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THE BROMINATION OF 3-BROMO-6,7-BENZOBICYCLO[3.2.1]OCTA-2,6-DIENE AND CHARACTERIZATION OF THE PRODUCTS

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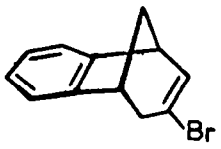
Summary: The bromination of 3-bromo-6,7-benzobicyclo[3.2.1]octa-2,6-diene at -50°C has been found to give only one product, the tribromide 8 produced via Wagner-Meerwein rearrangement with accompanying aryl migration. The bromination at 0°C produced nonrearranged tribromides beside the rearranged tribromide and the ketone 12. The structures of the products were determined by ^1H-, ^{13}C-NMR data and single X-ray structural analysis. The addition mechanism is discussed in terms of exo- and endo-attack.

INTRODUCTION

Recently, we reported our initial results[2] on the addition of bromine to 3-bromo-6,7-benzobicyclo-[3.2.1]octa-2,6-diene (1) in connection with our work on bicyclic allenes[3]. In this paper we describe the full characterization of these products and their spectroscopic properties.



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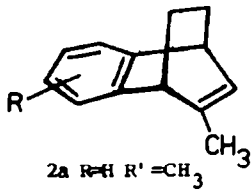
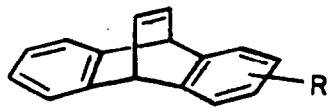


2a R=H R' =CH_3
2b R=5,8-$(OCH_3)_2$ R'=CH_3
2c R=5,6,7,8-$(F)_4$ R'=CH_3



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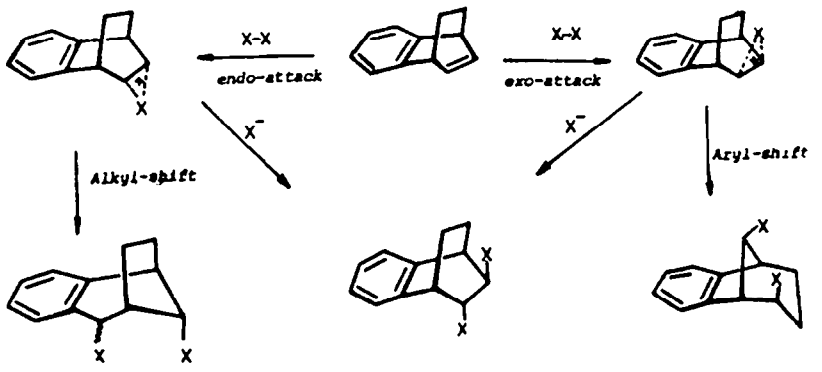
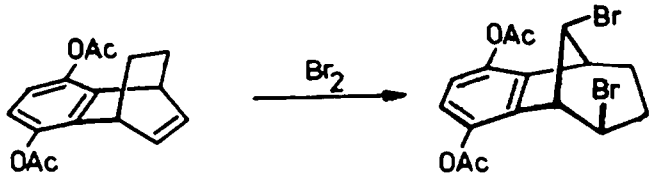
It has been shown that electrophilic addition to bicyclic systems such as (2) and (3) can lead to a multiplicity of products[4]. Attack on the double bond may be endo or exo. The intermediate may react with nucleophiles to give nonrearranged products or undergo Wagner-Meerwein rearrangement involving either aryl group or alkyl bridge before reacting to give rearranged products (Scheme 1). Paquette et al.[5] have studied the photooxygenation, oxymercuration and hydroboration of three differently substitiuted 2-methylbenzobicyclo[2.2.2]octadienes (2). Syn stereoselectivity was observed in every case. Electronic interactions in these molecules were explored by photoelectron spectroscopy and MINDO/3 calculations. These combined tools served to show that through-space interaction is absent in these molecules. Smith et al.[6] have observed similar results by epoxidation of benzobicyclo[2.2.2]octadiene systems. They found that m-chloroperbenzoic acid reacts in methylene chloride, acetonitrile, primarily with syn-attack. However, in oxygen containing solvents (diethyl ether, ethyl acetate) the rate of the reaction was considerably decreased but the stereochemistry



