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Evidence for the Intermediacy of an Alkyne rather than an Allene in the Base-Induced Reaction of 3-Bromo-6,7-benzobicyclo[3.2.1]octa-2,6-diene

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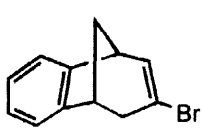
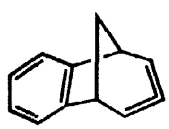
Abstract: In order to reveal the real intermediate in the base-promoted reaction of **1**, 2-methyl derivative **16** has been synthesized and its HBr elimination reaction studied. Reaction of **16** with potassium *t*-butoxide did not form the corresponding allene intermediate **17** under the same reaction conditions as described for **1**. Under more drastic conditions exocyclic diene **18** was formed. These results provide evidence for the intermediacy of the alkyne **3** in the base-promoted reaction of **1**.

Introduction

Recent interests have focused on attempts to synthesize highly strained cyclic allenes and to study their properties.[1] Decreasing the ring size of cyclic allenes results in deviation of both the normal C=C=C linearity and the orthogonality of the dihedral angle.[1a] The smallest isolable carbocyclic allene is 1-*tert*-butyl-cycloocta-1,2-diene.[2] Seven- and six-membered cyclic allenes are elusive compounds for isolation and they easily undergo dimerization or trapping reactions.[1a,3] In a previous paper,[4] we reported that the highly strained bicyclic allene **2** is the intermediate in the base-induced elimination of HBr from **1** which gives allene-like cycloadducts **7** in the presence of 1,3-diphenylisobenzofuran (DPIBF) as a trapping agent. However, we proposed an alternative mechanism for the formation of cycloadducts **7**. According to this mechanism the dehydrobromination of **1** yields the bicyclic alkyne **3** which undergoes cycloaddition with DPIBF to give **6**. The base-promoted isomerization of the double bond in **6** would give the observed adducts **7** (Eq.1).



1



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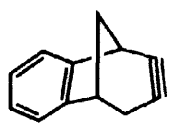

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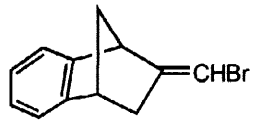

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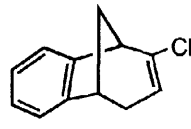

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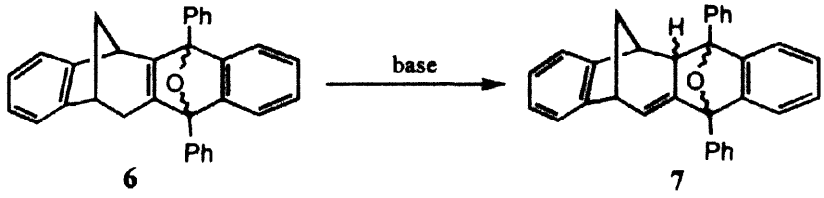
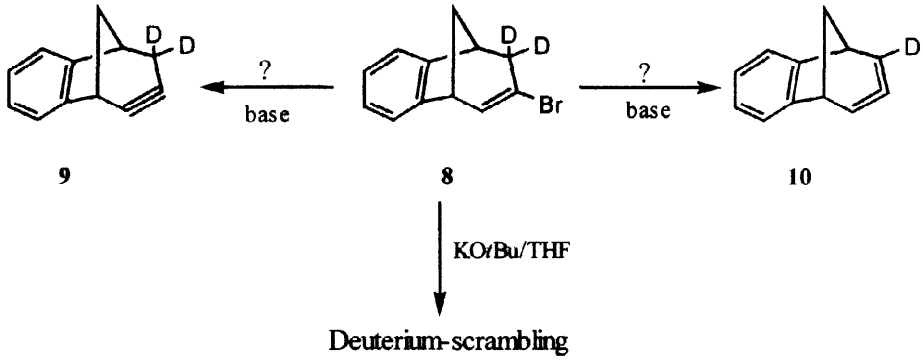


6 7 (1)

In order to distinguish between these two possible mechanisms, we recently investigated the generation and trapping of the alkyne **3** by alternative procedures.[5] The alkyne **3** was generated by the base-induced rearrangement of the bromomethylidene compound **4**. When **4** was subjected to dehydrobromination with potassium *t*-butoxide in the presence of DPBIF, the same allenic adducts **7** were obtained.[5a] This experiment indicates that the alkyne **3** initially reacts with DPIBF to give the alkyne-like cycloadducts **6** which then isomerize completely to the allene-like adducts **7** in the presence of excess base (Eq.1). The identical product distribution from two different reactions implies that the intermediates must have the same structure. Since the allene intermediate cannot be generated from the base-promoted reaction of **4**, it was concluded that the intermediate was the alkyne **3**.

