

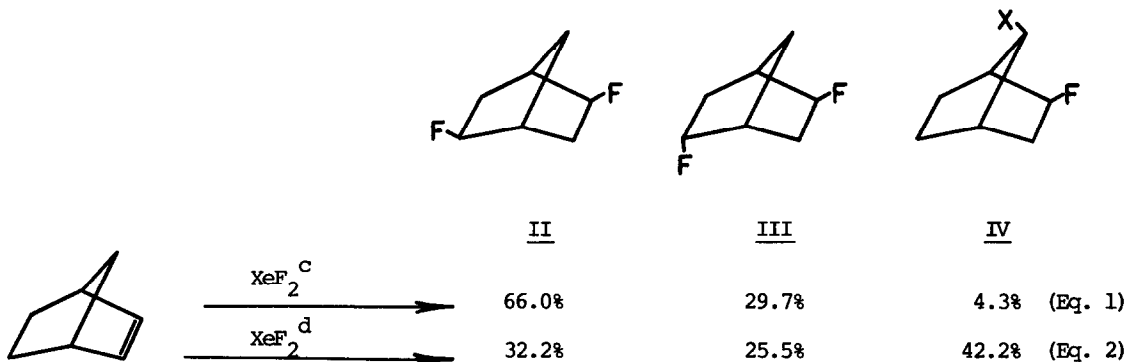
XENON DIFLUORIDE FLUORINATION. II.  
 SELECTIVE SYNTHESIS OF THE NOVEL 2-EXO-5-EXO-  
 AND 2-ENDO-5-EXO-DIFLUORONORBORNANE ISOMERS

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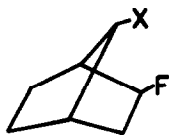
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Fluorination of norbornene I with xenon difluoride using a recently reported benchtop procedure<sup>1</sup> selectively produced 2-exo-5-exo-difluoronorbornane II and the analogous 2-endo-5-exo-difluoronorbornane III. This selective, direct synthesis of the two isomeric 2,5-difluoronorbornanes as major products is without precedence in previously reported studies of halogen and interhalogen additions to norbornene.<sup>2-9</sup>



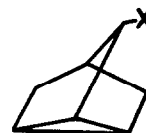
I (a) X=F (b) X=Br (c) -78°C to R.T., 20-22 hr (d) -46 to -39°C, 1½ hr



V



VI



VII

Past norbornene fluorinations<sup>2-3</sup> and one interhalogen "bromine fluoride" addition to norbornene<sup>4</sup> resulted in three major products common to each reaction system. Fluorination with lead tetraacetate/hydrogen fluoride in a Freon 112/methylene chloride solvent produced 2-exo-7-anti-difluoronorbornane IVa, 2-exo-7-syn-difluoronorbornane Va, and a nortricycyl fluoride VIa as the major reaction products.<sup>2</sup> A reported reaction between substituted difluoroiodobenzenes and norbornene in a methylene chloride/hydrogen fluoride solvent yielded the same three products<sup>3</sup>; and in both cases cited, the 2-exo-7-syn-difluoronorbornane Va was the predominant species. Reaction between norbornene, N-bromoacetamide, and hydrogen fluoride in ether generated "bromine fluoride" and resulted in the same two analogous 2,7-disubstituted products IVb, Vb plus a different isomeric nortricycyl derivative VIIb.<sup>4</sup> Very recently a hydrogen fluoride catalyzed reaction between norbornene and xenon difluoride in methylene chloride solvent was reported.<sup>5</sup> Seven products were isolated with the major product being a nortricycyl fluoride VIIa (37-44%). Compounds II (6-12%), III (13-23%), IVa (16-20%), Va (5-6%), 2-exo-3-exo-difluoronorbornane (1-6%), and 2-endo-3-exo-difluoronorbornane (1-11%) were present in low to moderate distribution. Coincidentally, this laboratory conducted similar norbornene/xenon difluoride additions using boron trifluoride etherate as the Lewis Acid initiating species.

