Synthesis of Medium and Large Rings, XLVII[◇]

Selective Reactions, Resolution and Absolute Configuration of Bridged Hydroazulenes☆

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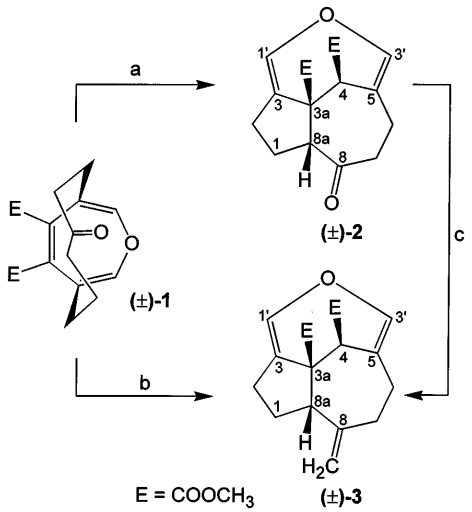
Treatment of the bridged oxepine **(±)-1** with a large excess of powdered sodium methoxide in Et_2O or with triphenylphosphonium methylide leads to the functionalized hydroazulenes **(±)-2** (69%) and **(±)-3** (81%). Regioselective and stereoselective cyclopropanation of **(±)-2** leads to the dibromocyclopropane derivative **(±)-4**. Epoxidation gives the epoxides **(±)-5** and **(±)-6**. The resolution of the hydroazulenone **(±)-2** is achieved by fractional crystallization of the quinine salt **(−)-8** of the corresponding mono acid **(±)-7**. The absolute configuration of **(+)-7** is established by X-ray analysis of the quinine salt **(−)-8**.

In previous papers[1][2] we reported on several approaches to functionalized hydroazulenes which are useful starting materials for the total synthesis of sesquiterpenoids isolated from fungi. Recently the lactarane 2(3)-8(9)-bisanhydrolactarorufin A[3] and an epimer of the naturally occurring tremulane tremulenolide B[4] could be synthesized by us from hydroazulene precursors[5].



Reagents: a: NaOMe, Et_2O. − b: Methyltriphenylphosphonium bromide, KO*t*Bu, Et_2O. − c: Methyltriphenylphosphonium bromide, KHMDS, toluene or Nysted reagent, $TiCl_4$, THF. For racemic compounds only one enantiomer is drawn.

Our approach to the tremulane skeleton[5] started with the hydroazulenone **(±)-2**[1][6] that is formed from the oxepine **(±)-1** and powdered sodium methoxide in Et_2O in a transannular Michael addition of the keto enolate to the C(4)=C(5) double bond of the oxepine ring[7].

In the course of our syntheses of bridged furanosides from related oxepines[8] we wanted to convert **(±)-1** into the corresponding methylene derivative [C=CH_2 instead of C=O] by Wittig methylenation. For this purpose a solution of **(±)-1** in Et_2O was added to triphenylphosphonium methylide generated by treatment of the corresponding phosphonium bromide with potassium *tert*-butoxide in the same solvent. After the usual work-up procedures to our surprise the methylenated hydroazulene **(±)-3** was isolated in 81% yield. The constitution and relative (3a*R**,4*S**,8a*S**)-configuration of **(±)-3** was established by X-ray analysis[9].

Normally the Wittig reaction is famous for the olefination of carbonyl groups in their original position[10].

The unexpected course of the methylenation of **(±)-1** to give **(±)-3** can be explained as follows: It is well-known[11] that carbonyl groups in medium rings undergo addition reactions very slowly because of the strain in the resulting intermediates or products. Therefore the ylide reacts with **(±)-1** as base in the first step to furnish a keto enolate that undergoes transannular cyclization as described earlier[1][6]. The carbonyl group in the seven-membered ring of **(±)-2** is now more reactive towards addition reactions and undergoes clean methylenation to furnish finally **(±)-3** in excellent yield.

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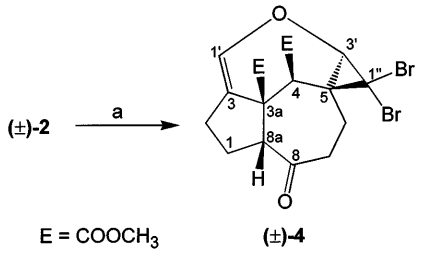
(±)-3 can also be obtained in 76% yield from **(±)-2** using the Lewis acidic conditions of the Nysted methylenation[12] (See Experimental Section). The Wittig methylenation of **(±)-2** has the problem that an epimer of **(±)-3** with 4*R** instead of 4*S** configuration can be formed as by-product (See Experimental Section). Therefore the above one-pot conversion of **(±)-1** in high yield to **(±)-3** which is a key intermediate of our tremulane approach[5] is not only of mechanistic interest but also of significant preparative value.

In this context it should be noted that the methylenation of **(±)-1** into its *exo* methylene derivative [C=CH_2 instead of C=O] is possible in 41% yield with the Nysted reagent[12] that avoids basic reaction conditions (See Experimental Section).



Reagents: a: $CHBr_3$, 50% aqueous NaOH, $BzlEt_3N^+Cl^-$, CH_2Cl_2

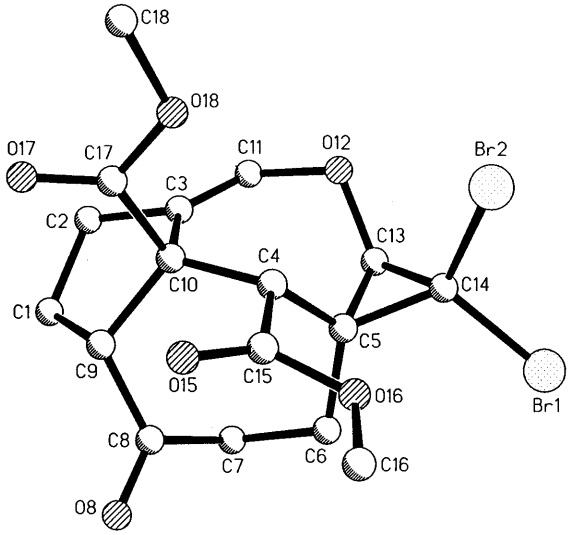
In our previous work[1][5] we also observed a regioselective hydrogenation of the C(3′)=C(5) enol ether double bond of **(±)-2** with the C(1′)=C(3) double bond being retained. This result encouraged us to study the cycloaddition of **(±)-2** with dibromocarbene because tetracylic hydroazulenes with a cyclopropane ring can have interesting biological activities[13].

