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# REGIOSPECIFIC BRIDGEHEAD BROMINATION IN TRICYCLO[4.3.1.1$^{2,5}$]-UNDECANE. HIGH REACTIVITY OF THE 1- OVER THE 2-CARBON ATOM IN A CARBOCATION REACTION

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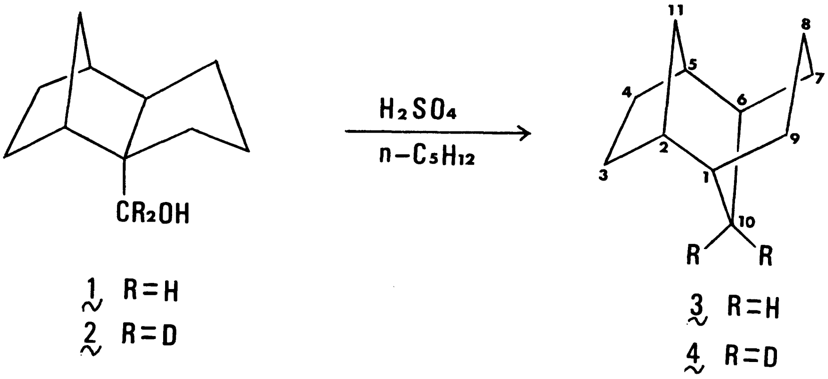
Bromination of tricyclo[4.3.1.1$^{2,5}$]undecane (3) gave exclusively the 1-bromo derivative (5). The structure of 5 was determined unequivocally by making use of deuterium isotope effects on $^{13}$C NMR signals of 1-deuterio-3 (6) derived from 5 and 10,10-dideuterio-3 (4) prepared from the dideuterated alcohol 2.

Functionalization reactions of polycycloalkanes offer convenient means of comparing the reactivities of bridgeheads within a molecules as well as among different molecules.[1] Thus bromination of 4-homoisotwistane (tricyclo[5.3.1.-0$^{3,8}$]undecane)[2] distinguished among the reactivities of three kinds of bridgeheads in this substrate, while acetamidation[3] made clear a high reactivity of 4-homoisotwistane as compared to those of bicyclo[3.3.1]nonane, 4-homobrendane (tricyclo[5.2.1.0$^{3,8}$]decane), and adamantane. We describe here the bromination of tricyclo[4.3.1.1$^{2,5}$]undecane (3).[4] It is intriguing with this $C_s$-symmetrical molecule which of the two bridgeheads, C-1 (and C-6) or C-2 (and C-5), is more reactive toward bromine cation.

The hydrocarbon 3 was stirred with excess bromine at room temperature overnight to give a single bromide 5 (checked on Golay column VPC) isolated in 68% yield: mp 57.5 - 58.5°C; $^{1}$H NMR ($CDCl_3$) $\delta$ 0.8 - 2.6 (m); $^{13}$C NMR ($CDCl_3$) $\delta_C$ 22.46 (t), 26.52 (t), 27.98 (t and t), 34.27 (t), 37.77 (d), 39.35 (t), 39.80 (d), 41.18 (t), 51.41 (d), 75.08 (s); mass spectrum *m/e* (rel intensity) 230 (1, $M^+$), 228 (2, $M^+$), 149 (100), 93 (18), 91 (15), 83 (18), 81 (44), 79 (23), 67 (82), 41 (24), 39 (18). In $^{1}$H NMR was found neither proton geminal to the bromine nor olefinic proton. The result of $^{13}$C NMR was consistent with this. The lowest field signal ($\delta_C$ 75.08), which should be assigned to the bromine-substituted carbon atom, appeared as a singlet on off-resonance proton decoupling, thus suggesting the absence of the proton geminal to the bromine. In the spectrum was also absent any signal at as low a field as $\delta_C$ $\sim$100 that corresponded to olefinic carbon atoms. Reduction of the bromide 5 with lithium in *t*-butyl alcohol[2] regenerated the parent hydrocarbon 3 to show the intactness of the skeleton during the bromination reaction. These results indicated 5 to be a monobromotricyclo-[4.3.1.1$^{2,5}$]undecane with the bromine substituent at a bridgehead.