Even with these results, allene formation cannot be excluded in the base-promoted reaction of **1**. In order to reveal whether the real intermediate in the dehydrobromination of **1** is **2** or **3** it was necessary to undertake another independent generation of alkyne **3** where the formation of allene **2** was excluded. For this reason, chloroalkene **5** was synthesized and submitted to dehydrochlorination with potassium *t*-butoxide. In contrast to expectation, the base-promoted reaction of **5** did not form the alkyne intermediate **3**.[5b]

At this stage the question 'what is the real intermediate in the base-promoted reaction of vinyl bromide **1**?' still remained open. In order to solve this problem, the 4,4-dideuterio derivative **8** was synthesized and its dehydrobromination reaction studied (Scheme 1).[6]



9 8 10

Scheme 1

Formation of an allene intermediate **10** by dehydrobromination of **8** would result in the scrambling of deuterium atoms. However, alkyne formation will give product **9** which, after trapping with DPIBF and double bond isomerization, would have deuterium located at the double bond (Scheme 1). Unfortunately, substrate **8** underwent H/D exchange *before* HBr-elimination.[6]

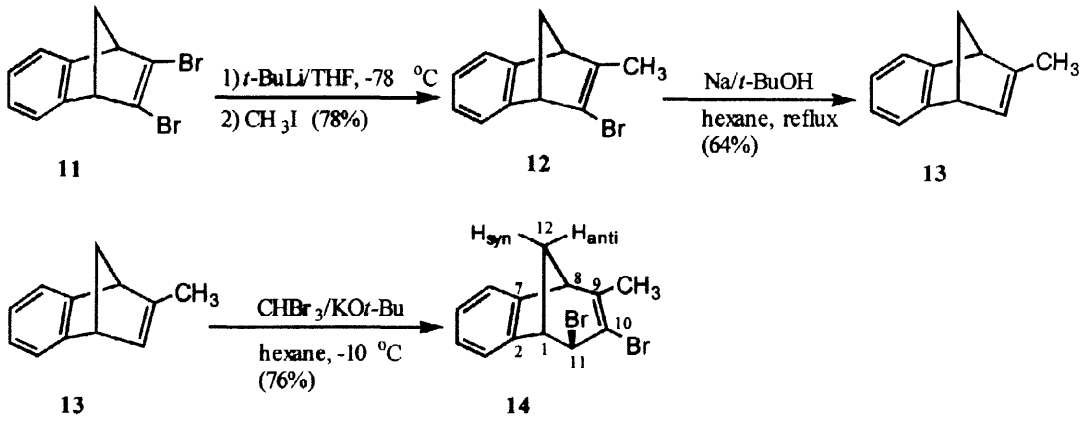
After the failure of this attempt to determine the real structure of the intermediate we decided to force the system to undergo allene formation by replacing the double bond proton in **1** by an alkyl group. In this paper, we describe the synthesis and base-promoted reaction of 2-methyl derivative **16**.

Results and Discussion

Dibromobenzonorbornadiene **11**, the starting material for the synthesis of **16**, was prepared by our published method.[7] Reaction of **11** with *t*-BuLi followed by CH_3I in THF at –78 °C gave bromide **12** whose structure was established unambiguously by ^1H and ^{13}C NMR spectra. Subsequent reductive debromination of **12** gave the known 2-methylbenzonorbornadiene **13**[8] in a yield of 64% (Scheme 2).