Reported in this paper is the first selective, high yield synthesis of the exo-exo- and endo-exo-2,5-difluoronorbornane isomers by this boron trifluoride etherate initiated norbornene/xenon difluoride reaction. Additional characterization of these novel compounds is also provided. Interestingly, the 2-exo-7-syn-difluoronorbornane Va, produced as the predominant derivative in all but one previous norbornene fluorination,<sup>2-5</sup> was not detected even as a trace product from this boron trifluoride initiated reaction.

Fluorination of norbornene with xenon difluoride in a stirred methylene chloride suspension was initiated with boron trifluoride etherate in a standard pyrex round bottom flask. At -78°C reaction was extremely slow during the first 5-6 hours. The cooling bath was then insulated and allowed to warm gradually toward ambient temperature during the next 15-16 hours. The reaction was worked-up as previously outlined.<sup>1</sup> Isomeric product analysis, separation, and isolation by glpc was generally accomplished prior to final solvent removal using a 10 ft. by ¼ in. 10% Carbowax 20M column packed with 80/100 mesh Chromasorb W. Despite the highly volatile nature of the difluoronorbornane isomers, in vacuo solvent removal did provide a 51-76% crude yield of brownish waxy solid comprised of the three isomeric difluoronorbornanes (Equation 1).<sup>10</sup>

Spectral characterization of II, III, and the analogous 2,3-isomers only recently was reported.<sup>5</sup> However, due to an expected spectral similarity between 2,5- and 2,3-difluoronorbornane isomers,<sup>11</sup> deuterium labeling on one vinyl position of the norbornene reactant<sup>12</sup> was employed to establish unambiguously II and III as being 2-exo-5-exo-difluoronorbornane and 2-endo-5-exo-difluoronorbornane respectively. The 2-exo-5-exo-difluoronorbornane II is a volatile white solid (mp 106.0-107.2°C, sealed capillary)<sup>13</sup> and gives the <sup>1</sup>H nmr spectrum illustrated in Figure 1. Figure 2 provides the <sup>1</sup>H nmr spectrum displayed by 2-endo-5-exo-difluoronorbornane III, which also is a volatile white solid (mp 105.0-107.0°C, sealed capillary).<sup>14</sup> Mass spectral data which shows the 2,5-difluoronorbornane isomers with a base peak m/e = 86 and the 2,7-difluoronorbornane providing an 81 base peak is identical to that reported.<sup>5</sup>

