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Tetrahedron
Tetrahedron 62 (2006) 12318–12325

Reactions of 3,10-epoxycyclo[10.2.2.0^{2,11}.0^{4,9}]hexadeca-4,6,8,13-tetraene: a new intramolecular 1,5-oxygen migration

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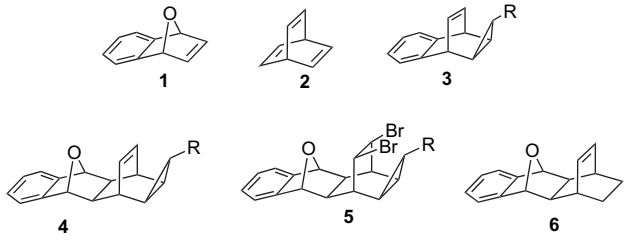
Received 18 June 2006; revised 18 September 2006; accepted 5 October 2006
Available online 31 October 2006

Abstract—Bromination of 3,10-epoxycyclo[10.2.2.0^{2,11}.0^{4,9}]hexadeca-4,6,8,13-tetraene gave 13-bromo-11-oxapentacyclo[8.7.0.0^{2,4}.0^{12,17}]-heptadeca-4,6,8-triene-3-ol, 12-bromo-1,2,3,4-tetrahydro-1,4-ethano-antracen-11-ol, 13-hydroxy-3,14-dibromotetracyclo[10.2.2.0^{2,11}.0^{4,9}]-hexadeca-2,4,6,8,10-pentaene, and 13-hydroxy-3,10,14-tribromotetracyclo[10.2.2.0^{2,11}.0^{4,9}]hexadeca-2,4,6,8,10-pentaene by cleavage of the carbon–oxygen bonds and intramolecular 1,5-migration of the oxygen atom of 1,4-epoxide. Reactions of epoxide 14,18-dioxahexacyclo[10.3.2.1^{3,10}.0^{2,11}.0^{4,9}.0^{13,15}]octadeca-4,6,8-triene obtained from 3,10-epoxycyclo[10.2.2.0^{2,11}.0^{4,9}]hexadeca-4,6,8,13-tetraene gave also similar products, in acidic media. Compound 3,10-epoxycyclo[10.2.2.0^{2,11}.0^{4,9}]hexadeca-4,6,8,13-tetraene was converted into tetracyclo[10.2.2.0^{2,11}.0^{4,9}]hexadeca-2(11),3,9-triene in two ways. The reactions, especially intramolecular oxygen migration, are discussed.

1. Introduction

Molecular rearrangements occur in some reactions of organic compounds. According to the processes desired in the synthesis, rearrangements may be of value or a disadvantage for researchers. These rearrangements depend on the structures of the compounds and reaction conditions.[1] Oxabenzonorbornadiene (**1**), barralene (**2**), and benzhomobarralene derivative **3** give skeleton rearrangements.[1a,2] The structures of compounds **4** and **6** include both oxabenzonorbornane and barrelene derivatives as annulated structures. Dibromide **5**[3] was selectively formed in the bromination of compound **4** by neighboring group participation of the oxygen atom in **4** (Scheme 1).



Scheme 1.

The structure of 3,10-epoxycyclo[10.2.2.0^{2,11}.0^{4,9}]hexadeca-4,6,8,13-tetraene (**6**) is similar to that of **4** as it includes 1,4-epoxide, an isolated double bond, and a benzene ring as functional groups. Its reactions with reagents such as bromine and *meta*-chloroperbenzoic acid (*m*-CPBA) will be important. Its importance is the following: (1) From which face does bromine or *m*-CPBA attack the double bond in **6**? (2) How does epoxide act in **6** when the reagents such as Br_2 or *m*-CPBA react with the double bond? Does a *cis*-dibromide **7** similar to **5** happen? Or does this epoxide in **6** rearrange? (3) Does anthracene derivative **8** obtained from **6**, by elimination of water? At the same time, **8** is an adduct of cyclohexadiene and was obtained by two different ways (from reactions of 1,3-cyclohexadiene with naphthyne and 1,4-naphthoquinone separately).[4] (4) It will also be possible that the aromatic ring shifts from terminal ring to the central ring in the same compound if **9** is obtained from **6** by reduction reactions from **6** (Scheme 2). Therefore, reactions of the compound **6** with these reagents were investigated separately.

2. Results and discussion

Adduct **6** was obtained from the Diels–Alder cycloaddition reaction of 1,4-dihydronaphthalene-1,4-epoxide with cyclohexadiene.[3] Adduct **6** was reacted with Br_2 (1.1 equiv) in a CCl_4 solution at 0 °C for 30 min (Scheme 3). It was seen that adduct **6** was absent in the ^{1}H NMR spectrum of the reaction mixture. Careful PLC (preparative thick-layer chromatography) allowed us to isolated two products, **10** and **11**.

Keywords: Aromatization; Bromination; Epoxide; Epoxidation; Naphthyne; Oxygen migration; Rearrangement; Reduction.
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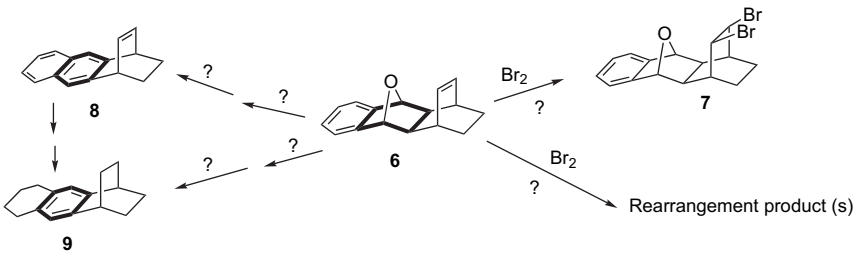
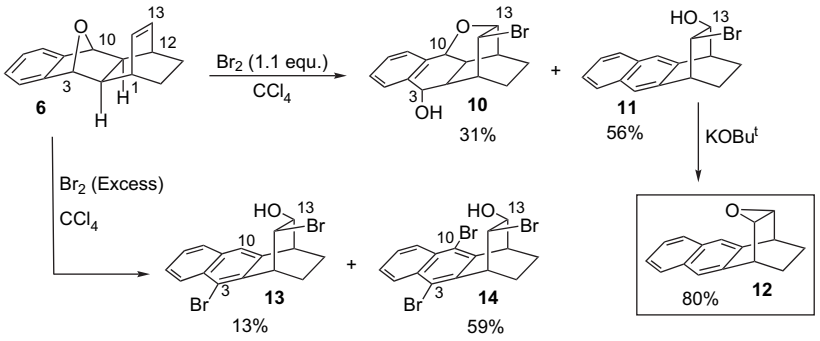
doi:10.1016/j.tet.2006.10.012



Scheme 2.



