Bromination of Tricyclo[7.2.1.0^{2,7}]dodeca-2,4,6,10-tetraene Derivatives: Highly Brominated Benzobicyclic Systems

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The bromination reaction of tricyclo[7.2.1.0^{2,7}]dodeca-2,4,6,10-tetraene derivatives was studied and the possible role of a substituent in rearrangements is discussed.

Key Words: bromination, Wagner-Meerwein rearrangement and poly-bromides.

Introduction

In addition to numerous industrial applications, such as pesticides, plastics, fire retardants and pharmaceutical chemicals, the halogen derivatives of a compound are valuable as a model for synthesizing other derivatives. Therefore, the halogenation of organic compounds is an important process. The addition of bromine to the carbon-carbon double bond with molecular bromine is formally one of the simplest reactions typical of unsaturated compounds[1]. The nature of the intermediates of the addition depends on temperature, steric factors, torsional effects, π- and σ-participation in the transition state and the formation of *non*-classical ions or a fast equilibrium of classical ions[2]. The bromination of unsaturated bicyclic systems with molecular bromine leads to rearrangements of the molecular skeleton.[2−8] Furthermore, we have shown previously that high temperature bromination of a bicylic system gives mainly *non*-rearrangement products[3−8].

Earlier we showed that[3] during the bromination of benzobarrelene (**1**), both at high and low temperatures, one mole of bromine is absorbed, and only dibromides **2-12** are formed (Scheme 1).

Results and Discussion

In the present work, we are interested in the further bromination of dibromides **4/5/11/12**, both in order to investigate the behaviour of dibromo derivatives of tricyclo [7.2.1.0^{2,7}]dodeca-2,4,6,10-tetraenes and to obtain highly brominated benzobicyclic systems, which may be important for research into insecticide activity.

Starting materials **4**, **5**, **11** and **12** were synthesized by the procedure described in the literature[3]. Firstly, the bromination of dibromide **4** in chloroform at 10°C was investigated. From this reaction, only

