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Synthetic Approach to the Grayanotoxins and Asebotoxins: A New Construction of A, B, and C Ring System of Grayanotoxan[1)]

Tetsuji Kametani, Masayoshi Tsubuki, Hideo Nemoto, and Keiichiro Fukumoto

Pharmaceutical Institute, Tohoku University[2)]

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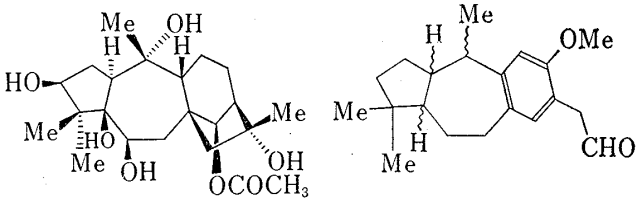
1,2,3,4,9,10-Hexahydro-6-methoxy-1,1,4-trimethylbenz[*f*]azulene (**15**) was synthesized by a rearrangement of 2,3,3a,4,5,9b-hexahydro-9b-(1-hydroxyethyl)-8-methoxy-3,3-dimethyl-1H-benz[*e*]indene (**14**), which was in turn obtained from a thermolysis of the olefinic benzocyclobutene (**11**) followed by treatment with methyllithium. The hexahydrobenzazulene (**15**) was converted into 7-formylmethyl-1,2,3,3a,4,9,10,10a-octahydro-6-methoxy-1,1,4-trimethylbenz[*f*]azulene (**1**) through the compounds **16**—**21**. The synthesis of 1,2,3,4,10,11-hexahydro-7-methoxy-5H-dibenzo[*a,d*]cycloheptene (**6**) by a rearrangement of 1,2,3,4,4a,9,10,10a-octahydro-4a-hydroxymethyl-6-methoxyphenanthrene (**5**) was also described.

Keywords——cycloaddition of benzocyclobutene; Wagner–Meerwein rearrangement; synthesis of 1,2,3,3a,4,9,10,10a-octahydro-1,1,4-trimethylbenz[*f*]azulene; synthesis of 1,2,3,4,4a,9,10,10a-octahydrophenanthrene; synthesis of A, B and C part of grayanotoxins

The tetracyclic diterpenoids related to grayanotoxins and asebotoxins which have a perhydroazulene skeleton fused with bicyclo[3.2.1]octane system are the interesting substances because of their structural characteristics and biological activities.[3)] Although a few papers concerning with the synthetic approach to this type of compounds have been reported,[4–6)] major obstacles in these methods are the construction of hydroazulene and bicyclo[3.2.1]-octane parts. We have been investigating a development of new synthetic route of the tetracyclic diterpenoids having bicyclo[3.2.1]octane system[7)] as a continuation of natural product synthesis by using cycloaddition reaction of *o*-quinodimethane in this laboratory.[8,9)] Now our attention has been focused on the synthesis of a hydroazulene part of grayanotoxin skeleton and we wish to report a new synthesis of hydroazulene fused with six membered ring (**1**), which constitutes A, B, and C rings of grayanotoxin skeleton and has the suitable substituents for the construction of D ring.



