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Low and high temperature bromination of exocyclic dienes: high temperature bromination. Part 16☆

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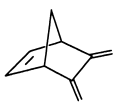
Abstract—The electrophilic addition of bromine to an exocyclic diene, 5,6-dimethylenebicyclo[2.2.1]hept-2-ene, in CCl_4 at 0°C led to the formation of non-rearranged (73%) and rearranged products (27%). However, high temperature bromination of the exocyclic diene at 77°C suppressed the formation of the rearranged products. Similarly, bromination of 9,10-dimethylenetricyclo[6.2.1.$0^{2,7}$]undeca-2,4,6-triene at −10°C gave only the *exo*-1,2-addition product. Bromination at +5°C resulted in the formation of a mixture consisting of *exo*-1,2- and 1,4-addition products in a ratio of (1:4). High temperature bromination at 77°C resulted in the formation of the *endo*-1,2-addition product. Furthermore, it has been shown that the 1,4-addition product converts smoothly to the 1,2-addition product. The formation mechanism of the products is discussed and supported by calculations.

1. Introduction

The constitution and configuration of products formed by electrophilic additions to norbornene and norbornadines are interesting.[2] The reaction of these systems has been used as a mechanistic probe to elucidate the mechanism of different reactions. The halogenation of norbornadiene has been studied less intensively.[3] Winstein studied the bromination of norbornadiene and reported the formation of products of Wagner–Meerwein rearrangement and homoallylic conjugation (Scheme 1).[4] The *trans*-addition product was not detected.

In the course of studying the bromination reaction of unsaturated bicyclic systems we observed that the reaction temperature has a dramatic influence on product distribution.[5] Therefore, we have investigated the high temperature bromination of norbornadiene,[6] benzonorbornadiene,[7] and some derivatives of benzonorbornadiene.[8] The bromination of these hydrocarbons at higher temperatures (77–150°C) resulted in the formation of non-rearranged products. For example, high temperature bromination of **1** gave a mixture of the rearranged (54%) and non-rearranged products whereas, in the latter case, skeletal rearrangement was prevented (Scheme 1).[6]

When electrophilic addition is carried out on a compound having nonconjugated dienes, the 1,2-addition product is often obtained. In conjugated systems, the 1,4-addition product is the most stable species (thermodynamically controlled product), and it predominates. In most cases, under the reaction conditions, the 1,2-addition product (kinetically controlled product) converts into a mixture of 1,2- and 1,4-addition products that is richer in the 1,4-addition product.[9]



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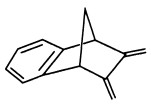

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To study the competition between an isolated olefin and conjugated diene and the effect of temperature on skeletal rearrangement we have studied the low and high temperature bromination reactions of the hydrocarbons **8** and **9**. Furthermore, diene units in **8** and **9** are a part of a cyclic system, and therefore it will also be interesting to compare the behavior of these diene units with acyclic systems.

2. Results and discussions

The starting material **8** was synthesized by the Diels–Alder cycloaddition of *trans*-2,3-dichloro-2-butene to cyclopentadiene as reported in the literature.[10] The bromination of **8** was carried out in carbon tetrachloride at 0°C. 200 MHz ^{1}H

☆ See Ref. 1.

Keywords: halogenation; alkenes; bicyclic aliphatic compounds; alkyl halides.

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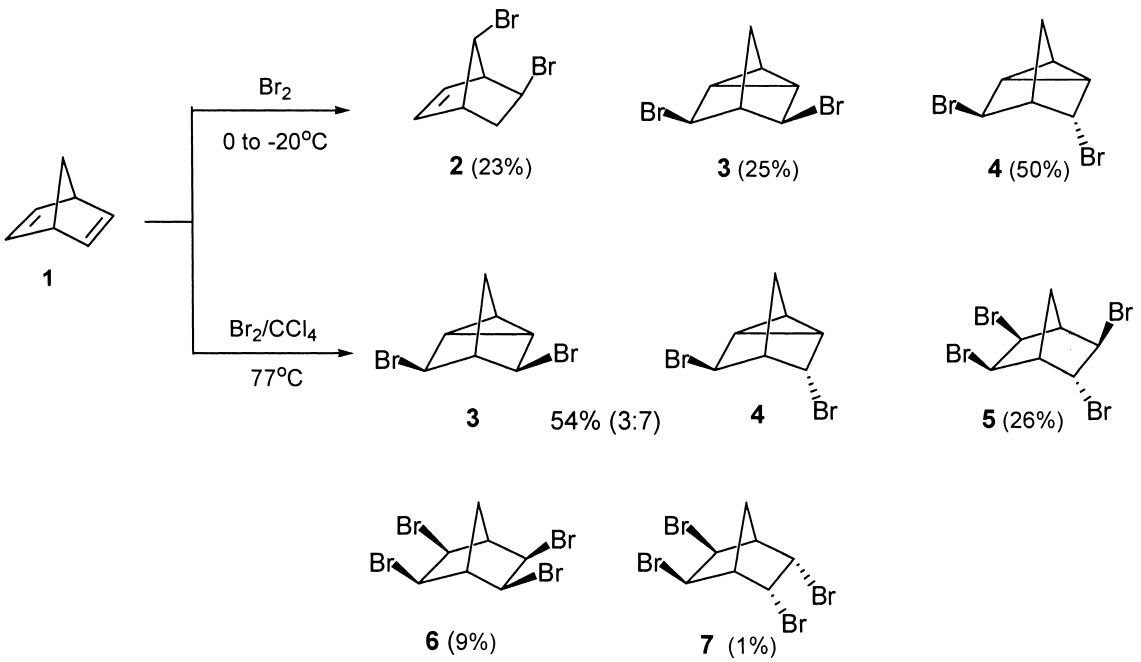
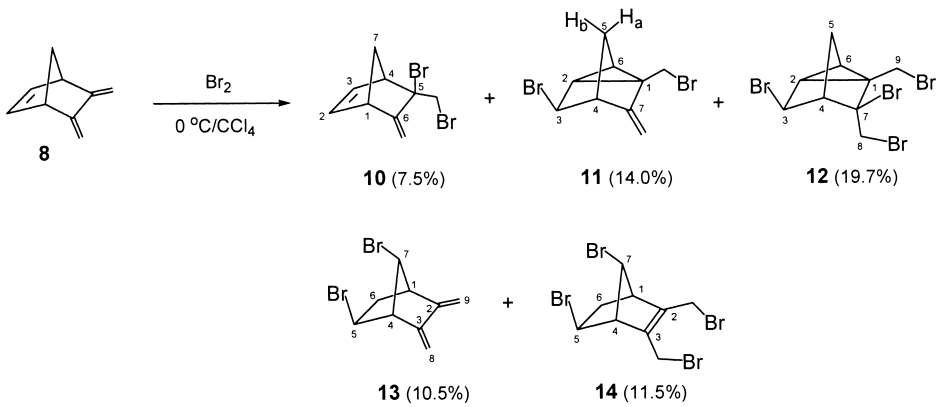


