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Weakly Nucleophilic Conjugate Bases of Superacids as Powerful Nucleophiles in Vinylic Bimolecular Nucleophilic Substitutions of Simple β-Alkylvinyl(aryl)-λ^3-bromanes

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Supporting Information

ABSTRACT: We report herein, for the first time, the stereoselective synthesis of simple (*E*)-β-alkylvinyl(aryl)-λ^3-bromanes via a boron-λ^3-bromane exchange reaction and their unique bimolecular nucleophilic substitutions at the vinylic ipso carbon atom under mild conditions. Interestingly, even weakly nucleophilic anions such as conjugate bases of superacids (HBF_4, TfOH, Tf_2CH_2, Tf_3CH, Tf_2NH, etc.) function as nucleophiles toward the vinyl-λ^3-bromanes. For instance, the vinylic S_N2 reaction of (*E*)-vinyl-λ^3-bromanes with potassium bis(triflyl)methanide stereoselectively produced (*Z*)-vinyloxy oxosulfonium ylides with exclusive inversion of configuration via oxygen attack, while that with potassium bis(triflyl)imide afforded predominantly (*Z*)-vinyloxysulfoximines. In marked contrast, (*E*)-β-alkylvinyl-λ^3-iodanes do not undergo the vinylic S_N2 reaction with these conjugate bases of superacids. The differences between the nucleofugalities of aryl-λ^3-iodanyl and aryl-λ^3-bromanyl groups (the latter being greater) probably play a pivotal role in these unique reactions.

Bimolecular nucleophilic substitution at an sp^2 vinylic carbon atom (S_N2V reaction), in which a nucleophile attacks the σ^* orbital of the $C_{vinylic}-LG$ bond from the side opposite the leaving group (LG) to give an inverted product, has been considered to be a high-energy process and for a long time has been excluded as a viable pathway on both theoretical and experimental grounds.[1] A unique but unambiguous example of intermolecular S_N2V displacement [2] relies heavily on the use of a highly powerful hypernucleofuge such as a phenyl-λ^3-iodanyl group,[3] which is a better LG than superleaving triflate.[4]

On the other hand, in the intramolecular version, even a common nucleofuge such as bromide can serve as a good LG:[5] for instance, 2-bromobut-2-enylamines cyclize to 2-ethyleneaziridines via base-induced nucleophilic substitutions with stereochemical inversion at the vinylic carbon atom. These reactions, however, cannot be applied to the intermolecular S_N2V displacement because of the modest nucleofugality of the LG. It occurred to us that instead of bromine, use of hypervalent λ^3-bromanes as LGs with an increased nucleofugality[6] would make possible the realization of an intermolecular S_N2V version. We report herein, for the first time, the stereoselective synthesis of highly active (*E*)-β-alkylvinyl(aryl)-λ^3-bromanes **3** via boron-λ^3-bromane exchange and their facile bimolecular nucleophilic substitutions at the vinylic ipso carbon atom under mild conditions. Much to our surprise, even weakly nucleophilic anions such as the conjugate bases of superacids[7] function as nucleophiles toward vinyl-λ^3-bromanes **3**. The vastly enhanced nucleofugality of aryl-λ^3-bromanyl groups in comparison with aryl-λ^3-iodanyl groups is a driving force for the unique S_N2V reactions.[6]

(*E*)-1-Decenyl(*p*-trifluoromethylphenyl)-λ^3-bromane (**3a**) was prepared stereoselectively via the ligand exchange reaction of the Frohn reagent $p\text{-}CF_3C_6H_4BrF_2$[8] on Br(III) with (*E*)-1-decenyldifluoroborane (**2a**) [2 equiv; generated in situ from potassium decenylborate (**1a**) by the reaction with $BF_3 \cdot OEt_2$ at low temperature in a Teflon PFA vessel under argon[9]] in dichloromethane at −78 °C for 1 h (Scheme 1).[10] After removal of precipitated KBF_4 by rapid filtration at 0 °C, evaporation of dichloromethane in vacuo at −30 °C followed by repeated decantation with pentane at −78 °C afforded (*E*)-vinyl-λ^3-bromane **3a** as an amorphous solid in 85% yield. All of the vinyl-λ^3-bromanes **3a**−**c** synthesized are thermally labile at ambient temperature and moisture-sensitive; hence, their yields were determined by ^1H NMR spectroscopy at −40 °C with 1,1,2,2-tetrachloroethane as an internal standard. In $CDCl_3$ solution at 0 °C, **3a** gradually decomposed to a mixture of inverted (*Z*)-1-decenyl fluoride (**6**) and $p\text{-}CF_3C_6H_4Br$ with a half-life ($t_{1/2}$) of 23 min, probably via S_N2V reaction with BF_4^- anion (see Scheme S1 and Figure S1 in the Supporting Information).[11] In the solid state, however, bromane **3a** can be stored at −78 °C for several weeks without any decomposition.