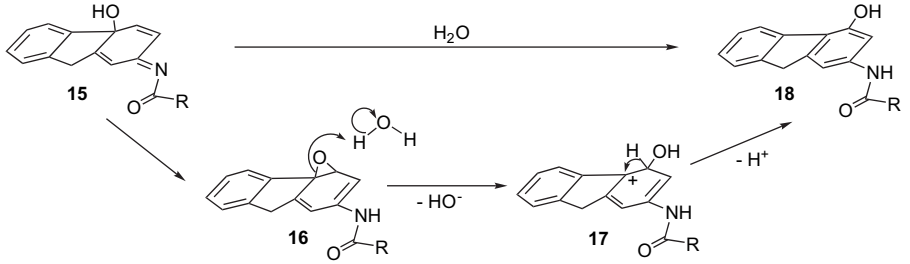
Scheme 3.

On the basis of the NMR spectra of these compounds, it was determined that they are asymmetrical structures, but it was not easy to establish their exact configurations. NMR spectroscopic data of **11** indicated that it is a naphthalene derivative with Br and OH functional groups. To confirm the configuration of Br and OH groups in **11**, compound **11** was reacted with potassium *tert*-butoxide to give epoxide **12**. Epoxide **12**[4a] has a symmetrical structure and its structure is consistent with its NMR spectra (Scheme 3). To determine the exact structures of **10** and **11**, X-ray crystallographic analyses were carried out.[5] We assumed that **10** might be formed during PLC by the hydrolysis of intermediate bromide (probable **24**, Scheme 5) whose structure is not known.

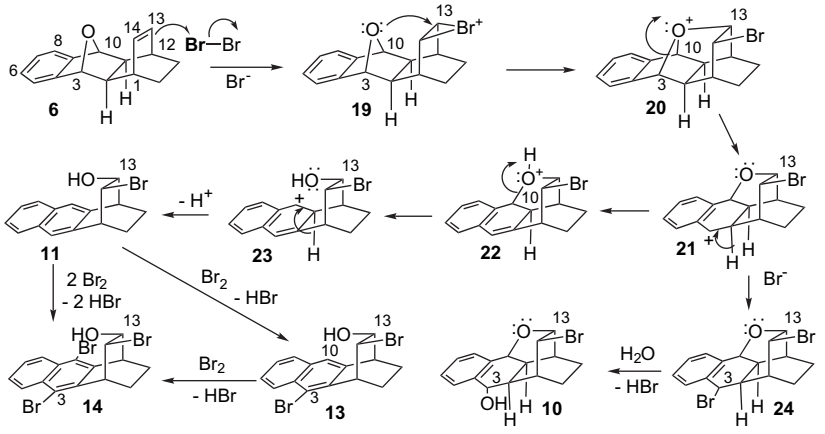
In a similar manner, adduct **6** was reacted with excess Br_2. After evaporation of excess Br_2 and solvent, dibromide **13** and tribromide **14** were isolated in this bromination reaction by column chromatography (Scheme 3). The ^{1}H NMR spectrum of dibromide **13** showed absorptions at δ 8.29 (d), 7.81 (d), 7.64 (s), and 7.63–7.27 (m), with relative intensities of 1:1:1:2. However, dibromide **13** does not have a symmetrical structure and exhibits ten lines in the aromatic and six lines in the aliphatic regions of its ^{13}C NMR spectrum. One of the five quaternary carbons should be CBr and other substituent groups (Br and OH) should be at the bridgehead as in **11**. The region of Br at aromatic carbon (C_3) was regarded as compound **13** because greater steric effect(s) can occur between the Br and OH groups in it and its intermediate(s) if Br is at C_{10} rather than the other position (if Br is at C_3). Tribromide **14** does not have a symmetrical structure and is consistent with its NMR spectra.

In the reactions of compound **6** with bromine, the epoxide ring of **6** is opened and tetrahydrofuran rings occur in this structure, as in **10**, by intramolecular 1,5-migration of the oxygen atom. Then halohydrins **11**, **13**, and **14** occur by the aromatization of these structures.

Intramolecular 1,5-migration of the oxygen atom and formation of tetrahydrofuran derivative are important in the bromination of **6**. There are intramolecular oxygen migrations.[6] One of them is migration of the oxygen atom, which is observed in the conversion of compound **15** to compound **18**.[6b] According to the data, epoxide (oxa norcaradiene) **16** was formed by nucleophilic attack of oxygen, and then **18** was formed (via **17**) by ring opening of epoxide and aromatization of ring in this reaction (Scheme 4). The migration of the oxygen atom in the formation of **18** is an intramolecular 1,2-migration and is similar to that of **6**. However, the



Scheme 4.

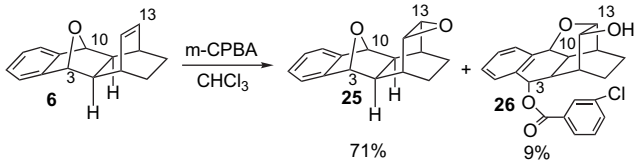


Scheme 5.

intramolecular 1,5-migration of the oxygen atom is a new oxygen migration.