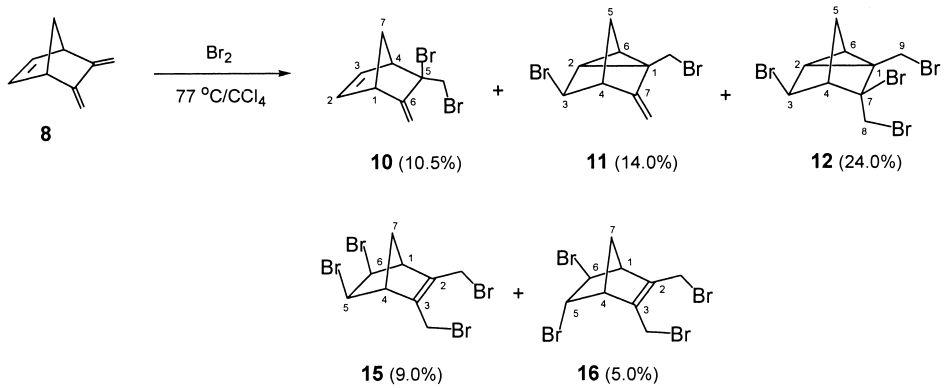
Scheme 1.

NMR spectroscopic analysis of the crude product indicated a complex mixture. After the mixture was subjected to column chromatography on silica gel we isolated five products, **10**, **11**, **12**, **13** and **14**, at ratios of 7.5, 14.0, 19.7, 10.5 and 11.5%, respectively (Scheme 2).

The structural proof of these compounds was carried out primarily with ^{1}H NMR and ^{13}C NMR spectra. The 200 MHz ^{1}H NMR and 50 MHz ^{13}C NMR spectra of **10** show the presence of four olefinic protons arising from an endocyclic and an exocyclic double bond, which clearly shows that 1,2-addition of bromine took place to one of the exocyclic double bonds. The configuration of the bromine atoms has been confirmed by nuclear Overhauser enhancement (NOE) experiments. Irradiation at the resonance frequency δ 6.25 caused enhancement of the signals for bridgehead protons H_1 and H_4 (3.42 ppm) and for B-part of AB system at δ 3.36 arising from methylene protons (C*H*HBr). Dibromo- and tetrabromo-nortricyclanes derivatives **11** and **12** formed by the homo-conjugative addition of bromine to **8** were the main products. Treatment of **11** with bromine under the given reaction conditions resulted in the formation of **12**. Proton coupled ^{13}C NMR spectra of **11** and **12** in particular were decisive for the formation of cyclopropane rings. The determined coupling constants in the sp^3 region (J_{CH}=178.4, 183.0 Hz for **11** and J_{CH}=174.0, 184.8.0 Hz for **12**) are in agreement only with the presence of cyclopropane rings. Further configurational assignments to **11** and **12** have been done with differential ^{1}H NMR NOE measurements and correlation spectroscopy (COSY). The bonding arrangement of the coupled protons H_3 and H_{5a} in **11** and **12** meets the M or W criterion. Irradiation at the resonance frequency of the H_3 proton in **11** and **12** removes the long-range coupling in the resonance signal of H_{5a}. Irradiation of the H_3 proton in **12** at δ 4.05 induces an enhancement at one of the methylene protons ($-CH_2Br$), H_2 and H_4 protons, not at the bridge protons, which clearly indicates the *exo*-orientation of the bromine atom attached to C_3 and the *endo*-orientation of the $-CH_2Br$ group. Furthermore, there was no measurable coupling between H_3 and H_4 due to the nearly 90° dihedral angle.



Scheme 2.

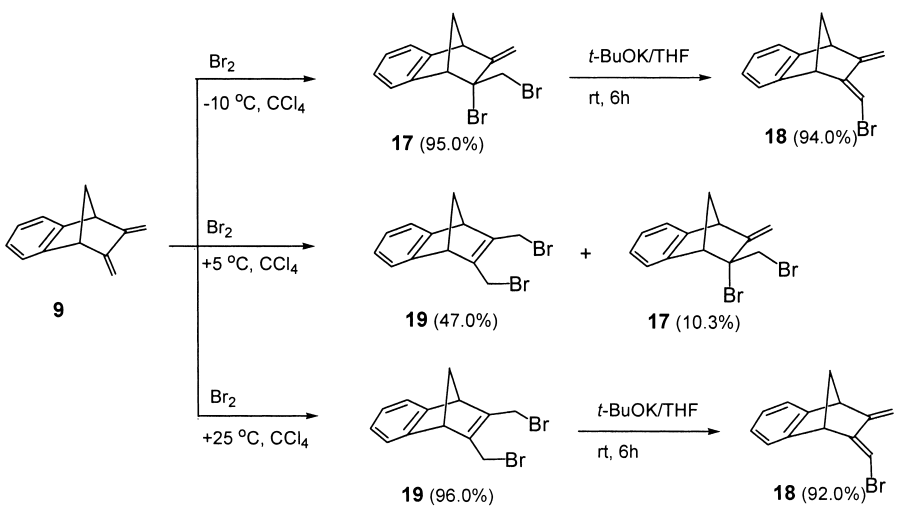


Scheme 3.

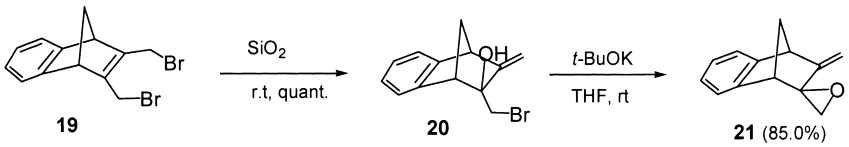
Besides these products we isolated two Wagner–Meerwein rearrangement products **13** and **14** in a total yield of 22%. Dibromide **13** is not stable and decomposes to a complex mixture if left standing at room temperature. Control experiments on NMR scale showed that **14** is formed through the 1,4-addition of bromine to **13**. The fact that H_5 showed no coupling with the adjacent bridgehead proton H_4 indicated the *exo*-configuration of the bromine atom.