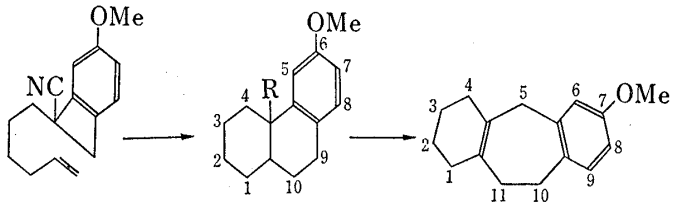
grayanotoxin-1 **1**

Chart 1

1) A part of this work has been presented in the 98th Annual Meeting of the Pharmaceutical Society of Japan, Abstracts of Papers, p. 228, 5H 3-1, April 5, 1978, Okayama.
2) Location: *Aobayama, Sendai 980, Japan.*
3) T.K. Devon and A.I. Scott, "Handbook of Naturally Occurring Compounds," Vol. II, Terpenes, Academic Press, New York, 1972.
4) M. Shiozaki, K. Mori, M. Matsui, and T. Hiraoka, *Tetrahedron Lett.*, **1972**, 657.
5) T. Okuno and T. Matsumoto, *Tetrahedron Lett.*, **1969**, 4071.
6) S. Gasa, N. Hamanaka, S. Matsunaga, T. Okuno, N. Takeda, and T. Matsumoto, *Tetrahedron Lett.*, **1976**, 553.
7) T. Kametani, H. Nemoto, and K. Fukumoto, *J.C.S. Chem. Commun.*, **1976**, 400.
8) T. Kametani and K. Fukumoto, *Heterocycles*, **3**, 29 (1975); **8**, 465 (1977).
9) T. Kametani, H. Matsumoto, H. Nemoto, and K. Fumumoto, *Tetrahedron Lett.*, **1978**, 2425; *idem*, *J. Am. Chem. Soc.*, **100**, 6219 (1978), and references cited herein.

Firstly we investigated Wagner–Meerwein type rearrangement using the readily available alcohol (**5**) to find out whether the aromatic group is preferred to migrate giving the desired compound (**6**).

The nitrile (**3**),[10] obtained by a thermolysis of the benzocyclobutene (**2**), was reduced with diisobutylaluminum hydride (DIBAL) to give, in 49.4% yield, the aldehyde (**4**), showing carbonyl absorption at 1720 cm^{-1} in its infrared (IR) spectrum. The aldehyde (**4**) was successively reduced again with lithium aluminum hydride to afford the alcohol (**5**) [$\nu_{max}^{CHCl_3}$ cm^{-1}: 3480 (OH)], in 95.1% yield, whose methylene protons attached to hydroxyl group were observed at 3.60 ppm as broad singlet in the nuclear magnetic resonance (NMR) spectrum. The alcohol (**5**) thus obtained was treated with *p*-toluenesulfonyl chloride in pyridine at room temperature to give the hexahydrodibenzo[*a*,*d*]cycloheptene (**6**) in 89.9% yield, whose NMR spectrum showed methylene protons adjacent to olefin and aromatic ring at 3.20 ppm as broad singlet, but lacked a resonance of olefinic protons. Moreover, molecular ion peak was observed at *m/e* 228 (M^+) in its mass spectrum, thus confirming the structure of the product.



2 **3**: R=CN; **4**: R=CHO; **5**: R=CH_2OH **6**

Chart 2

By having the result in hand that aromatic ring is preferred to migrate, a synthesis of the hydroazulene (**1**) was investigated by the same method.

The 3-methyl-3-vinylbutyl bromide (**9**), which was derived from the 3-methyl-3-vinylbutyl alcohol (**7**)[11] *via* the tosylate (**8**), was condensed with 1-cyano-5-methoxybenzocyclobutene (**10**)[12] in the presence of sodium amide in liquid ammonia to give the 1,1-disubstituted benzocyclobutene (**11**) [*m/e* 255 (M^+), $\nu_{max}^{CHCl_3}$ cm^{-1}: 2230 (CN)] in 54% yield, whose vinyl protons resonated at 4.7—6.0 ppm as multiplet in the NMR spectrum. Then, the olefinic benzocyclobutene (**11**) was heated at 170° for 5 hr to give the benz[*e*]indene (**12**) [*m/e* 255 (M^+); $\nu_{max}^{CHCl_3}$ cm^{-1}: 2240 (CN)][13] in 80.7% yield. The signals due to vinyl group, which were observed in the NMR spectrum of the starting compound (**11**), were not detected in this product (**12**). This nitrile (**12**) was treated with methyllithium to afford the ketone (**13**) [$\nu_{max}^{CHCl_3}$ cm^{-1}: 1695 (CO)], in 71.9% yield, which was successively reduced with sodium borohydride to give the alcohol (**14**) [$\nu_{max}^{CHCl_3}$ cm^{-1}: 3500 (OH)]. By treatment of the alcohol (**14**) with *p*-toluenesulfonyl chloride in pyridine, the hydroazulene (**15**) was obtained in 82.1% yield, which exhibited the signal due to methyl group at the 4 position at 1.36 ppm as doublet (J=7 Hz) in the NMR spectrum and showed the molecular ion peak at *m/e* 256 in the mass spectrum.