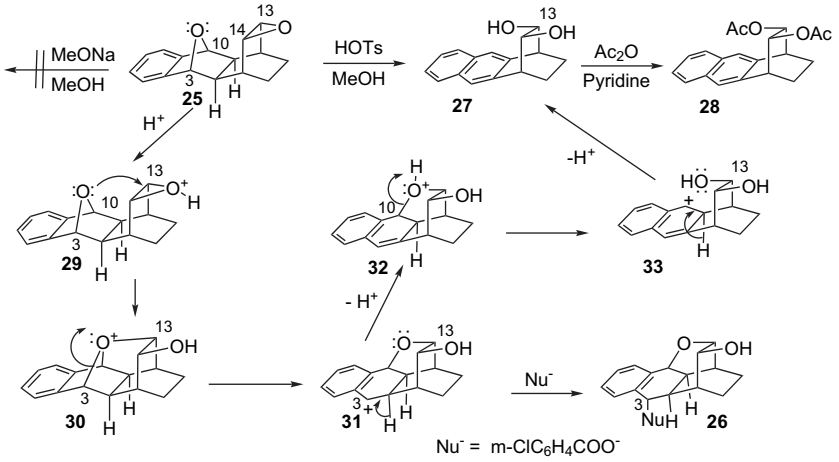
To rationalize the formation of compounds **10**, **11**, **13**, and **14**, we propose the following reaction mechanism as favorable mechanism. As shown in the bromination of compound **5**,[3] bromine can attack the double bond in **6** from the *exo* face (Scheme 5). A bridged bromonium ion **19** is produced and the oxygen of the epoxide acts as a nucleophile to yield **20**. Intermediate **21** is produced from **20** by the opening of the epoxide ring. Br^- can attack intermediate **21** to give **24** (probable) as a nucleophile. Intermediate **24** whose structure is not known may hydrolyze to give **10**. Intermediate **21** is converted into **11** through intermediates **22** and **23** by aromatization of the ring. As reported in the literature,[7] bromine is added to naphthalene and its derivatives, and then brominated naphthalenes are produced by the elimination of HBr. Compound **11** is a naphthalene derivative, and bromine will be added to its ring, which is electron-rich. Compound **11** is converted into **13** by the addition of Br_2 and then the elimination of HBr. Compound **14** can be formed by either the addition of 2 equiv of Br_2 to **11** and then the elimination of 2 equiv of HBr or the addition of Br_2 to **13** and then the elimination of HBr.

As mentioned above, bromine attacks the double bond in **4** and **6** from the *exo* face. *m*-CPBA can attack the double bound in **6** by approach from *exo* and *endo* (toward 1,4-epoxide) faces. To investigate the approach of *m*-CPBA to the double bond in **6** and to confirm the intramolecular 1,5-migration of the oxygen atom, compound **6** was reacted with *m*-CPBA (Scheme 6). In this epoxidation, epoxide **25** and ester **26**[8] were obtained. According to its NMR data such as HETCOR and COSY, **25** has a symmetrical structure and is consistent with the proposed structure. In the formation of epoxide **25**, *m*-CPBA also attacks the double bond in **6**. As shown in Scheme 7, ester **26** is a secondary product formed from **25**.



Scheme 6.

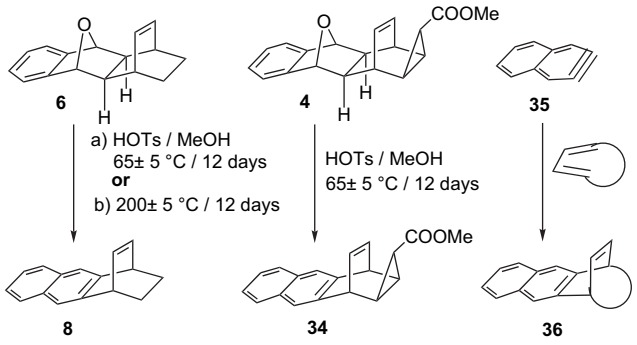
Epoxide **25** was refluxed with TsOH (*p*-toluenesulfonic acid) in MeOH for 1 week (Scheme 7). In this reaction, only diol **27** was obtained and epoxide **25** was not present. However, when the opening of the ring of epoxide **25** with NaOMe in similar conditions was attempted, we isolated only unreacted starting material.



Scheme 7.

For the formation of diol **27**, we can propose the following reaction mechanism as favorable mechanism. The fact that no product with OMe was observed in either of them by the opening of 1,2-epoxide, which shows that the oxygen of 1,4-epoxide only attacked the 1,2-epoxide as a nucleophile. First, 1,2-epoxide is protonated with TsOH and it converts into structure **31** via **29** and **30** because it is more strained than the 1,4-epoxide.[9] Intermediate **31** can convert into both **32**, by the departure of the proton and the formation of a double bond, and **26** by the attack of a nucleophile. Ester **26**,[8] a substitution product, was obtained in the epoxidation of compound **6** because *m*-chlorobenzoic acid (*m*-ClC_6H_4COOH) or *m*-chlorobenzoate (*m*-$ClC_6H_4COO^-$) transferred from *m*-CPBA is present. Intermediate **32**, a protonated tetrahydrofuran derivative, can convert into diol **27** via **33** by the opening of the tetrahydrofuran ring, the departure of the proton, and aromatization of ring. The synthesis and structure of diacetate **28** also confirm diol **27**.

A compound such as epoxide **6** reacted with acids gives an aromatic product by the elimination of water.[10] Epoxide **6** was reacted with TsOH in a methanol solution at 65±5 °C (in a sealed tube) for 12 days and only an anthracene derivative **8** was isolated (Scheme 8). However, anthracene derivative **8** was also obtained when epoxide **6** was heated at 200±5 °C (in a sealed tube) for 12 days. In a similar manner, the reaction of compound **4** with TsOH in a methanol solution at 65±5 °C (in a sealed tube) for 12 days gave only an anthracene derivative **34** (Scheme 8). According their NMR data, both **8**[4a] and **34** have symmetrical structures. Aromatic protons of **34** resonate as an AA′BB′ system and a singlet. Compounds **8** and **34** represented by a generic structure **36** are adducts of naphthyne with cyclohexadiene and 7-methoxycarbonylcycloheptatriene, respectively, and they were obtained from adducts **6** and **4**, which were synthesized from reactions of 1,4-dihydronaphthalene-1,4-epoxide with cyclohexadiene and 7-methoxycarbonylcycloheptatriene, respectively.[3] However, a diol derivative of **34** was synthesized from reaction of 1,4-naphthoquinone with 7-methoxycarbonylcycloheptatriene as adduct.[11] Therefore, 1,4-dihydronaphthalene-1,4-epoxide can act as a synthetic equivalent of naphthyne.