Large vicinal coupling constants of 12.3−12.4 Hz between the vinylic protons of λ^3-bromanes **3** ($CDCl_3$/−40 °C) indicate exclusive retention of stereochemistry during the boron-λ^3-bromane exchange reaction. These coupling constants for **3** are smaller than the value of 13.7 Hz for a λ^3-iodane analogue, (*E*)-1-decenyl(phenyl)(tetrafluoroborato)-λ^3-iodane (**4**),[12] probably reflecting the greater electron-withdrawing power of phenyl-λ^3-bromanyl groups than of phenyl-λ^3-iodanyl groups.[13,14] ESI-MS data for **3a** acquired in positive-ion mode in chloroform revealed prominent ion peaks derived from monomeric, dimeric, and trimeric species at *m*/*z* 363, 813, and 1267, respectively (see Figure S2).[15]

Upon exposure to excess amounts of potassium triflate, a conjugate base of superacidic TfOH with H_0 acidity of −14.1 (see Scheme S2),[16] in dichloromethane at −78 °C to room temperature, alkenyl-λ^3-bromane **3a** underwent an S_N2V reaction and afforded inverted (*Z*)-vinyl triflate **5** stereoselectively in 54% yield along with another S_N2V product, **6** (41%) (Scheme 2). In marked contrast, (*E*)-decenyl-λ^3-iodane **4** did not undergo the vinylic S_N2 reaction under these conditions because of the weak nucleophilicities of triflate and borate anions (see Scheme S3). Use of trimethylsilyl

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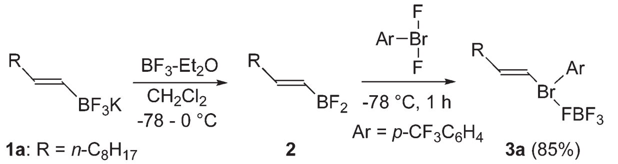
Scheme 1

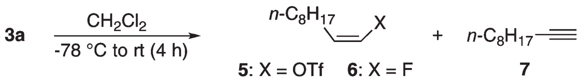


1a: R = *n*-C_8H_{17}
1b: R = *n*-Bu
1c: R = *t*-Bu

2

3a (85%)
3b (63%)
3c (86%)

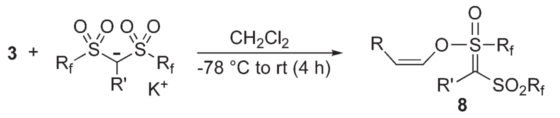
Scheme 2[a]



	5: X = OTf	**6**: X = F	**7**
KOTf (5 equiv)	54%	41%	5%
TMSOTf (3 equiv)	72%	6%	7%

[a] GC yields.

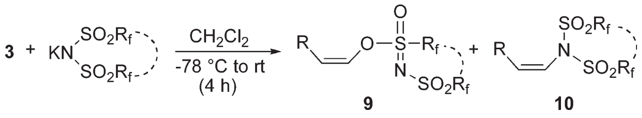
Table 1. S_N2V Reaction with Perfluoroalkanesulfonylmethanide Anions[a]



entry	3	R_f	R′	8	yield (%)[b]
1	**3a**	CF_3	H	**8a**	81
2	**3b**	CF_3	H	**8b**	84
3	**3c**	CF_3	H	**8c**	43[c]
4	**3a**	*n*-C_4F_9	H	**8d**	93
5	**3b**	*n*-C_4F_9	H	**8e**	68 (77)
6	**3c**	*n*-C_4F_9	H	**8f**	31[c]
7	**3a**	CF_3	CF_3SO_2[d]	**8g**	49 (80)

[a] Conditions: **3**/potassium sulfonylmethanide (5 equiv)/Ar. [b] Isolated yields. Numbers in parentheses are ^1H NMR yields. [c] 3,3-Dimethyl-1-butyne (38% for entry 3 and 15% for entry 6) was produced. [d] $KCTf_3$ (10 equiv) was used.