rearranged product **13** was obtained. The bromination of the *exo* isomer **5** under the same reaction conditions as for compound **4** gave exactly the same product in almost the same yield (Scheme 2).
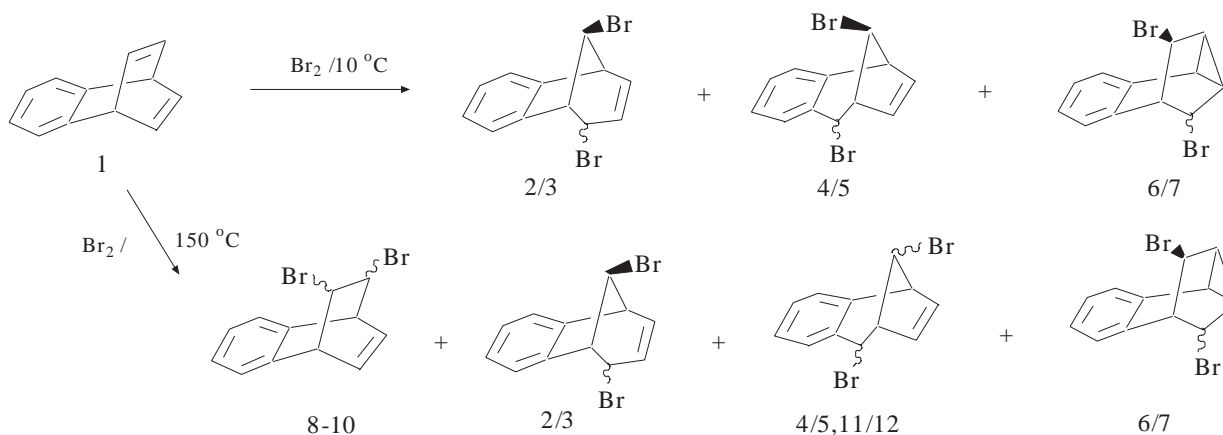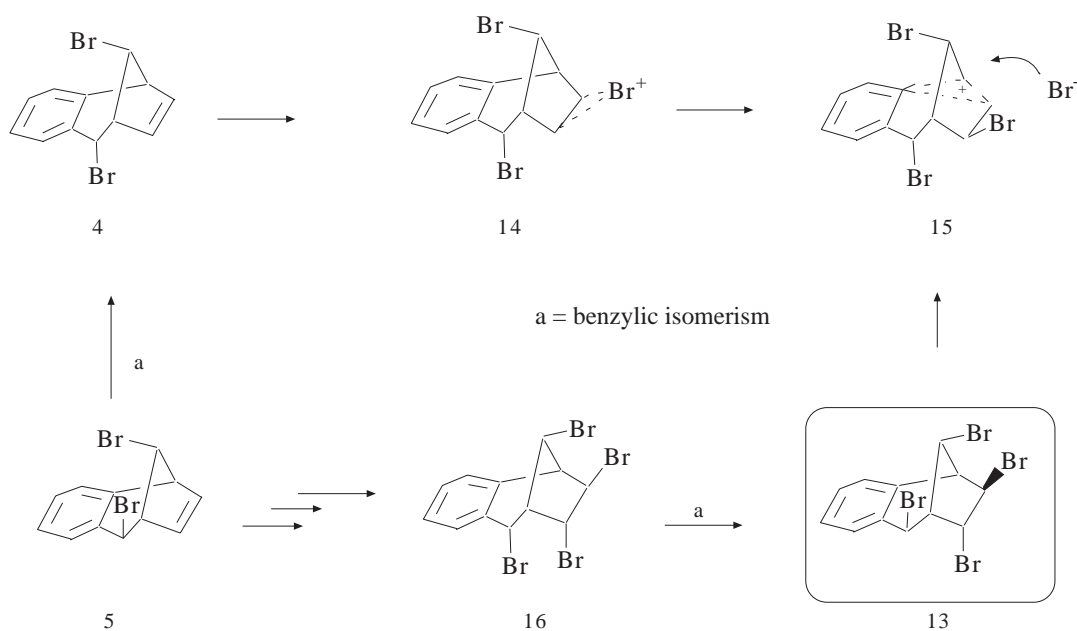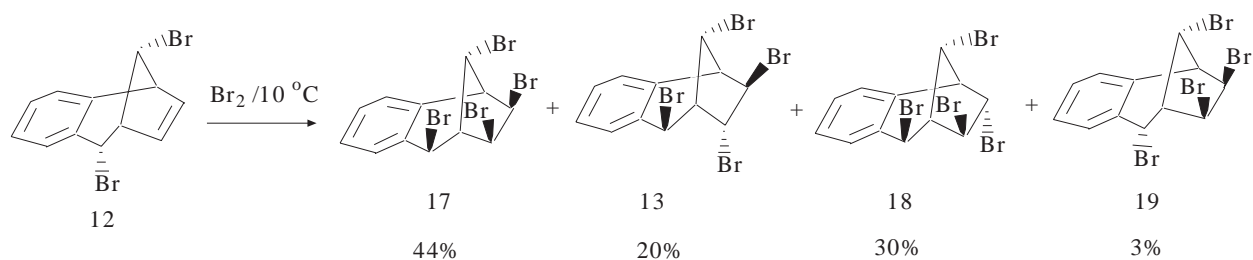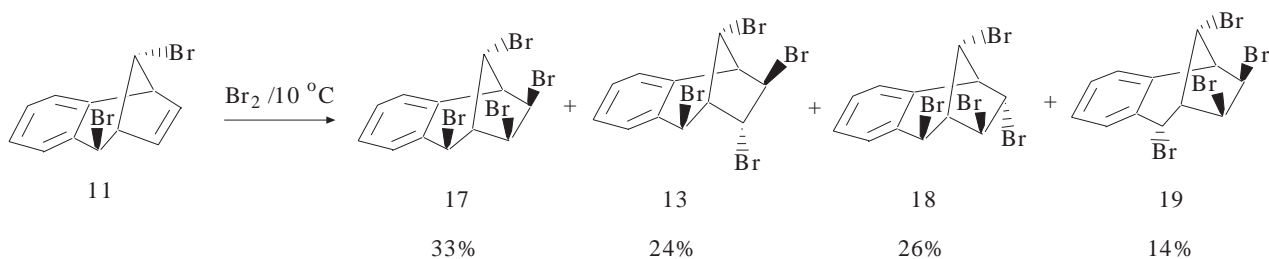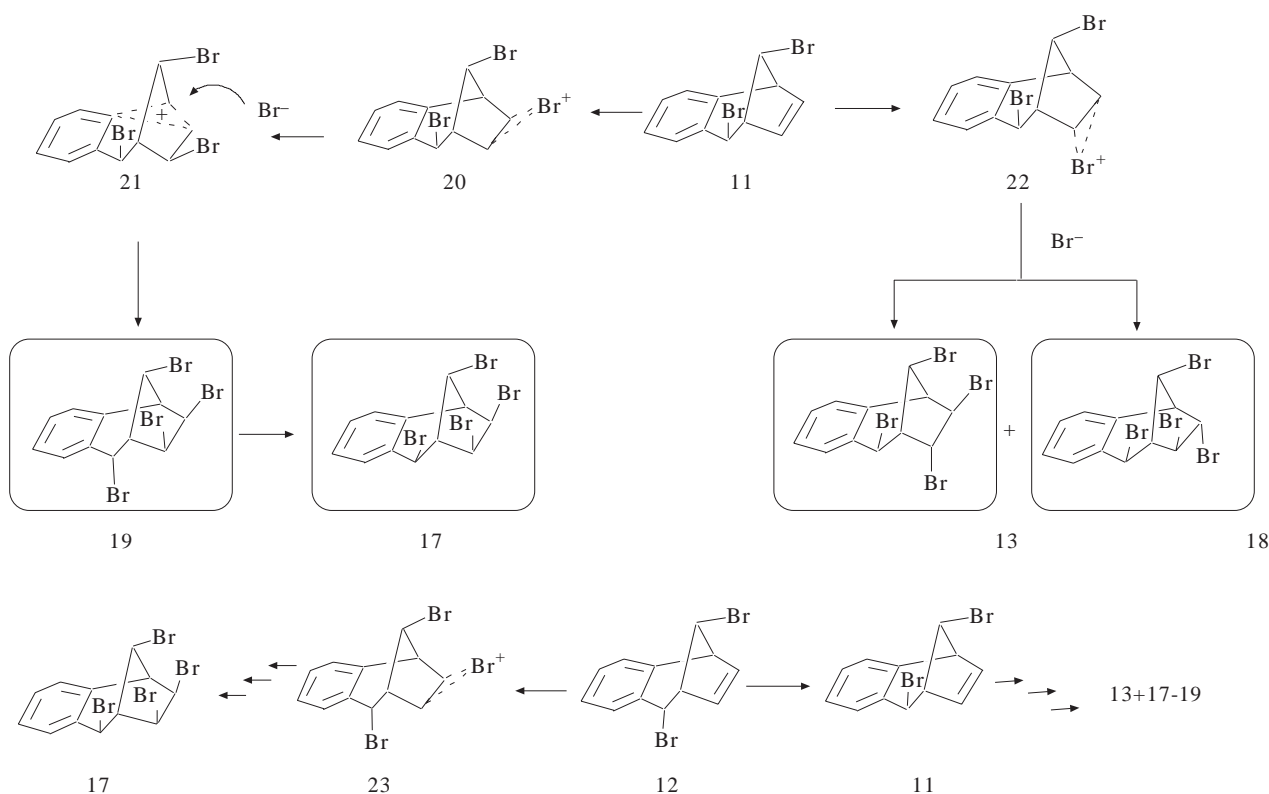

