Tetrahedron Vol 33, pp. 2847 to 2849 Pergamon Press 1977 Printed in Great Britain

THE BROMINATION OF BICYCLO[3.2.1]OCTA-2,6-DIENE WITH N-BROMOSUCCINIMIDE

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(*Received in UK* 12 *April* 1977; *Accepted for publication* 16 *May* 1977)

Abstract—The bromination of bicyclo[3.2.1]octa-2,6-diene (3) by NBS does not follow the familiar free-radical course but proceeds through the cyclopropylcarbinyl cation 7. 7 can be trapped by addition of small amounts of methanol. The bicyclo[3.2.1]octa-2,6-dien-4-yl radical is involved in the reduction of exo-6-bromotricyclo[3.2.1.$0^{2,7}$]oct-3-ene by tributyltin hydride.

The bromination of bicyclo[3.2.1]oct-2-ene (**1**) with N-bromosuccinimide (NBS) under conditions which promote radical chain reactions (CCl_4 as the solvent; activation by UV-light) gives rise to the expected allylic bromination product exo-4-bromobicyclo[3.2.1]oct-2-ene (**2**, eqn 1).[1] We discovered that when the related bicyclo[3.2.1]octa-2,6-diene (**3**) is treated with NBS under comparable conditions (CCl_4 as the solvent; activation by benzoyl peroxide (BPO) and visible light) no product of allylic bromination is formed. Instead, the bromination results in the formation of exo-6-bromotricyclo[3.2.1.$0^{2,7}$]oct-3-ene (**4**)[2], due to participation of the C(6)=C(7) double bond in **3** (eqn 2). The most widely accepted mechanism for bromination by NBS involves the formation of an allylic radical through hydrogen abstraction by a Br atom followed by attack of the allylic radical upon a molecule of bromine.[3] After hydrogen abstraction from C(4) participation of the C(6)=C(7) bond in **3** would then probably lead to a delocalized radical, either cyclic (**5**) or open (**6**)[4]. Attack of a bromine molecule on C(6) or C(7) in **5** or on C(6) in **6** would then result in chain propagation and the formation of product.

If an intermediate like **5** or **6** is involved, it is surprising that no products resulting from an attack of bromine on another C-atom in **5** or **6** are formed together with **4**, e.g.: endo-6-bromotricyclo[3.2.1.$0^{2,7}$]oct-3-ene, exo- and endo-4-bromobicyclo[3.2.1]octa-2,6-diene, because radicals like these probably react further quite indiscriminately, as is also shown by our work on a radical debromination of **4**, described below.

In order to evaluate the mechanism we repeated the reaction using deuterated starting material, bicyclo[3.2.1]octa-2,6-diene-4-d_2 (**3d**).[5] Bromination of **3d** produced exo-6-bromotricyclo[3.2.1.$0^{2,7}$]oct-3-ene deuterated on the C(4)-site exclusively (**4d**, eqn 3). This result does not agree with the intermediacy of **5**, while **6** also is not very likely to be an intermediate, because it would not be allowed to interchange with its enantiomer

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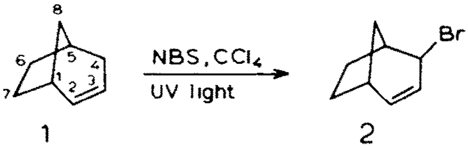

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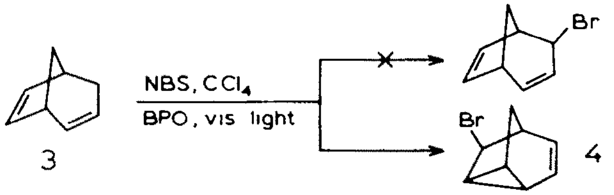


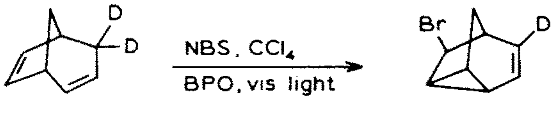
3

5

6

8

(3)



3-d 4-d

or with **5**.[6] The exclusive attack of the bromine molecule on C(6) in **6** also is not easily understood.