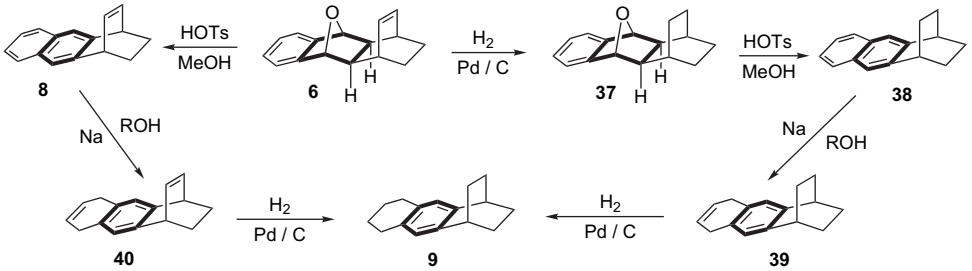
Scheme 8.

In compound **6**, aromatic and olefinic double bonds can be reduced, and these reduced products will be interesting. With this in mind, reduction reactions of **6** were investigated in two ways. One synthetic path is via **6**, **37**, **38**, **39**, and **9**, while the other is via **6**, **8**, **40**, and **9** (Scheme 9). Catalytic hydrogenation of compound **6** quantitatively gave **37** (Scheme 9). Reaction of compound **37** with TsOH gave anthracene derivative **38** in 72% yield. The data of **38**[4a] and **39** are in complete agreement with the proposed structures. We performed the reductions of aromatic compounds such as naphthalene with alkali metals and *tert*-butyl alcohol in high yield at room temperature.[12] Reduction reactions of **8** and **38** with Na/^{t}BuOH were carried out separately. Reduction of **8** produced a mixture of **8** and **40** while reduction of **38** produced a mixture of **38** and **39**. These mixtures could not be separated by chromatographic methods. Unsubstituted aromatic rings of **8** and **38** were reduced in these reactions because their electron densities are less than the others.[13] Catalytic hydrogenations of **39** and **40** in these mixtures gave compound **9** in high yields (Scheme 9). The aromatic protons of **9**, **39**, and **40** resonate at 6.91, 6.98, and 6.98 ppm, respectively, as singlets.

There is an aromatic ring in compounds **6** and **9**, but these aromatic rings are in different units of these structures. Therefore, the aromatic ring in **6** was transferred into another ring in **9** by chemical reactions.

3. Conclusion

The reaction of compound **6** with Br_2 (1.1 equiv) gave tetrahydrofuran derivative **10** and anthracene derivative **11**, while with excess Br_2 it gave anthracene derivatives **13** and **14**. As shown in Scheme 5, compounds **13** and **14** are not primary products and they are formed from **11**. Compound **10** is formed by the cleavage of a carbon–oxygen bond and intramolecular 1,5-migration of the oxygen atom of 1,4-epoxide. Compound **11** can also be formed from products and intermediate(s) such as **21** and **24** by cleavage of the tetrahydrofuran rings in them. Reactions of epoxide **25** obtained from **6** also gave similar products, **26** and **27**, in acidic media. In these reactions, the observed intramolecular 1,5-migration of the oxygen atom of 1,4-epoxide is important and new.



Scheme 9.

Compounds **8** and **34** represented by a generic structure **36** were formed from the reactions of **6** and **4** with TsOH, are adducts of naphthyne with cyclohexadiene and 7-methoxycarbonylcycloheptatriene, respectively. Therefore, 1,4-dihydronaphthalene-1,4-epoxide can be used as a synthetic equivalent of naphthyne.

Compound **6** was converted into **9** by reactions of TsOH and reduction. Aromatic rings are found in different units in the structures of **6** and **9**. Therefore, the aromatic ring in **6** was transferred into another ring in **9** by these reactions.

4. Experimental

4.1. General methods

All chemicals and solvents are commercially available and were used after distillation or treatment with drying agents. Melting points were determined on Thomas-Hoover capillary melting apparatus and are uncorrected. IR spectra were obtained from solutions in 0.1 mm cells with a *Perkin–Elmer* spectrophotometer. The ^{1}H and ^{13}C NMR spectra were recorded on a 200 (50) and 400 (100)-MHz *Varian spectrometer*; δ in parts per million, Me_4Si as the internal standard. Mass spectra were determined on VG ZabSpec, double focusing, magnetic sector (100.000 resolution) max. range 1000 for EI and 10,000 for HRMS. Elemental analyses were performed on Carlo Erba 1106 apparatus. All column chromatography was performed on silica gel (60-mesh, Merck). PLC is preparative thick-layer chromatography: 1 mm of silica gel 60 PF (Merck) on glass plates.

4.2. Bromination of the compound 6 with bromine (1.1 equiv)

To a stirred solution of compound **6** (200 mg, 0.89 mmol) in CCl_4 (20 mL) was added Br_2 (158 mg, 0.99 mmol, in 1 mL of CCl_4) dropwise at 0 °C over 5 min. The mixture was stirred for 30 min, and then the solvent was evaporated. According to the NMR spectrum of the residue, compound **6** was absent. The residue was submitted to PLC with ether/hexane (1:1). Compounds **11**[5b] (150 mg, 0.50 mmol, 56%) and **10**[5a] (90 mg, 0.28 mmol, 31%) were isolated pure.