Scheme 1
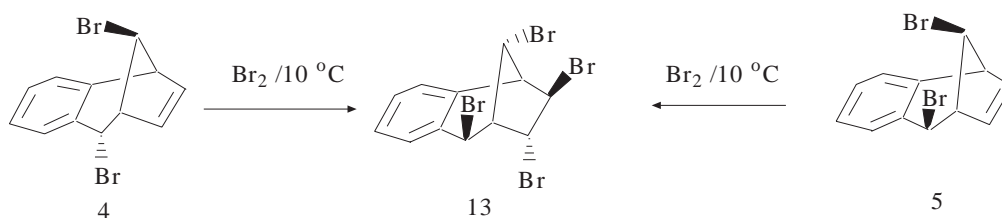
Scheme 2

As can be seen from this scheme, the bromine adds, as a rule, from the *exo* side (Scheme 3). This cannot entirely be explained by the assumption that the aromatic ring sterically screens the *endo* side. The selective *exo* addition of bromine may be explained by the hypothesis that in the formation of the *exo* brominium ion **14** the latter will be stabilized by the π-participation of the aromatic ring, which leads to rapid conversion of the brominium ions into the more energetically favourable homobenzyl ion **(15)**. The ion **15** may be subjected to attack by a nucleophile at C11 only from the *exo* side with the formation of 2,3-cis-di-*exo* derivative; but this did not take place, apparently because of the unfavourable steric or polar interactions with the bromine ion already present at C10 carbon (Scheme 3).

The homobenzyl ion **(15)**, which is attacked by the nucleophile from the *exo* side at C1, giving a product of Wagner-Meerwein rearrangement, may be transferred into the tetrabromide **13**. Such high stereoselectivity is difficult to explain for the rearranged classical ion.

The bromination of dibromides **11/12**, which have an *anti* bromine atom at C12 carbons, was also studied in order to investigate the steric effect of *anti* substituent at C12 carbon on bromination in the tricyclo [7.2.1.0^{2,7}]dodeca-2,4,6,10-tetraene system. The bromination of compounds **11** and **12** with bromine in chloroform at 10°C leads to a reaction mixture consisting of four compounds (**13, 17-19**). After repeated column chromatography, we were able to separate four compounds (Scheme 4).

a = benzylic isomerism

Scheme 3

Scheme 4

In these reactions, tetrabromides **17** and **19** are Wagner-Meerwein rearrangement products, obtained via *exo* brominium ions **20/23** (Scheme 5). It is not possible to explain the formation of these products by the classical addition of bromine to the double bond. In addition, the formation of the other products, **13/18**, can be explained only by the conversion of the skeletal system. For compounds **13/18**, if rearrangement occurred the bromine atoms at C10 and C11 carbons must be *exo*, like in molecules **17** and **19** (Scheme 5).

Scheme 5

Comparison of the results obtained during the halogenation of **4** and **5** shows that the bromine atom at C$_{12anti}$ affects the skeletal rearrangements. Steric hindrance of the bromine atom at C$_{12}$ carbons comparatively prevents the formation of *exo* bromine ions **20/23**, and supports the formation of *endo* brominium ions **22**.

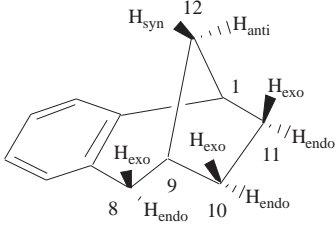## NMR Spectral Studies and Configurational Assignments

The structures of these compounds have been elucidated on the basis of ^{1}H and ^{13}C NMR spectral data and extensive double resonance experiments, and by comparison of some spectral data of similar compounds and related systems reported in the literature[4]. For all compounds which completely follow skeletal systems, structural analysis was achieved according to the coupling constant and chemical shifts. The coupling patterns important for the stereochemical characterization of bromine atoms at C$_8$, C$_{10}$, C$_{11}$, and C$_{12}$ carbons are J$_{8,9}$, J$_{9,10}$, J$_{10,11}$, J$_{1,11}$, J$_{1,12}$, J$_{9,12}$, J$_{10,12}$ and J$_{11,12}$. As a consequence of the rigid geometry and the reliability of the Karplus rule[15] in [3.2.1]octane systems,[9−14] the dihedral relationship of these protons is sufficiently distinctive to be revealed by the magnitude of the spin-spin interaction (Table).