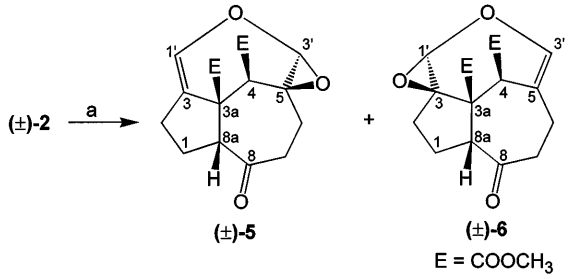
The reaction of **(±)-2** with this carbene, generated under phase-transfer catalysis conditions from tribromomethane, yielded the dibromocyclopropane **(±)-4** in 62% yield as the only isolated product besides 33% of the starting material. The constitution and relative (3′*R**,3a*R**,4*S**,5*S**,8a*R**)-configuration of **(±)-4** was established by X-ray analysis (See Figure 1)[14]. Thus, dibromocarbene adds regio- and stereoselectively to the C(3′)=C(5) enol ether double bond of **(±)-2**.

A tentative explanation for this selectivity depends on the structure of the starting material. The tricyclic system of **(±)-2** has the shape of a bowl (see ref.[6]). The attack of dibromocarbene to the C(3′)=C(5) enol ether double bond of **(±)-2** has taken place from the outer side of the bowl, which is less sterically hindered by the methoxycarbonyl group on C(4) than the C(1′)=C(3) enol ether double bond by the methoxycarbonyl group on the quarternary carbon C(3a). This can be derived from the torsion angles C(1′)=C(3)−C(3a)−C(ester) of 155.9° and C(3′)=C(5)−C(4)−C(ester) of 120.5°, respectively[7]. **(±)-4** has a similar bowl shape (See Figure 1).

In contrast to the above results epoxidation of **(±)-2** with *m*-chloroperbenzoic acid (*m*CPBA) led to a mixture of the epoxides **(±)-5** (30%) and **(±)-6** (38%), which can be easily separated by column chromatography.

Figure 1. A molecule of **(±)-4** in the crystal; arbitrary numbering





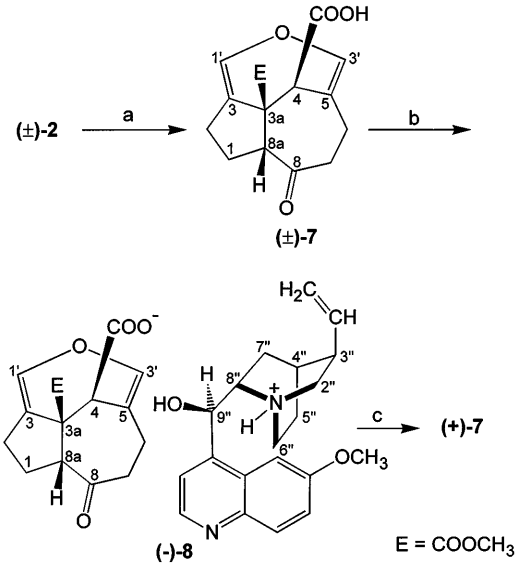
Reagents: a: *m*-CPBA, CH_2Cl_2

The structure of **(±)-5** was derived from the NMR spectra (see Experimental Section). The relative configuration at C(3′) follows from a n.O.e. between 3′-H and 4-H. The constitution and relative (1′*R**,3*R**,3a*R**,4*S**,8a*R**) configuration of **(±)-6** was established by X-ray analysis[15].

It may be summarized at present that highly selective additions [hydrogenation with a Pd[1] or the Wilkinson catalyst[5], dibromocarbene addition on the C(3′)=C(5) site] are possible in high yield, whereas more reactive systems (hydrogenation with a Pt catalyst[1], *m*CPBA) react with both enol ether double bonds.

All compounds described here and earlier[1][5] were obtained in racemic form. For the synthesis of natural products f. i. in the tremulane series[5] enantiomerically pure compounds are necessary. The racemic oxepine **(±)-1** was earlier resolved into its enantiomers with the (−)-(*P*)-configuration being determined[16], however by a rather tedious reaction sequence. Our continuous efforts finally led to the following very simple preparative procedure:

Regioselective saponification with 2 M NaOH at room temp. of the methoxycarbonyl group on C(4) in **(±)-2** leads to the mono carboxylic acid **(±)-7** in 89% yield. Under these conditions the ester group on the quaternary C(3a) is not hydrolysed. Treatment of **(±)-7** with the cheap base (−)-quinine in methanol gave the diastereomerically pure (de ≥ 97%, NMR) crystalline salt **(−)-8** in 48% yield. The

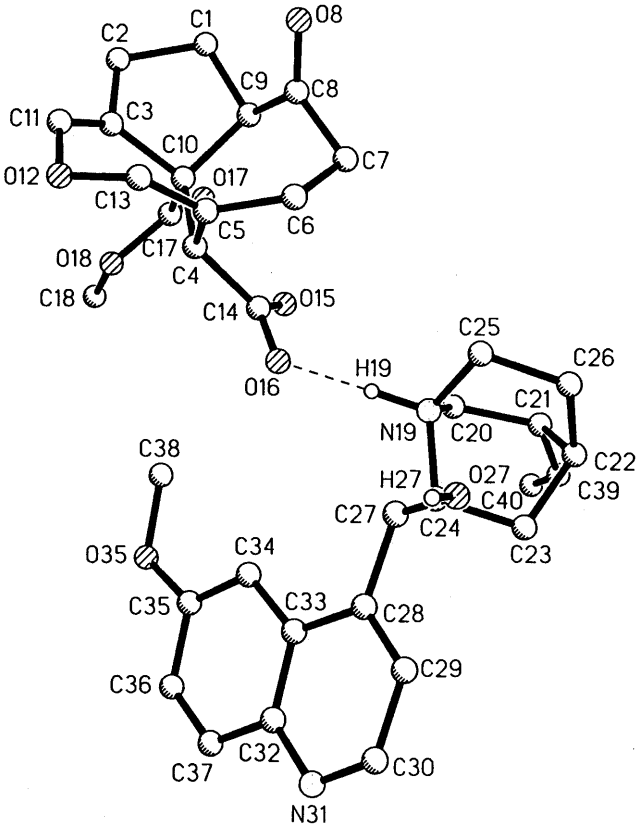


Reagents: a: 2 M NaOH, CH_2Cl_2. b: (−)-quinine, MeOH. c: 2 M HCl, CH_2Cl_2.

(3′′*R*,3a*R*,4*S*,4′′*S*,8′′*S*,8a*R*,9′′*R*) configuration of **(−)-8** was established by X-ray analysis (See Figure 2)[14].

(−)-8 was converted into the free carboxylic acid **(+)-7** by treatment with 2 M HCl. The enantiomeric excess of **(+)-7** (ee ≥ 97%) was derived from the ^{13}C-NMR spectrum of the quinine salt **(−)-8**, that only shows the signals of one diastereomer and could be finally established by NMR shift experiments with **(±)-7** and **(+)-7** (see Experimental Section).

Figure 2. A molecule of **(−)-8** in the crystal; arbitrary numbering



tion). Esterification of **(+)-7** with diazomethane furnished **(−)-2** in 96% yield. The (3a*R*,4*S*,8a*R*) configuration of **(−)-2** follows from the X-ray analysis of the quinine salt **(−)-8**[14]. Work-up of the mother liquor of **(−)-8** furnished in an analogous way **(−)-7**.