SCHEME 1

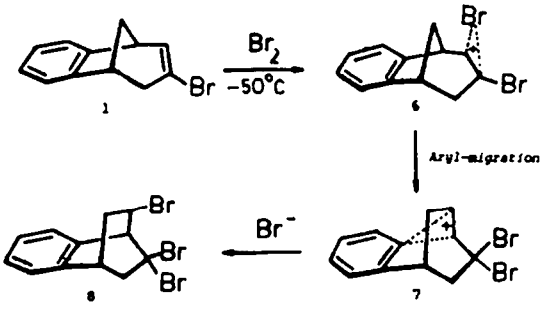
of the reagent changed in favor of the formation of the sterically less favored anti-epoxides. The enhanced stereoselectivity of the peracid was discussed in terms of homo-conjugation in the transition state being important in determining the product selectivity. More recently, Smith[6] has studied the addition of bromine to 5,8-diacetoxy-1,4-ethanonaphthalene (4) and obtained only one product (5). Clearly attack of bromine has occured from the sterically less favored side of the double bond with subsequent aryl migration.



4 5

RESULTS AND DISCUSSIONS

3-Bromo-6,7-benzobicyclo[3.2.1]octa-2,6-diene (1) was prepared by the published method[7] and subjected in $CHCl_3$ to bromination at 0°C and -50°C. Suprisingly, we obtained a completely different product distribution. From the reaction at -50°C we isolated a single tribromide (8) in quantitative yield. While 90 MHz ^{1}H-NMR spectrum clearly showed the tree methine protons and two AB-systems, successful analysis of the stereochemistry of the bromine even with the aid of proton decoupling was not possible. ^{13}C-NMR data was consistent with the proposed structure showing 6 aliphatic carbons and 6 aromatic carbons (Table 1). On the basis of these data the correct configuration of (8) could not be established.



1 6 8 7

SCHEME 2

Therefore, the product was subjected to single-crystal X-ray analysis which revealed the compound to be (1SR, 4SR, 10RS)-2,2,10-tribromo-1,2,3,4-tetrahydro-1,4-ethanonaphthalene (8)[8] (Figure 1).

It is evident from the bromine configuration in (8) that the initial attack by the bromine has occurred from the sterically less favored side of the π-system. There is no question that the hyd-

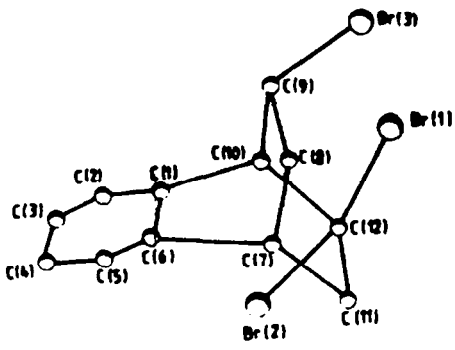
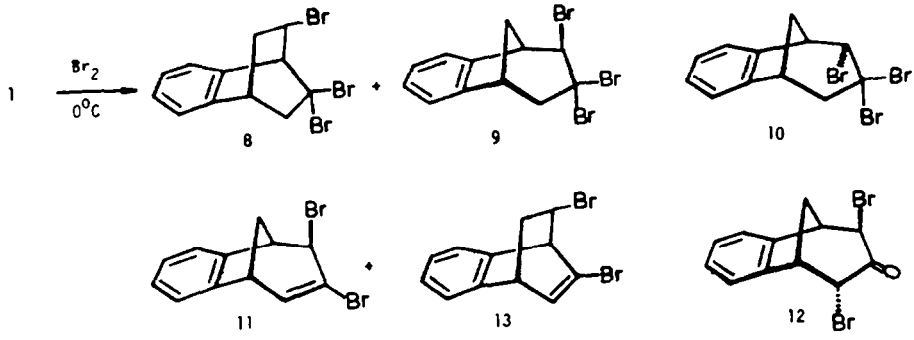


Figure 1. X-ray crystal structure of 8.

rogen atom of the methano bridge can provide sufficient bulk to divert an incoming bromide preferentially away from the exo-face to the double bond. However, the fact that we obtained only the rearranged product shows that this effect is clearly not overwhelming. The homoconjugative interaction between the developing cationic center and the aryl-π-electroncenter plays an important role in promoting attack from the less favored side of the double bond. This reasoning explains the sole formation of (8). In the case of endo attack we should expect either unrearranged products (9 and 10) or products involving alkyl bridge shift.