Conclusions

The results of the present work demonstrate that tricyclo[7.2.1.0^{2,7}]dodeca-2,4,6,10-tetraene systems tend to undergo skeletal rearrangement in bromination reactions. The steric effect of the substituent also orientates the reaction tendency. The skeletal rearrangement in the bromination reactions is determined by the configuration of the initially formed brominium ion. The *exo* brominium ion is eligible for rearrangement

by aryl shifts. The *endo* brominium ion gives addition products without skeletal rearrangement. The steric hindrance at C_{12} carbons supports predominantly the formation of *endo* brominium ions. Consequently, we think that the stereochemistry of the electrophilic addition in tricyclo[7.2.1.0^{2,7}]dodeca-2,4,6,10-tetraene systems was controlled by the π-delocalization in the transition ion and the possibility of the formation of *non*-classical ions as intermediate particles.

Table. Typical spin-spin interaction in tricyclo[7.2.1.0^{2,7}]dodeca-2,4,6,10-tetraene systems.

$J_{1,11endo} = J_{9,10endo} = 0- < 1$ Hz	$J_{10endo,11endo} = 8.2 \pm 0.4$
$J_{1,11exo} = J_{9,10exo} = 6.3 \pm 0.5$ Hz	$J_{10endo,11exo} = J_{10exo,11endo} = 5.0 \pm 0.2$ Hz
$J_{1,12syn} = J_{9,12syn} = 0- < 1$ Hz	$J_{11endo,12} = J_{10endo,12} = 1.2 \pm 0.5$ Hz
$J_{1,12anti} = J_{9,12anti} = 4.7 \pm 0.3$ Hz	$J_{1,9} = 2.1 \pm 0.6$ Hz
$J_{8endo,9} = 2.3 \pm 0.3$ Hz	
$J_{8exo,9} = 4.9 \pm 0.2$ Hz	

Experimental Section

General: Melting points are uncorrected. Infrared spectra were obtained from solution in 0.1 mm cells or KBr pellets on a regular instrument. The ^{1}H and ^{13}C NMR spectra were recorded on 200 (50)-MHz spectrometers. Apparent splitting is given in all cases. Column chromatography was performed on silica gel (60-mesh, Merck). TLC was carried out on Merck 0.2 mm silica gel 60 F$_{254}$ analytical aluminium plates. All substances reported in this paper are in their racemic form.

Caution: It has been reported[16] that of three laboratory workers who have used dibromides and a bromohydrin derived from norbornadiene, two later developed similar pulmonary disorders, which contributed to their subsequent deaths. The third exhibited minor skin sensitivity reactions. In the case of dibromide derived from benzonorbornadiene, there is no report in the literature about the toxicological effect. However, we recommend that these compounds be handled only with extreme caution.

Bromination of (1S(R),8*S(R)*,9*S(R)*,12*R(S)*)-8,12-dibromotricyclo[7.2.1.0^{2,7}]dodeca-2,4, 6,10-tetraene (4)[3]:

To a magnetically stirred solution of **4** (100 mg, 0.32 mmol) in 5 mL dry chloroform cooled to 10 °C was added dropwise a solution of bromine (54 mg, 0.33 mmol) in 2 mL chloroform. The resulting solution was stirred for 30 min. The solvent was removed and the residue was crystallized from methylene chloride/hexane (1:3): (143 mg, 95%, mp 118-119 °C, colourless crystals).

