.3 [CH, Ar−C3(5)], 130.0 (CH, Ar−C4), 137.2 [CH, Ar−C2(6)], 177.5 (C, C1), 178.6 (C, C3). HRMS (ESI) (m/z) calcd for $[C_{15}H_{16}INO_2{}^{80}Se + H]^+$ 449.9463. Found: 449.9475. Anal. Calcd for $C_{15}H_{16}INO_2Se \cdot 0.05$hexane (452.47): C 40.61, H 3.72, N 3.10; I, 28.05. Found: C 40.90, H 3.75, N 3.18; I, 28.11.

Mixture of Methyl (1*RS*)- and (1*SR*)-1-{[(3a*RS*,5*SR*,6a*SR*)-2-methyl-3a-(phenylselanyl)-1,3-dioxooctahydrocyclopenta[c]-pyrrol-5-yl]methyl}-2-oxocyclopentanecarboxylate, 24. To a cold (0 °C, ice−water bath), magnetically stirred suspension of NaH (14 mg, 60% content, 0.36 mmol) in anhydrous DMF (0.5 mL), a solution of methyl 2-oxocyclopentanecarboxylate (66 mg, 60 μL, 95% content, 0.44 mmol) was added dropwise, and the mixture was stirred for 1 h at this temperature. Then, a solution of iodide **23** (80.3 mg, 0.18 mmol) in anhydrous DMF (0.8 mL) was added dropwise, and the reaction mixture was stirred at 0 °C for 2 h and at room temperature for 67 h. A saturated aqueous solution of NH_4Cl (0.5 mL) and water (0.8 mL) were added, and the mixture was extracted with EtOAc (3 × 4 mL). The combined organic extracts were washed with water, dried (anhydrous Na_2SO_4) and concentrated in vacuo. The obtained residue (331 mg) was subjected to column chromatography (silica gel, 15 g, hexane/EtOAc mixtures). On elution with hexane/EtOAc 1:1, product **24** (59.2 mg, 71% yield) was isolated as a thick yellow oil: R_f = 0.36 (silica gel, 9.5 cm, hexane/EtOAc 1:1); IR (ATR) ν 2952 (w), 1770 (w), 1749 (w), 1697 (s), 1429 (m), 1378 (m), 1283 (m), 1222 (m), 1147 (m), 1119 (m), 1088 (m), 1021 (m), 744 (m), 694 (m) cm^{-1}; ^1H NMR δ 1.51−1.60 (complex signal, 2H, 4′-H_x and C5′-CH_a), 1.62−1.75 (complex signal, 3H, 5-H_a, 5′-H and 6′-H_x), 1.82−1.99 (complex signal, 2H, 4-H_a and 4-H_b), 2.02−2.14 (complex signal, 2H, 4′-H_n and 6′-H_n), 2.14−2.26 (m, 1H, 3-H_a), 2.33−2.43 (m, 1H, 3-H_b), 2.43−2.54 (complex signal, 2H, 5-H_b and C5′-CH_b), 2.72 (s) and 2.73 (s) (total 3H, N−CH_3), 3.13 (br s) and 3.15 (br s) (total 1H, 6a′-H), 3.64 (s) and 3.65 (s) (total 3H, OCH_3), 7.27−7.31 [complex signal, 2H, Ar-3(5)-H], 7.38 (tm, J = 7.4 Hz, 1H, Ar-4-H), 7.56−7.59 [complex signal, 2H, Ar-2(6)-H]; ^{13}C NMR δ 19.5 (CH_2, C4), 25.1 (CH_3) and 25.2 (CH_3) (*N*-CH_3), 32.8 (CH_2) and 32.9 (CH_2) (C5), 35.8 (CH, C5′), 36.1 (CH_2) and 36.4 (CH_2) (C6′), 37.3 (CH_2, C3), 37.57 (CH_2) and 37.64 (CH_2) (C4′), 43.1 (CH_2) and 43.4 (CH_2) (C5′-CH_2), 52.7 [CH_3, OCH_3], 52.9 (CH) and 53.1 (CH) (C6a′), 53.3 (C) and 53.6 (C) (C3a′), 60.0 (C, C1), 125.6 (C) and 125.7 (C) (Ar−C1), 129.2 [CH, Ar−C3(5)], 129.87 (CH) and 129.90 (CH) (Ar−C4), 137.1 [CH, Ar−C2(6)], 170.7 [C, $COOCH_3$], 177.79 (C) and 177.83 (C) (C1′), 178.8 (C, C3′), 213.8 (C, C2). HRMS (ESI) (m/z) calcd for $[C_{22}H_{25}NO_5Se + H]^+$: 464.0970. Found: 464.0968. Anal. Calcd for $C_{22}H_{25}NO_5Se$ (462.40): C, 57.14; H, 5.45; N, 3.03. Found: C, 57.31; H, 5.73; N, 2.85.