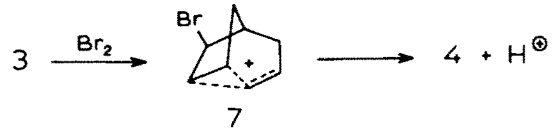
As an alternative to radical chain mechanisms we therefore propose a cationic mechanism for the reaction between **3** and NBS (eqn 4). It involves attack of Br_2 upon C(6) of **3** leading ultimately to the cyclopropylcarbinyl cation **7**. **7** is a bromo derivative of cation **8**, which has been shown by Grob *et al.*[7] to be the common intermediate of solvolyses of esters of tricyclo[3.2.1.0^{2,7}]octan-3-ol, endo- and exo-tricyclo[3.2.1.0^{3,6}]octan-4-ol and of exo-bicyclo[3.2.1]oct-2-en-17-ol. Olah and Liang[8] have shown that under long-lived ion conditions at −78° **8** and derivatives thereof are the most stable species that are formed from bicyclo[3.2.1]oct-2-en-3-ol and from bicyclo[3.2.1]octa-2,6-dienes. In kinetically controlled reactions, which are postulated to proceed via cyclopropylcarbinyl cations a tendency can be seen towards formation of products retaining the cyclopropane ring.[9,10] In our case this is achieved through loss of one of the protons at C(4) of **7**.

Another case, where formation of a favorable cyclopropylcarbinyl cation supersedes the usual radical-chain mechanism of bromination by NBS has been described in the literature.[11] Direct evidence for the intermediacy of cation **7** was obtained by trapping it with methanol. When the bromination was carried out in the presence of low concentrations of methanol three methoxy bromides were formed which, however, were thermally unstable. In order to alleviate the thermal instability the mixture of methoxy bromides was reduced with Na/t-butanol in THF, which produced three methyl ethers in the ratio 80:18:2 (eqn 5). By comparison with authentic materials the main component appeared to be 3-methoxytricyclo[3.2.1.0^{2,7}]octane (**9**) while the second was exo-7-methoxybicyclo[3.2.1]oct-2-ene (**10**). The structure of the 2%-component was not affirmed. Both **9** and **10** result from methoxy bromides that are expected from trapping of the postulated cation **7**. It is noted that in both reactions of **7**, deprotonation (as in the formation of **4** from **3** in the absence of methanol) and addition of methanol, formation of tricyclic product is favored. However, methanol apparently can also add to (one of) the other positively charged C atoms of **7**, whereas of the three possible modes of deprotonation of **7** only the one leading to **4** is realized.

Support for the proposed cationic mechanism is also provided by a radical debromination-experiment with **4d** which illustrates the behaviour to be expected when radicals are generated in our bicyclic system. Treatment of **4d** with $(n\text{-}Bu)_3SnH$[12] or with Na/t-butanol in THF produces bicyclo[3.2.1]octa-2,6-diene deuterated on the C(2)- and C(4)-site as shown in eqn 6. This scrambling of deuterium can be explained by postulating the intermediacy of the delocalized radicals **5** or **12** through rearrangement of the cyclopropylcarbinyl radical **11** first formed.[13] If **5** is formed, it must be attacked by tin hydride at the three-carbon-bridge selectively, no tricyclic olefin being formed.

This difference in regioselectivity provides evidence against a radical mechanism in the bromination of **3**, although, of course, the reactivity of a radical like **5**, **6** or **12** may be different if it reacts with a hydrogen donor like $(n\text{-}Bu)_3SnH$ instead of with molecular bromine.

(4)



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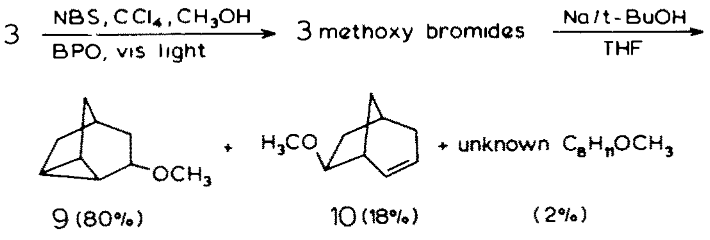

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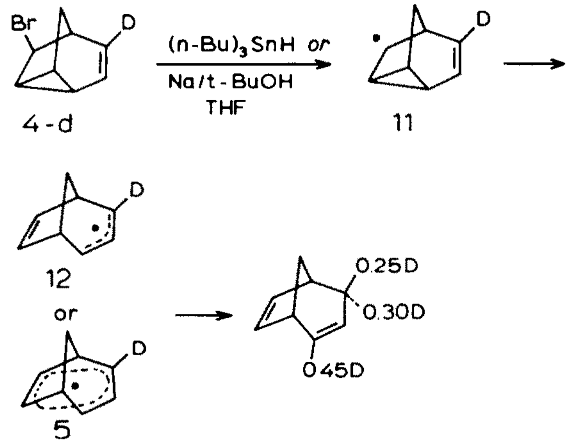