In summary this study has shown that the above described reactions of the readily available ketooxepine **1**[17] lead to functionalized hydroazulenes in good to excellent yield that can be used for further transformations. In addition these compounds are now available for the syntheses of sesquiterpenoids on a preparative scale in enantiomerically pure form with established absolute configurations.

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Experimental Section

IR: Perkin-Elmer 1600 FTIR. − ^{1}H NMR: TMS int., Bruker AC 200 P, ARX 300, DRX 500. − ^{13}C NMR: TMS int., Bruker AC 200 P, ARX 300, DRX 500. The assignment of signals marked with asterisks is arbitrary. − MS: Finnigan-MAT 8230; direct inlet (CI: isobutane). − UV: Zeiss DMR 10. − Column chromatography (CC): Baker Silica gel 40−60 μm. − TLC: Macherey−Nagel SIL G/UV$_{254}$. − Melting points: Büchi 510 (uncorrected). − Optical rotations: Perkin−Elmer polarimeter 241. − Elemental analysis: Mikroanalytisches Laboratorium Ilse Beetz, D-96301 Kronach. − All solvents and reagents were purified and dried according to common procedures.

1. *(3aR*,4S*,8aS*)-(±)-Dimethyl Decahydro-8-methylene-3,5-(2′-oxapropanediylidene)azulene-3a,4-dicarboxylate* [**(±)-3**]: To a suspension of 5.13 g (14.4 mmol) of methyltriphenylphosphonium bromide in 50 ml of Et_2O 1.54 g (13.7 mmol) of potassium *tert*-butoxide was added. The yellow mixture was refluxed under nitrogen for 40 min. After cooling to room temp. a solution of 2.00 g (6.53 mmol) of **(±)-1**[17] in 70 ml of Et_2O was added dropwise, the reaction mixture was then stirred for 15 min. The reaction was cooled to 0°C and quenched with water. The aqueous layer was extracted with Et_2O. The combined organic fractions were washed with water and satd. NaCl, dried and concentrated. The crude product was purified by CC [Et_2O/*n*-pentane (2:3)] to give 1.62 g (81%) of **(±)-3** (R_f = 0.50), m. p. 121−122°C (Et_2O/*n*-pentane). − IR (KBr): $\tilde{\nu}$ = 1735 cm^{-1} (s, C=O). − ^{1}H NMR ($CDCl_3$, 200 MHz, 55°C): δ = 1.50 (m, 1 H, 1-H), 2.05−2.25 (m, 7 H, CH_2), 3.66 (s, 3 H, $COOCH_3$), 3.71 (s, 3 H, $COOCH_3$), 3.83 (m, 1 H, 8a-H), 4.81 (m, therein ^2J = 2.1 Hz, 1 H, =CH_2), 4.86 (m, therein ^2J = 2.1 Hz, 1 H, =CH_2), 5.22 (s, 1 H, 4-H), 6.45 (m, 1 H, 3′-H), 6.56 (m, 1 H, 1′-H). − ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 26.65 (t, C-2), 28.01 (t, C-1), 30.06 (t, C-6), 34.82 (t, C-7), 46.64 (d, C-4), 49.43 (d, C-8a), 51.70 (q, $COOCH_3$), 52.80 (q, $COOCH_3$), 55.74 (s, C-3a), 117.45 (t, =CH_2), 127.48 (s, C-5)*, 129.98 (s, C-3)*, 142.46 (d, C-1′)**, 148.05 (d, C-3′)**, 148.30 (s, C-8), 171.87 (s, *C*O-OCH_3), 173.40 (s, *C*$OOCH_3$). The above assignments were derived from COSY, NOESY and ^{1}H ^{13}C shift-shift correlation spectra. − MS (CI): *m/z* (%): 305 (100) [M^+ + H], 245 (18) [M^+ + H − $HCOOCH_3$]. − $C_{17}H_{20}O_5$ (304.3): calcd. C 67.09, H 6.62, found C 67.10, H 6.54.

2. *(3aR*,4S*,8aS*)-(±)-Dimethyl Decahydro-8-methylene-3,5-(2′-oxapropanediylidene)azulene-3a,4-dicarboxylate* [**(±)-3**] by Nysted methylenation of **(±)-2**: Under nitrogen 7.35 g (3.22 mmol) of Nysted reagent[12] (20% in THF) was diluted with 12 ml of THF. After cooling to −78°C 711 mg (2.32 mmol) of **(±)-2** in 7 ml of

THF was dropped so slowly to the suspension that the temp. did not exceed −60°C. At the same temp. 0.26 ml (2.32 mmol) of $TiCl_4$ was added. The reaction mixture was warmed to room temp. over a period of 2 h and then refluxed for 20 h. After cooling to room temp. the reaction was quenched with water. The aqueous layer was extracted with Et_2O. The combined organic fractions were washed with water and satd. NaCl, dried and concentrated. After filtration through an aluminium oxide (neutral, act. I) column with Et_2O/*n*-pentane (1:1) the solvent was removed under reduced pressure. Crystallization of the crude product from CH_2Cl_2/*n*-pentane afforded 535 mg (76%) of **(±)-3**, m. p.: 121−122°C. − The spectroscopic data of **(±)-3** are identical with those reported above.