Methyl (1*RS*,2*RS*)-2-hydroxy-1-[(2-methyl-1,3-dioxo-1,2,3,4,5,6-hexahydrocyclopenta[c]pyrrol-5-yl)methyl]-cyclopent-3-enecarboxylate, 25. *a. Reaction of Enone **21** with Furan.* A solution of enone **21** (104 mg, 0,34 mmol) in furan (3.2 mL) was heated at 80 °C for 24 h in a closed glass vessel. The solution was allowed to cool to room temperature and was concentrated in vacuo to give a mixture of four diastereomeric pairs of the Diels−Alder adduct **26** (145 mg, quantitative yield), which was used as such in the next step.

Significant ^1H NMR data of the stereoisomeric mixture **26** (the given values for each kind of proton are given in decreasing relative ratio): 2.80/2.96/2.82/3.00 (s, *N*-CH_3), 3.70/3.68/3.69/3.67 (s, $COOCH_3$), 6.13−6.18 (complex signal, cyclopentenone 3-H), 6.43/6.59/6.38/6.40 (t, J = 1.2 Hz, olefinic protons from the dihydrofuran moiety), 7.72−7.80 (complex signal, cyclopentenone 4-H).

*b. Reduction of the Mixture of Diels−Alder Adducts **26** with $NaBH_4/CeCl_3 \cdot 7H_2O$.* To a cold (−40 °C, cryocool) solution of the above mixture of Diels−Alder adducts **26** (127 mg, 0.34 mmol) and $CeCl_3 \cdot 7H_2O$ (357 mg, 0.96 mmol) in a mixture of THF (3.1 mL)/MeOH (3.4 mL), $NaBH_4$ (50 mg, 1.33 mmol) was added portionwise, and the mixture was stirred at this temperature for 1 h. Then, saturated aqueous $NaHCO_3$ solution (1.3 mL) and water (1.5 mL) were added, and the mixture was extracted with CH_2Cl_2 (3 × 12 mL). The combined organic phases were dried (anhydrous Na_2SO_4) and concentrated in vacuo to give a mixture of diastereomeric alcohols **27** (135 mg, quantitative yield) as a white solid, which was used as such in the next step.

Significant ^1H NMR data of the stereoisomeric mixture **27** (the given values for each kind of proton are given in decreasing relative ratio): 2.80/2.96/2.83/3.02 (s, *N*-CH_3), 3.70/3.74/3.680/3.683/other minor signals (s, $COOCH_3$), 4.93/5.09/4.85/5.04/5.04/5.01 (br, cyclopentenol 2-H plus allylic protons from the dihydrofuran moiety), 5.75−5.79 (complex signal, cyclopentenol 4-H), 5.88−5.95 (complex signal, cyclopentenol 3-H), 6.43/6.60/6.38/6.58 (br s, olefinic protons from the dihydrofuran moiety).

*c. Retro-Diels−Alder Reaction from the Reduced Adducts **27**.* A solution of the above stereoisomeric mixture **27** in toluene (17 mL) was heated under reflux for 4 d. The solution was allowed to cool to room temperature and concentrated in vacuo, and the residue (113 mg) was subjected to column chromatography (silica gel 35−70 μm, 7 g, hexane/EtOAc mixtures). On elution with hexane/EtOAc 65:35, stereoisomerically pure alcohol **25** (48.4 mg) and a mixture of **25** and its epimer at the cyclopentene C2 carbon atom (28.5 mg, ratio **25**/C2 epimer about 2:1 by ^1H NMR), both as thick white oils, were successively isolated (total 76.9 mg, 74% yield from enone **21**). On increasing the polarity of the eluent until hexane/EtOAc 4:6, a stereoisomeric mixture of the two originally minor adducts **27** (22.5 mg) was recovered as brown oil.