EXPERIMENTAL

General and analytical procedures. All reactions were carried out in previously dried glassware and under N_2. IR spectra were recorded in CCl_4 on a Perkin-Elmer Model 237 spectrophotometer. Only the most important absorptions are given with a precision of 5 cm^{-1}. PMR spectra (δ_{TMS}, ppm) were recorded on Varian A-60, Varian XL-100 and Bruker WH90 spectrometers. Abbreviations used: s-singlet, d = doublet, m = multiplet, pq pseudo-quartet. Mass spectra were obtained from a Varian Mat CH5 spectrometer. Analytical and preparative gaschromatographic separations were carried out on Varian Aerographs 90P and 920. Columns used: 0.5 × 150 cm copper 10% SE-30 (A) and 0.5 × 150 cm copper 20% DEGS (B), both on Chromosorb W

Exo-6-*Bromotricyclo*[3.2.1.0^{2,7}]*oct-3-ene* (**4**). A mixture of **3** (5 mmol), NBS (5 mmol) and benzoylperoxide (5–10 mg) in 5 ml CCl_4 (freshly distilled from P_2O_5) was refluxed under visible light (Philips 13352E/44) until the NBS had disappeared (0.5–1 hr) and changed into white material floating on the surface of the soln (succinimide). The mixture was cooled to room temp, filtered and extracted twice with water. The solvent was removed under reduced pressure and the residue was distilled in a short-path apparatus (15 Torr, 40–70°). The yield of **4** was 35–40%. PMR (60 MHz; CCl_4): 0.86 (d, 1 H, J = 11.4 Hz); 1.70 (s, 3 H); 2.10–2.44 (m, 1 H); 2.67 (pq, 1H); 3.56 (s, 3 H); 5.85 (pq, 2 H). IR: 3060, 2990, 2965, 2940, 2875, 1620, 1450, 1360, 1315, 1290, 1250, 1195, 1175, 1025, 920, 910, 855, 840, 700, 645 The sequence and shapes of the PMR signals closely correspond to the ones given for **4** in Ref. 2. However, in our case all absorptions are shifted to higher field by approximately 0.27 ppm.

Bicyclo[3.2.1]*octa-2,6-diene-4-*d_1 (**3d**). Prepared after Brown.[5] Deuterium-content: 90–95%.

Exo-6-*Bromotricyclo*[3.2.1.0^{2,7}]*oct-3-ene-4-d* (**4d**) Prepared as **4** using the sample of **3d** described above as starting material. PMR spectrum: same as **4**, except that both the olefinic signal at 5.85 ppm and the C(5)H signal at 2.67 ppm have changed from (pseudo)quartets into broad doublets, the intensity of the 5.85 signal approximately being halved relative to **4**.

Bromination of **3** *in the presence of methanol.* The bromination of **3** was carried out as mentioned above in the presence of three equivs MeOH. The mixture was worked up as before and distilled in a short-path apparatus at 2 Torr and 80-120°. Gaschromatographic separation of the resulting mixture failed under all conditions tried probably due to metal-catalyzed thermal decomposition. Characteristic absorptions in the 60 MHz-PMR spectrum (CCl_4) of the distillate are: 1.12–2.37 (m, 7.8 H); 3.21 (s, 3 H); 3.5–3.85 (m, 1 H); 4.23 (s, 0.3 H); 4.39 (s, 0.5 H); 5.27–6.0 (m, 0.4 H).

Debromination of the mixture of methoxy bromides with Na/t-BuOH/THF. The mixture of methoxy bromides (400 mg) obtained from the short-path distillation described above, t-BuOH (1 ml) and 4 ml THF (distilled from LAH) were heated to 50°. Under continuous stirring, Na (0.3 g) was added and the resulting mixture was refluxed for 10 hr. After cooling the excess Na was destroyed with MeOH and water was added. After 4 extractions with petroleum ether 28–40 the organic layer was washed four times with water and then dried with $MgSO_4$. The solvent was removed under normal pressure and after distillation in a short-path apparatus the distillate was analyzed by GLC [A, 100°; relative yields (relative retention-times)]: **3** (originating from **4** contained in the mixture of methoxy bromides), trace (1.0); **10**, 18% (3.8); unidentified component, $m/e = 138$, 2% (3.9); **9**, 80% (5.2). **10** and the unidentified component were collected together and separated on B, 120°.