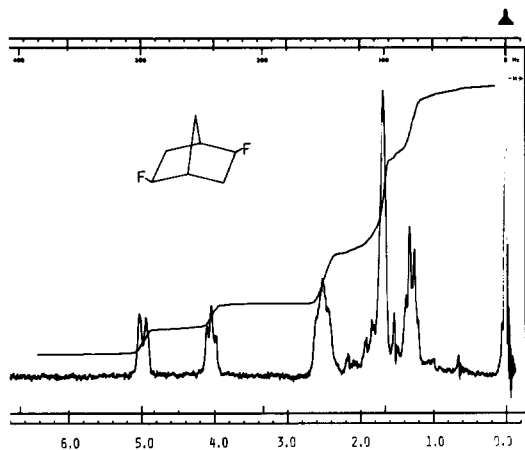


Figure 1

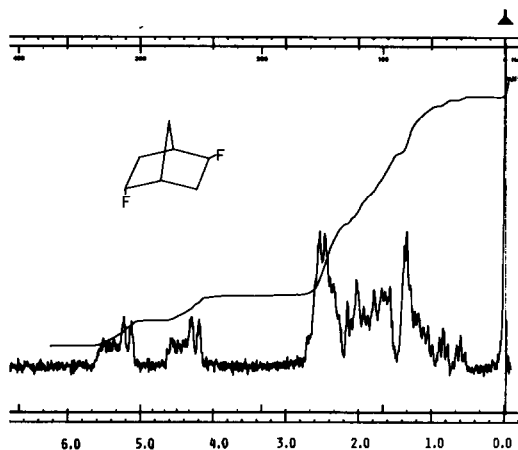


Figure 2

Equation 1 outlines the highly selective nature of this reaction when run over the entire 20-22 hour duration at  $-78^{\circ}\text{C}$  to near room temperature. When the same reaction is conducted at  $-46^{\circ}\text{C}$  to  $-39^{\circ}\text{C}$  for 1-1/4 hours and quenched, glpc analysis reveals II, III, and IVa are initially present; however IVa constitutes the predominant isomer (Equation 2). Studies conducted with monodeuterovinyl norbornene indicate II and III are directly formed fluorination products. Selective isomerization of IVa mostly to II and to III in minor amounts occurred during the extended 20-22 hour reaction conditions to provide the more selective distribution displayed by Equation 1. The isomerization of norbornane fluorides in the presence of hydrogen fluoride has been reported.<sup>5</sup> It is reasonable to suspect that boron trifluoride etherate catalyzes a similar Lewis Acid isomerization during the reaction described. The mechanism of our boron trifluoride etherate initiated reaction appears to proceed through a monofluoronorbornyl cation rearrangement and is supported by our monodeuterovinyl norbornene fluorination results. Recent fluorination of norbornene with xenon difluoride using hydrogen fluoride catalysis produced two difluoronorbornane isomers proposed to result from a radical cation or pure radical pathway.<sup>5</sup> The analogous boron trifluoride etherate initiated reaction gave no products corresponding to those formed from the proposed radical cation or pure radical mechanism.

The striking preference of boron trifluoride etherate initiated norbornene/xenon difluoride fluorination to provide major isomeric difluorides not encountered in other fluorination, halogenation, or interhalogenation addition reactions is quite unique. The substantially more selective product formation compared to the analogous hydrogen fluoride initiated reaction defines a direct fluorination procedure that provides a high yield synthesis of the exo-exo- and endo-exo-2,5-difluoronorbornane isomers. The unique selectivity demonstrated by the boron trifluoride etherate catalyst with the conveniently handled xenon difluoride reagent is a significant contribution to the direct synthesis of novel or important organic fluoride products.

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9. D. R. Marshall, P. R. Warnhoff, E. W. Warnhoff, and J. R. Robinson, Can. J. Chem., 49, 885 (1971).
10. Compounds II, III, and IVa in equations 1 and 2 represent 90% (or greater) of the reaction products. One minor product with an extremely high glpc retention time was present. This material remains unidentified; however, it is not Va, VI, VIIa nor is it either of the 2,3-difluoronorbomane isomers.
11. The fluorination reaction described herein comprised a portion of material presented at the 172nd American Chemical Society National Meeting, 29 Aug - 3 Sep 1976, San Francisco, CA. Preliminary spectral data and current analogous halogenation literature suggested II and III likely to be the new compounds, 2-exo-3-exo- and 2-endo-3-exo-difluoronorbomane respectively, although the analogous unreported 2,5-isomers could not be totally dismissed. Subsequent investigation resulted in conducting the deuterium labeled norbornene fluorination to resolve this structural assignment dilemma.
12. J. E. Franz, C. Osuch, and M. W. Dietrich, J. Org. Chem., 29, 2922 (1964); A. A. Morton, M. L. Brown, M. E. T. Holden, R. L. Letsinger, and E. E. Maget, J. Am. Chem. Soc., 67, 2224 (1945), and R. Finnegan and R. McNees, J. Org. Chem., 29, 3234 (1964). The metalation reaction required to synthesize our monodeuterovinyl norbornene proved hazardous and quite unpredictable. Proper shielding and care should be taken when attempting the referenced procedures.
13. Reference 5 (mp 96-98°C, sealed capillary).
14. Reference 5 (mp 82-84°C, sealed capillary).