Since the hydroazulene (**15**) having three methyl groups required for the A and B rings of grayanotoxin skeleton was synthesized, our attention was turned into the introduction of a suitable substituent on the aromatic ring which could be used for the construction of ring D of grayanotoxin skeleton.

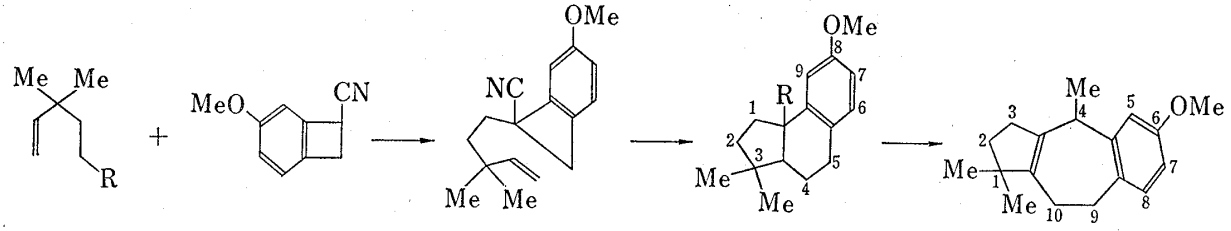
The hydroazulene (**15**) was heated in the presence of pyridine hydrochloride to afford, in 82.5% yield, the phenol (**16**) [$\nu_{max}^{CHCl_3}$ cm^{-1}: 3340 (OH)] involving the migration of double

10) T. Kametani, M. Tsubuki, Y. Shiratori, Y. Kato, H. Nemoto, M. Ihara, K. Fukumoto, F. Satoh, and H. Inoue, *J. Org. Chem.*, **42**, 2672 (1977).

11) P. Cresson, *Bull. Soc. Chim. France*, **1964**, 2618.

12) T. Kametani, M. Kajiwara, and K. Fukumoto, *Chem. Ind.* (London), **1973**, 1165; *idem*, *Tetrahedron*, **30**, 1053 (1974).

13) The stereochemistry of this compound (**12**) has not been determined because it was expected that the rearrangement of the alcohol (**14**) would give the olefinic product (**15**), which has only one asymmetric center, by the consideration based on the experiment of the rearrangement of the model compound (**5**) into the olefinic compound (**6**).

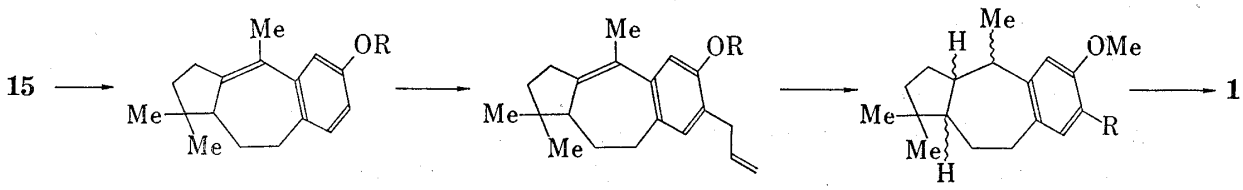


7: R=OH
8: R=OTs
9: R=Br

10 **11** **12**: R=CN **15**
13: R=COMe
14: R=CHMe (OH)

Chart 3

bond, which showed the signal due to olefinic methyl group at 1.90 ppm in its NMR spectrum. The phenol (**16**) was treated with allyl chloride in the presence of potassium carbonate and potassium iodide to give the allyl ether (**17**), in 68.8% yield, which was successively subjected to the Claisen rearrangement at 210° for 10 hr to afford the allylbenzene (**18**) in 58.5% yield, the phenolic hydroxyl group of which was observed at 3350 cm^{-1} in its IR spectrum. The presence of the allyl substituent at the ortho position to phenolic hydroxyl group was supported by the signals due to methylene protons adjacent to allyl and aromatic group at 3.30 ppm as doublet (J=6 Hz) and aromatic protons at 6.55 and 6.75 ppm as a singlet, respectively, in its NMR spectrum. After methylation of phenolic hydroxyl group of the hexahydrobenz-[*f*]azulene (**18**) with methyl iodide in the presence of potassium carbonate, the resulting methyl ether (**19**) was treated with lithium in liquid ammonia in the presence of ethanol to give the octahydrobenzazulene (**20**) in 65.6% yield.[14] Finally the reduction product (**20**) was converted into the aldehyde (**1**)[14] by treatment of **20** with osmium tetraoxide followed by sodium metaperiodate in 15.7% yield. The absorption due to formyl group was observed at 1720 cm^{-1} in its IR spectrum and the molecular ion peak was also observed at *m/e* 300 in the mass spectrum.