The bromination of 1 at 0°C was suprising. The ^{1}H-NMR studies revealed that the reaction mixture was very complex. After repeated column chromatography we isolated six products, the identification of which was no trivial task. As a major product we isolated 8 in a yield of 42%. 8 and 11[7] were identified by comparison of the spectroscopic data with those of authentic samples. The structures of 9 and 10 were determined on the basis of spectral data. The ^{1}H- and ^{13}C-NMR spectrum pattern of 9 was very similar to that of 10 which indicates that they are stereoisomers. The protons on the bridging methylene group (C_8) in 9 and 10 gave rise to an AB-system whose internal proton (H_{8i}) is further coupled with the adjacent bridgehead protons where the external proton (H_{8e}) does not show any measurable coupling with bridgehead protons H_1 and H_5. Inspection of Dreidings models indicates that the dihedral angle between H_{8e} and bridgehead protons H_1 and H_5 is near 90° and dihedral angle between H_{8i} and bridgehead protons is near 20-30°. An interesting feature of these AB-systems is the chemical shift differences (Δδ 0.55 ppm) between the external bridge protons H_{8e} in 9 and 10.



SCHEME 3

There is no considerable chemical shift difference between the resonances of internal hydrogens in 9 and 10 (in both cases the splitting pattern of the AB-system remained). H_{8e} in 10 resonates at higher field compared to H_{8e} in 9. This observation can be explained on the basis of strong steric interaction between the proton H_{8e} in 9 and the neighboring bromine in the exo-position. Any steric repulsion between H_{8e} in 9 and the geminal bromines at C_3 is out of the question due to the chair conformation of the cyclohexane ring. It is well known that interactions related to the van der Waals effect causes a paramagnetic contribution to the shielding constants which results in a shift to lower field[9]. This observation strongly supports the configurational assignment of 9 and 10. This finding was also supported by the ^{13}C-NMR chemical shifts. In saturated open-chain and cyclic systems the steric effect on carbon shielding is observed when two hydrogenated carbons are γ-gauche relative to each other[10]. Typical γ-gauche effects are observed in configurationally rigid systems such as methylcyclohexanes[11] and methylnorbornanes[10]. Other substituents, e.g. halogens raises the γ-effect to -7 ppm.

