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DIFFERENT SELECTIVITIES IN BROMOFLUORINATION REACTIONS USING N-BROMOSUCCINIMIDE/TRIETHYLAMINE TRIS HYDROFLUORIDE OR OLAH'S REAGENT[1]

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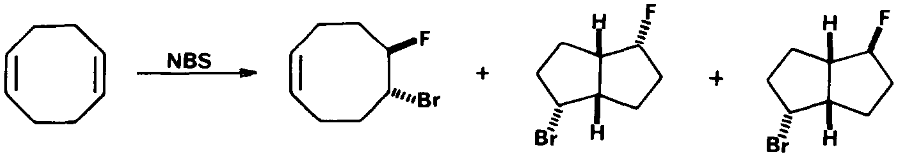
Summary : A new reagent is used for bromofluorination. Its selectivity is compared with that of a known one in the competition between normal 1,2-addition and transannular π-cyclisation of cycloalka-1,5-dienes ***1*** *and* ***5****.*

Recently, we showed that the course of ring opening of 9-oxabicyclo[6.1.0]non-4-ene can be directed by the fluorinating agent employed[2].

Continuing our investigations on the introduction of fluorine into organic substrates[2,3], as well as studies on transannular cyclisations of unsaturated medium-sized rings[4], we wish now to describe the different selectivities in bromofluorinations of (Z,Z)-cycloocta-1,5-diene and (E,Z)-cyclodeca-1,5-diene using N-bromosuccinimide (NBS) as a source of positive halogen and Olah's reagent or Et$_3$N/3HF, respectively as the source for the fluoride ion. The combination of N-bromosuccinimide with the latter (commercially available from Fluka) is a very convenient and effective reagent for halofluorinations of unsaturated compounds, which allows working at room temperature in normal glass apparatus, while hydrogen fluoride in combination with pyridine[5] or solvents like ether or dichloromethane[6] require a polyethylenic equipment and working at low temperatures.

The reaction of (Z,Z)-cycloocta-1,5-diene **1** with one equivalent of NBS and 5 equivalents of Et$_3$N/3HF in dichloromethane or ether at room temperature for 3 h leads to a mixture of three products (GC), whose relative amounts were determined by ^{19}F-NMR spectroscopy of the crude product mixture. These products were separated by chromatography (Kieselgel 100, Merck, petroleum ether) and identified by spectroscopic methods (cf. Table) to be trans-5-bromo-6-fluorocyclooctene (**2**, 92 %), endo,endo-2-bromo-6-fluoro-cis-bicyclo[3.3.0]octane (**3**, 2 %) and endo,exo-2-bromo-6-fluoro-cis-bicyclo[3.3.0]octane (**4**, 6 %). With a decreasing amount of Et$_3$N/3HF the portion of **3** and **4** increases. On the other hand the reaction of **1** with one equivalent of NBS and a ten fold excess of Olah's reagent in ether at 20°C for 4 h leads to a mixture of 26 % **3**, 66 % **4** and three other products (together 8 %), which could not be separated.