The orientation of the bromine atom in 5 was determined unambiguously with reference to deuterium isotope effects on $^{13}$C NMR.[5] In order to obtain 10,10-

dideuterio derivative (4) of 3, the dideuterio analog (2) of the alcohol 1 was synthesized by the same procedure as that for the protium compound 1.[4] Use of lithium aluminum deuteride in place of the hydride for the preparation gave the dideuterio alcohol 2: mp 75 - 76°C; IR (neat) 2210, 2190, 2120, 2090 ($\nu_{C-D}$) $cm^{-1}$; $\delta$ 0.8 - 2.2 (m); *m/e* 150 (50), 136 (12), 135 (100), 107 (12), 93 (17), 91 (11), 81 (14), 79 (20), 67 (36), 66 (10). Treatment of 2 with sulfuric acid and *n*-



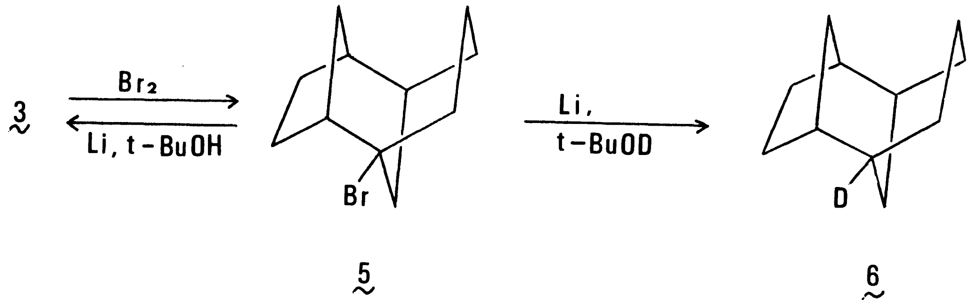


Table I. $^{13}C$ NMR Chemical Shifts of Tricyclo[4.3.1.1$^{2,5}$]undecane (3) and Its Deuterated Analogs

| Compound | $\delta_C$[a] | | | | | | |
|---|---|---|---|---|---|---|---|
| | C-1,6 (d) | C-2,5 (d) | C-3,4 (t) | C-7,9 (t) | C-8 (t) | C-10 (t) | C-11 (t) |
| 3 | 33.14 | 41.16 | 28.39 | 27.94 | 18.42 | 26.41 | 31.77 |
| 4 | 32.90[b] | 41.09[c] | 28.39 | 27.89[b] | 18.41 | -[d] | 31.77 |
| 6 | 33.15<br>[32.52[e] | 41.21<br>[41.15[b] | 28.39 | 27.94<br>[27.89[b] | 18.41[b] | 26.28[b] | 31.76[b] |

[a] ppm from internal TMS standard, measured with resolution of ±0.02 ppm for 2.8 M solution in $CDCl_3$ at 15.03 MHz on a JEOL JNM FX-60 FT spectrometer. Temperature, 25°C; tube, 10 mm; repetition time, 5.0 sec; pulse width, 11 μsec (45°); data points, 4096; no of pulses, 600; spectral width, 1000 Hz. [b] Broadened band. [c] Triplet, $J \sim 1.0$ Hz. [d] Band (quintet) hidden in the noise signals. [e] Triplet, $J \sim 20$ Hz.

pentane[4] gave a dideuterio hydrocarbon **4**: mp 58 - 59°C; IR 2220, 2190, 2120 cm$^{-1}$; *m/e* 152 (42, M$^{+}$), 124 (100), 83 (32), 82 (39), 81 (71), 80 (58), 69 (31), 68 (48), 67 (65), 41 (39). The location of the deuterium atoms in **4** is considered evident from the mechanism of the ring enlargement involved in the synthesis.[4] The $^{13}$C NMR spectrum of **4** (Table I) is also consistent with this structure, as described below. Reduction of the bromide **5** with lithium in *O*-deuterio-*t*-butyl alcohol gave a monodeuterio derivative (**6**) of **3**: mp 58 - 59°C; IR 2170, 2140 cm$^{-1}$; *m/e* 151 (66, M$^{+}$), 123 (100), 122 (42), 82 (42), 81 (81), 80 (62), 79 (36), 68 (55), 67 (78), 41 (29). Chemical shifts of the total proton decoupled $^{13}$C NMR signals for **3**, **4**, and **6** are listed in Table I, together with the fine structures of the signals of **3** found on off-resonance proton decoupling in parentheses.