16: R=H
17: R=CH_2-CH=CH_2

18: R=H
19: R=Me

20: R=$CH_2CH=CH_2$
21: R=$CH_2CH(OH)-CH_2(OH)$

Chart 4

Thus, we could succeed in developing a new route for a synthesis of the hydroazulene derivative (**1**) which contains A, B, and C rings of grayanotoxin skeleton and also have the suitable substituent on C ring for the construction of D ring.

14) These compounds were obtained as a diastereomeric mixture and could not be separated into the diastereomerically pure form.

Experimental[15]

4a-Formyl-1,2,3,4,4a,9,10,10a-octahydro-6-methoxyphenanthrene (4)——To a solution of the nitrile (3)[10] (5.0 g) in dry benzene (50 ml) was added diisobutylaluminum hydride (25% toluene solution) (20 g) and the solution was stirred for 1 hr at room temperature. After quenching the reaction mixture with water–methanol (1: 2, v/v), filtration of inorganic compound, and evaporation of the solvent, the residue was extracted with ether. The extract was washed with saturated aqueous NaCl solution and dried over anhydrous Na_2SO_4. Evaporation of ether afforded an oil, which was purified by column chromatography on silica gel using *n*-hexane–benzene as an eluent to give the aldehyde (4) (2.5 g, 49.4%) as a colorless powder after recrystallization from *n*-hexane–benzene, mp 65—66°. *Anal.* Calcd. for $C_{16}H_{20}O_2$: C, 78.65; H, 8.25. Found: C, 78.44; H, 8.24. IR$\nu_{max}^{CHCl_3}$ cm^{-1}: 1720 (CHO). NMR (CCl_4) δ: 1.1—3.1 (13H, m, methylene and methine protons), 3.7 (3H, s, OMe), 6.7—7.1 (3H, m, ArH), 9.3 and 9.5 (1H, each s, CHO). MS *m/e*: 244 (M^+).

1,2,3,4,4a,9,10,10a-Octahydro-4a-hydroxymethyl-6-methoxyphenanthrene (5)——To a suspension of lithium aluminum hydride (550 mg) in anhydrous tetrahydrofuran (10 ml) was added dropwise a solution of the aldehyde (4) (2.4 g) in anhydrous tetrahydrofuran (20 ml), and the mixture was stirred for 5 hr at room temperature. After quenching the reaction mixture with 15% aqueous KOH solution, filtration of inorganic compound, and evaporation of tetrahydrofuran, the residue was extracted with ether. The extract was washed with saturated aqueous NaCl solution and dried over anhydrous Na_2SO_4. Evaporation of ether afforded an oil, which was purified by column chromatography on silica gel using benzene as an eluent to give the alcohol (5) (2.3 g, 95.1%) as a colorless oil. *Anal.* Calcd. for $C_{16}H_{22}O_2 \cdot 0.4H_2O$: C, 75.79; H, 9.06. Found: C, 75.32; H, 8.76. IR$\nu_{max}^{CHCl_3}$ cm^{-1}: 3480 (OH). NMR (CCl_4) δ: 1.1—3.1 (13H, m, methylene and methine protons), 3.60 (2H, br s, $C\underline{H}_2OH$), 3.80 (3H, s, OMe), 6.6—7.1 (3H, m, ArH). MS *m/e*: 246 (M^+).