*Analytical and Spectroscopic Data of the Main Diastereoisomer **25**.* Thick white oil: R_f = 0.33 (silica gel, 8 cm, hexane/EtOAc 4:6); IR (ATR) ν 3600−3300 (m), 2947 (w), 1770 (w), 1695 (s), 1432 (m), 1377 (m), 1230 (m), 1203 (m), 1167 (m), 1031 (m), 982 (m), 728 (m) cm^{-1}; ^1H NMR δ 1.80 (s, 1H, OH), 1.98 (dd, J = 14.4 Hz, J' = 5.6 Hz, 1H, C5′-CH_a), 2.23 (dd, J = 14.4 Hz, J' = 7.2 Hz, 1H, C5′-CH_b), 2.32−2.37 (complex signal, 3H, 4′-H_a, 5-H_{trans} and 6′-H_a), 2.70−2.87 (complex signal, 3H, 4′-H_b, 5′-H and 6′-H_b), 2.93 (s, 3H, *N*-CH_3), 2.93−2.99 (dm, J = 16.8 Hz, 1H, 5-H_{cis}), 3.66 (s, 3H, $COOCH_3$), 4.92−4.95 (br s, 1H, 2-H), 5.80 (dq, J = 6.0 Hz, J' = 2.0 Hz, 1H, 4-H), 5.92−5.95 (m, 1H, 3-H); ^{13}C NMR δ 23.7 (CH_3, N−CH_3), 33.2 (CH_2) and 34.0 (CH_2) (C4′ and C6′), 38.5 (CH_2, C5′-CH_2), 39.2 (CH_2, C5), 41.3 (CH, C5′), 52.3 (CH_3, $COOCH_3$), 57.3 (C, C1), 80.2 (CH, C2), 132.0 (CH, C4), 133.9 (CH, C3), 152.1 (C) and 152.4 (C) (C3a′ and C6a′), 167.3 (C, C1′ and C3′), 176.5 (C, COOMe). HRMS (ESI) (m/z) calcd for $[C_{16}H_{19}NO_5 + NH_4]^+$ 323.1601. Found: 323.1593. Anal. Calcd for $C_{16}H_{19}NO_5$ (305.33): C 62.94, H 6.27, N 4.59. Found: C 63.24, H 6.45, N 4.27.

*Significant NMR Data of the Minor Diastereoisomer of **25** from the Spectra of the Diastereomeric Mixture.* ^1H NMR δ 1.87 (dd, J =

13.8 Hz, J' = 5.8 Hz, 1H, C5′-CH_a), 2.14 (dd, J = 13.8 Hz, J' = 7.8 Hz, 1H, C5′-CH_b), 2.97 (s, 3H, N−CH_3), 3.07−3.14 (dm, J = 17.6 Hz, 1H, 5-H_{cis}), 3.75 (s, 3H, $COOCH_3$), 4.48−4.52 (br s, 1H, 2-H); ^{13}C NMR δ 23.8 (CH_3, *N*-CH_3), 33.3 (CH_2) and 34.2 (CH_2) (C4′ and C6′), 38.3 (CH_2, C5′-CH_2), 41.0 (CH, C5′), 43.0 (CH_2, C5), 52.1 (CH_3, $COOCH_3$), 57.6 (C, C1), 83.5 (CH, C2), 130.9 (CH, C4), 134.0 (CH, C3), 151.9 (C) and 152.3 (C) (C3a′ and C6a′), 167.20 and 167.22 (C, C1′ and C3′), 175.2 (C, $COOCH_3$).