3-*Methoxytricyclo*[3.2.1.0^{2,7}]*octane* (**9**). To a mixture of pentane-washed NaH (1 mmol) and 10 ml THF (distilled from LAH) gaschromatographically purified tricyclo[3.2.1.0^{2,7}]octanol-3[14] (70 mg; 0.57 mmol) was added. The resulting mixture was stirred for 2.5 hr to form the Na salt, then MeI (290 mg; 2 mmol) was added. After stirring for 21 hr the excess NaH was destroyed with water and after addition of ether the mixture was filtered, washed four times with water and one time with sat NaClaq, then dried with $MgSO_4$. The ether was removed under normal pressure and the residue subjected to GLC (A, 105°). The main component ($m/e = 138$) was isolated. PMR (100 MHz, $CDCl_3$): 0.95–1.2 (m, 1 H); 1.2–2.0 (m, 9 H); 3.29 (s, 3H); 3.6–3.85 (m, 1 H). IR: 3045, 2940, 2865, 2820, 1465, 1450, 1440, 1365, 1330, 1200, 1095, 1070, 1050, 985, 940, 895.

Compound **9** is unstable at higher temps. Thus, material isolated by GLC always contains small percentages of **10** and of tricyclo[3.2.1.0^{2,7}]oct-3-ene. Flow-pyrolysis of **9** (245°, *ca.* 2 sec) yields MeOH, tricyclo[3.2.1.0^{2,7}]oct-3-ene (*ca.* 55%) and **10** (*ca.* 15%) besides starting material (*ca.* 30%). Therefore the question arises, whether **10** shown by GLC to be present in the mixture resulting from Na/t-BuOH/THF reduction of the mixture of methoxy bromides is an artefact or whether it had been present in the original mixture. We think the latter to be the case, because otherwise the presence of *ca.* 20% of olefinic material (on a $C_8H_{10}BrOCH_3$ basis in the PMR spectrum) in the original methoxy bromide mixture cannot be explained; furthermore under the GLC conditions used only a few percent of **10** and no large amounts of tricyclo[3.2.1.0^{2,7}]oct-3-ene are formed.

Exo-7-*Methoxybicyclo*[3.2.1]*oct-2-ene* (**10**). Prepared as **9**, using exo-7-hydroxybicyclo[3.2.1]oct-2-ene.[14] PMR (90 MHz, $CDCl_3$): 1.4–1.95 (m, 5 H); 2.2–2.6 (m, 3 H); 3.29 (s, 3 H); 3.6–3.75 (m, 1 H); 5.35–5.55 (m, 1 H); 5.65–5.9 (m, 1 H). IR: 3030, 2940, 2880, 2840, 1450, 1440, 1355, 1260, 1215, 1200, 1095, 980, 900, 690. $m/e = 138$.

Debromination of **4** *and* **4d** *with* Na/t-BuOH/THF. The procedure followed was the same as described above for the mixture of methoxy bromides. The product, **3** was isolated by GLC. Deuteriated **3** obtained from **4d**, which itself had been prepared from **3d** deuteriated at C(4) for *ca* 90–95% (see above) showed the following PMR absorptions (100 MHz, $CDCl_3$): 1.6–2.1 (m, 2.76 H); 2.15–2.5 (m, 0.78 H); 2.6–2.8 (m, 2 H); 5.2–5.3 (m, 1 H); 5.6–5.8 (pq, 1 H); 5.9–6.15 (m, 0.63 H); 6.15–6.3 (pq, 1 H). The numbers given in eqn 6 have been adjusted to correspond to the presence of 100% of one deuterium atom in **3**.

Debromination of **4** *and* **4d** *with* (n-Bu)$_3$SnH

A mixture of 1 mmol of **4** (**4d**) and 2 mmol (n-Bu)$_3$SnH was kept at 110° for 5 hr; the course of the reaction was followed by PMR. **3** was isolated by distillation and purified by GLC (yield: 90–100%). Deuteriated **3** obtained from the sample of **4d** described above showed a distribution of deuterium, which was identical within experimental error with the one obtained by debromination of **4d** with Na/t-BuOH/THF.

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