1,2,3,4,10,11-Hexahydro-7-methoxy-5H-dibenzo[*a*,*d*]cycloheptene (6)——To a solution of the alcohol (5) (1.8 g) in pyridine (20 ml) was added *p*-toluenesulfonyl chloride (2.1 g) and the mixture was stirred for 8 hr at room temperature, and then poured into water and extracted with ether. The ethereal phase was washed with 5% HCl, water and saturated aqueous NaCl solution. After drying over anhydrous Na_2SO_4, the organic solvent was removed to give an oil, which was purified by column chromatography on silica gel using *n*-hexane as an eluent to afford the hexahydrodibenzo[*a*,*d*]cycloheptene (6) (1.5 g, 89.9%) as a colorless oil. *Anal.* Calcd. for $C_{16}H_{20}O$: C, 84.16; H, 8.83. Found: C, 83.83; H, 8.76. NMR (CCl_4) δ: 1.2—2.5 (10H, m, methylene protons), 2.5—3.1 (2H, m, $ArC\underline{H}_2CH_2$), 3.20 (2H, br s, $ArC\underline{H}_2C=$), 3.7 (3H, s, OMe), 6.4—7.0 (3H, m, ArH). MS *m/e*: 228 (M^+).

1-Bromo-3,3-dimethyl-4-pentene (9)——To a solution of the 3-methyl-3-vinylbutyl alcohol (7) (13.5 g) in pyridine (80 ml) was added *p*-toluenesulfonyl chloride (25 g) and the solution was stirred for 4 hr at room temperature. The resulting mixture was poured into water and extracted with ether. The extract was washed with 5% HCl and saturated aqueous NaCl solution. After drying over anhydrous Na_2SO_4, the organic solvent was evaporated to give the tosylate (8) (27.6 g, 87%) as an oil. This crude tosylate was used for the next reaction without further purification. A part of product (8) was purified by distillation, bp 118°/0.02 mmHg, for an analysis. NMR (CCl_4) δ: 1.0 (6H, s, 2×Me), 1.7 (2H, t, J=8 Hz, $C\underline{H}_2CH_2OTs$), 2.5 (3H, s, $ArCH_3$), 4.0 (2H, t, J=8 Hz, $CH_2C\underline{H}_2OTs$), 4.7—6.0 (3H, m, $CH=CH_2$), 7.3 (2H, d, J=8 Hz, ArH), 7.7 (2H, d, J=8 Hz, ArH).

A solution of the tosylate (8) (27.6 g) and lithium bromide (25 g) in acetone (500 ml) was refluxed for 5 hr. After evaporation of acetone by using Widmer column, the residue was extracted with ether. The ethereal solution was washed with saturated aqueous NaCl solution and dried over anhydrous Na_2SO_4. After evaporation of ether, the resulting residue was distilled to give the bromide (9) [15.77 g, 75.2% from the alcohol (7)], bp 78°/50 mmHg. NMR (CCl_4) δ: 1.0 (6H, s, 2×Me), 1.8—2.1 (2H, m, $C\underline{H}_2CH_2Br$), 3.0—3.4 (2H, m, $CH_2C\underline{H}_2Br$), 4.7—6.0 (3H, m, $CH=CH_2$). MS *m/e*: 177 (M^+), 179 (M^++2).

1-Cyano-5-methoxy-1-(3,3-dimethyl-4-pentenyl)benzocyclobutene (11)——A solution of 1-cyano-5-methoxybenzocyclobutene (10)[12] (12.9 g) in anhydrous tetrahydrofuran (30 ml) was added to a solution of sodium amide [prepared from sodium (2.8 g) in liquid ammonia] in liquid ammonia (800 ml). After the mixture was stirred for 10 min at −78°, a solution of the bromide (9) (15.8 g) in anhydrous tetrahydrofuran (50 ml) was added dropwise at −78°, and the mixture was further stirred for 3 hr at −33°. This was treated with an excess of crystalline ammonium chloride and the solvent was removed to give a reddish residue, which was diluted with water and extracted with ether. The organic layer was washed with 5% HCl and saturated aqueous NaCl solution, and dried over anhydrous Na_2SO_4. Removal of the solvent gave a reddish gum, which was purified by column chromatography on silica gel using *n*-hexane–benzene as an eluent to

15) All melting points were measured with a Yanagimoto micro melting point apparatus (MP-S2) and are uncorrected. IR spectra were taken with a Hitachi 215 grating spectrophotometer, NMR spectra with a JNM-PMX-60 (60 MHz) instrument (for solution in carbon tetrachloride with tetramethylsilane as internal standard). MS spectra were measured with Hitachi RMU-7 and JEOL JMX-D 100 mass spectrometers.