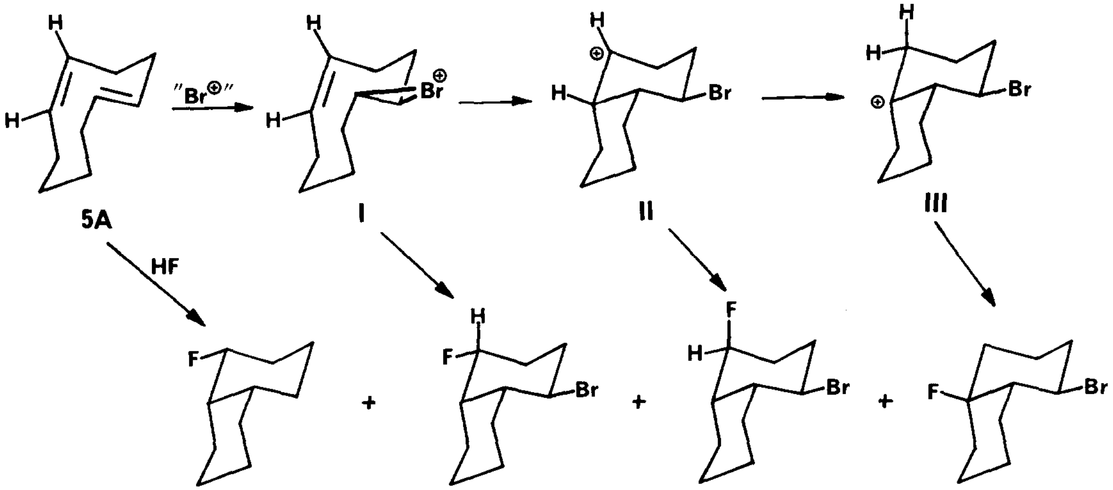


1

	2	**3**	**4**
Et$_3$N/3HF	92 %	2 %	6 %
Pyridine/10HF	0	26 %	66 %

Under similar conditions the reaction of (E,Z)-cyclodeca-1,5-diene **5** with NBS and $Et_3N/3HF$ gave exo-2-bromo-endo-5-fluoro-cis-bicyclo[4.4.0]decane (**6**, 78 %), exo-2-bromo-exo-5-fluoro-cis-bicyclo-[4.4.0]decane (**7**, 12 %), exo-2-bromo-6-fluoro-cis-bicyclo[4.4.0]decane (**8**, < 1 %) and endo-2-fluoro-cis-bicyclo[4.4.0]decane (**9**, 8 %). With Olah's reagent as the source of the fluoride ion the same compounds are formed in relative amounts given in the upper scheme. The structure of the compounds was established again by spectroscopic methods (cf. Table). Furthermore compound **9** could be synthesized in 75 % yield by treatment of **1** with Olah's reagent at room temperature for 20 h.

In the first step of these electrophilic additions[7] to the most stable[8] chair-boat-chair conformation **5A** of (E,Z)-cyclodeca-1,5-diene **5** a cationic intermediate which is probably the bridged bromonium ion **I** is formed from the more reactive[9] E-double bond. A parallel transannular π-cyclisation[10] may lead either to the carbenium ion **II**, or preferably directly to the main product **6** by concerted nucleophilic attack of the fluoride ion. With **5**, cyclisation is preferred particularly[11] because the structure of cis-decalin is closely preformed in the starting diene, and carbons C-1 and C-6 are in close spatial neighborhood. Moreover, the attack of the fluoride ion on C-1 or C-2 of **I** is sterically hindered.



	9	**6**	**7**	**8**
$Et_3N/3HF$:	8 %	78 %	12 %	1 %
Pyridine/10HF :	17 %	46 %	19 %	18 %

The cation **II** is attacked by the nucleophile from the axial direction producing the second product **7**. Moreover, especially under the strong acidic conditions in the reaction with Olah's reagent, the secondary cation **II** is transformed by 1,2-hydride shift to the tertiary carbenion ion **III**, from which **8** is derived under retention of the configuration at C-6. Such a hydride shift during an electrophilic addition to **5** to the best of our knowledge is unknown up to now, but it is throughout known for other systems. Compound **9** is formed directly from **5** by reaction with hydrogen fluoride from the fluorinating agents.

Analogously, the bicyclic products from (Z,Z)-cycloocta-1,5-diene **1** are formed by crossed[10] transannular π-cyclisation as already known from some other electrophilic halogenations of this and other dienes[11-13].

Chemical shifts (δ , $CDCl_3$/TMS ($CFCl_3$) [ppm]) and coupling constants J_{CF} and J_{HF} [Hz] in ^{1}H-, ^{13}C- and ^{19}F-n.m.r. spectra