Methyl (1*RS*,2*RS*)-2-acetoxy-1-[(2-methyl-1,3-dioxo-1,2,3,4,5,6-hexahydrocyclopenta[c]pyrrol-5-yl)methyl]-cyclopent-3-enecarboxylate, 29. *a. Oxidation of the Stereoisomeric Mixture **22** with MnO_2.* To a solution of the stereoisomeric mixture of diols **22** (210 mg, 0.68 mmol) in anhydrous CH_2Cl_2 (130 mL), MnO_2 (418 mg, 85% content, 4.1 mmol) was added at once under an Ar atmosphere, and the mixture was heated under reflux for 36 h. The solution was allowed to cool to room temperature, filtered through a pad of Celite, and the solid was washed with CH_2Cl_2 (3 × 35 mL). Concentration in vacuo of the combined filtrate and washings gave a residue (204 mg), which was subjected to column chromatography (silica gel 35−70 μm, 12 g, hexane/EtOAc mixtures). In order of elution, a mixture of the main stereoisomeric allylic alcohol **25** and enone **21** (hexane/EtOAc 4:1, 75 mg, approximate ratio by ^{1}H NMR alcohol **25**/enone **21** = 3:1), a mixture of alcohol **25**, its C2 epimer and enone **21** (hexane/EtOAc 7:3, 28 mg, approximate ratio by ^{1}H NMR alcohol **25**/C2 epimer of **25**/enone **21** = 4:3:1.5) and a mixture of starting diol **22** and hydroxylactam **28** (hexane/EtOAc 1:1, 48.5 mg, approximate ratio by ^{1}H NMR diol **22**/hydroxylactam **28** = 3:4) were obtained. Altogether, the approximate yield for the different compounds were alcohol **25** and its C2 epimer (43%), enone **21** (12%), hydroxylactam **28** (13%) and starting diol **22** (10%).

*b. Acetylation of the Mixture of Alcohol **25** and Enone **21**.* To a solution of the above mixture of alcohol **25** and enone **21** (75 mg, ratio alcohol **25**/enone **21** = 3:1, 0.18 mmol alcohol **25**) in anhydrous CH_2Cl_2 (1.5 mL) under an Ar atmosphere, anhydrous pyridine (0.11 mL, 1.35 mmol), acetic anhydride (0.11 mL, 1.16 mmol) and DMAP (14.9 mg, 0.122 mmol) were successively added, and the solution was stirred at room temperature for 15 h. The solution was made acidic by addition of an aqueous 0.1 N HCl solution (4.5 mL); the organic phase was separated and washed with aqueous 0.1 N HCl solution (2 × 4.5 mL), brine (6 mL), saturated aqueous $NaHCO_3$ solution (2 × 6 mL) and brine (6 mL), dried (anhydrous Na_2SO_4) and concentrated in vacuo to give a yellowish oily residue (76 mg), which was subjected to column chromatography (silica gel 35−70 μm, 4.0 g, hexane/EtOAc mixtures). In order of elution, pure acetate **29** as colorless oil (hexane/EtOAc 9:1, 59 mg, 92% yield) and enone **21** (hexane/EtOAc 4:1, 18 mg) were isolated. Spectroscopic data of acetate **29**: IR (ATR) ν 3055 (w), 2946 (w), 1771 (w), 1695 (s), 1428 (m), 1377 (m), 1288 (m), 1275 (m), 1180 (m), 1086 (m), 1006 (m), 742 (m), 692 (m), 633 (m) cm^{-1}; ^{1}H NMR δ 2.00 (dd, J = 14.0 Hz, J' = 6.4 Hz, 1H, C5′-CH_a), 2.06 (s, 3H, CH_3COO), 2.18 (dd, J = 14.0 Hz, J' = 5.6 Hz, 1H, C5′-CH_b), 2.20−2.34 (m, 2H, 4′-H_a and 6′-H_a), 2.38 (dq, J = 16.8 Hz, J' = 2.0 Hz, 1H, 5-H_{cis}), 2.71−2.83 (complex signal, 3H, 4′-H_b, 6′-H_b and 5′-H), 2.93 (s, 3H, *N*-CH_3), 3.06 (dt, J = 16.8 Hz, J' = 2.0 Hz, 1H, 5-H_{trans}), 3.71 (s, 3H, $COOCH_3$), 5.78−5.81 (m, 1H, 4-H), 5.94−5.96 (m, 1H, 2-H), 6.06 (dt, J = 5.6 Hz, J' = 2.0 Hz, 1H, 3-H); ^{13}C NMR δ 21.0 (CH_3, CH_3COO), 23.7 (CH_3, *N*-CH_3), 33.7 (CH_2) and 33.9 (CH_2) (C4′ and C6′), 38.8 (CH_2, C5′-CH_2), 40.3 (CH_2, C5), 41.2 (CH, C5′), 52.5 (CH_3, $COOCH_3$), 56.4 (C, C1), 81.5 (CH, C2), 128.9 (CH, C4), 136.5 (CH, C3), 152.05 (C) and 152.12 (C) (C3a′ and C6a′), 167.2 (C, C1′ and C3′), 170.2 (C, CH_3COO), 175.3 (C, $COOCH_3$). HRMS (ESI) (m/z) calcd for $[C_{18}H_{21}NO_6 + NH_4]^+$ 365.1707. Found: 365.1709. Anal. Calcd for $C_{18}H_{21}NO_6$ (347.36): C 62.24, H 6.09, N 4.03. Found: C 62.54, H 6.39, N 3.80.