4.3. Treatment of halohydrine 11 with ^{t}BuOK

To a stirred solution of compound **11**[5b] (520 mg, 1.72 mmol) in dry tetrahydrofuran (40 mL) was added ^{t}BuOK (1.5 g, 13.40 mmol) at room temperature. The mixture was stirred for 5 days. After the evaporation of solvent, a cold solution of NH_4Cl (5%, 100 mL) was added. The mixture was extracted with $CHCl_3$ (3×50 mL). The combined organic layer was dried over $CaCl_2$ and filtered by a small column (2–3 g silica gel). After the evaporation of solvent, epoxide **12**[4a] (305 mg, 1.37 mmol, 80%) was crystallized from $CHCl_3$/hexane as white crystals.

4.3.1. 14-Oxo-1*S*(*R*),12*R*(*S*),13*S*(*R*),15*R*(*S*)-pentacyclo-[10.3.2.0^{2,11}.0^{4,9}.0^{13,15}]heptadeca-2(11),3,5,7,9-pentaene (12). Mp 166–168 °C (lit. 173–174 °C[4a]); ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.91–7.85 (AA′ of AA′BB′, aromatic, 2H), 7.61 (s, aromatic, 2H), 7.53–7.47 (BB′ of AA′BB′, aromatic, 2H), 3.68–3.66 (m, 2H), 3.60–3.54 (m, 2H), 1.98–1.88 (m, methylenic, 2H), 1.57–1.48 (m, methylenic, 2H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 139.5 (C), 135.1 (C), 129.6 (CH), 127.1 (CH), 124.3 (CH), 52.0 (CH), 39.1, 24.9; Anal. Calcd for $C_{16}H_{14}O$: C 86.45, H 6.35; found: C 86.29, H 6.37.

4.4. Bromination of the compound 6 with excess bromine

To a stirred solution of compound **6** (1 g, 4.46 mmol) in CCl_4 (45 mL) was added Br_2 (2–3 mL, excess) dropwise at 0 °C over 5 min. The temperature of the bath was allowed to rise gradually to room temperature. After the addition of Br_2 was completed, the reaction mixture was stirred for 19 h. Solvent and excess Br_2 were evaporated. Chromatography of the residue on silica gel (60 g) with hexane/ether (10/1) gave the first fraction tribromide **14** (1.2 g, 2.61 mmol, 59%) and the second fraction dibromide **13** (186 mg, 0.57 mmol, 13%).

4.4.1. 1(*R*)*S*,12(*S*)*R*,13(*R*)*S*,14(*R*)*S*-13-Hydroxy-3,14-dibromotetracyclo[10.2.2.0^{2,11}.0^{4,9}]hexadeca-2,4,6,8,10-pentaene (13). Mp 178–180 °C; white crystal from ethyl acetate/hexane; ^{1}H NMR (200 MHz, $CDCl_3$) δ 8.29 (d, aromatic, J=8.3 Hz, 1H), 7.81 (d, aromatic, J=6.7 Hz, 1H), 7.64 (s, aromatic, 1H), 7.63–7.27 (m, aromatic, 2H), 4.36 (m, CH-O, 1H), 3.39 (m, 1H), 4.01 (m, 1H), 3.14 (m, 1H), 2.39 (m, methylenic, 1H), 1.95 (m, methylenic, 1H), 1.84 (br d, J=6.5 Hz, OH, 1H), 1.69–1.40 (m, methylenic, 2H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 140.6 (C), 138.5 (C), 136.0 (C), 133.7 (C), 129.8 (CH), 129.6 (CH), 128.9 (CH), 128.4 (CH), 126.8 (CH), 121.5 (C), 81.7 (CH-O), 60.0 (CH), 45.2 (CH), 44.8 (CH), 25.0 (CH_2), 20.9 (CH_2); *m*/*z*: 384.2/382.3/380.2 (61/41/41), 259.2/257.2 (54/47), 194.2/192.2/191.2 (22/16/15), 178.2/179.2 (100/52), 166.2/165.2/164.2 (13/29/6); IR ($CHCl_3$) 3301, 3270, 3062, 2939, 2869, 1496, 1419, 1326, 1257, 1187, 1064, 1033, 933, 887, 794, 775, 686 cm^{-1}. HRMS: Anal. Calcd for $C_{16}H_{14}O^{79}Br_2$ 381.9568, found 381.9557.

4.4.2. 1(*R*)*S*,12(*S*)*R*,13(*R*)*S*,14(*R*)*S*-13-Hydroxy-3,10,14-tribromotetracyclo[10.2.2.0^{2,11}.0^{4,9}]hexadeca-2,4,6,8,10-pentaene (14). Mp 171–173 °C; white crystal from ethyl acetate/pentane; ^{1}H NMR (200 MHz, $CDCl_3$) δ 8.37–8.32 (m, aromatic, 2H), 7.68–7.60 (m, aromatic, 2H), 4.44 (m, CH-O, 1H), 4.07 (m, 1H), 3.91 (m, 1H), 3.83 (m, 1H), 2.39 (m, methylenic, 1H), 1.97 (m, methylenic, 1H), 1.83 (br d, J=5.5 Hz, OH, 1H), 1.70–1.27 (m, methylenic, 2H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 141.0 (C), 138.7 (C), 134.6 (C), 134.4 (C), 130.1 (CH), 129.9 (CH), 129.7 (CH), 129.0 (CH), 123.9 (C), 121.4 (C), 81.8 (CH-O), 59.0 (CH), 45.3 (2CH), 23.8 (CH_2), 20.5 (CH_2); *m*/*z*: 464.1/462.2/460.2/452.2 (35/76/76/35), 384.2/382.2/380.2 (18/34/20), 339.1/337.1 (35/48), 259.2/258.2/256.2 (50/86/81), 192.2/191.2/189.2 (31/35/37), 179.2/178.2 (40/100), 165.2/163.2 (48/23); IR ($CHCl_3$) 3284, 3228, 3096, 2916, 2869, 1592, 1492, 1446, 1323, 1253, 1192, 1176, 1076, 1038, 930, 761, 700, 684 cm^{-1}. HRMS: Anal. Calcd for $C_{16}H_{13}O^{79}Br_3$ 459.8673, found 459.8686.