Compound	^{1}H-n.m.r.	^{13}C-n.m.r.	^{19}F-n.m.r.
<u>2</u>	5.58 (m, 2H, -CH=CH-), 4.81 (dm, 1 H_6, J_{HF}=47.0), 4.35 (m, 1 H_5), 2.7-1.5 (m, 8H), -CH_2-).	129.5, 126.4 (C_1, C_2), 95.2 (C_6, ^1J=173.7), 55.1 (C_5, ^2J=20.2), 33.9 (C_4, ^3J=5.4), 30.9 (C_7, ^2J=23.5), 24.8 (C_3), 23.4 (C_8, ^3J=5.5).	162.9
<u>3</u>	5.04 (dm, 1 H_{6e}, J_{HF}=54.6, $J_{H6e\,H5}$=5.8, $J_{H6e\,H7e}$=3, $J_{H6e\,H7a}$=1.8), 4.19 (m, 1 H_{2a}, $J_{H2a\,H3a}$=10.6, $J_{H2a\,H3e}$= 6.2, $J_{H2a\,H1}$=7.2), 2.70 (m, 2H), 2.50 (m, 1H, J_1= 10.5, J_2=9.1, J_3=5.6), 2.2-1.4 (m, 7H).	97.15 (C_6, ^1J=179.1), 53.3 (C_2), 47.75 (C_1), 46.3 (C_5, ^2J=18.9), 36.6 (C_3, ^4J=1.8), 34.4 (C_7, ^2J=21.9), 28.6 (C_4), 23.7 (C_8, ^3J=13.6).	190.5
<u>4</u>	4.88 (dm, 1 H_{6a}, J_{HF}=54.2), 4.40 (m, 1 H_{2a}, $J_{H2a\,H3a}$= 8.5, $J_{H2a\,H3e}$=6.5, $J_{H2a\,H1}$=7.0), 2.9-2.6 (m, 2H), 2.15-1.75 (m, 7H), 1.40 (m, 1H).	101.55 (C_6, ^1J=173.6), 56.7 (C_2), 49.5 (C_5, ^2J=20.7), 46.9 (C_1), 36.5 (C_3), 33.0 (C_7, ^2J=20,9), 27.8 (C_4), 27.2 (C_8, ^3J=9.1).	170.4
<u>6</u>	4.67 (dm, 1 H_{5a}, J_{HF}=48.2, $J_{H5a\,H4a}$=9.0, $J_{H5a\,H4e}$= $J_{H5a\,H6a}$=4.3), 4.34 (m, 1 H_{2a}, $J_{H2a\,H3a}$=9.1, $J_{H2a\,H1a}$= 8.8, $J_{H2a\,H3e}$=4.1), 2.37 (m, 1H), 2.23 (m, 2H), 2.1-1.2 (m, 11H).	92.6 (C_5, ^1J=176.1), 51.7 (C_2), 42.5 (C_1, ^3J=2.1), 42.0 (C_6, ^2J=13.0), 35.1 (C_3, ^3J=11.9), 29.4 (C_{10}, ^4J=1.2), 27.9 (C_4, ^2J=19.4), 25.3 (C_9), 20.35 (C_8), 19.4 (C_7, ^3J=3.9) §.	181.6
<u>7</u>	4.65 (dm, 1_{H5e}, J_{HF}=48.3), 4.33 (m, 1H), 2.45-2.15 (m, 4H), 2.0-1.75 (m, 4H), 1.7-1.2 (m, 6H).	92.3 (C_5, ^1J=168.6), 53.5 (C_2), 42.5 (C_6, ^2J=19.4), 38.8 (C_1), 32.5 (C_3), 28.8 (C_{10}), 28.0 (C_4, ^2J=20.9), 25.9 (C_9), 23.95 (C_7, ^3J=10.7), 20.1 (C_8) §.	180.6
<u>8</u>	4.5-3.9 (bm, 1 H_2), 2.5-1.0 (bm, 15 H).	95.3 (C_6, ^1J=174.6), 56.2 (C_2), 51.1 (C_1, ^2J=20.3), 38,5 (C_3), 37,0 ($C_5{}^x$, ^2J=22.5), 36.55 ($C_7{}^x$, ^2J=22.8), 26.9 ($C_{10}{}^+$), 25.5 ($C_9{}^+$), 22.2 ($C_4{}^*$, ^3J=2.1), 21.4 (C_8*, ^3J=1.3).	174,0
<u>9</u>	4.52 (dm, 1 H_{5a}, J_{HF}=48.4, J_{H5aH4a}=10.7, J_{H5aH4e}= J_{H5aH6e}=4.9), 2.04 (m, 1H), 1.80 (m, 2H), 1.75-0.9 (m, 13H).	94.7 (C_2, ^1J=175.4), 41.2 (C_1, ^2J=16.8), 35.2 (C_6, ^3J= 7.9), 31.3 (C_7, ^4J=2.4), 27.2 (C_3, ^2J=18.7), 23.0 (C_4, ^2J=11.4), 20.15 (C_{10}, ^3J=3.8), 25.85, 24.9, 21.9 (C_8, C_5,C_9).	179.4

§spectra registred at -60°C ; ^{x}, $^+$, * or reverse

These results show that in the reaction of 1 with NBS/Et_3N,3HF the fluoride ion is sufficiently nucleophilic for successful competition with the internal double bond toward the bromonium ion. The relatively high nucleophilicity of the fluoride ion in the Et_3N/3HF reagent was already obtained in our former studies on ring opening of aziridinium ions[14] as well as epoxides[2]. On the other hand, in the reaction with the more acidic combination NBS/Olah's reagent the second double bond in transannular position competes successfully with the fluoride ion, which is a weaker nucleophile in this reagent. Thus, first a crossed transannular π-cyclisation leads to a 2-bromo-cis-bicyclo[3.3.0]-oct-6-yl carbenium ion which is then attacked by the fluorinating agent from one or the other side leading to the epimeric bromo-fluoro compounds 3 or 4.

In contrast, in the reactions of 5 the intramolecular nucleophilic attack of the Z-double bond on the cationic center is the exclusive process, even in the presence of Et_3N/3HF, depending from the large strain release forming the nearly strainless cis-decalin system from the highly strained medium-sized ring[11,15]. So, by proper choice of the fluorinating agent, it is possible to direct the bromofluorination of unsaturated medium-sized rings.

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