give a powder. This was recrystallized from *n*-hexane to afford the benzocyclobutene (**11**) (11.7 g, 54%) as colorless prisms, mp 50.5—51.5°. *Anal.* Calcd. for $C_{17}H_{21}NO \cdot 1/6H_2O$: C, 79.03; H, 8.32; N, 5.42. Found: C, 78.85; H, 8.32; N, 5.52. IR$\nu_{max}^{CHCl_3}$ cm^{-1}: 2230 (CN). NMR (CCl_4) δ: 1.0 (6H, s, 2×Me), 1.5—1.9 (4H, m, 2×CH_2), 3.05 and 3.58 (each 1H, each d, J=14 Hz, Ar$C\underline{H}_2$), 3.7 (3H, s, OMe), 4.7—6.0 (3H, m, CH=CH_2), 6.7—7.1 (3H, m, ArH). MS *m/e*: 255 (M^+).

9b-Cyano-2,3,3a,4,5,9b-hexahydro-8-methoxy-3,3-dimethyl-1H-benz[*e*]indene (12)——A solution of the benzocyclobutene (**11**) (2.6 g) in *o*-dichlorobenzene (800 ml) was heated for 5 hr at 170° under an atmosphere of nitrogen. After evaporation of the solvent, the residue was recrystallized from *n*-hexane to give the compound (**12**) (2.1 g, 80.7%) as colorless prisms, mp 61.5—62°. *Anal.* Calcd. for $C_{17}H_{21}NO$: C, 79.96; H, 8.29. Found: C, 79.86; H, 8.46. IR$\nu_{max}^{CHCl_3}$ cm^{-1}: 2240 (CN). NMR (CCl_4) δ: 0.9 (3H, s, Me), 1.3 (3H, s, Me), 3.8 (3H, s, OMe), 6.5—7.0 (3H, m, ArH). MS *m/e*: 255 (M^+).

9b-Acetyl-2,3,3a,4,5,9b-hexahydro-8-methoxy-3,3-dimethyl-1H-benz[*e*]indene (13)——To a solution of methyllithium [prepared from lithium (5 g) and methyl iodide (20 ml) in anhydrous ether (200 ml)] was added dropwise a solution of the nitrile (**12**) (3.0 g) in anhydrous ether (30 ml) at −20° and the solution was stirred for 2 hr at 0°. After quenching the reaction mixture with water, a solution of 6 N sulfuric acid–dioxane (1: 2, v/v) (200 ml) was added and the mixture was heated for 8 hr at 60°. The organic phase was separated and washed with saturated aqueous NaCl solution. After drying over anhydrous Na_2SO_4, the organic solvent was removed to give the ketone (**13**) (2.3 g, 71.9%). IR$\nu_{max}^{CHCl_3}$ cm^{-1}: 1695 (CO). NMR (CCl_4) δ: 0.95 (3H, s, Me), 1.05 (3H, s, Me), 1.82 (3H, s, COMe), 3.7 (3H, s, OMe), 6.4—7.0 (3H, m, ArH). MS *m/e*: 272 (M^+). 2,4-Dinitrophenylhydrazone of the ketone (**13**) forms yellow needles, mp 184—185°, after recrystallization from EtOH. *Anal.* Calcd. for $C_{24}H_{28}N_4O_5 \cdot 0.25C_2H_5OH$: C, 63.41; H, 6.41; N, 12.08. Found: C, 62.97; H, 6.16; N, 11.87.

2,3,3a,4,5,9b-Hexahydro-9b-(1-hydroxyethyl)-8-methoxy-3,3-dimethyl-1H-benz[*e*]indene (14)——To a solution of the ketone (**13**) (3.0 g) in methanol (50 ml) was added in portions in sodium borohydride (0.2 g) at 0° and the solution was stirred for 2 hr at room temperature. After evaporation of the solvent, the residue was extracted with ether and the ethereal layer was washed with 5% HCl and saturated aqueous NaCl solution. After drying over anhydrous Na_2SO_4, the solvent was removed to give an oil, which was purified by column chromatography on silica gel using benzene for elution to afford the alcohol (**14**) (2.8 g, 92.7%) as a colorless oil. *Anal.* Calcd. for $C_{18}H_{26}O_2$: C, 78.79; H, 9.55. Found: C, 78.67; H, 9.64. IR$\nu_{max}^{CHCl_3}$ cm^{-1}: 3500 (OH). NMR (CCl_4) δ: 0.8 (3H, s, Me), 0.92 (3H, d, J=3 Hz, Me), 1.1 (3H, s, Me), 3.7 (3H, s, OMe), 6.4—7.0 (3H, m, ArH). MS *m/e*: 274 (M^+).