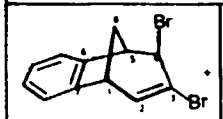
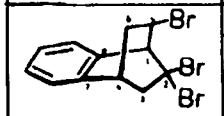
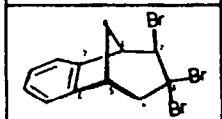
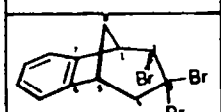
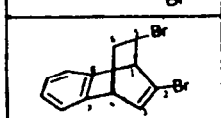
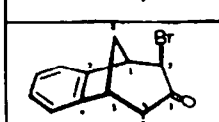
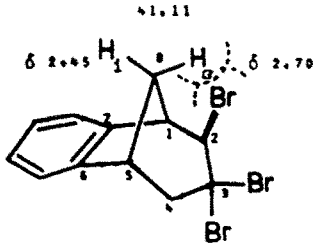
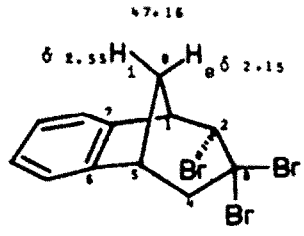
	^{1}H- and ^{13}C-NMR Chemical Shifts							Aromatic Protons	Olefinic and Aromatic Carbons	Coupling Constants (Hz)
	1	2	3	4	5	δ_1	δ_e			
	3.6 dd 42.87	6.88 dd	----	4.8 d 56.18	3.9 m 50.45	2.6 dt 37.93	2.3 d	7.4-6.5 m	151.76 141.07 140.41 127.16 126.91 125.21 120.02 121.54	J_{12}=7.0, J_{45}=2.1, $^4J_{24}$=1.0 $J_{1e1}=J_{5e5}$=4.4 J_{e1e5}=10.4
	4.15 d	----	2.8-3.65 AB-System	3.0 m	4.0-4.4 ddd	2.0-2.45 m (H_6)		7.0-7.4 m	140.35 136.98 128.46 127.21 125.69 124.51 59.58 58.38 55.81 44.95 36.52 34.27	
	3.7 t 50.08	5.15 dd 63.01	---- 62.41	3.1 m 49.41	3.2 m 41.41	2.45 dtt 41.11	2.7 d	7.1 br. s	144.26 143.95 128.32 127.47 124.17 124.06	
	3.6 dd 51.19	4.95 d 65.27	---- 65.27	3.4 m 53.38	3.4 m 41.68	2.55 47.16	2.15	7.2-7.5 m	143.81 139.92 128.21 127.31 125.43 123.90	
	4.35 t 46.11	----	6.85 dd	3.9 dt 42.51	4.1 p 57.46	-CH_2-protons 2.45-1.9 AB-System ddd ddd 37.94		7.1-7.4 m	141.41 139.86 133.94 127.04 125.94 124.10 123.76 122.97	
	3.64 t 49.67	4.45 t 51.40	---- 193.71	5.42 d 57.60	3.75 t 48 19	2.58 ddt 50.59	2.93 d	7.45 m 7.25 m	141.91 141.31 128.98 128.49 126.47 124.20	J_{12}=3.2 J_{45}=3.0 $J_{1e1}=J_{5e1}$=4.6 J_{ee1}=12.0 J_{4e1}=2.3

Table 1. 400 MHz ^{1}H- and 100 MHz ^{13}C-NMR Spectra of the compounds 8, 9, 10, 11, 12, and 13 in $CDCl_3$.

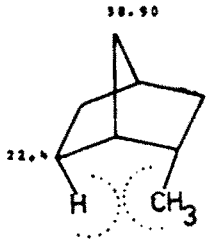


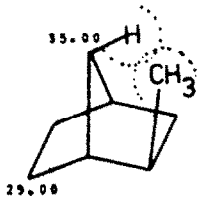
9



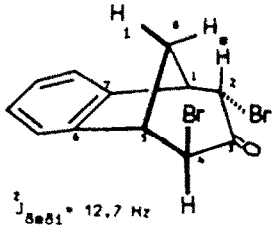
10

The steric perturbation of the C-H bond involved causes the charge to drift towards carbons; the bonding orbitals at carbon expand and shielding will arise. The bridging carbons in 9 and 10 are resonating at 41.11 ppm and 47.16 ppm, respectively. Therefore, the high field resonance at 41.11 ppm was assigned to the methylene carbon C_8 in 9 where the bromine atom is in the exo-position. Other chemical shifts (see Table 1) were also consistent with the proposed structures 9 and 10. Finally the correct configuration of the exo-isomer (9) was assigned by X-ray crystallographic analysis[12] (Fig. 2). The position of the bromine in 9 could also be established by means of chemical reactions. Treatment of (8) with one mol potassium tert. butoxide gave the known exo-dibromide (11).





In addition to the products mentioned above we isolated one more polar product in a yield of 3%. The IR showed a carbonyl group. The mass spectrum (M^+ 338/340/342) and analysis of the ^{1}H- and ^{13}C-NMR spectra indicated the presence of two bromine atoms. ^{13}C-NMR data were consistent with a [3.2.1]-bicyclic structure showing 5 aliphatic carbons, 6 aromatic carbons and one carbonyl carbon. The stereochemistry assigned to 12 has an experimental basis from its 400 MHz ^{1}H-NMR in the δ 2.5-3.0 region. The bridge protons at C_8 in 12 appear as an AB-system. B-part (H_{8e}) shows a doublet. There is no further coupling with the adjacent bridgehead protons H_1 and H_5. However, the A-part (high field resonance) is split into triplets of doublets of doublets. Triplet splitting arises from the hydrogens at bridgehead H_1 and H_5. Doublet splitting (^{4}J,low coupling constant) originates from the proton on C_4 which is in the endo-position. In the cases of ^{4}J one speaks of the M or a W arrangement. In the bicyclic systems 12 the bonding arrangement of the coupled protons meets the M criterion. For the assignment of the stereochemistry in isomeric endo- and exo-bicycloheptane derivatives the magnitude of ^{4}J is of importance, since only the endo proton couples with the anti bridge protons.