(1S(R),8R(S),9S(R),10*R(S)*,11*R(S)*,12*S(R)*)-8,10,11,12-tetrabromotricyclo[7.2.1.0^{2,7}] dodeca-2,4,6-triene (13): [Found: C, 31.34; H, 2.09 $C_{12}H_{10}Br_4$ requires C, 30.42; H, 2.13%]; ^{1}H-NMR (200 MHz, CDCl$_3$): 7.51-7.02 (m, 4H, aryl), 5.91 (d, $J_{8,9}$=2.2 Hz, 1H, H$_8$), 5.14 (dd, $J_{9,10}$=6.7 Hz, $J_{10,11}$=5.1 Hz, 1H, H$_{10}$), 5.04 (d, $J_{11,12}$=1.7 Hz, $J_{1,12}$=$J_{9,12}$=0 Hz, 1H, H$_{12}$), 4.03 (dd, $J_{10,11}$=5.1 Hz, $J_{11,12}$=1.7 Hz, 1H, H$_{11}$), 3.69 (m, 1H, H$_1$), 3.42 (ddd, $J_{9,10}$=6.7 Hz, $J_{8,9}$=2.2 Hz, $J_{1,9}$=1.5 Hz, 1H, H$_9$),^{13}C-NMR (50 MHz, CDCl$_3$): 141.81, 134.67, 134.08, 131.81, 131.00, 128.30, 61.47, 60.21, 58.78, 58.38, 54.03, 50.86, IR (KBr, cm^{-1}): 3081, 3055, 3030, 2979, 2953, 1472, 1447, 1319, 1268, 1243, 1191, 1140, 1114, 936, 885, 783, 757.

Bromination of (1S(R),8R(S),9S(R),12R(S))-8,12-dibromotricyclo[7.2.1.0^{2,7}]dodeca-2,4, 6,10-tetraene (5)[3]: The reaction was carried out as described above by using 100 mg (0.32 mmol) of dibromide **5**, and tetrabromide **13** was obtained as the sole product. (142 mg, 94%) (For the spectral data see above).

Bromination of (1S(R),8R(S),9S(R),12S(R))-8,12-dibromotricyclo[7.2.1.0^{2,7}]dodeca-2,4, 6,10-tetraene (11)[3]: The reaction was carried out as described above by using 200 mg (0.64 mmol) of dibromide **11**. The solvent was evaporated and the residue was subjected to silica gel (90 g) chromatography eluting with n-hexane.

The first fraction: **(1S(R),8R(S),9S(R),10R(S),11R(S),12S(R))-8,10,11,12-tetrabromo- tricyclo[7.2.1.0^{2,7}] dodeca-2,4,6-triene (13):** (72 mg, 24%). (For the spectral data see above).

The second fraction: **(1S(R),8R(S),9S(R),10S(R),11S(R),12S(R))-8,10,11,12-tetrabromo-tricyclo[7.2.1.0^{2,7}] dodeca-2,4,6-triene (18):** (78 mg, 26%, pale yellow oily residue); [Found: C, 29.93; H, 2.17 $C_{12}H_{10}Br_4$ requires C, 30.42; H, 2.13%]; ^{1}H-NMR (200 MHz, CDCl$_3$): 7.44-7.03 (m, 4H, aryl), 5.43 (d, $J_{8,9}$=2.0 Hz, 1H, H$_8$), 5.31 (dd, $J_{1,11}$=6.6 Hz, $J_{10,11}$=5.1 Hz, 1H, H$_{11}$), 5.07 (d, $J_{10,12}$=1.1 Hz, $J_{1,12}$=$J_{9,12}$=0 Hz, 1H, H$_{12}$), 3.77 (bd, $J_{1,11}$=6.6 Hz, 1H, H$_1$), 3.53 (m, 2H, H$_9$ and H$_{10}$), ^{13}C-NMR (50 MHz, CDCl$_3$): 135.76, 132.43, 132.00, 131.22, 129.81, 129.25, 62.72, 61.02, 56.42, 53.15, 51.98, 49.20, IR (KBr, cm^{-1}): 3081, 3030, 2979, 2953, 2928, 1472, 1447, 1319, 1294, 1243, 1166, 834, 783, 757.