Next, 5,6-dimethylenebicyclo[2.2.1]hept-2-ene (**8**) was submitted to high temperature bromination. To a refluxing solution of **8** in carbon tetrachloride was added a hot solution of bromine in carbon tetrachloride in one portion. The color of bromine disappeared immediately. After removal of the solvent, the reaction mixture was chromatographed on silica gel to give five products, three of which, **10**, **11** and **12**, were observed previously with low temperature bromination. Besides these products, we isolated an additional two non-rearranged tetrabromo compounds, **15** and **16**, with a norbornene structure (Scheme 3). A careful examination of the reaction mixture revealed no formation of any trace of Wagner–Meerwein rearrangement products **13** and **14**. The structural assignments of the tetrabromo compounds **15** and **16** were achieved by means of proton and carbon NMR spectra. The ^{1}H NMR and ^{13}C NMR spectra of **15** were highly symmetrical according to the symmetry in the molecule. In particular, the five-line ^{13}C NMR spectrum of **15** is completely in agreement with the *cis*-configuration of the bromine atoms. The *exo*-configuration of the bromine atoms has been confirmed by the observed long-range coupling between the bridgehead proton H_7 and H_5 and H_6 ($^4J_{7,5(6)}$=2.0 Hz), respectively. For **16**, the ^{1}H NMR and ^{13}C NMR spectra were decisive. The nine-line ^{13}C NMR spectrum in particular confirms the presence of asymmetry in the molecule.

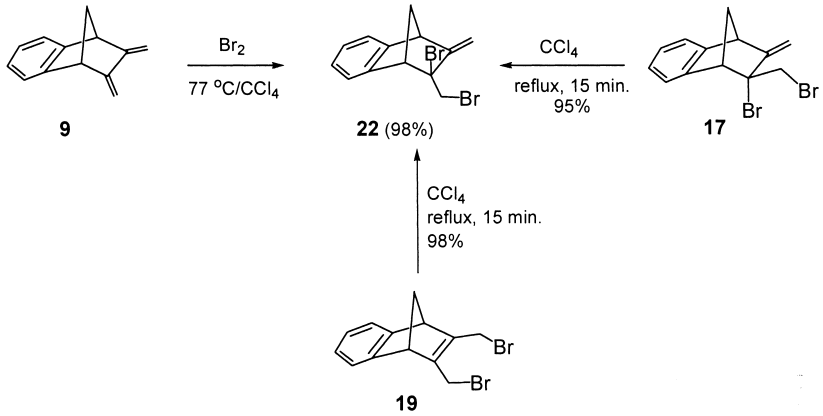
To see the behavior of an exocyclic diene unit against bromination reactions (to cancel the competition between an isolated double bond and an exocyclic diene unit) we have incorporated the double bond in **8** in a benzene ring. For that reason, we have brominated **9**[11] at −10°C and isolated **17** as the sole product, which is formed by the 1,2–addition of bromine to the exocyclic double bond (Scheme 4). The structural assignment to dibromide **17** was achieved by means of proton and carbon NMR data. The *endo*-configuration of the bromine atom was established by differential NOE experiments. Irradiation of bridge methylene protons at δ 2.09 induces an enhancement of the B-part of the AB system arising from methylene protons ($-CH_2Br$) as well as of bridgehead protons. This observation clearly indicates the *endo*-configuration of the bromine atom in **17**. For further structural proof, the dibromide **17** was submitted to a base-supported elimination reaction with *t*-BuOK to give **18** in high yield. The bromination of **9** at +5°C gave a mixture consisting of **17**



Scheme 4.



Scheme 5.



Scheme 6.

and **19** in a ratio of 1:4 (determined by ^{1}H NMR spectroscopy). Preparative liquid column chromatography of the reaction mixture using silica gel gave **17** and **20**, which is considered to be the hydrolyzed product of **19** under silica gel column conditions. The formation of **20** can be explained by the attack of a water molecule present in silica gel stereospecifically on C_9 from the *exo*-face of the molecule, the bromine at C_{13} being displaced according to an S_N2' mechanism (Scheme 5). The structure of **20** was ascertained from its ^{1}H NMR spectrum, which is very similar to that of **22** (see below), indicating that the two products have the same configuration. For further structural proof, **20** was converted easily into the corresponding epoxide **21** in 85% yield upon treatment with *t*-BuOK in THF at room temperature (Scheme 5).

Bromination of **9** at ambient temperature gave only the symmetrical dibromo compound **19** in almost quantitative yield (Scheme 4). Compound **19** exhibits an AA′BB′ system arising from the aromatic protons, which indicates clearly the symmetrical 1,4-addition of bromine to the exocyclic diene unit in **9** (Scheme 6).

For the high temperature bromination reaction, a hot solution of bromine in carbon tetrachloride was added directly to a refluxing solution of **9** in carbon tetrachloride. Analysis of the crude product indicated that **22** was formed as the sole product, which is a configurational isomer of **17** (Scheme 6). The structure **22** was determined by extensive double resonance experiments. The ^{13}C NMR data is consistent with the proposed structure, which displays 5 sp^2 and 8 sp^3 carbon atoms. A comparison of the chemical shifts of the bridge protons in **17** and **22** shows that the bridge protons of **17** resonate at δ 2.09 as a triplet (J=1.5 Hz) due to coupling with the bridgehead protons, whereas the bridge protons of **22** resonate at δ 2.21 and 2.61 ppm as a well-resolved AB system. The chemical shifts of the bridge protons are highly sensitive to the configuration of the substituents. Any steric repulsion between the bridgehead proton and the substituent (in this case bromine) related to the van der Waals effect causes a paramagnetic contribution to the shielding constants of the bridge proton resulting in a shift to a lower field.[12] The *exo*-orientation of the bromine atom causes a remarkable chemical shift difference ($\Delta\delta$=0.4 ppm) of bridge protons in **22**. This phenomenon, the low field shift of one of the bridge protons, can be explained only by the *exo*-configuration of the bromine atom in **22**. Furthermore, one of the methylenic protons ($-CH_2Br$) in **22** resonates at an unusually high field (δ=2.61 and 3.70 ppm), which can only be attributed to the *endo*-configuration of the bromomethylene group. AM1 geometry optimization shows that one of the methylene protons is located in the shielding zone of the aromatic ring (Fig. 1).

A solution of **17** and **19** in carbon tetrachloride was refluxed for 15 min. NMR spectral analysis showed that both starting materials were converted into **22** in almost quantitative yield (Scheme 6). These experiments implied that **22** is the most thermodynamically stable compound.