The addition of dihalocarbene halogen: (Cl or Br) to benzonorbornadiene provided the most direct route to compounds having the benzobicyclo[3.2.1]octyl ring system.[9] The reaction involves addition of the carbene to the *exo* face of the bicyclic alkene to give initially a *gem*-dihalocyclopropane, which under the reaction conditions usually undergoes ring opening to afford a rearranged, ring-expanded dihalide with *exo*-halogen orientation.[10]

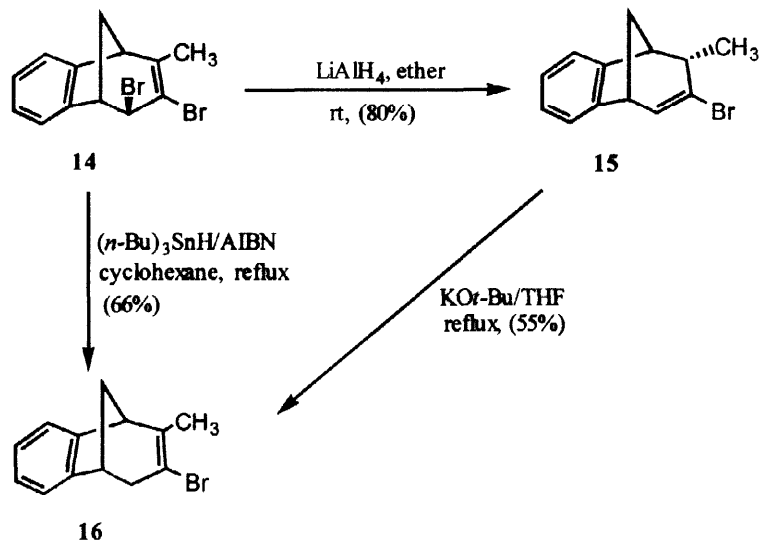
Addition of dibromocarbene, generated from $CHBr_3$ and potassium *t*-butoxide, to 2-methylbenzonorbornadiene **13** afforded the *exo*-dibromide **14** as the sole product in high yield (76%) (Scheme 2). No trace of the other possible ring-expanded was observed.



Scheme 2

The structure of **14** has been elucidated on the basis of ^1H and ^{13}C NMR spectral data. The *exo*-configuration of bromine at C_{11} has been established by analysis of the AB system arising from the bridge methylene protons by comparison with analogous systems[11]. The *exo*-configuration of bromine at C_{11} was also confirmed by differential ^1H NMR nuclear Overhauser enhancement (NOE) studies. Irradiation of H_{11} proton at δ 4.71 induces a peak enhancement only of the bridgehead proton H_1 not the bridge methylene proton H_{12anti} which supports the *exo*-orientation of bromine atom at C_{11} .

$LiAlH_4$ reduction of **14** furnished the *endo*-methyl bromide **15** as a rearranged product (Scheme 3). This is a stereospecific *cis* process involving a S_N2' mechanism. Recently, we have observed a similar stereochemical course in the same ring system.[11a] Jefford *et al.*[12] have also reported similar results for *exo*-3,4-dichloro-2-methylbicyclo[3.2.1]oct-2-ene. Synthesis of the target compound **16** was achieved by treatment of **14** with tri-*n*-butyltin hydride. Potassium *tert*-butoxide catalyzed double bond isomerization in **15** gave also the desired compound **16** (Scheme 3).