The third fraction: **(1S(R),8S(R),9S(R),10S(R),11R(S),12S(R))-8,10,11,12-tetrabromo- tricyclo[7.2.1.0^{2,7}] dodeca-2,4,6-triene (19):** (42 mg, 14%, mp 190-191°C, colourless crystals from methylene chloride/hexane (1:3); [Found: C, 30.34; H, 2.18 $C_{12}H_{10}Br_4$ requires C, 30.42; H, 2.13%]; ^{1}H-NMR (200 MHz, CDCl$_3$): 7.59-7.05 (m, 4H, aryl), 5.74 (d, $J_{8,9}$=4.8, Hz, 1H, H$_8$), 5.14 (bd, $J_{10,11}$=8.0 Hz, 1H, H$_{11}$), 4.70 (bd, $J_{10,11}$=8.0 Hz, 1H, H$_{10}$), 4.44 (t, $J_{10,12}$=$J_{11,12}$=1.0 Hz, $J_{1,12}$=$J_{9,12}$=0 Hz, 1H, H$_{12}$), 3.89 (d, $J_{1,9}$=2.6 Hz, 1H, H$_1$), 3.69 (dd, $J_{8,9}$=4.8 Hz, $J_{1,9}$=2.6 Hz, 1H, H$_9$), ^{13}C-NMR (50 MHz, CDCl$_3$): 141.46, 133.80, 133.18, 131.66, 131.34, 128.99, 65.36, 61.05, 57.74, 55.99, 52.40, 50.10, IR (KBr, cm^{-1}): 3055, 3030, 2979, 2953, 1472, 1447, 1294, 1268, 1243, 1191, 1165, 834, 757.

The fourth fraction: **(1S(R),8R(S),9S(R),10S(R),11R(S),12S(R))-8,10,11,12-tetrabromo-tricyclo[7.2.1.0^{2,7}] dodeca-2,4,6-triene (17):** (100 mg, 33%, mp 133-134°C, colourless crystals from methylene chloride/ hexane (1:3); [Found: C, 31.23; H, 2.17 $C_{12}H_{10}Br_4$ requires C, 30.42; H, 2.13%]; ^{1}H-NMR (200 MHz, CDCl$_3$): 7.42-7.08 (m, 4H, aryl), 5.41 (d, $J_{8,9}$=2.9 Hz, 1H, H$_8$), 5.00 (t, $J_{10,12}$=$J_{11,12}$=0.8 Hz, $J_{1,12}$=$J_{9,12}$=0 Hz, 1H, H$_{12}$), 4.50 (bd, A part of AB system, $J_{10,11}$=7.9 Hz, 1H, H$_{11}$), 4.35 (bd, B part of AB system, 1H, $J_{10,11}$=7.9 Hz, H$_{10}$), 3.93 (d, $J_{1,9}$=2.2 Hz, 1H, H$_1$), 3.72 (dd, $J_{8,9}$=2.9 Hz, $J_{1,9}$=2.2 Hz, 1H, H$_9$), ^{13}C-NMR (50 MHz, CDCl$_3$): 141.30, 134.03, 133.32, 132.06, 131.27, 129.29, 66.21, 60.62, 57.98, 54.25, 51.69, 49.31, IR (KBr, cm^{-1}): 3055, 3030, 2979, 2953, 1447, 1421, 1395, 1319, 1268, 1243, 1191, 885, 757.

Bromination of (1S(R),8S(R),9S(R),12S(R))-8,12-dibromotricyclo[7.2.1.0^{2,7}]dodeca-2,4, 6,10-tetraene (12)[3]: The reaction was carried out as described above by using 200 mg (0.64 mmol) of dibromide **12**. The solvent was evaporated and the ^{1}H-NMR spectrum of the residue revealed the formation of tetrabromides **17** (44%), **13** (20%), **18** (30%) and **19** (3%).

Acknowledgements

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