Electrophilic addition to conjugated dienes usually involves allylic cations as intermediates. Unlike simple carbocations, an allylic cation can react with a nucleophile at either of its

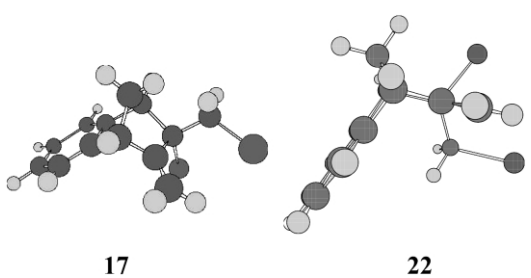
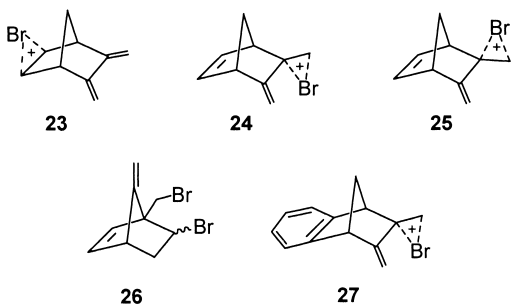


Figure 1. AM1 optimized geometries for compounds **11** and **12**.

positive centers to give 1,2-addition and 1,4-addition products, respectively. One of the interesting peculiarities of the reaction of conjugated dienes with electrophiles is the effect of temperature on the products. If the reaction is carried out at lower temperatures <0°C, the 1,2-addition product predominates, whereas higher temperatures favor the 1,4-addition product. The exocyclic diene provides an isolated double bond as well as a conjugated diene. The electrophile, bromine, can attack both systems. Analysis of the product mixture indicates that 22% of the products (**13** and **14**) arises from the attack on the isolated double bond. On the other hand, the major products (**11**, **12** and **10**) are formed from the attack on the conjugated system. It is well known that conjugated systems are often more stable than unconjugated systems. By contrast they are more reactive due to having higher HOMO than isolated olefins.[13] Therefore, the formation of the products **11**, **12** and **10** as the major products can be easily rationalized. Furthermore, HOMO of **8** (calculated by AM1 method) shows that the reactive side of the molecule is the diene unit as indicated by the experiments. The products **13** and **14** are formed via Wagner–Meerwein rearrangement. Since the bromine attacks benzonorbornadiene exclusively from the *exo*-face of the double bond,[7,8] we assume that in the case of **8** bromine also attacks the double bond from the *exo*-face of the double bond to generate *exo*-bromonium cation **23**, which can easily rearrange to **13**. Furthermore, the configurations of the bromine atoms also support the formation of *exo*-bromonium ion **23**.

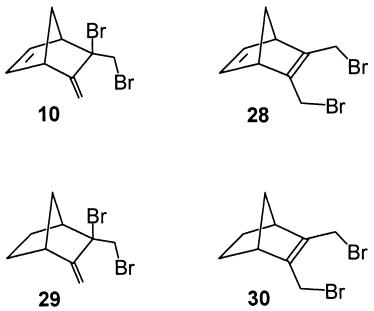


23 **24** **25** **26** **27**

The formation mechanism of the products **10**, **11** and **12** can be rationalized in term of two different cyclic bromonium ions **24** and **25**. In the case of the formation of an *exo*-bromonium ion **25** the system can undergo Wagner–Meerwein rearrangement to form rearranged products of type **26**. However, we were not able to determine any trace of this type of product. Therefore, we assume that the bromine attacks the double bond from the *endo*-face to form **24**. Recently, a similar *endo*-attack has been demonstrated by Sataka et al. during the bromination reaction of bicyclo[2.2.2]octa-2,5-diene.[14] Furthermore, we have performed some calculations based on the B3LYP/3-21G** level for the ions **24** and **25** and found that bromonium ion **24** is 2.7 kcal/mol more stable than **25**. However, it is very difficult to predict at this stage whether the products **10**–**12** are formed from the *endo*-bromonium ion **24** or not. Those products can be actually formed from **24** as well as from **25**.

The high-temperature bromination of **8** did not reveal any trace of Wagner–Meerwein products **13** and **14**. The formation of these products was completely suppressed. We additionally isolated two new products, **15** and **16**, arising from normal 1,2-addition to the double bond in **8**. In order to test the reaction mechanism at high temperature, the bromination of **8** was carried out at the reflux temperature of carbon tetrachloride in the presence of free radical inhibitors like 2,4-di-*tert*-butylphenol, which suppressed the formation of the non-rearranged products **15** and **16**. This observation strongly supports the assumption that there is competition between radical and ionic reactions at 77°C. The products **15** and **16** are likely formed by a radical mechanism.

From the bromination reactions of **9** we isolated different products at various temperatures. The reaction at −10°C gave **17** exclusively, which is a normal 1,2-addition product. At +5°C we mostly isolated 1,4-addition product. These observations indicate that the activation barrier for the formation of **19** is higher than that of **17**, which is in agreement with the findings from acyclic systems. On the other hand, the 1,2-addition product **17**, as well as the 1,4-addition product **19**, rearranged completely to the isomeric 1,2-addition product **22**. This means that the 1,4-addition product **19** is not the most thermodynamically stable product. To support this finding we have calculated these three isomers, **17**, **19** and **22**, with geometry optimizations at Becke3LYP/-21G** level and found that the 1,4-addition product **19** is 5.8 kcal/mol higher in energy than **22** and 4.2 kcal/mol higher than **17** (Table 1). These results are completely in agreement with our observations. Furthermore, we have optimized the geometries of **10/28** and **29/30**.



10 **28** **29** **30**

In these systems we have also found that the 1,4-addition products **28** and **30** are about 8.3 and 3.2 kcal in higher energy than the corresponding 1,2-addition products **10** and **29**, respectively. These calculations show us that the

Table 1. Absolute energies of the 1,2- and 1,4-addition products. The optimized geometries are calculated DFT at B3LYP/6-31G**

Compounds	*E* (a.u.)	Relative energies (kcal/mol)
28	−5471.14128	8.3
10	−5471.15481	0.0
30	−5472.39567	3.2
29	−5472.40001	0.0
19	−5623.96982	5.8
17	−5623.97616	1.6
22	−5623.97883	0.0

formation of a 1,4-addition product, where the double bond is incorporated in a ring, causes an additional increase in the ring strain. Therefore, the formation of an exocyclic double bond (1,2-addition) is preferred. The ring strain in **29** is reduced due to the removal of the endocyclic double bond. Therefore, the energy gap between 1,2- and 1,4-addition products is reduced (from 8.3 to 3.2 kcal/mol). In conclusion, 1,2-addition products derived by the addition of bromine to exocyclic double bonds, in contrast to acyclic systems, are thermodynamically more stable than the corresponding 1,4-addition products; however, the activation barrier for the 1,4-addition to **9** is higher than that of 1,2-addition as in the case of acyclic systems.

3. Experimental

3.1. General

Melting points were determined on a melting apparatus. Infrared spectra were obtained from films on NaCl Plate for liquids or from solution in 0.1 mm cells or KBr pellets for solids on a regular instrument. The ^{1}H and ^{13}C NMR spectra were recorded on 200 (50)-MHz spectrometers. Mass spectra (electron impact) were recorded at 70 eV as *m/z*. Column chromatography was performed on silica gel (60-mesh, Merck).