3. *(3aR*,4S*,8aS*)-(±)-Dimethyl Decahydro-8-methylene-3,5-(2′-oxapropanediylidene)azulene-3a,4-dicarboxylate* [**(±)-3**] *and Its (3aR*,4R*,8aS*)-(±)-Epimer* [**(±)-3**, 4*R** instead of 4*S**] by Wittig methylenation of **(±)-2**: To 643 mg (1.80 mmol) of methyltriphenylphosphonium bromide in 3 ml of toluene 2.60 ml (1.71mmol) of potassium bis(trimethylsilyl)amide (15% in toluene) was added and the mixture was warmed to 50°C under nitrogen for 15 min. After cooling to room temp. 500 mg (1.63 mmol) of **(±)-2** in 7 ml of toluene was added and stirring was continued for 90 min. The reaction was quenched with water. The aqueous layer was extracted with Et_2O. The combined organic fractions were washed with satd. NaCl, dried and concentrated. After filtration over a small silica-gel column with Et_2O/*n*-pentane (1:1) the crude product was purified by CC [Et_2O/*n*-pentane (2:3)] yielding 262 mg (53%) of **(±)-3** (R_f = 0.50) as colorless crystals and 137 mg (28%) of **(±)-3**, 4*R** instead of 4*S**, (R_f = 0.40) as a colorless oil. − The spectroscopic data of **(±)-3** are identical with those reported above. − Epimer **(±)-3**, 4*R** instead of 4*S**: m. p. 103−105°C (Et_2O/*n*-pentane). − IR (KBr): $\tilde{\nu}$ = 1740 cm^{-1} (s, C=O), 1715 cm^{-1} (s, C=O). − ^1H NMR ($CDCl_3$, 200 MHz, 55°C): δ = 1.64 (dddd, ^2J = 13.2 Hz, $^3J_{1,2}$ = 8.3 Hz, $^3J_{1,2}$ = 6.9 Hz, $^3J_{1,8a}$ = 4.5 Hz, 1 H, 1-H), 1.80 (dddd, ^2J = 13.2 Hz, $^3J_{1,8a}$ = 8.5 Hz, $^3J_{1,2}$ = 5.0 Hz, $^3J_{1,2}$ = 4.8 Hz, 1 H, 1-H), 2.11 (ddddd, ^2J = 13.0 Hz, $^3J_{2,1}$ = 8.3 Hz, $^3J_{2,1}$ = 5.0 Hz, $^4J_{2,8a}$ = 1.0 Hz, $^4J_{2,1'}$ = 0.8 Hz, 1 H, 2-H), 2.15−2.35 (m, 4 H, 2CH_2), 2.69 (dddd, ^2J = 13.0 Hz, $^3J_{2,1}$ = 6.9 Hz, $^3J_{2,1}$ = 4.8 Hz, $^4J_{2,1'}$ = 2.5 Hz, 1 H, 2-H), 2.82 (m, therein $^3J_{8a,1}$ = 8.5 Hz, $^3J_{8a,1}$ = 4.5 Hz, 1 H, 8a-H), 3.65 (s, 3 H, COOCH_3), 3.71 (s, 1 H, 4-H), 3.74 (s, 3 H, COOCH_3), 4.83 (m, therein ^2J = 1.4 Hz, 1 H, =CH_2), 4.88 (m, therein ^2J = 1.4 Hz, 1 H, =CH_2), 6.31 (d, $^4J_{3',6}$ = 1.5 Hz, 1 H, 3′-H), 6.49 (dd, $^4J_{1',2}$ = 2.5 Hz, $^4J_{1',2}$ = 0.8 Hz, 1 H, 1′-H). − ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 26.68 (t, C-7)*, 27.34 (t, C-1)*, 30.69 (t, C-6), 34.08 (t, C-2), 48.34 (d, C-4), 52.14 (q, COOCH_3), 52.35 (q, COOCH_3), 54.88 (d, C-8a), 55.54 (s, C-3a), 115.28 (t, =CH_2), 127.85 (s, C-3), 128.28 (s, C-5), 143.58 (d, C-1′), 146.56 (s, C-8), 148.11 (d, C-3′), 172.31 (s, *C*OOCH$_3$), 175.61 (s, *C*OOCH$_3$). The above assignments were derived from COSY, NOESY, HMQC and HMBC spectra. − MS (CI): *m/z* (%): 305 (100) [M^+ + H], 245 (48) [M^+ + H − $HCOOCH_3$]. − $C_{17}H_{20}O_5$ (304.3): calcd. C 67.09, H 6.62, found C 67.03, H 6.50.

4. *(±)-Dimethyl 10-Methylene-3,6-hexanooxepine-4,5-dicarboxylate* [**(±)-1**, C(10)=CH_2 instead of C(10)=O]: Under argon 5.05 g (2.20 mmol) of Nysted reagent[12] (20% in THF) was diluted with 8 ml of THF. After cooling to −78°C 500 mg (1.63 mmol) of **(±)-1** in 5 ml of THF was dropped so slowly to the suspension, that the temp. did not exceed −60°C. At the same temp. 0.18 ml (1.63 mmol) of $TiCl_4$ was added. The reaction mixture was warmed to room temp. over a period of 2 h and then refluxed for 24 h. After cooling to room temp. the reaction was quenched with water. The aqueous layer was extracted with Et_2O. The combined organic fractions were washed with water and satd. NaCl, dried and concentrated. The crude product was purified by CC [Et_2O/*n*-pentane (1:2)] to give 203 mg (41%) of the methylene oxepine [**(±)-1**, C=CH_2 instead of C=O], (R_f = 0.37) as a colorless oil. − IR (film): $\tilde{\nu}$ = 1726 cm^{-1} (s, C=O). − UV (ethanol): λ_{max} (lg ε) = 280 nm (3.17), 213 nm (3.63). − ^1H NMR ($CDCl_3$, 300 MHz): δ = 1.67−1.77 (m, 5 H, CH_2), 1.87−2.17 (m, 2 H, CH_2), 2.29 (ddd, ^2J = 13.4 Hz, ^3J = 8.5 Hz, ^3J = 5.6 Hz, 1 H, 8-H)*, 2.45 (dddd, ^2J = 13.4 Hz, ^3J = 6.1 Hz, ^3J = 4.9 Hz, ^4J = 1.3 Hz, 1 H, 13-H)*, 2.58 (dddd, ^2J = 13.4 Hz, ^3J = 6.1 Hz, ^3J = 4.9 Hz, ^4J = 1.3 Hz, 1 H, 8-H)*, 3.81 (s, 6 H, 2 $COOCH_3$), 4.68 (ddd, ^2J = 1.5 Hz, ^4J = 1.0 Hz, ^4J = 1.0 Hz, 1 H, 14-H), 4.93 (ddd, ^2J = 1.5 Hz, ^4J = 1.2 Hz, ^4J = 1.2 Hz, 1 H, 14-H), 6.31 (ddd, ^4J = 1.3 Hz, ^4J = 0.5 Hz, ^4J = 0.5 Hz, 1 H, 7-H)**, 6.33 (d, ^4J = 1.3 Hz, ^4J = 0.8 Hz, ^4J = 0.8 Hz, 1 H, 2-H)**. − ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 26.56 (t, CH_2), 28.51 (t, CH_2), 29.28 (t, CH_2), 34.85 (t, CH_2), 35.53 (t, CH_2), 52.11 (q, COOCH_3), 52.14 (q, COOCH_3), 112.23 (t, C-14), 125.41 (s, C-3)*, 126.38 (s, C-6)*, 137.51 (s, C-4)**, 137.99 (s, C-5)**, 147.12 (d, C-7)***, 147.44 (d, C-2)***, 148.22 (s, C-10), 165.90 (s, *C*OOCH$_3$), 166.20 (s, *C*OOCH$_3$). − MS (CI): *m/z* (%) = 305 (25) [M^+ + H], 289 (17) [M^+ + H − CH_4], 273 (100) [M^+ + H − CH_3OH]. − $C_{17}H_{20}O_5$ (304.3): calcd. C 67.09, H 6.62, found C 67.00, H 6.55.