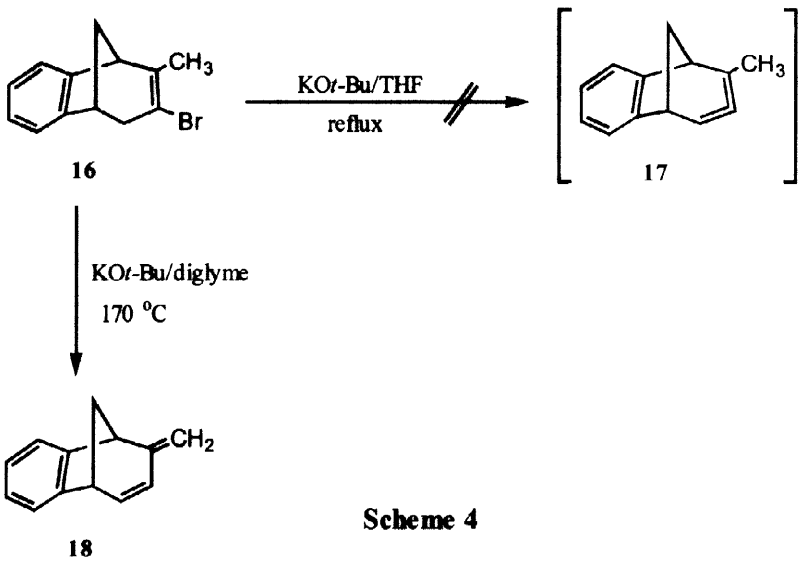


Scheme 3

The structures of **15** and **16** were evident from their NMR spectroscopic properties. Methyl protons in **16** show a triplet (J=2.2 Hz) while a doublet (J=7.2 Hz) in **15**. Analysis of the AB system arising from methylene protons (H_{11}) in **16** show that the down field part (2.96 ppm) is split into doublets of doublets of quartets (J=17.2, 4.9, 2.2 Hz). The third quartet splitting is reconcilable only by long-range coupling (^5J, homoallylic coupling) between methyl protons and methylenic H_{11} protons which was confirmed by extensive double resonance experiments. ^{13}C NMR spectra of **15** and **16** are completely in agreement with these unsymmetrical structures.

After successful synthesis of the target compound **16** it was submitted to the base-promoted HBr-elimination reaction (Scheme 4). No reaction was observed when **16** was subjected to dehydrobromination with potassium *t*-butoxide under the same reaction conditions as reported for **1**. When the more drastic conditions of diglyme at 170 °C were employed, dehydrobromination occurred and exocyclic olefin **18**[9c] was formed; primarily base abstracts a hydrogen atom from the methyl group. This result indicates that **16** has no tendency for dehydrobromination to form allene **17**. On the basis of these results we conclude that the intermediate which is formed from the base-promoted reaction of **1** is the alkyne **3** not the the allene **2**. Alkyne **3** is calculated to be

11 kcal/mol (MOPAC) and 16 kcal/mol (PCMODEL) more stable than the allene.[5a] These calculations are also in agreement with our experimental findings.



Scheme 4

Experimental Section

General. Melting points were determined on a Büchi model 530 apparatus and are uncorrected. Infrared spectra were recorded on a Mattson model 1000 FT-IR spectrometer. ^{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 (60-200 mesh). TLC was carried out on Merck 0.2 mm silica gel 60 F_{254} analytical aluminum plates.

9-Bromo-10-methyltricyclo[6.2.1.0^{2,7}]undeca-2,4,6,9-tetraene 12. A stirred solution of **11** (3.0 g, 10.0 mmol) in dry THF (20 mL) was cooled to –78 °C under a nitrogen atmosphere and treated dropwise with a solution of *t*-BuLi (1.7 M, 5.94 mL, 10.1 mmol) in pentane. After completion of the addition, stirring was continued for 30 min, 1.44 g of CH_3I (10.1 mmol) was added at –78 °C and the solution was stirred for a further 30 min. The cold bath was removed and the reaction mixture was allowed to warm to room temperature. After a major part of the THF was removed, the mixture was treated with water (25 mL) and extracted with ether (3x50 mL). The combined ether layers were washed with water, dried over Na_2SO_4, and filtered. The solvent was removed, and the oily residue was chromatographed over silica gel with hexane to afford 1.72 g (78%) of **12** as a colorless liquid; [Found: C, 61.49; H, 4.63. $C_{12}H_{11}Br$ requires C, 61.30; H, 4.72%]; ^{1}H NMR δ_H (200 MHz, $CDCl_3$) 7.37-7.23 (2H, m, ArH), 6.98 (2H, m, ArH), 3.79 (1H, br s, bridgehead H), 3.68 (1H, br s, bridgehead H), 2.52 (1H, dd, A part of AB system, *J* 7.2, 1.5 Hz, bridge H), 2.26 (1H, dd, B part of AB system, *J* 7.2, 1.5

Hz, bridge H), 1.76 (3H, d, J 1.6 Hz, Me); δ_H ^{13}C NMR (50 MHz, $CDCl_3$) 151.97, 151.46, 150.02, 131.74, 126.99, 126.89, 123.62, 123.25, 68.58, 60.25, 57.58, 17.01; IR ($CHCl_3$, cm^{-1}) 3106-2902, 1600, 1472, 1293, 1063, 1012, 757.