3.2. Caution

It has been reported[4] that of the three laboratory workers who has used dibromides and bromohydrin derived from norbornadiene, two later developed similar pulmonary disorders which contributed to their subsequent deaths. The third exhibited minor skin sensitivity reaction. In the case of the dibromides derived from benzonorbornadiene there is no report in the literature about the toxicological effect. However, we recommend that the compounds must be handled only with extreme caution.

3.3. Calculation methods

The initial geometries with the global energy minima were calculated by using AM1 self-consistent fields molecular orbital method at the restricted Hartree-Fock (RHF) level.[15] After that, all obtained geometries were fully optimized again at the B3LYP/3-21G** level. Energies were refined using B3LYP/3-21G** single point evaluations. For this purpose, Density functional theory (DFT)[16] employing Beckee's three-parameter hybrid method[4,17] and the exchange functional of Lee, Yang, and Parr (B3LYP)[18] as implemented in the Gaussian 98W[19] program suite were used.

3.4. Bromination of 5,6-dimethylenebicyclo[2.2.1]hept-2-ene (8) at 0°C

To a magnetically stirred solution 5,6-dimethylenebicyclo[2.2.1]hept-2-ene (**8**) (1.0 g, 8.5 mmol) in 40 mL dry CCl_4 was added drop wise a solution of bromine (2.0 g, 12.5 mmol) in 40 mL dry CCl_4 during 10 min at 0°C. After completion of the addition, the solution was allowed to warm to 20°C. The solvent was removed under reduced pressure. Oily residue was chromotographed on silica gel (45 g, 100 cm, 1 cm) eluting with hexane to give as the first fraction **10**.

3.4.1. (1*S*(*R*),4*R*(*S*),5*R*(*S*)) 5-Bromo-5-(bromomethyl)-6-methylenebicyclo[2.2.1]hept-2-ene (10). 175 mg 7.5%, isolated yield as colorless oil; [Found: C, 39.0; H, 3.6. $C_9H_{10}Br_2$ requires C, 38.89; H, 3.63%]; ν_{max} (liquid film) 2929, 2856, 1458, 1381, 1297 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 6.25 (1H, bs, *H*C═C*H*), 5.20 (1H, bs, C═C*H*H), 5.18 (1H, bs, C═CH*H*), 3.81 (1H, d, A part of AB system, *J*=9.3 Hz, –CH*H*Br), 3.42 (2H, m, H_1 and H_4), 3.36 (d, B part of AB system, *J*=9.3 Hz, –C*H*HBr), 2.28 (1H, bd, A part of AB system, *J*=9.2 Hz, H_{7endo}), 1.92 (1H, bd, B part of AB system, *J*=9.2 Hz, H_{7exo}); δ_C (50 MHz, $CDCl_3$) 156.1 (C_6), 140.3 (C_2 or C_3), 135.6 (C_2 or C_3), 111.3 (C_8), 72.5 (C_5), 58.0 (C_9), 53.9 (C_1 or C_4), 51.5 (C_1 or C_4), 46.9 (C_7). The second fraction gave **13**.

3.4.2. (1*R*(*S*),4*R*(*S*)-5*S*(*R*),7*R*(*S*))-5,7-Dibromo-2,3-dimethylenebicyclo[2.2.1]heptane (13). 373 mg, 10.5%, isolated yield as colorless oil; [Found: C, 38.99, H, 3.52. $C_9H_{10}Br_2$ requires C, 38.89, H, 3.63%]; ν_{max} (KBr) 3029, 2978, 2876, 1446, 1319, 1268, 1242, 1191, 1114, 1038, 936, 834, 609 cm^{-1}. δ_H (200 MHz, $CDCl_3$) 5.26 (1H, bs, C═C*H*H), 5.23 (1H, bs, C═CH*H*), 5.02 (1H, bs, C═C*H*H), 4.94 (1H, bs, C═CH*H*), 4.08 (1H, m, H_7), 4.01 (1H, m, H_5), 3.26 (1H, bs, H_4), 2.99 (1H, m, H_1), 2.77 (1H, dt, A part of AB system, *J*=13.8, 4.5 Hz, H_{6exo}), 2.35 (1H, dd, B part of AB system, *J*=13.8, 8.4 Hz, H_{6endo}); δ_C (50 MHz, $CDCl_3$) 148.1 (C), 147.6 (C), 106.5 (CH_2), 106.2 (CH_2), 60.8 (CH), 55.4 (CH), 53.8 (CH), 47.5 (CH), 42.2 (CH_2). As the third fraction we isolated **11**.

3.4.3. (1*R*(*S*),2*S*(*R*),3*S*(*R*),4*R*(*S*),6*R*(*S*))-3-Bromo-1-(bromomethyl)tricyclo[2.2.1.0^{2,6}]heptane (11). 329 mg (14%, isolated yield) as colorless oil; [Found: C, 38.7, H, 3.5. $C_9H_{10}Br_2$ requires C, 38.89, H, 3.63%]; ν_{max} (liquid film) 3106, 3029, 2978, 2953, 2876, 1472, 1446, 1319, 1268, 1242, 1217, 1038, 911, 885, 834, 757 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 4.83 (1H, C═C*H*H), 4.70 (1H, s, C═CH*H*), 4.07 (1H, t, J_{34}=J_{5a}=1.6 Hz, C*H*Br), 3.59 (2H, s, CH_2), 2.51 (1H, bs, H_4), 2.01–2.07 (m, A-parts of two AB systems, H_6 and H_{5b}), 1.88 (1H, bd, B part of AB system, *J*=5.2 Hz, H_2), 1.57 (1H, dt, B part of AB system, *J*=10.7, 1,6 Hz, H_{5a}); δ_C (50 MHz, gated-coupled, $CDCl_3$) 151.1 (s, C_7), 103.3 (t, *J*=158.8 Hz, C_8), 56.1 (d, *J*=165.9 Hz, C_3), 47.3 (d, *J*=155.0 Hz, C_4), 35.8 (s, C_1), 34.7 (d, *J*=183.0 Hz, C_2), 34.65 (t, *J*=136.6 Hz, C_5), 32.4 (t, *J*=153.9 Hz, C_9), 29.0 (d, *J*=178.0 Hz, C_6). The fourth fraction gave **12**.