4.5. Reaction of the compound 6 with *m*-CPBA

A solution of *m*-CPBA (2.392 g, 10.40 mmol) whose water is 25% in $CHCl_3$ (50 mL) was dried over Na_2SO_4 and filtered. To this solution was added compound **6** (1.164 g,

5.20 mmol). After stirring at room temperature for 1 day, the reaction mixture was washed with a solution of NaOH (0.5%, 500 mL) and water (500 mL), dried over Na_2SO_4, and the solvent was evaporated. The reaction mixture was crystallized from $CHCl_3$/ether, and epoxide **25** (735 mg, 3.10 mmol, 59%) was obtained as colorless crystals. The residue was submitted to preparative thick-layer chromatography (PLC) with ethyl acetate/hexane (1/1). Epoxide **25** (150 mg, 0.60 mmol, 12%) and compound **26**[8] (468 mg, 1.20 mmol, 9%) were obtained.

4.5.1. 1*R*(*S*),2*R*(*S*),3*R*(*S*),10*S*(*R*),11*S*(*R*),12*S*(*R*),13*S*(*R*),15*R*(*S*)-14,18-Dioxahexacyclo[10.3.2.1^{3,10}.0^{2,11}.0^{4,9}.0^{13,15}]-octadeca-4,6,8-triene (25). Mp 202–204 °C; colorless crystals; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.24–7.22 (AA′ of AA′BB′, aromatic, 2H), 7.15–7.13 (BB′ of AA′BB′, aromatic, 2H), 5.22 (s, epoxide, H_3–H_{10}, 2H), 3.29 (br s, epoxide, H_{13}–H_{15}, 2H), 2.46 (br s, bridgehead, H_1–H_{12}, 2H), 1.86 (br s, H_2–H_{11}, 2H), 1.75 (br d, A of AABB, J=8.1 Hz, methylenic, 2H), 1.06 (br d, B of AABB, J=8.1 Hz, methylenic, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 146.4 (C), 126.8 (CH), 119.1 (CH), 82.7 (CH, C_3–C_{10}), 52.3 (CH, C_{14}–C_{15}), 43.8 (CH, C_1–C_{12}), 31.3 (CH, C_2–C_{11}), 24.0 (CH_2); IR ($CHCl_3$) 3077, 3023, 2939, 2861, 1457, 1419, 1272, 1133, 1079 cm^{-1}. Anal. Calcd for $C_{16}H_{16}O_2$: C 79.97, H 6.71; found: C 79.76, H 6.68.

4.6. Reaction of epoxide 25 with TsOH

A mixture of epoxide **25** (335 mg, 1.40 mmol), TsOH (200 mg, 1.16 mmol), and MeOH (50 mL) was refluxed for 1 week. After the solvent of the mixture was evaporated, water (50 mL) was added and it was extracted with ethyl acetate (3×50 mL). The combined organic layers were washed with $NaHCO_3$ (5%, 100 mL) and water (100 mL), dried over $CaCl_2$, and the solvent was evaporated. Diol **27** (175 mg, 73%) was crystallized from ethyl acetate.

4.6.1. 1(*R*)*S*,12(*S*)*R*,13(*S*)*R*,14(*S*)*R*-Tetracyclo-[10.2.2.0^{2,11}.0^{4,9}]hexadeca-2,4,6,8,10-pentaene-13,14-diol (27). Mp 182–184 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82–7.80 (AA′ of AA′BB, aromatic, 2H), 7.66 (s, aromatic, 1H), 7.64 (s, aromatic, 1H), 7.47–7.42 (BB′ of AA′BB, aromatic, 2H), 3.84 (br s, OCH, 1H), 3.62 (br s, OCH, 1H), 3.20 (m, bridgehead, 1H), 3.15 (m, bridgehead, 1H), 2.19 (m, methylenic, 1H), 1.92 (m, methylenic, 1H), 1.72 (m, OH, 1H), 1.59 (tt, J=12.7, 4.03 Hz, 1H), 1.31 (m, methylenic, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.4 (C), 137.4 (C), 133.2 (C), 133.0 (C), 127.8 (CH), 127.7 (CH), 125.7 (2CH), 124.7 (CH), 123.1 (CH), 79.7 (C–O), 78.8 (C–O), 42.8, 42.1, 23.7, 17.7.

4.7. Synthesis of diacetate 28

Diol **27** (600 mg, 2.50 mmol) was allowed to react at room temperature for 3 days with pyridine (2 mL) and acetic anhydride (Ac_2O) (3 mL). The reaction mixture was poured into dilute aqueous HCl (100 g) with ice and checked with pH paper. It was extracted with $CHCl_3$ (2×40 mL), the extract was washed with $NaHCO_3$ (5%, 100 mL) and water (100 mL), and dried over $CaCl_2$. The solvent was evaporated and diacetate **28** (486 mg, 1.50 mmol, 60%) was obtained in a refrigerator from $CHCl_3$/hexane as white crystals.

4.7.1. 1(*R*)*S*,12(*S*)*R*,13(*S*)*R*,14(*S*)*R*-14-(Acetyloxy)tetracyclo[10.2.2.0^{2,11}.0^{4,9}]hexadeca-2,4,6,8,10-pentaen-13-yl acetate (28). Mp 87–89 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87–7.81 (AA′ of AA′BB′, aromatic, 2H), 7.70 (s, aromatic, 1H), 7.61 (s, aromatic, 1H), 7.50–7.44 (BB′ of AA′BB′, aromatic, 2H), 5.06 (t, J=2.6 Hz, H_{14}, 1H), 4.80–4.76 (m, H_{13}, 1H), 3.43–3.41 (m, bridgehead, H_{12}, 1H), 3.33–3.30 (m, bridgehead, H_{13}, 1H), 2.33–2.00 (m, methylenic, 2H), 2.17 (s, methyl, 3H), 1.91 (s, methyl, 3H), 1.62 (tt, J=12.5, 4.03 Hz, methylenic, 1H), 1.45–1.33 (m, methylenic, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.7 (CO), 170.5 (CO), 137.8 (C), 137.4 (C), 133.3 (C), 133.2 (C), 128.0 (CH), 127.8 (CH), 125.8 (CH), 125.7 (CH), 124.0 (CH), 123.5 (CH), 77.8 (C–O), 77.7 (C–O), 39.3 (CH), 39.0 (CH), 23.4 (CH), 21.5 (CH_3), 21.3 (CH_3), 18.6 (CH); IR ($CHCl_3$) 3055, 3018, 2953, 2872, 1739, 1371, 1245, 1214, 1054, 1039, 879, 752 cm^{-1}; Anal. Calcd for $C_{20}H_{20}O_4$: C 74.06, H 6.21; found: C 73.81, H 6.23.