5. *(3′R*,3aR*,4S*,5S*,8aR*)-(±)-Dimethyl Decahydro-3,5-(3′,5-dibromomethano-2′-oxa-3′-propane-1′-ylidene)-8-oxoazulene-3a,4-dicarboxylate* [**(±)-4**]. To a solution of 300 mg (0.98 mmol) of **(±)-2** in 45 ml of CH_2Cl_2 and 3 ml of $CHBr_3$ 37 mg (0.199 mmol) of benzyltriethylammonium chloride and 1.5 ml of 50% aqueous NaOH were added. After refluxing for 11 h the reaction was cooled to room temp. and quenched with 150 ml of water and 50 ml of 5 M HCl. The aqueous layer was extracted with CH_2Cl_2. The combined organic phases were dried and concentrated. The crude product was purified by CC [Et_2O/*n*-pentane (1:1)] yielding 288 mg (62%) of **(±)-4** (R_f = 0.16) as colorless crystals besides 100 mg (33%) of unreacted starting material **(±)-2** (R_f = 0.27). − M. p. 173−175°C (CH_2Cl_2/Et_2O). − IR (KBr): $\tilde{\nu}$ = 1732 cm^{-1} (s, ester C=O), 1699 cm^{-1} (s, ketone C=O). − ^1H NMR ($CDCl_3$, 500 MHz): δ = 1.67 (dddd, ^2J = 12.9 Hz, $^3J_{6,7}$ = 8.2 Hz, $^3J_{6,7}$ = 4.0 Hz, $^4J_{6,3'}$ = 1.5 Hz, 1 H, 6-H), 1.91 (ddd, ^2J = 12.4 Hz, ^3J = 8.5 Hz, $^3J_{1,8a}$ = 3.8 Hz, 1 H, 1-H), 2.26 (m, 1 H, 2-H), 2.27 (m, 1 H, 6-H), 2.32 (m, 1 H, 2-H), 2.33 (m, 1 H, 1-H), 2.39 (dddd, ^2J = 11.6 Hz, $^3J_{7,6}$ = 8.2 Hz, ^3J = 3.7 Hz, ^4J = 1.2 Hz, 1 H, 7-H), 2.72 (ddd, ^2J = 11.6 Hz, ^3J = 10.4 Hz, $^3J_{7,6}$ = 4.0 Hz, 1 H, 7-H), 3.75 (s, 3 H, $COOCH_3$), 3.79 (s, 3 H, $COOCH_3$), 3.83 (s, 1 H, 4-H), 3.89 (dd, $^3J_{8a,1}$ = 8.8 Hz, $^3J_{8a,1}$ = 3.8 Hz, 1 H, 8a-H), 4.85 (d, $^4J_{3',6}$ = 1.5 Hz, 1 H, 3′-H), 6.53 (dd, ^4J = 2.3 Hz, ^4J = 1.2 Hz, 1 H, 1′-H). − ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 24.22 (t, C-1), 26.01 (t, C-2)*, 31.15 (t, C-6)*, 34.87 (s, C-5), 36.94 (t, C-7), 40.18 (s, C-1′′), 49.34 (d, C-4), 52.79 (q, COOCH_3), 53.63 (q, COOCH_3), 57.22 (d, C-8a), 59.61 (s, C-3a), 72.96 (d, C-3′), 130.52 (s, C-3), 141.04 (d, C-1′), 170.48 (s, *C*OOCH$_3$), 171.73 (s, *C*OOCH$_3$), 209.80 (s, C-8). The above assignments were derived from COSY and NOESY spectra. − MS (CI, ^{79}Br): *m/z* (%) = 477 (51) [M^+ + 1], 479 (100) [M^+ + 3], 481 (49) [M^+ + 5]. − HRMS calcd. for $C_{17}H_{18}{}^{79}Br_2O_6$ [M^+]: 475.9470, found 475.9470. − $C_{17}H_{18}Br_2O_6$ (478.1): calcd. C 42.71, H 3.79, found C 42.77, H 3.89.

X-ray Structure Analysis of **(±)-4**[14]: The data of a crystal (CH_2Cl_2/*n*-pentane) were obtained with a Siemens P4-diffractometer (Mo-K_α radiation, graphite monochromator). Cell dimensions were refined from 61 reflections; *a* = 1246.5(1), *b* = 994.89(7), *c* = 1446.8(1) pm, β = 93.368(6)°, *V* = 1791.1(3) · 10^6 pm^3, monoclinic, space group $P2_1/c$, *Z* = 4, $\rho_{calcd.}$ = 1.773 g/cm^3, 3812 unique intensities, of which 3041 [$F_o > 3\,\sigma(F)$] were observed in the θ range 1.75−27.5°, measured with ω-scan technique. The

structure was solved by using direct-phase determination and refined on *F* by using SHELXTL-Plus. Positional parameters, anisotropic displacement parameters for all atoms except for hydrogen atoms, groupwise isotropic displacement parameters for all hydrogen atoms, treated as rigid groups. $R = 0.051$, $R_w = 0.046$, $w = 1/\sigma^2(F)$.

6. *(3′S*,3aR*,4S*,5S*,8aR*)-(±)-Dimethyl 3′,5-Epoxy-decahydro-8-oxo-3,5-(2′-oxapropanylidene)azulene-3a,4-dicarboxylate* [**(±)-5**] *and (1′R*,3R*,3aR*,4S*,8aR*)-(±)-Dimethyl 1′,3-Epoxy-decahydro-8-oxo-3,5-(2′-oxapropaneylidene)azulene-3a,4-dicarboxylate* [**(±)-6**]: To a solution of 200 mg (0.654 mmol) of **(±)-2** in 20 ml of CH_2Cl_2 232 mg (1.34 mmol) of *m*CPBA in 10 ml of CH_2Cl_2 was added at 0°C and stirred for 1.5 h at the same temp. After warming up to room temp. stirring was continued for 23 h. The reaction mixture was diluted with 30 ml of CH_2Cl_2, washed with 2 M HCl and water, dried and concentrated. The crude product was purified by CC [Et_2O/*n*-pentane (3:1)] yielding 79 mg (38%) of **(±)-5** ($R_f = 0.31$) as colorless crystals and 64 mg (30%) of **(±)-6** ($R_f = 0.38$) as colorless crystals besides 15 mg (8%) of unreacted starting material **(±)-2** ($R_f = 0.45$).