3.4.4. (1*R*(*S*),2*S*(*R*),3*S*(*R*),4*S*(*R*),6*R*(*S*))-3,7-Dibromo-1,7-bis(bromomethyl)tricyclo-[2.2.1.0^{2,6}] heptane (12). 464 mg, 19.7%, isolated yield as white crystals from CCl_4/hexane (1:4), mp 70–71°C; [Found: C, 24.75, H, 2.28. $C_9H_{10}Br_4$ requires C, 24.69, H, 2.30%]; ν_{max} (liquid film) 3029, 2978, 2876, 1444, 1319, 1268, 1242, 1191, 1038, 936, 885, 834, 609 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 4.17 (1H, bs, C*H*Br), 4.05 (1H, d, A part of AB system, *J*=11.8 Hz, –C*H*HBr), 3.97 (1H, d, A part of AB system, *J*=12.7 Hz, –C*H*HBr), 3.70 (1H, d, B part of AB system, *J*=12.7 Hz, –CH*H*Br), 3.24 (1H, d, B part of AB system, *J*=11.8 Hz, –CH*H*Br), 2.62 (1H, bs, H_4), 2.30 (1H, bd, A

part of AB system, J=12.1 Hz, H_5), 2.16 (1H, bd, B part of AB system, J=12.1 Hz, H_5'), 2.00 (1H, dt, A part of AB system, J=5.1, 1.3 Hz, H_2), 1.87 (1H, dt, B part of AB system, J=5.1, 1.3 Hz, H_6); δ_C (50 MHz, gated-coupled, $CDCl_3$) 77.6 (s, C_7), 52.3 (dd, ^1J=159.6 Hz, ^2J=4.6 Hz, C_4), 50.8 (dd, ^1J=163.9 Hz, ^2J=8.2 Hz, C_3), 41.9 (dd, ^1J=158.4, 150.0 Hz, C_9), 41.5 (bs, C_1), 34.2 (bt, J=135.5 Hz, C_5), 32.5 (t, ^1J=154.36 Hz, C_8), 32.3 (bd, J=174.0 Hz, C_6), 31.3 (bd, ^1J=184.8 Hz, C_2).

Elution was continued with hexane/chloroform (3:1) to give **14**.

3.4.5. (1*S*(*R*),4*R*(*S*)-5*S*(*R*),7*R*(*S*))-5,7-Dibromo-2,3-bis-(bromomethyl)bicyclo[2.2.1]hept-2-ene (14). 426 mg (11.5%) as white crystals from CCl_4/hexane (1:4), mp 87–88°C; [Found: C, 24.53, H, 2.21. $C_9H_{10}Br_4$ requires C, 24.69, H, 2.30%]; ν_{max} (KBr) 3004, 2978, 1446, 1293, 1268, 1217, 834, 731, 629 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 4.09 (1H, m, H_5), 4.00 (5H, m, 2 CH_2–Br and H_7), 3.32 (1H, bs, H_4), 3.06 (1H, m, H_1), 2.76 (1H, dt, A part of AB system, J=13.3, 4.1 Hz, H_{6exo}), 2.37 (1H, dd, B part of AB system, J=13.3, 8.1 Hz, H_{6endo}); δ_C (50 MHz, $CDCl_3$) 145.4, 143.5, 60.4, 56.4, 55.1, 45.6, 37.7, 25.5, 24.3; *m/z* M^+ (–HBr): 439/437/435 (50, 100, 55, M^+), 455/457/459/461 (25, 95, 90, 22, M^+–HBr), 275/277/279 (25, 45, 27, M^+–2HBr), 197/199 (50, 45, M^+–3HBr), 170 (18, M^+–3HBr, $-CH_2-$).

3.5. Bromination of 5,6-dimethylenebicyclo[2.2.1]hept-2-ene (8) at 77°C

5,6-Dimethylenebicyclo[2.2.1]hept-2-ene (**8**) (1.0 g, 8.5 mmol) was dissolved in 40 mL CCl_4 in a 100 mL two-necked flask equipped with reflux condenser and an inlet glass-tube touching the bottom of the reaction flask. The inlet glass-tube was connected to a 25 mL round-bottom flask which contains (2.0 g, 12.5 mmol) bromine. Bromine vapors obtained by heating of the flask to 100°C was transferred directly to CCl_4 solution having a temperature of 77°C in 10 min while stirring magnetically. The reaction mixture was refluxed for 5 min. After cooling of the reaction mixture to room temperature, the solvent was evaporated, the residue was chromatographed on silica gel (45.0 g) eluting with hexane. Five compounds were isolated in the following order: **10**, **11**, **16**, **12**, and the last product **15** eluting with chloroform/hexane (1:1).

1. Fraction: **10** (246.0 mg, 10.5%)
2. Fraction: **11** (329.0 mg, 14.0%)
3. Fraction: **16** (183.0 mg, 5.0%)
4. Fraction: **12** (880.0 mg, 24.0%)
5. Fraction: **15** (330.0 mg, 9.0%)

3.5.1. (1*R*(*S*),4*S*(*R*),5*R*(*S*),6*R*(*S*))-5,6-Dibromo-2,3-bis-(bromomethyl)bicyclo[2.2.1]hept-2-ene (15). White crystals from hexane, mp 115–116°C; [Found: C, 24.55, H, 2.24. $C_9H_{10}Br_4$ requires C, 24.69, H, 2.30%]; ν_{max} (KBr) 3004, 2978, 2953, 2876, 1446, 1293, 1268, 1217, 1191, 834, 629 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 4.36 (2H, d, $^4J_{5(6)7endo}$=2.0 Hz, H_5 and H_6), 4.05 (4H, s, $-CH_2Br$), 3.20 (2H, bs, H_1 and H_4), 2.35 (1H, dt, A part of AB system, ^2J=9.6 Hz, $^3J_{7exo,1(4)}$=0.9 Hz, H_{7exo}), 1.91 (1H, dqui, B-part of AB-system, ^2J=9.6 Hz, $^3J_{7endo,1(4)}$=$^4J_{7endo,5(6)}$=2.0 Hz, H_{7endo}); δ_C (50 MHz, $CDCl_3$) 144.7, 59.4, 54.6, 45.8, 26.0; *m/z* M^+ 439/437/435 (4, 8, 4, M^+), 455/457/459/461 (25, 100, 90, 20, M^+–HBr), 275/277/279 (20, 40, 25, M^+–2HBr), 197/199 (55, 45, M^+–3HBr), 170 (25, M^+–3HBr, $-CH_2-$).