4.8. Synthesis of anthracene derivative 8[4a] from 6

This product **8** was synthesized in two different ways.

(a) A mixture of compound **6** (591 mg, 2.46 mmol), TsOH (156 mg, 0.91 mmol), and MeOH (20 mL) in a sealed tube was heated at 95±5 °C for 12 days. The other parts of the reaction were studied in the same manner as for epoxide **25**. $CHCl_3$ (3×50 mL) was used in the extraction and anthracene derivative **8** was obtained as 350 mg (1.70 mmol, 69%).

(b) Compound **6** (112 mg, 0.50 mmol) was heated at 200±5 °C for 12 days alone. After the reaction mixture with silica gel (2–3 g) was filtered by $CHCl_3$ and the solvent was evaporated, **8** (55 mg, 0.20 mmol, 40%) was obtained.

4.8.1. 1(*R*)*S*,12(*S*)*R*-Tetracyclo[10.2.2.0^{2,11}.0^{4,9}]hexadeca-2,4,6,8,10,13-hexaene (8). Mp 102–104 °C (lit. 112–114 °C[4a]); white crystals were obtained from $CHCl_3$/hexane; ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.86–7.80 (AA′ of AA′BB′, aromatic, 2H), 7.63 (s, aromatic, 2H), 7.48–7.42 (BB′ of AA′BB′, aromatic, 2H), 6.63 (m, olefinic, 2H), 4.09 (m, bridgehead, 2H), 1.73–1.60 (m, methylenic, 4H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 144.8 (C), 137.1 (CH), 134.2 (C), 129.4 (CH), 126.9 (CH), 122.3 (CH), 42.2, 28.1; Anal. Calcd for $C_{16}H_{14}$: C 93.16, H 6.84; found: C 92.99, H 6.86.

4.9. Synthesis of anthracene derivative 34

A mixture of compound **4**[3] (125 mg, 0.43 mmol), TsOH (160 mg, 0.93 mmol), and MeOH (25 mL) in a sealed tube was heated at 95±5 °C for 12 days. The other parts of the reaction were studied in the same manner as for epoxide **25**. $CHCl_3$ (3×50 mL) was used in the extraction and chromatography of the residue on PLC with hexane/ether (7/3) given as an anthracene derivative **34** (80 mg, 0.29 mmol, 67%).

4.9.1. 1(*R*)*S*,12(*S*)*R*,13(*S*)*R*,14(*R*)*S*-Methylpentacyclo-[10.3.2.0^{2,11}.0^{4,9}.0^{13,15}]heptadeca-2,4,6,8,10,16-hexaene-14-carboxylate (34). Mp (amorf) 146–148 °C; ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.80–7.72 (AA′ of AA′BB′, aromatic, 2H), 7.61 (s, aromatic, 2H), 7.47–7.27 (BB′ of AA′BB′, aromatic, 2H), 6.26 (m, olefinic, 2H), 4.20 (m, bridgehead,

2H), 3.67 (s, OMe, 3H), 1.98–1.92 (m, cyclopropane, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 174.4 (CO), 144.9 (C), 134.0 (C), 133.5 (CH), 129.5 (CH), 127.4 (CH), 123.3 (CH), 53.5 (OMe), 42.7, 28.5, 27.5; IR ($CHCl_3$) 3080, 3029, 3004, 2953, 1710, 1676, 1625, 1497, 1472, 1319, 1242, 1191, 1165, 1114, 1063, 936, 885, 757 cm^{-1}; Anal. Calcd for $C_{19}H_{16}O_2$: C 82.55, H 5.84; found: C 82.24, H 5.81.

4.10. Catalytic hydrogenation of the compound 6

Into a 250 mL, two necked, round-bottomed flask fitted with a spinbar were placed 60 mg of Pd/C (5%) catalyst and **6** (1.04 g, 5.00 mmol) in ethyl acetate (100 mL). One of the necks was attached to a hydrogen manifold with a three-way stopcock and the other neck was capped with a rubber septum, degassed and flushed with hydrogen gas, while stirring magnetically. After stirring for 9 h the solution was decanted to separate it from the catalyst, and the solvent was evaporated. Compound **37** was quantitatively obtained and crystallized from hexane as white crystals.

4.10.1. 2*R*(*S*),3*R*(*S*),10*S*(*R*),11*S*(*R*)-3,10-Epoxytetracyclo-[10.2.2.0^{2,11}.0^{4,9}]hexadeca-4,6,8-triene (37). Mp 127–129 °C; ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.27–7.21 (AA′ of AA′BB′, aromatic, 2H), 7.19–7.12 (BB′ of AA′BB′, aromatic, 2H), 5.17 (s, epoxide, 2H), 1.94–1.87 (m, 4H), 1.70 (m, 2H), 1.62–1.30 (m, 6H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 149.0 (C), 128.1 (CH), 120.7 (CH), 84.3 (OCH), 44.7, 29.7, 28.7, 24.2; IR ($CHCl_3$) 2914, 1458, 1351, 1247, 1208, 1023, 965, 919, 850, 758, 657 cm^{-1}; Anal. Calcd for $C_{16}H_{18}O$: C 84.91, H 8.02; found: C 84.68, H 8.05.