(±)-5: m. p. 128−130°C (Et_2O/*n*-pentane). − IR (KBr): $\tilde{\nu} = 1735$ cm^{-1} (s, ester C=O), 1698 cm^{-1} (s, ketone C=O). − ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 1.35 (dddd, ^2J = 13.8 Hz, $^3J_{6,7}$ = 10.9 Hz, $^3J_{6,7}$ = 6.5 Hz, J = 0.9 Hz, 1 H, 6-H), 2.08 (m, 1 H, 1-H), 2.12 (m, 1 H, 2-H), 2.22 (m, 1 H, 1-H), 2.24 (m, 1 H, 2-H), 2.27 (ddd, ^2J = 13.8 Hz, $^3J_{6,7}$ = 6.5 Hz, $^3J_{6,7}$ = 4.6 Hz, 1 H, 6-H), 2.47 (ddd, ^2J = 11.9 Hz, $^3J_{7,6}$ = 6.5 Hz, $^3J_{7,6}$ = 4.6 Hz, 1 H, 7-H), 2.59 (dddd, ^2J = 11.9 Hz, $^3J_{7,6}$ = 10.9 Hz, $^3J_{7,6}$ = 6.5 Hz, J = 0.8 Hz, 1 H, 7-H), 3.73 (s, 3 H, $COOCH_3$), 3.86 (s, 3 H, $COOCH_3$), 3.93 (dd, ^3J = 7.9 Hz, ^3J = 1.73 Hz, 1 H, 8a-H), 4.38 (s, 1 H, 4-H), 4.70 (s, 1 H, 3′-H), 6.29 (dd, ^4J = 2.5 Hz, ^4J = 0.8 Hz, 1 H, 1′-H). − ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 21.97 (t, C-1), 24.73 (t, C-2), 26.85 (t, C-6), 36.36 (t, C-7), 50.76 (d, C-4), 52.78 (q, $COOCH_3$), 53.44 (q, $COOCH_3$), 56.66 (d, C-8a), 58.66 (s, C-3a), 60.14 (s, C-5), 87.04 (d, C-3′), 129.83 (s, C-3), 137.10 (d, C-1′), 171.42 (s, $COOCH_3$), 171.56 (s, $COOCH_3$), 209.11 (s, C-8). The above assignments were derived from COSY, NOESY, HMBC and HSQC spectra. MS (CI): *m/z* (%) = 323 (100) [M^+ + H]. − $C_{16}H_{18}O_7$ (322.3): calcd. C 59.62, H 5.63, found C 59.61, H 5.65.

(±)-6: m. p. 143−145°C (Et_2O/*n*-pentane). − IR (KBr): $\tilde{\nu} = 1745$ cm^{-1} (s, ester C=O), 1708 cm^{-1} (s, ketone C=O). − ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 1.59 (ddd, ^2J = 14.4 Hz, $^3J_{2,1}$ = 10.3 Hz, $^3J_{2,1}$ = 4.8 Hz, 1 H, 2-H), 1.79 (ddd, ^2J = 14.4 Hz, $^3J_{2,1}$ = 12.3 Hz, $^3J_{2,1}$ = 6.4 Hz, 1 H, 2-H), 2.13 (dddd, ^2J = 13.5 Hz, $^3J_{1,2}$ = 12.3 Hz, $^3J_{1,8a}$ = 8.7 Hz, $^3J_{1,2}$ = 4.8 Hz, 1 H, 1-H), 2.19 (ddd, ^2J = 13.7 Hz, $^3J_{6,7}$ = 11.2 Hz, $^3J_{6,7}$ = 8.2 Hz, 1 H, 6-H), 2.29 (ddddd, ^2J = 13.7 Hz, $^3J_{6,7}$ = 8.8 Hz, $^3J_{6,7}$ = 2.0 Hz, $^4J_{6,3'}$ = 1.5 Hz, J = 0.6 Hz, 1 H, 6-H), 2.44 (ddd, ^2J = 11.3 Hz, $^3J_{7,6}$ = 8.2 Hz, $^3J_{7,6}$ = 2.0 Hz, 1 H, 7-H), 2.45 (dddd, ^2J = 13.5 Hz, $^3J_{1,2}$ = 10.3 Hz, $^3J_{1,2}$ = 6.4 Hz, $^3J_{1,8a}$ = 2.2 Hz, 1 H, 1-H), 2.84 (dddd, ^2J = 11.3 Hz, $^3J_{7,6}$ = 11.2 Hz, $^3J_{7,6}$ = 8.8 Hz, J = 0.5 Hz, 1 H, 7-H), 3.80 (s, 3 H, $COOCH_3$), 3.81 (s, 3 H, $COOCH_3$), 3.88 (dd, $^3J_{8a,1}$ = 8.7 Hz, $^3J_{8a,1}$ = 2.2 Hz, 1 H, 8a-H), 4.61 (s, 1 H, 4-H), 4.76 (s, 1 H, 1′-H), 6.25 (ddd, $^4J_{3',6}$ = 1.5 Hz, J = 1.0 Hz, J = 0.5 Hz, 1 H, 3′-H). − ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 19.85 (t, C-1), 22.95 (t, C-6), 27.11 (t, C-2), 38.75 (t, C-7), 44.42 (d, C-4), 52.57 (q, $COOCH_3$), 53.12 (q, $COOCH_3$), 54.32 (s, C-3a), 55.08 (d, C-8a), 69.13 (s, C-3), 85.48 (d, C-1′), 124.67 (s, C-5), 142.17 (d, C-3′), 171.42 (s, $COOCH_3$), 171.56 (s, $COOCH_3$), 208.39 (s, C-8). The above assignments were derived from COSY, NOESY, HMBC and HSQC spectra. − MS (CI): *m/z* (%) = 323 (100) [M^+ + H]. − $C_{16}H_{18}O_7$ (322.3): calcd. C 59.62, H 5.63, found C 59.40, H 5.72.

7. *(3aR*,4S*,8aR*)-(±)-Decahydro-3a-methoxycarbonyl-8-oxo-3,5-(2′-oxapropanediylidene)azulene-4-carboxylic Acid* [**(±)-7**]: To 510 mg (1.67 mmol) of **(±)-2** in 3.5 ml of CH_2Cl_2 and 17 ml of methanol 7 ml of 2 M NaOH was added at 0°C and stirred at the same temp. for 15 min. After warming up to room temp. the reaction mixture was stirred for 14 h, concentrated and dissolved in 10 ml of diethyl ether/10 ml of water. The aqueous layer was washed with water, acidified with 5 M HCl and extracted with CH_2Cl_2. The organic layer was dried and concentrated. The resulting residue was recrystallized (acetone/*n*-pentane) to afford 435 mg (89%) of **(±)-7** as colorless crystals. − M. p. 196−197°C (acetone/*n*-pentane). − IR (KBr): $\tilde{\nu} = 3600-2900$ cm^{-1} (br., OH), 1745 cm^{-1} (s, ester C=O), 1680 cm^{-1} (s, acid C=O). − ^{1}H NMR ([D_6]acetone, 300 MHz): δ = 1.76−1.99 (m, 3 H), 2.32 (ddd, ^2J = 11.5 Hz, $^3J_{7,6}$ = 8.0 Hz, $^3J_{7,6}$ = 1.0 Hz, 1 H, 7-H), 2.37 (m, 1 H, 1-H), 2.55 (m, therein ^2J = 13.0 Hz, $^3J_{6,7}$ = 8.3 Hz, $^3J_{6,7}$ = 1.0 Hz, 1 H, 6-H), 2.71 (ddd, ^2J = 13.0 Hz, $^3J_{6,7}$ = 11.5 Hz, $^3J_{6,7}$ = 8.0 Hz, 1 H, 6-H), 2.84 (ddd, ^2J = 11.5 Hz, $^3J_{7,6}$ = 11.5 Hz, $^3J_{7,6}$ = 8.3 Hz, 1 H, 7-H), 3.70 (s, 3 H, $COOCH_3$), 3.72 (dd, $^3J_{8a,1}$ = 8.4 Hz, $^3J_{8a,1}$ = 2.3 Hz, 1 H, 8a-H), 4.20−5.90 (br. s, 1 H, COOH, exchangeable), 5.23 (s, 1 H, 4-H), 6.41 (m, 1 H, 3′-H), 6.46 (m, 1 H, 1′-H). − ^{13}C NMR ([D_6]acetone, 75 MHz): δ = 21.69 (t, C-1), 23.82 (t, C-6), 25.01 (t, C-2), 38.92 (t, C-7), 46.86 (d, C-4), 53.05 (q, $COOCH_3$), 55.99 (d, C-8a), 56.22 (s, C-3a), 125.58 (s, C-5), 128.12 (s, C-3), 142.38 (d, C-1′), 148.57 (d, C-3′), 172.28 (s, $COOCH_3$), 173.60 (s, COOH), 205.99 (s, C-8). The above assignments were derived from COSY, NOESY, HMBC and ^{1}H ^{13}C shift-shift correlation spectra. MS (CI): *m/z* (%) = 293 (100) [M^+ + H] − $C_{15}H_{16}O_6$ (292.3): calcd. C 61.64, H 5.52, found C 61.49, H 5.43.