9-Methyltricyclo[6.2.1.0^{2,7}]undeca-2,4,6,9-tetraene 13. Metallic sodium (1.95 g, 84.78 mmol) was cut into small pieces and combined with 30 mL of dry hexane . The stirred mixture was heated to reflux and a solution of **12** (2.0 g, 8.54 mmol) and t-butyl alcohol (4.91 g, 66.35 mmol) in dry ether (5 mL) was added dropwise during 1 h. After stirring at reflux overnight, the reaction mixture was cooled and methanol was added carefully to destroy unreacted sodium. The resulting mixture was poured into water (50 mL) and extracted with ether (3x50 mL). The combined organic layers were washed with water, dried over $MgSO_4$, and filtered. After removal of the solvent, the residue was purified on a short silica gel column, eluting with hexane, to give 0.89 g (64%) of **13** as a colorless liquid, with identical analytical data to that in the literature.[8]

***Exo*-10,11-dibromo-9-methyltricyclo[6.3.1.0^{2,7}]dodeca-2,4,6,9-tetraene 14.** To a stirred solution of **13** (2.0 g, 12.82 mmol) in 40 mL of dry hexane was added 1.60 g (14.28 mmol) of potassium t-butoxide. The reaction mixture was cooled to –10 °C with an ice-salt bath, and a solution of $CHBr_3$ (3.47 g, 13.71 mmol) in 10 mL of hexane was added dropwise over a period of 1 h. The resulting reaction mixture was stirred for an additional 1 h at room temperature. The mixture was diluted with water and the aqueous solution was extracted with ether, washed with water, and dried over Na_2SO_4. After removal of the solvent, the oily viscous residue was crystallized from ether/hexane (1/3) to give 3.2 g (76%) of *exo*-dibromide **14** as a colorless crystals. mp 85-86 °C; [Found: C, 47.29; H, 3.54. $C_{13}H_{12}Br_2$ requires C, 47.60; H, 3.69 %]; δ_H (200 MHz, $CDCl_3$) 7.37-7.11 (4H, m, ArH), 4.71 (1H, m, H_{11}), 3.78 (1H, m, H_1), 3.35 (1H, d, J 4.3 Hz, H_8), 2.70 (1H, d, A part of AB system, J 10.9 Hz, H_{12anti}), 2.37 (1H, dt, B part of AB system, J 10.9, 4.2 Hz, H_{12syn}), 1.95 (3H, d, J 1.3 Hz, Me); δ_C (50 MHz, $CDCl_3$) 153.10, 147.96, 143.52, 129.13 (2x), 126.92, 122.71, 118.26, 60.11, 52.89, 50.61, 40.53, 24.91; IR (KBr, cm^{-1}) 3080-2876, 1651, 1472, 1395, 1191.

Reduction of exo-Dibromide 14 with $LiAlH_4$: *endo*-10-Bromo-11-methyltricyclo[6.3.1.0^{2,7}]dodeca-2,4,6,9-tetraene 15. To a suspension of 25 mg (0.66 mmol) of $LiAlH_4$ in 30 mL of dry and freshly distilled ether was added dropwise a solution of 0.2 g (0.61 mmol) of *exo*-dibromide **14** in 10 mL of dry ether during 20 min. The resulting reaction mixture was stirred magnetically at room temperature for 20 h. Wet ether was added to the reaction mixture (while cooling with an ice-bath) until no reaction was observed. The resulting precipitate was dissolved by adding dilute HCl solution. The organic layer was washed with water, dried over $CaCl_2$, filtered, and concentrated to give an oil. The oily residue was filtered over 20 g of silica gel, eluting with hexane to give 0.12 g (80%) of *endo*-methyl bromide **15** as a colorless liquid; [Found: C, 62.52; H, 5.41. $C_{13}H_{13}Br$ requires C, 62.67; H, 5.26 %]; δ_H (200 MHz, $CDCl_3$) 7.26-7.08 (4H, m, ArH), 6.49 (1H, d, J 7.4 Hz,