4.11. Synthesis of anthracene derivative 38[4a]

This reaction was also studied in the same manner as for compound **6**. Compound **37** (904 mg, 4.00 mmol), TsOH (172 mg, 1.00 mmol), and MeOH (25 mL) were used for this reaction. Compound **38** (600 mg, 72%) was obtained and crystallized from ethanol.

4.11.1. Tetracyclo[10.2.2.0^{2,11}.0^{4,9}]hexadeca-2,4,6,8,10-pentaene (38). Mp 111–113 °C (lit. 112–113 °C[4a]); ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.91–7.84 (AA′ of AA′BB′, aromatic, 2H), 7.65 (s, aromatic, 2H), 7.52–7.45 (BB′ of AA′BB′, aromatic, 2H), 3.17 (m, bridgehead, 2H), 1.97–1.91 (m, methylenic, 4H), 1.59–1.54 (m, methylenic, 4H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 145.4 (C), 134.8 (C), 129.5 (CH), 127.7 (CH), 123.2 (CH), 36.2 (CH), 28.5 (CH_2); Anal. Calcd for $C_{16}H_{18}$: C 91.37, H 8.63; found: C 91.28, H 8.65.

4.12. Reduction of anthracene derivative 8

Anthracene derivative **8** (340 mg, 1.65 mmol) and ^{t}BuOH (2 mL) were dissolved in dry ether (30 mL). Excess metallic Na (1 g, 43.48 mmol), in small pieces, was added over 10 min. After stirring at room temperature for 4 days, unreacted Na and solid ^{t}BuOK were removed by filtration and washed with ether (40 mL). The solution was poured into water (100 mL) and the mixture formed was shaken. The organic layer was separated, and the water layer was extracted twice with ether (2×30 mL). The combined organic layer was washed with water (20 mL), dried over $CaCl_2$, and then the solvent was evaporated. A mixture of **8** and **40** (278 mg) was obtained (**8**:**40**=1:9). They were not isolated by chromatographic methods.

4.12.1. 1(*R*)*S*,12(*S*)*R*-Tetracyclo[10.2.2.0^{2,11}.0^{4,9}]hexadeca-2(10),3,5,8,13-pentaene (40). ^{1}H NMR (200 MHz, $CDCl_3$) δ 6.98 (s, aromatic, 2H), 6.57–6.53 (m, olefinic, 2H), 5.95 (s, olefinic, 2H), 3.94 (m, bridgehead, 2H), 3.41 (s, methylenic, 4H), 1.68–1.54 (m, methylenic, 4H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 144.3 (C), 137.3 (CH), 132.4 (C), 127.0 (CH), 124.6 (CH), 41.0, 31.0, 28.1.

4.13. Reduction of anthracene derivative 38

This reaction was also studied in the same manner as for compound **8**. A mixture of anthracene derivative **38** (600 mg, 2.88 mmol), ^{t}BuOH (2 mL), dry ether (40 mL), and excess metallic Na (6 equiv) was stirred for 1 week. A mixture of **38** and **39** (430 mg) was obtained (**38**:**39**=1:6). They were also not isolated by chromatographic methods.

4.13.1. Tetracyclo[10.2.2.0^{2,11}.0^{4,9}]hexadeca-2(10),3,5,8-tetraene (39). ^{1}H NMR (200 MHz, $CDCl_3$) δ 6.98 (s, aromatic, 2H), 5.98 (s, olefinic, 2H), 3.46 (br s, methylenic, 4H), 3.00 (m, bridgehead, 2H), 1.83 (bd, A of AB, J= 8.2 Hz, methylenic, 4H), 1.47 (bd, B of AB, J=8.2 Hz, methylenic, 4H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 144.2 (C), 133.3 (C), 129.0 (CH), 125.5 (CH), 35.7, 28.6, 20.4.

4.14. Synthesis of compound 9

This compound was synthesized by two ways.

(a) Catalytic hydrogenation of the compound **39**: This reaction was also studied in the same manner as for compound **6**. A mixture of compounds **38** and **39** (300 mg, **38**:**39**=1:6), Pd/C (25 mg, 5%) catalyst, and ethyl acetate (30 mL) were used for this reaction. The residue was submitted to PLC with hexane and compound **9** (75 mg) was obtained and crystallized from ethanol.
(b) Catalytic hydrogenation of the compound **40**: This reaction was also studied in the same manner as for compound **37**. A mixture of compounds **8** and **40** (300 mg, **8**:**40**=1:9), Pd/C (25 mg, 5%) catalyst, and ethyl acetate (40 mL) were used for this reaction. The residue was submitted to PLC with hexane and compound **9** (155 mg) was obtained and crystallized from ethanol.

4.14.1. Tetracyclo[10.2.2.0^{2,11}.0^{4,9}]hexadeca-2(11),3,9-triene (9). Mp 88–90 °C; ^{1}H NMR (200 MHz, $CDCl_3$) δ 6.91 (s, aromatic, 2H), 2.95 (m, bridgehead, 2H), 2.86–2.80 (m, methylenic, 4H), 1.89–1.78 (m, methylenic, 8H), 1.46 (br d, B of AB, J=8.0 Hz, methylenic, 4H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 143.6 (C), 136.2 (C), 126.2 (CH), 35.7, 31.4, 28.6, 25.5; IR ($CHCl_3$) 2929, 2864, 1466, 1143, 893, 630 cm^{-1}; *m/z*: 213.1/212.0 (8/49), 185.0/184.0/182.9 (8/60/100), 169.0 (12), 156.0 (16), 142.0/140.9 (24/86), 128.0 (22), 114.9 (20), 18.41 (100); Anal. Calcd for $C_{16}H_{22}$: C 89.65, H 10.35; found: C 89.60, H 10.37.

Acknowledgements

The authors are indebted to the Department of Chemistry (Atatürk University) for financial support, associate

Professor Dr. Cavit Kazaz for technical assistant and associate Professor Dr. Thomas J. Cronin (SUNY Cobleskill, NY) for proofread.

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