Assignment of all the $^{13}$C NMR signals, except for those of C-8 and C-11, of **3** was possible with the use of deuterium isotope effects observed for the dideuterio hydrocarbon **4**. The vanished signal ($\delta_C$ 26.41) must belong to C-10 substituted by two deuterium atoms which split the signal into a quintet with as low peak heights as those of noise signals. A geminal effect, upfield shift of the signal with peak broadening,[5] was shown only in one ($\delta_C$ 33.14) of the two double-intensity doublet (bridgehead) signals. Accordingly, this signal should be assigned to C-1 and C-6. Vicinal effects, coupling without any appreciable chemical shift change,[5] were exhibited in the other bridgehead ($\delta_C$ 41.16) and in one ($\delta_C$ 27.94) of the double-intensity methylene carbon signals. Therefore, these signals are assigned to C-2 (and C-6) and C-7 (and C-9), respectively. The deuterium isotope effects and the signal assignment based on them are thus consistent with the 10,10-dideuterio-**3** structure for **4**.

In the $^{13}$C NMR spectrum of the monodeuterio compound **6**, the signal assigned to C-1 and C-6 in the above appeared as two peaks. One ($\delta_C$ 33.15) was almost unchanged compared to the corresponding signal of the undeuterated compound **3**, while the other ($\delta_C$ 32.25) was split into a large triplet with an upfield shift. The result definitely demonstrated that one of the carbon atoms of this bridgehead was substituted by deuterium. Deuterium isotope effects on the other carbon atoms of **6** are also fully consistent with the 1-deuterio-**3** structure for **6**: geminal effects on the signal for C-2 and C-5 as well as on that for C-7 and C-9, and vicinal effects on the C-10 signal and two other single-intensity triplets (for C-8 and C-11).[6,7]

Since the deuterium atom in **6** was shown to be substituted at C-1, so should be the bromine in **5**. Thus the C-1 bridgehead was found to be more reactive than the C-2. The rate-determining step in the bromination of the bridged hydrocarbon lies in the generation of the bridgehead cation through abstraction of the hydride by bromine cation.[1,2] Therefore, the relative reactivities of the bridgeheads in carbocation reactions are determined by the relative stabilities of the corresponding carbocations. The present bromination result signifies that **3**-1-yl cation is more stable than **3**-2-yl. This seems to be easily understood by reference to relative stabilities of bridgehead cations of bicyclic compounds as measured by their relative solvolysis rates.[9] The stability of **3**-1-yl cation may be represented by that of bicyclo[3.3.1]non-1-yl cation, because **3**-1-yl cation is constructed by adding to bicyclo[3.3.1]non-1-yl cation the *exo*-2,4-ethano bridge which should not cause any additional strain to the parent bicyclononyl cation. **3**-2-yl cation may likewise be approximated to bicyclo[3.2.1]oct-1-yl cation with the *exo*-2,4-trimethylene bridge. Bicyclo[3.3.1]non-1-yl cation has been shown $3 \times 10^5$ times more stable than bicyclo[3.2.1]oct-1-yl.[9] This stability difference is enough to explain an entire absence (below 0.2%, the accuracy of the Golay column VPC) of **3**-2-yl bromide in the product. A generalization now seems to be possible from the present bromination and that of 4-homoisotwistane[2] that the relative reactivities of bridgeheads in an unstrained tricycloalkane can be predicted from those in bicyclic compounds which the tricycloalkane contains as partial structures.

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6) The signal for C-3 ($\delta_C$ 28.39) was unaffected by the 1-deuterium atom, although it was also vicinal. This is considered to arise from little coupling due to an unfavorable dihedral angle.[5]

7) Signal assignment to C-8 and C-11 can not be made only on the basis of the deuterium isotope effects in 4 and 6, but could be achieved by reference to some bicyclic model compounds. C-8 of 3 may be structurally correspond to C-3 of bicyclo[3.3.1]nonane ($\delta_C$ 22.5) and C-11 of 3 to C-8 of bicyclo[3.2.1]octane ($\delta_C$ 39.7).[8] Accordingly, the higher field signal ($\delta_C$ 18.42) was assigned to C-8, and the lower field one ($\delta_C$ 31.77) to C-11.

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