8. *(3′′R,4′′S,8′′S,9′′R)-(−)-Quinine Salt of (3aR,4S,8aR)-(−)-Decahydro-3a-methoxycarbonyl-8-oxo-3,5-(2′-oxapropanediylidene)azulene-4-carboxylic Acid* [**(−)-8**]: To a refluxing solution of 5.80 g (20.0 mmol) of **(±)-7** in 100 ml of methanol 6.40 g (20.0 mmol) of (−)-quinine in 50 ml of methanol was added dropwise. After refluxing for 1 h the solvent was removed in vacuo. The crude product was resolved in 425 ml of methanol and left to crystallize for 48 h at room temp. yielding 4.53 g (37%) of **(−)-8**. One half of the mother liquor was removed in vacuo and the remainder left to stand for 48 h yielding additional 1.33 g (11%) of **(−)-8**. Total yield of **(−)-8**: 5.86 g (48%) as colorless crystals, m. p. 229−231°C, specific rotations (c = 0.50, methanol): $[\alpha]_{589}^{20}$= −107, $[\alpha]_{578}^{20}$= −113, $[\alpha]_{546}^{20}$= −132, $[\alpha]_{436}^{20}$= −271, $[\alpha]_{365}^{20}$= −685. − IR (KBr): $\tilde{\nu} = 3388$ cm^{-1} (OH), 1733 cm^{-1} (ester C=O), 1702 cm^{-1} (ketone C=O). − ^{1}H NMR ([D_4]methanol, 500 MHz): δ = 1.58 (dddd, ^2J = 14.2 Hz, $^3J_{7'',8''}$ = 11.0 Hz, J = 4.0 Hz, J = 2.7 Hz, 1 H, 7′′-H), 1.82 (dddd, ^2J = 12.4 Hz, ^3J = 9.0 Hz, ^3J = 7.9 Hz, ^3J = 4.7 Hz, 1 H, 1-H), 1.89 (ddd, ^2J = 13.7 Hz, ^3J = 7.4 Hz, ^3J = 2.0 Hz, 1 H, 5′′-H), 1.93 (m, 1 H, 2-H), 1.95 (m, 1 H, 2-H), 2.06 (ddd, ^2J = 12.7 Hz, $^3J_{6,7}$ = 11.3 Hz, $^3J_{6,7}$ = 7.9 Hz, 1 H, 6-H), 2.07 (m, 1 H, 4′′-H), 2.16 (m, 1 H, 7′′-H), 2.19 (m, 1 H, 6′′-H), 2.25 (ddd, ^2J = 11.3 Hz, $^3J_{7,6}$ = 7.9 Hz, $^3J_{7,6}$ = 1.1 Hz, 1 H, 7-H), 2.33 (dddd, ^2J = 12.4 Hz, ^3J = 9.2 Hz, ^3J = 7.0 Hz, $^3J_{1,8a}$ = 2.1 Hz, 1 H, 1-H), 2.66 (ddddd, ^2J = 12.7 Hz, $^3J_{6,7}$ = 8.3 Hz, J = 2.0 Hz, $^3J_{6,7}$ = 1.1 Hz, $^4J_{6,3'}$ = 0.9 Hz, 1 H, 6-H), 2.75 (m, 1 H, 3′′-H), 3.08 (ddd, ^2J = 11.3 Hz, $^3J_{7,6}$ = 11.3 Hz, $^3J_{7,6}$ = 8.3 Hz, 1 H, 7-H), 3.23 (m, 1 H, 2′′-H), 3.26 (m, 1 H, 5′′-H), 3.56 (dd, ^2J = 13.2 Hz, ^3J = 10.7 Hz, 1 H, 2′′-H), 3.59 (m, 1 H, 6′′-H), 3.69 (s, 3 H, $COOCH_3$), 3.83 (dd, J = 8.2 Hz, $^3J_{8a,1}$ = 2.1 Hz, 1 H, 8a-H), 4.00 (s, 3 H, OCH_3), 4.16 (dddd, J = 13.2 Hz, $^3J_{8'',7''}$ = 11.0 Hz, J = 5.0 Hz, $^3J_{8'',9''}$ = 2.3 Hz, 1 H, 8′′-H), 5.03

(ddd, ^3J = 10.5 Hz, ^2J = 1.2 Hz, J = 1.2 Hz, 1 H, C=CH_2), 5.09 (s, 1 H, 4-H), 5.12 (ddd, ^3J = 17.2 Hz, ^2J = 1.2 Hz, J = 1.3 Hz, 1 H, C=CH_2), 5.79 (ddd, ^3J = 17.2 Hz, ^3J = 10.5 Hz, J = 7.2 Hz. 1 H, CH=C), 5.92 (d, $^3J_{9'',8''}$ = 2.3 Hz, 1 H, 9′′-H), 6.28 (dd, ^4J = 2.2 Hz, $^4J_{3',6}$ = 0.9 Hz, 1 H, 3′-H), 6.38 (dd, ^4J = 2.0 Hz, ^4J = 1.2 Hz, 1 H, 1′-H), 7.42 (d, J = 2.7 Hz, 1 H, aromatic H), 7.49 (dd, J = 9.2 Hz, J = 2.7 Hz, 1 H, aromatic H), 7.77 (dd, J = 4.5 Hz, J = 0.8 Hz, 1 H, aromatic H), 7.99 (d, J = 9.2 Hz, 1 H, aromatic H). 8.72 (d, J = 4.6 Hz, 1 H, aromatic H).The OH and NH signals were not detectable in [D_4]methanol. – ^{13}C NMR ([D_4]methanol, 125 MHz): δ = 21.90 (t, C-1), 24.75 (t, C-6), 25.55 (t, C-2), 28.50 (d, C-4′′), 38.95 (d, C-3′′), 39.66 (t, C-7), 45.10 (t, C-6′′), 49.17 (d, C-4), 49.63 (t, C-7′′)*, 49.51 (t, C-5′′)* 53.13 (q, COOCH_3), 55.73 (t, C-2′′), 56.63 (q, OCH_3), 56.94 (d, C-8a), 58.07 (s, C-3a), 61.31 (d, C-8′′), 69.00 (d, C-9′′), 102.57 (d, aromatic C), 116.90 (t, C=CH_2), 120.51 (d, aromatic C), 123.20 (d, aromatic C), 127.59 (s, aromatic C), 128.31 (s, C-5), 128.78 (s, C-3), 131.69 (d, aromatic C), 139.78 (d, -CH=), 142.70 (d, C-1′), 144.80 (s, aromatic C), 147.45 (s, aromatic C), 148.14 (d, C-3′), 148.26 (d, aromatic C), 160.15 (s, aromatic C), 174.80 (s, COOCH$_3$), 178.35 (s, COO$^-$), 212.20 (s, C-8). The above assignments were derived from COSY, HSQC and HMBC spectra. MS (CI): *m/z* (%) = 325 (100) [quinine + H], 293 (22) [acid + H]. – $C_{35}H_{40}N_2O_8$ (616.7): calcd. C 68.17, H 6.54, found C 68.16, H 6.48.