H_9), 3.30 (2H, m, H_1 and H_8), 2.89 (1H, m, H_{11}), 2.39 (1H, dt, A part of AB system, *J* 10.3, 4.5 Hz, H_{12syn}), 2.17 (1H, d, B part of AB system, *J* 10.3 Hz, H_{12anti}), 1.03 (3H, d, *J* 7.2 Hz, Me); δ_C (50 MHz, $CDCl_3$) 153.63, 144.14, 136.88, 128.45, 128.05, 127.77, 123.02, 122.37, 49.86, 45.46, 45.08, 43.84, 20.06; IR (neat, cm^{-1}) 3080-2876, 1625, 1472, 1395, 1038.

Reduction of exo-Dibromide 14 with Tri-*n*-butyltin Hydride: 10-Bromo-9-methyltricyclo-[6.3.1.$0^{2,7}$]dodeca-2,4,6,9-tetraene 16. A mixture of *exo*-dibromide **14** (1.2 g, 3.66 mmol), tri-*n*-butyltin hydride (1.42 g, 4.88 mmol), AIBN (20 mg), and cyclohexane (40 mL) was heated at reflux temperature for 6 h and then cooled to room temperature. The resulting mixture was diluted with water and the aqueous solution was extracted with ether, washed with water, and dried over Na_2SO_4. After removal of the solvent, the oily residue was purified by repeated column chromatography (silica gel/hexane) to give 0.6 g (66%) of **16** as a colorless liquid; ; [Found: C, 62.38; H, 5.21. $C_{13}H_{13}Br$ requires C, 62.67; H, 5.26 %]; δ_H (200 MHz, $CDCl_3$) 7.30-7.04 (4H, m, ArH), 3.24 (2H, m, H_1 and H_8), 2.96 (1H, ddq, A part of AB system, *J* 17.2, 4.9, 2.2 Hz, H_{11}), 2.36 (1H, dm, B part of AB system, *J* 17.2 Hz, H_{11}), 2.25 (1H, dt, A part of AB system, *J* 10.1, 5.4 Hz, H_{12syn}), 2.08 (1H, d, B part of AB system, *J* 10.1 Hz, H_{12anti}), 1.90 (3H, t, *J* 2.2 Hz, Me); δ_C (50 MHz, $CDCl_3$) 147.48, 141.09, 136.82, 128.64, 128.30, 125.30, 122.05, 117.11, 49.93, 44.24, 44.14, 43.18, 24.19; IR (neat, cm^{-1}) 3080-2876, 1472, 1395, 1217, 1012.

Reaction of 15 with Potassium *t*-Butoxide. To a stirred solution of *endo*-methyl bromide **15** (0.3 g, 1.21 mmol) in 20 mL of dry and freshly distilled THF was added 150 mg (1.28 mmol) of potassium *t*-butoxide. The reaction mixture was refluxed for 6 h and then cooled to room temperature. After a major part of the THF was removed, the mixture was diluted with water and the aqueous solution was extracted with ether, washed with water, and dried over $MgSO_4$. After removal of the solvent, the oily residue was filtered on a short silica gel column eluted with hexane to give 165 mg (55%) of **16** as a colorless liquid.

Reaction of 16 with Potassium *t*-Butoxide: 11-Methylenetricyclo[6.3.1.$0^{2,7}$]dodeca-2,4,6,9-tetraene 18. To a stirred solution of **16** (0.4 g, 1.61 mmol) in 20 mL of dry diglyme was added 0.21 g (1.87 mmol) of potassium *tert*-butoxide. The reaction mixture was refluxed for 24 h and then cooled to room temperature. The resulting mixture was diluted with water and the aqueous solution was extracted with ether, washed with water, and dried over Na_2SO_4. After removal of the solvent, the residue was filtered on a short silica gel column eluted with hexane to give 0.23 g (85.5%) of exocyclic methylene compound **18** as a colorless liquid. The ^1H NMR and IR spectra were identical to that reported.[9] ^{13}C NMR ($CDCl_3$) δ 151.14, 147.67, 146.93, 137.08, 128.11 (2x), 127.39, 125.34, 123.11, 110.86, 51.91, 46.73, 43.88.

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References and Notes

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