Methyl 2-methyl-1,3-dioxo-1,2,3,4,5,6,7,8-octahydro-3a,7,8-(epiprop[2]ene[1,1,3]triyl)-5,8a-methanocyclohepta[c]pyrrole-7-carboxylate, 1 (R = COOMe). *a. From Acetate **29**.* To a solution of acetate **29** (27.8 mg, 80 μmol) in benzene (16 mL), *p*-TsOH·H_2O (3.0 mg, 16 μmol) was added, and the solution was heated under reflux in a Dean−Stark equipment for 24 h. The solution was allowed to cool to room temperature, treated with solid K_2CO_3 (about 60 mg) and was filtered. Concentration of the filtrate in vacuo gave a white solid (41.4 mg), which was subjected to column chromatography (silica gel, 2.0 g, hexane/EtOAc mixtures). On elution with hexane/EtOAc 85:15, product **1** (R= COOMe) (20.7 mg, 90% yield) was obtained as a white solid. The analytical sample of **1** (R = COOMe) was obtained as white solid: mp 166−167 °C, by sublimation at 110 °C/0.2−0.5 Torr; R_f = 0.32 (silica gel, 10 cm, hexane/EtOAc 1:1); IR (ATR) ν 2953 (w), 2860 (w), 1754 (w), 1731 (m), 1691 (s), 1424 (m), 1374 (m), 1327 (m), 1307 (m), 1253 (s), 1145 (m), 1110 (m), 1053 (m), 780 (m), 730 (m) cm^{-1}; ^{1}H NMR δ 1.88−1.89 (dm, J = 2.8 Hz, 2H, 6-H_2), 1.93−1.97 [ddm, J = 11.6 Hz, J' = 3.6 Hz, 2H, 4(12)-H_b], 2.04−2.07 [dm, J = 11.6 Hz, 2H, 4(12)-H_a], 2.62−2.65 (m, 1H, 5-H), 2.81 (s, 3H, *N*-CH_3), 3.25 [t, J = 2.0 Hz, 2H, 8(11)-H], 3.59 (s, 3H, OCH_3), 6.17 [t, J = 2.0 Hz, 2H, 9(10)-H]; ^{13}C NMR δ 24.4 (CH_3, *N*-CH_3), 35.3 (CH_2, C6), 38.2 (CH, C5), 38.6 [CH_2, C4(12)], 52.0 (CH_3, OCH_3), 55.5 [CH, C8(11)], 59.5 [C, C3a(8a)], 72.2 (C, C7), 135.5 [C, C9(10)], 173.3 (C, $COOCH_3$), 177.3 [C, C1(3)]. HRMS (ESI) (m/z) calcd for $[C_{16}H_{17}NO_4 + H]^+$ 288.1230. Found: 288.1217. Anal. Calcd for $C_{16}H_{17}NO_4$ (287.31): C 66.89, H 5.96, N 4.88. Found: C 66.80, H 6.15, N 4.67.

*b. From Alcohol **25**.* To a solution of alcohol **25** (33.5 mg, 0.11 mmol) in benzene (16 mL), *p*-TsOH·H_2O (4.2 mg, 22 μmol) was added, and the solution was heated under reflux with azeotropic distillation of water with a Dean−Stark equipment for 24 h. The solution was allowed to cool to room temperature, treated with solid K_2CO_3 (about 60 mg) and was filtered. Concentration of the filtrate in vacuo gave a brown solid (39.7 mg), which was subjected to column chromatography (silica gel, 2.0 g, hexane/EtOAc mixtures). On elution with hexane/EtOAc 85:15, product **1** (R = COOMe) (28.6 mg, 91% yield) was obtained as a white solid. A similar reaction starting from a mixture of **25** and its C2 epimer (134 mg, 0.44 mmol) gave **1** (R = COOMe) in 85% yield.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

^{1}H and ^{13}C NMR spectra for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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