3.5.2. (1*S*(*R*),4*R*(*S*),5*S*(*R*),6*S*(*R*))-5,7-Dibromo-2,3-bis-(bromomethyl)bicyclo[2.2.1]hept-2-ene (16). Colorless oil. [Found: C, 24.55, H, 2.24. $C_9H_{10}Br_4$ requires C, 24.69, H, 2.30%]; ν_{max} (liquid film) 3004, 2953, 2851, 1472, 1293, 1268, 1217, 1191, 1114, 808, 757 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 4.61 (1H, t, $^3J_{5,4}$=$^3J_{5,6}$=3.1 Hz, H_5), 4.30–4.05 (5H, m, H_6 and $-CH_2Br$), 3.27 (1H, m, H_4), 3.17 (1H, m, H_1), 2.15 (1H, bd, A part of AB system, $^2J_{7exo,7endo}$=9.9 Hz, H_{7exo}), 2.00 (1H, dq, B-part of AB system, $^2J_{7exo,7endo}$=9.9 Hz, $^3J_{7endo,1(4)}$=$^4J_{7endo,5}$=1.9 Hz, H_{7endo}); δ_C (50 MHz, APT, $CDCl_3$) 146.5 (+), 142.2 (+), 59.3 (−), 57.6 (−), 57.3 (−), 55.1 (−), 47.6 (+), 28.3 (+), 25.7 (+).

3.6. Bromination of 5,6-dimethylenebicyclo[2.2.1]hept-2-ene (8) in the presence of free radical inhibitor at 77°C

To a refluxing solution of **8** (300 mg, 2.5 mmol) and 2,4-di-*tert*-buthylphenol (515 mg, 2.5 mmol) in 40 mL of CCl_4 was added a hot solution of bromine (488 mg, 3 mmol) in 5 mL of CCl_4. The resulting mixture was kept at the reflux temperature for 5 min. After cooling to room temperature the solvent was removed under reduced pressure. The oily residue was chromatographed on silica gel (30 g). The compounds **10**, **11** and **12**, were isolated in 20.6% (146 mg), 23.0% (162 mg) and 24.9% (277 mg) yields, respectively.

3.7. Bromination of 9,10-dimethylenetricyclo-[6.2.1.0^{2,7}]undeca-2,4,6-triene (9) at −10°C

To a magnetically stirred solution of **9** (200 mg, 1.19 mmol) in 20 mL dry CCl_4 cooled to −10°C was added dropwise a solution of bromine (224 mg, 1.4 mmol) in 20 mL dry CCl_4 during 10 min. After completion of the addition, the solution was allowed to warm to 20°C. The solvent was removed under reduced pressure. The residue was filtered on silica gel (5 g) eluting with hexane gave **17**.

3.7.1. (1*S*(*R*),8*R*(*S*),9*S*(*R*))-9-Bromo-9-(bromomethyl)-10-methylenetricyclo[6.2.1.0^{2,7}]undeca-2,4,6-triene (17). This compound as colorless oil (370.0 mg, 95.0%); [Found: C, 47.17, H, 3.53. $C_{13}H_{12}Br_2$ requires C, 47.60, 3.69%]. ν_{max}(liquid film) 3080, 3004, 2974, 1472, 1421, 1268, 1244, 987, 936, 782, 706 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 7.14–7.35 (4H, m, aromatic), 5.38 (1H, s, =C*H*H), 5.29 (s, =CH*H*), 4.0 (1H, d, A part of AB system, ^2J=11.9 Hz, $-CHH-Br$), 3.93 (1H, m, H_1 or H_8), 3.91 (1H, d, B part of AB system, ^2J=11.9 Hz, $-CHHBr$), 3.87 (1H, m, H_1 or H_8) 2.09 (2H, bt, ^3J=1.5 Hz, $-CH_2-$); δ_C (50 MHz, $CDCl_3$) 156.1, 147.9, 147.8, 129.0, 127.9, 126.4, 122.6, 112.1, 71.2, 56.7, 54.1, 49.6, 45.8.

3.8. Bromination of 9,10-dimethylenetricyclo-[6.2.1.0^{2,7}]undeca-2,4,6-triene (9) at 5°C

The reaction was carried out with 200.0 mg (1.19 mmol) of

9 at 5°C as described above. The NMR spectroscopic analysis of the residue showed that the reaction mixture consisted of 1,4- and 1,2-addition products in a ratio of 4:1. Crystallization of the mixture from carbon tetrachloride gave **19**.

3.8.1. (1*S*(*R*),8*R*(*S*))-9,10-Bis(bromomethyl)tricyclo-[6.2.1.0^{2,7}]undeca-2,4,6,9-tetraene (19). 180 mg, 47%, isolated yield as white crystals, mp 102–103°C; [Found: C, 47.2, H, 3.82. $C_{13}H_{12}Br_2$ requires C, 47.60, 3.69%]; ν_{max} (KBr) 3080, 3029, 2978, 2953, 2876, 1472, 1446, 1268, 1217, 1191, 1012, 936, 859, 782, 655 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 7.27 (4H, AA′BB′ system, aromatic), 4.22 (2H, d, A part of AB system, $^2J_{CH2}$=10.5 Hz, –C*H*$_2$Br), 4.07 (2H, d, B part of AB system, $^2J_{CH2}$=10.5 Hz, –C*H*$_2$Br), 3.93 (t, $^3J_{1(8),11}$=1.7 Hz, H_1 and H_8, 2H), 2.38 (1H, dt, A part of AB system, $^2J_{11exo,11endo}$=7.4 Hz, $^3J_{11,1(8)}$=1.7 Hz, H_{11endo} or H_{11exo}), 2.22 (1H, dt, B part of AB system, $^2J_{11exo,11endo}$=7.4 Hz, $^3J_{11,1(8)}$=1.7 Hz, H_{11endo} or H_{11exo}); δ_C (50 MHz, $CDCl_3$), 151.7 (s), 150.1 (s), 126.9 (dd, $^1J_{CH}$=160.0 Hz, $^2J_{CH}$=7.0 Hz, arom. C), 124.0 (dt, $^1J_{CH}$=158.8 Hz, $^2J_{CH}$=5.0 Hz, arom. C), 68.7 (t, $^1J_{CH}$=136.7 Hz, *C*H$_2$Br), 55.8 (d, $^1J_{CH}$=149.1 Hz, *C*H), 28.6 (t, $^1J_{CH}$=153.7 Hz, *C*H$_2$); *m/z* 329/327/325 (5, 10, 5, M$^+$), 247/249 (100, M$^+$−Br), 137 (30).

The residue was submitted to column chromatography (silica gel) eluting with hexane. As the first fraction we collected **17** as colorless oil (40.2 mg, 10.3.%, isolated yield) and the second fraction the alcohol **20**, respectively.