1,2,3,4,9,10-Hexahydro-6-methoxy-1,1,4-trimethylbenz[*f*]azulene (15)——To a solution of the alcohol (**14**) (3.0 g) in pyridine (30 ml) was added *p*-toluenesulfonyl chloride (2.8 g) and the solution was heated for 8 hr at 70° with stirring. The resulting mixture was poured into water and extracted with ether. The ethereal phase was washed with 5% HCl and saturated aqueous NaCl solution. After drying over anhydrous Na_2SO_4, the organic solvent was removed to give a yellow oil, which was purified by column chromatography on silica gel using *n*-hexane as an eluent to afford the benzazulene (**15**) (2.3 g, 82.1%) as a colorless oil. *Anal.* Calcd. for $C_{18}H_{24}O$: C, 84.32; H, 9.44. Found: C, 84.36; H, 9.68. NMR (CCl_4) δ: 0.9 and 1.0 (each 3H, each s, 2×Me), 1.36 (3H, d, J=7 Hz, $\underline{Me}$CH), 3.23 (1H, q, J=7 Hz, MeC$\underline{H}$), 3.7 (3H, s, OMe), 6.4—7.0 (3H, m, ArH). MS *m/e*: 256 (M^+).

1,2,3,9,10,10a-Hexahydro-6-hydroxy-1,1,4-trimethylbenz[*f*]azulene (16)——A mixture of the compound (**15**) (1.0 g) and pyridine hydrochloride (2.8 g) was heated for 1 hr at 220° under an atmosphere of nitrogen. After cooling, the precipitated solid was dissolved in water and then extracted with ether. The ethereal layer was washed with saturated aqueous NaCl solution and dried over anhydrous Na_2SO_4. The organic solvent was removed to leave an oil, which was purified by column chromatography on silica gel using *n*-hexane–benzene for elution to give the phenol (**16**) (0.78 g, 82.5%) as a colorless oil. IR$\nu_{max}^{CHCl_3}$ cm^{-1}: 3340 (OH). NMR (CCl_4) δ: 0.8 and 0.9 (each 3H, each s, 2×Me), 1.90 (3H, s, Me), 6.4—7.0 (3H, m, ArH). MS *m/e*: 242 (M^+).

1,2,3,9,10,10a-Hexahydro-1,1,4-trimethyl-6-(2-propenyloxy)benz[*f*]azulene (17)——A mixture of the phenol (**16**) (830 mg), potassium carbonate (473 mg), potassium iodide (285 mg), allyl chloride (315 mg) and acetone (10 ml) was refluxed for 10 hr. The solvent was removed to yield a residue, which was extracted with ether. The ethereal layer was washed with saturated aqueous NaCl solution, dried over anhydrous Na_2SO_4 and evaporated to give an oil which was purified by column chromatography on silica gel using *n*-hexane for elution to afford the allyl ether (**17**) (665 mg, 68.8%) as a colorless oil. *Anal.* Calcd. for $C_{20}H_{26}O_2$: C, 85.05; H, 9.28. Found: C, 84.95; H, 9.46. NMR (CCl_4) δ: 0.8 and 0.9 (each 3H, each s, 2×Me), 2.0 (3H, s, Me), 4.3 (2H, d, J=5 Hz, OC$\underline{H}_2$CH=CH_2), 5.0—6.3 (3H, m, CH=CH_2), 6.4—7.0 (3H, m, ArH). MS *m/e*: 282 (M^+).

1,2,3,9,10,10a-Hexahydro-6-hydroxy-1,1,4-trimethyl-7-(2-propenyl)benz[*f*]azulene (18)——A solution of the allyl ether (**17**) (140 mg) in xylene (20 ml) was heated for 10 hr at 210° in a sealed tube. After cooling, removal of the solvent afforded a yellow oil which was purified by column chromatography on silica gel using *n*-hexane–benzene for elution to afford the phenol (**18**) (90 mg, 58.5%) as a colorless oil. IR$\nu_{max}^{CHCl_3}$ cm^{-1}: 3350 (OH). NMR (CCl_4) δ: 0.8 and 0.9 (each 3H, each s, 2×Me), 2.0 (3H, s, Me), 3.30 (2H, d, J=6 Hz, Ar$C\underline{H}_2$CH=CH_2), 4.8—6.4 (3H, m, CH=CH_2), 6.55 and 6.75 (each 1H, each s, ArH). MS *m/e*: 282 (M^+).