$^2J_{8e8i}$ = 12.7 Hz
$^3J_{815}$ = $^3J_{811}$ = 5.0 Hz
$^3J_{8e5}$ = $^3J_{8e1}$ = 0.0 Hz
$^4J_{814}$ = 2.3 Hz $^4J_{812}$ = 0.0 Hz

12

$^4J_{HH}$ = 3.0–4.0 Hz

15

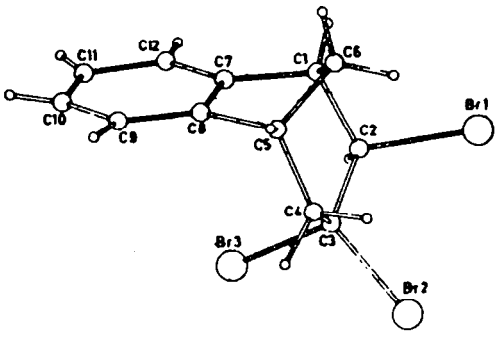


Figure 2. X-ray crystal structure of 9.

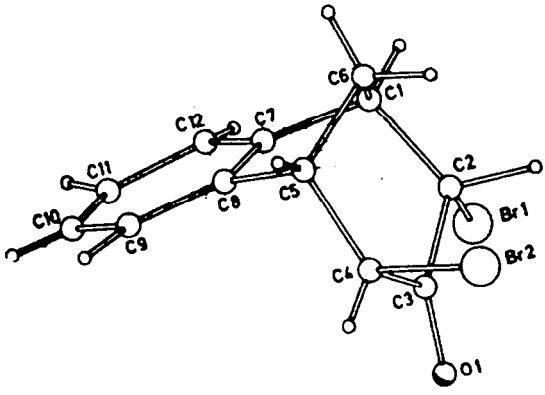
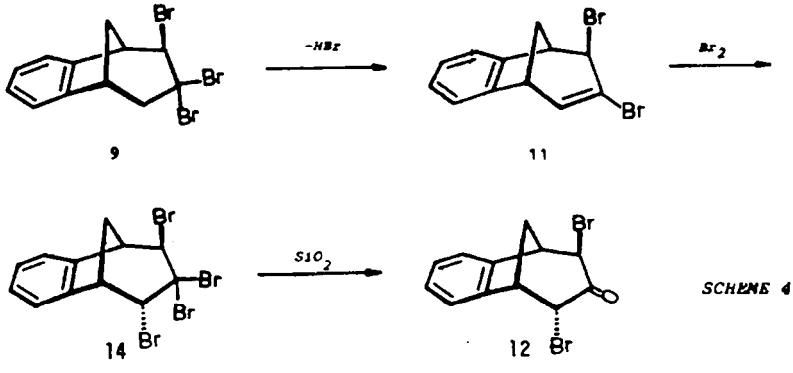


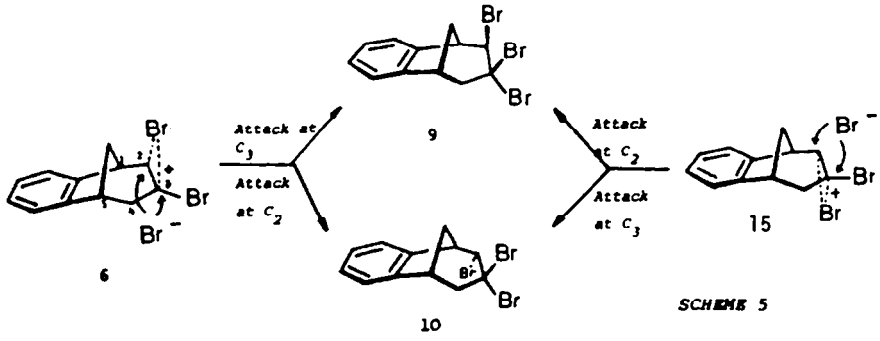
Figure 3. X-ray crystal structure of 12.