X-ray Structure Analysis of **(–)-8**[14]: The data of a crystal (methanol) with the approximate dimensions 0.45 × 0.55 × 0.20 mm were obtained with a Siemens P4 diffractometer (Mo-K_α radiation, graphite monochromator). Cell dimensions were refined from 62 reflections; a = 814.72(5), b = 1966.9(1), c = 1008.91(5) pm, β = 107.164(5)°, V = 1544.7(2) · 10^6 pm^3, monoclinic, space group $P2_1$, Z = 2, $\rho_{calcd.}$ = 1.326 g/cm^3, 7092 unique intensities, of which 5977 [$F_o > 3\sigma(F)$] were observed in the θ range 1.75–27.5°, measured with ω-scan technique. The structure was solved by using direct-phase determination and refined on F by using SHELXTL-Plus. Positional parameters, anisotropic displacement parameters for all atoms except for hydrogen atoms, groupwise isotropic displacement parameters for all hydrogen atoms, treated as rigid groups. R = 0.046, R_w = 0.043, $w = 1/\sigma^2(F)$.

9. *(3aR,4S,8aR)-(+)-Decahydro-3a-methoxycarbonyl-8-oxo-3,5-(2′-oxapropanediylidene)azulene-4-carboxylic Acid* [**(+)-7**]: To a suspension of 2.00 g (3.24 mmol) of **(–)-8** in 50 ml of CH_2Cl_2 50 ml of 2 M HCl was added and stirred for 90 min at room temp. The organic layer was washed with 2 M HCl and water, dried and concentrated. Crystallization from acetone/*n*-pentane afforded 715 mg (75%) of **(+)-7** as colorless needles, m. p. 186–187°C, specific rotations (c = 2.00, methanol): $[\alpha]_{589}^{20}$ = +9.8, $[\alpha]_{578}^{20}$ = +9.9, $[\alpha]_{546}^{20}$ = +10.3, $[\alpha]_{436}^{20}$ = +5.0, $[\alpha]_{365}^{20}$ = –43.7, specific rotations (c = 2.00, acetone): $[\alpha]_{589}^{20}$ = +2.7, $[\alpha]_{578}^{20}$ = +2.5, $[\alpha]_{546}^{20}$ = +1.7, $[\alpha]_{436}^{20}$ = –11.2, $[\alpha]_{365}^{20}$ = –74.9. The spectral data are identical with those of **(±)-7**. – $C_{15}H_{16}O_6$ (292.30): calcd. C 61.64, H 5.52, found C 61.68, H 5.52.

10. *^{1}H-NMR-Spectroscopic Determination of the Enantiomeric Excess of* **(+)-7** *by Shift Experiments of* **(±)-7** *and* **(+)-7 with Tris[3-***(trifluoromethylhydroxymethylene)-D-camphorato]europium(III):* 18.0 mg (0.062 mmol) of **(±)-7** and 20.0 mg (0.022 mmol) of the shift reagent were dissolved in 0.60 ml of [D_4]methanol. In the ^{1}H-NMR spectrum of the methyl ester group two singlets appeared. – ^{1}H NMR ([D_4]methanol, 200 MHz): δ = 3.96 (s, 0.49 CH_3 of COOCH_3), 3.98 (s, 0.51 CH_3 of COOCH_3). 18.0 mg (0.062 mmol) of **(+)-7** and 20.0 mg (0.022 mmol) of the shift reagent were dissolved in 0.60 ml of [D_4]methanol. Only one signal for the methyl ester group was observed there. – ^{1}H NMR ([D_4]methanol, 200 MHz): δ = 3.95 (s, 3 H, COOCH_3).

11. *(3aR,4S,8aR)-(+)-Dimethyl Decahydro-8-oxo-3,5-(2′-oxapropanediylidene)azulene-3a,4-dicarboxylate* [**(–)-2**]: To a solution of 115 mg (0.375 mmol) of **(+)-7** in 50 ml of CH_2Cl_2 an ethereal solution of CH_2N_2 was added until the mixture turned yellow. After stirring at room temp. for 1 h excess CH_2N_2 was destroyed with silica gel. After filtration the solvent was removed in vacuo and the resulting residue was purified by CC [Et_2O/*n*-pentane (1:1)] yielding 116 mg (96%) of **(–)-2** as colorless crystals, m. p. 108–110°C (Et_2O/*n*-pentane), specific rotations (c = 0.53, methanol): $[\alpha]_{589}^{20}$ = –1.2, $[\alpha]_{578}^{20}$ = –1.4, $[\alpha]_{546}^{20}$ = –2.6, $[\alpha]_{436}^{20}$ = –16.6, $[\alpha]_{365}^{20}$ = –78.0. The spectral data are identical with those of **(±)-2**[1].

12. *(3aS,4R,8aS)-(–)-Decahydro-3a-methoxycarbonyl-8-oxo-3,5-(2′-oxapropanediylidene)azulene-4-carboxylic Acid* [**(–)-7**]: The mother liquor of the above resolution procedure was concentrated in vacuo to give an oily residue. 2.00 g of this oil were dissolved in 100 ml of CH_2Cl_2 and treated with 50 ml of 2 N HCl. Working up as described above gave 725 mg (76%) of **(–)-7** as colorless crystals, m. p. 176–178°C (acetone/*n*-pentane), specific rotations (c = 2.00, methanol): $[\alpha]_{589}^{20}$ = –9.3, $[\alpha]_{578}^{20}$ = –9.4, $[\alpha]_{546}^{20}$ = –9.8, $[\alpha]_{436}^{20}$ = –5.2, $[\alpha]_{365}^{20}$ = +37.0. The spectral data are identical with those of **(±)-7**.

☆ Dedicated to Professor Dr. *Wolfgang Steglich* on the occasion of his 65th birthday.

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