1,2,3,9,10,10a-Hexahydro-6-methoxy-1,1,4-trimethyl-7-(2-propenyl)benz[*f*]azulene (19)——A mixture of the phenol (**18**) (75 mg), methyl iodide (5 ml), potassium carbonate (60 mg) and dimethylformamide (20 ml) was heated for 24 hr at 80° with stirring. The resulting mixture was poured into water and extracted with ether. The ethereal solution was washed with saturated aqueous NaCl solution and dried over anhydrous Na_2SO_4. The organic solvent was removed to give an oil, which was purified by column chromatography on silica gel to afford the methyl ether (**19**) (46 mg, 58.5%) as a colorless oil. *Anal.* Calcd. for $C_{21}H_{28}O$: C, 85.08; H, 9.52. Found: C, 84.87; H, 9.59. NMR (CCl_4) δ: 0.8 and 0.9 (each 3H, each s, 2×Me), 2.0 (3H, s, Me), 3.30 (2H, d, J=6 Hz, $ArC\underline{H}_2CH{=}CH_2$), 3.73 (3H, s, OMe), 4.8—6.3 (3H, m, $CH{=}CH_2$), 6.6 and 6.8 (each 1H, each s, ArH). MS *m/e*: 296 (M^+).

1,2,3,3a,4,9,10,10a-Octahydro-6-methoxy-1,1,4-trimethyl-7-(2-propenyl)benz[*f*]azulene (20)——Lithium wire (30 mg) was added in small pieces to a stirred solution of the compound (**19**) (50 mg) in anhydrous tetrahydrofuran (3 ml) and liquid ammonia at −33° and then absolute ethanol (1 ml) was added and the mixture was stirred for 1 hr at −33°. After treatment with an excess of crystalline ammonium chloride, the solvent was removed to give a reddish residue, which was extracted with ether. The organic solvent was washed with saturated aqueous NaCl solution and dried over anhydrous Na_2SO_4. Removal of the solvent afforded a reddish gum, which was purified by thick-layer chromatography on silica gel developing with *n*-hexane–benzene (9: 1, v/v) to give the octahydrobenzazulene (**20**) (33 mg, 65.6%) as a colorless oil. NMR (CCl_4) δ: 0.7—1.1 (9H, m, 3×Me), 3.30 (2H, d, J=6 Hz, $ArC\underline{H}_2CH{=}CH_2$), 3.8 (3H, s, OMe), 4.8—6.3 (3H, m, $CH{=}CH_2$), 6.5, 6.6, and 6.8 (2H, each s, ArH). MS *m/e*: 298 (M^+).

7-Formylmethyl-1,2,3,3a,4,9,10,10a-octahydro-6-methoxy-1,1,4-trimethylbenz[*f*]azulene (1)——A solution of the olefin (**20**) (38 mg) and osmium tetraoxide (33 mg) in tetrahydrofuran (10 ml) was stirred for 1 hr at room temperature, and to this solution was added sodium periodate (272 mg) in water (5 ml) and then the solution was stirred for 20 min at room temperature. The mixture was filtered and then diluted with ether. The ethereal phase was washed with saturated aqueous NaCl solution and dried over anhydrous Na_2SO_4. After evaporation of ether, the residue was purified by thick-layer chromatography on silica gel developing with *n*-hexane–benzene (1: 4, v/v) to give the aldehyde (**1**) (6 mg, 15.7%) as a colorless oil. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1720 (CHO). NMR (CCl_4) δ: 0.7—1.1 (9H, m, 3×Me), 3.42 (2H, br s, $ArC\underline{H}_2CHO$), 3.8 (3H, s, OMe), 6.5—6.8 (2H, m, ArH), 9.3—9.6 (1H, m, CHO). MS *m/e*: 300 (M^+).