The fact that the internal bridge proton (H_{81}) shows a long range coupling with only one proton (H_4) indicates that the stereochemistry of the bromine atoms in 12 are different. Asymmetry in the molecule supported by ^{13}C-NMR establishes unambiguously the exo- and endo-orientation of the bromine atoms. Finally X-ray structure analysis of 12 confirms the structural findings[13] (figure 3). The mechanism for formation of the dibromo ketone 12 is given below. We assume that the dibromide 11 is a secondary product formed by addition of bromine to 1 to give 9 followed by hydrogen bromide elimination. The reaction of 11 with bromine[14] gives the tetrabromo compound 14 which hydrolyses on silica gel during column chromatography to give 12 (Scheme 4).



SCHEME 4

In conclusion; we obtained a different product distribution in the reaction of bromine with 1 at 0°C. We assume that 8, 9, and 10 are primary products. The formation of both stereoisomers 9 and 10 does not give any indication of which of the two competing modes of endo- and exo-attack is preferred, since both isomers can be formed from endo-attack as well as exo-attack as shown below (Scheme 5). The fact that we did not observe any trace of alkyl shift products supports the exclusive formation of the exo-bromonium ion. The different product distribution at 0°C results from



SCHEME 5

the life time of the intermediate 6. At -50°C the life time of the intermediate is increased so that the rearrangement can take place completely. However, at 0°C bromine ion can attack the exo-intermediate before rearrangement since the life time of the intermediate is decreased.

EXPERIMENTAL SECTION

General. Melting points were determined in open capillary tubes and are uncorrected. Infrared spectra were obtained from KBr pellet on a Perkin Elmer 337 Infrared Recording Spectrophotometer. The NMR spectra were recorded with EM 360 Varian Spectrometer and Bruker 400 MHz Spectrometer. Mass spectra were recorded on a Finnigan-MAT MS Model 4000 mass spectrometer at an ionizing voltage 70 eV. Analytical thin-layer chromatography (TLC) was performed on silica gel 60_{254} plates. Column chromatography was done on silica gel (60-200 mesh) from Merck Chemical Company.

Bromination of 1. (1SR,4SR,10RS)-2,2,10-Tribromo-1,2,3,4-tetrahydro-1,4-ethanonaphthalene 8.

a) at -50°C

To a solution of 5.0 g (15.9 mmol) of 1 in 100 mL of CH_2Cl_2 was added dropwise, with stirring and during 1 h a solution of 2.6 g (16.25 mmol) of bromine in 25 mL of CH_2Cl_2 at -50°C. The reaction mixture was allowed to stir for 2h at -50°C and the solvent was removed by rotary evaporation. The ^1H- and ^{13}C-NMR of crude material indicated that only one product was formed quantitatively. Analytical pure sample was obtained by crystallization from n-hexane, mp; 101-102°C, MS, m/e 392/394/396/398 (M^+,11%), 313/315/317 (M^+-Br, 22), 234/236 (M^+-2Br, 10), 207/209 (19), 153 (22), 128 (100). IR (KBr, cm^{-1}) 3075, 3045, 3020, 2980, 1480, 1455, 1255, 1100, 1025, 955, 850, 765. Anal. $C_{12}H_{11}Br_3$ (395.41), Calcd.: C, 36.46, H, 2.81, Br, 60.63. Found: C, 36.41, H, 2.91, Br, 60.98.

b) at 0°C

To a solution of 3.0 g (9.55 mmol) of 1 in 100 mL of CH_2Cl_2 was added dropwise, and with stirring a solution of 1.6 g (10.0 mmol) of bromine in 25 mL of CH_2Cl_2 at 0°C. The reaction mixture was allowed to stir for 2h at 0°C and the solvent was removed under reduced pressure. The ^1H- and ^{13}C-NMR spectra of crude material indicated the existence of a complex mixture. Crude product was charged over a silica gel (150 g) column. Elution with petroleum ether furnished as first fraction the tribromide 9.