3.8.2. (1*S*(*R*),8*R*(*S*),9*S*(*R*))-9-(Bromomethyl)-10-methylenetricyclo[6.2.1.0^{2,7}]undeca-2,4,6-trien-9-ol (20). This compound as colorless liquid (47.0 mg, 15%); [Found: C, 59.38, H, 5.05. $C_{13}H_{13}BrO$ requires C, 58.89, 4.94%]; ν_{max} (liquid film) 3464, 3080, 2927, 2851, 1753, 1676, 1625, 1472, 1421, 1293, 1268, 1242, 1012, 910, 782 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 7.43–7.09 (4H, m, aromatic), 5.20 (s, =C*H*H, 1H), 5.05 (1H, s, =CH*H*), 3.83 (1H, bs, H_1 or H_8), 3.48 (1H, d, A part of AB system, ^2J=10.3 Hz, –C*H*H–Br), 3.47 (1H, bs, H_1 or H_8), 2.65 (1H, d, B part of AB system, ^2J=10.3 Hz, –CH*H*Br), 2.60 (1H, bs, –OH), 2.38 (1H, dt, A part of AB system, ^2J=9.1 Hz, $^3J_{11,1(8)}$=1.3 Hz,), 2.3 (1H, bd, B part of AB system, ^2J=9.1 Hz); δ_C (50 MHz, $CDCl_3$) 156.6, 148.2, 146.1, 129.0, 128.3, 125.2, 123.0, 109.3, 81.3, 56.4, 54.6, 50.1, 45.5.

3.9. Bromination of 9,10-dimethylenetricyclo-[6.2.1.0^{2,7}]undeca-2,4,6-triene (9) at 25°C

The reaction was carried out with 200.0 mg (1.19 mmol) of **9** at 25°C as described above. The formed product was identified as **19** in 96% yield.

3.10. Elimination of the dibromides 17 and 19 with *t*-BuOK in THF

To a stirred solution of dibromide **17** (or **19** or a mixture of **17** and **19**) (50 mg, 0.15 mmol) in dry and freshly distilled THF (5 mL) was added 34 mg (0.3 mmol) of *t*-BuOK solution in THF (10 mL). The resulting mixture was stirred at room temperature for 6 h. To the reaction mixture was then added water (50 mL) and the aqueous phase extracted with hexane (3×25 mL). The combined organic layers were washed with water, dried, filtered and evaporated to give **18**.

3.10.1. (1*S*(*R*),8*R*(*S*))-9-[(*E*)-Bromomethylidene]-10-methylenetricyclo[6.2.1.0^{2,7}]undeca-2,4,6-triene (18). 69.10 mg, 94% as colorless oil; [Found: C, 62.85, H, 4.38. $C_{13}H_{11}Br$ requires C, 63.18, 4.49%]; ν_{max} (liquid film) 3106, 3080, 3055, 3004, 2953, 2927, 2902, 1472, 1268, 1242, 987, 936, 910, 782 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 7.35–7.10 (4H, m, aromatic), 6.30 (1H, s, =C*H*Br), 5.08 (1H, s, =C*H*H), 5.07 (1H, s, =CH*H*), 4.32 (1H, bs, H_1 or H_8), 3.94 (1H, bs, H_1 or H_8), 2.13 (1H, dt, A part of AB system, ^2J=8.9 Hz, $^3J_{11,1(8)}$=1.6 Hz), 1.97 (1H, dt, B part of AB system, ^2J=8.9 Hz, $^3J_{11,1(8)}$=1.6 Hz); δ_C (50 MHz, $CDCl_3$) 150.23, 148.6, 147.9, 146.9, 128.5, 128.4, 123.5, 123.2, 104.4, 99.2, 55.3, 53.1, 52.9.

3.10.2. Synthesis of the epoxide 21. To a stirred solution of monobromide **20** (50 mg, 0.18 mmol) in dry and freshly distilled THF (5 mL) was added 63 mg (0.54 mmol) of *t*-BuOK. The resulting mixture was stirred at room temperature for 5 h. The solvent was evaporated and the mixture was diluted with water and the aqueous solution was extracted with hexane (3×10 mL), washed with water, and dried ($MgSO_4$). The evaporation of the solvent gave the epoxide **21** (30.0 mg 85%) as colorless oil (purity 90%); δ_H (200 MHz, $CDCl_3$) 7.26–7.10 (4H, m, aromatic), 5.13 1H, s, =C*H*H), 4.74 (1H, s, =C**H**H*H*), 3.88 (1H bs, H_1 or H_8), 3.00 (1H, bs, H_1 or H_8), 2.98 (1H, d, A part of AB system, ^2J=4.7 Hz, O–C*H*H), 2.87 (1H, d, B part of AB system, ^2J=4.7 Hz, O–CH*H*), 2.37 (1H, dt, ^2J=9.0 Hz, ^3J=1.6 Hz, –C*H*H–), 2.34 (1H, dt, ^2J=9.0 Hz, ^3J=1.5 Hz, –CH*H*–); δ_C (50 MHz, $CDCl_3$) 151.5, 148.9, 146.6, 128.9, 128.6, 124.2, 123.3, 106.2, 67.1, 54.0, 53.9, 52.4, 52.2.

3.11. Bromination of 9,10-dimethylenetricyclo-[6.2.1.0^{2,7}]undeca-2,4,6-triene (9) at 77°C

200 mg (1.19 mmol) of **9** was dissolved in 20 mL CCl_4 in a 100 mL flask, which was equipped with reflux condenser. The solution was heated until CCl_4 started to reflux while stirring magnetically. To the refluxing solution was added dropwise a hot solution of bromine (209 mg, 1.3 mmol) during 5 min. The resulting reaction mixture was heated for 15 min at reflux temperature. After cooling to room temperature the solvent was evaporated to give **22**.

3.11.1. (1*S*(*R*),8*R*(*S*),9*R*(*S*)-9-Bromo-9-(bromomethyl)-10-methylenetricyclo[6.2.1.0^{2,7}]undeca-2,4,6-triene (22). This compound as colorless oil (383 mg, 98%); [Found: C, 47.43, H, 3.48. $C_{13}H_{12}Br_2$ requires C, 47.60, 3.69%]; ν_{max} (liquid film) 3106, 3080, 3055, 3004, 2953, 2927, 2902, 1472, 1421, 1268, 1242, 987, 936, 910 cm^{-1}; δ_H (200 MHz, $CDCl_3$) 7.5–7.1 (4H, m, aromatic), 5.32 (1H, s, =C*H*H), 5.20 (1H, s, =CH*H*), 3.90 (2H, (2 bs, H_1 and H_8), 3.7 (1H, d, A part of AB system, ^2J=11.7 Hz, –C*H*HBr), 2.65 (1H, A part of AB system, *J*=9.5, 1.5 Hz, –C*H*H–), 2.61 (1H, d B part of AB system, ^2J=11.7 Hz, –CH*H*Br), 2.21 (1H, bd, *J*=9.5 Hz, B part of AB system, –CH*H*–); ^{13}C NMR (50 MHz, $CDCl_3$) 156.1, 147.8, 144.0, 129.7, 128.4, 126.0, 122.8, 112.2, 71.9, 59.3, 55.3, 51.9, 46.1.

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