(1RS,2RS,5RS)-2,3,3-Tribromo-6,7-benzobicyclo-[3.2.1]oct-6-ene 9. mp 105-106°C (from n- hexane), 1140 mg (22%), MS, m/e, 392/394/396/398 (M^+). IR (KBr, cm^{-1}) 3070, 3050, 3020, 2970, 2950, 1470, 1460, 1430, 1170, 1150, 945. Anal. $C_{12}H_{11}Br_3$ (395.41) Calcd.: C. 36.46, H, 2.81, Br, 60.63. Found: C, 36.32, H, 2,88, Br, 60,42.

Continued elution with the same solvent afforded as second fraction the dibromide 11.
(1RS,2RS,5RS)-2,3-Dibromo-6,7-benzobicyclo-[3.2.1]octa-3,6-diene 11. 450 mg(11%) recrystallized from n-hexane. Comparison of the spectral data of this compound with those reported in the literature[7] were in full agreement.

As third fraction we isolated the dibromide 13[15].
(1SR,4RS,5RS)-2,10-Dibromo-1,4-dihydro-1,4-ethanonaphthalene 13. mp 80-81°C, 155 mg (3.9 %) from $CHCl_3$/petroleum ether (1:6). IR (KBr, cm^{-1}) 3060, 2970, 1610, 1470. MS, m/e, 312/314/316 (8%), 208/206 (100), 153 (49). Anal. $C_{12}H_{10}Br_2$ (314.03) Calcd.: C, 45.89, H, 3.21, Br, 50.90. Found:C, 46.13, H, 3.25, Br, 50.63.

As forth fraction we isolated the tribromide 8, 2130 mg (42.2%). This product was identical with those obtained by the reaction at 0°C.

Further elution with petroleum ether furnished 10.
(1RS,2SR,5RS)-2,3,3-Tribromo-6,7-benzobicyclo[3.2.1]oct-6-ene 11. mp 169-170°C, 440 mg (8.7%) from CH_2Cl_2/petroleum ether (1:4). MS, m/e, 392/394/396/398 (M^+). IR ($CHCl_3$, cm^{-1}), 3070, 3050, 3020, 2950, 1430, 1355, 1295, 1250, 1230, 1195, 1120. Anal. $C_{12}H_{11}Br_3$ (395.41) Calcd.: C, 36.46, H, 2.81, Br, 60.63. Found: C, 36.71, H, 2.95, Br, 60.03.

Finally, elution with CH_2Cl_2/petroleum ether (1:1) gave as last fraction 12.
(1RS,2RS,4RS,5SR)-2,4-Dibromo-3-oxo-6,7-benzobicyclo[3.2.1]oct-6-ene 12. mp 128-130°C, 290 mg (6.9%) from CH_2Cl_2/petroleum ether (2:1). MS, m/e, 328/330/332 (M^+, 3%), 249/251 (M-Br, 68), 170 (M^+-2Br, 83), 151 (90), 128 (75), 115 (100). IR ($CHCl_3$, cm^{-1}) 2980, 2920, 1720, 1470, 1455. Anal. $C_{12}H_{10}Br_2O$ (330.03) Calcd.: C, 43.67, H, 3.05, Br, 48.43, O, 4.85. Found: C, 43.45, H, 3.15, Br, 48.10.

Reaction of 9 with potassium tert.-butoxide.

To a solution of 450 mg (1.14 mmol) of 9 in 10 mL of abs. THF was given t-BuOK (190 mg, 1.71 mmol) and the resulting mixture was refluxed for 3 h under nitrogen. After cooling to room temperature water was added and aqueous phase was extracted with n-hexane (2x50 mL), and the combined hexane extracts was washed with water, dried, filtered and evaporated in vacuo. The crude product was crystallized from n-pentane which was identical with this obtained by dibromocarbene addition to benzonorbornadiene and bromination of 1 as second fraction. 225 mg (77%).

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14) Independent reaction of isolated 11 with bromine followed by SiO_2 column chromatography gave 12.
15) The dibromide 13 was also synthesized independently by HBr elimination of 8 using one equivalent potassium tert.-butoxide.