Table 2. S_N2V Reaction with Bis(perfluoroalkanesulfonyl)imide Anions[a]



entry	3	R_f	product (% yield[b]) 9	10
1	**3a**	CF_3	**9a** (68)	**10a** (8)
2	**3b**	CF_3	**9b** (50)	**10b** (7[c])
3	**3c**	CF_3	**9c** (32)	**10c** (−)[d]
4	**3a**	*n*-C_4F_9	**9d** (73)	**10d** (6)
5	**3b**	*n*-C_4F_9	**9e** (74)	**10e** (6)
6	**3a**	($CF_2CF_2CF_2$)	**9f** (56)	**10f** (12)
7	**3b**	($CF_2CF_2CF_2$)	**9g** (43)	**10g** (3)

[a] Conditions: 3/potassium sulfonylimide (5 equiv)/Ar. [b] Isolated yields. [c] ^1H NMR yields. [d] 3,3-Dimethyl-1-butyne (18%) was produced.

triflate, which can capture fluoride from weak fluoride donors with formation of TMSF, markedly increased the selectivity for formation of (*Z*)-vinyl triflate **5** (72%).

Interestingly, superstrong CH acids with two perfluoroalkanesulfonyl groups[16] provide efficient nucleophiles for the substitution reactions of **3** (Table 1). Thus, reaction of **3a** with potassium bis(triflyl)methanide in dichloromethane at −78 °C to room temperature stereoselectively afforded a new type of (*Z*)-vinyl sulfinate derivative, oxosulfonium ylide **8a**, in 81% yield with exclusive inversion of configuration (entry 1). Ylide **8a** was produced via O-attack of the ambident methanide anion, and no formation of the C-attack product was detected. This is in marked contrast to the reported preferential C-alkylation of $Tf_2CHMgCl$ in the reaction with allyl bromide and benzyl chloride.[17] The unique structure of (*Z*)-ylide **8a** was identified by ^1H, ^{13}C, and ^{19}F NMR and MS spectral analyses, especially by (1) two peaks with 1:1 intensity at −75.6 and −80.5 ppm in the ^{19}F NMR spectrum, indicating the presence of different kinds of CF_3 groups, and (2) a small vicinal coupling constant of 5.6 Hz between the vinylic protons and a sharp singlet peak at 4.25 ppm assigned to the hydrogen atom attached to the ylidic C═S bond in the ^1H NMR spectrum (see Scheme S4).[18] Potassium bis(nonaflyl)methanide also afforded (*Z*)-ylide **8d** selectively in high yield (entry 4). The presence of a sterically demanding *β*-*tert*-butyl group in (*E*)-alkenyl(phenyl)-λ^3-iodanes completely inhibits the S_N2 displacement with halide anions but instead results in syn *β*-elimination, yielding a terminal alkyne;[2] however, *tert*-butylvinyl-λ^3-bromane **3c** did undergo the S_N2V reaction with bis(sulfonyl)methanide anions and afforded (*Z*)-sulfinates **8c** and **8f**, albeit in moderate yields. Unique but highly labile bis(triflyl)-oxosulfonium ylide **8g** was produced by the reaction of **3a** with O-nucleophilic tris(triflyl)methanide anion (entry 7).[19]

Potassium salts of bis(sulfonyl)imide superacids function as ambident nucleophiles in the S_N2V reaction and afforded a mixture of O- and N-attack products (Table 2). Thus, exposure of **3a** to $KNTf_2$ gave inverted (*Z*)-*N*-triflylsulfoximine **9a** as the major product via predominant O-attack of the imide anion, along with a small amount of (*Z*)-enimide **10a** (entry 1). Comparable results were obtained in the reaction with nonaflyl and cyclic potassium salts (entries 4−7). A similar preference for O-phenylation over N-phenylation has been reported in the S_N1-type thermolysis and photolysis of $PhN_2^+NTf_2^-$, which generates an active phenyl cation intermediate.[20] ^{19}F NMR spectroscopy of **9a**, **9b**, **10a**, and **10b** provided the most direct evidence for identification of these products, where the former pair exhibit two well-resolved singlets (1:1 ratio) and the latter a slightly more deshielded singlet (see Scheme S4).

Conjugate anions of these CH and NH superacids did not undergo the vinylic S_N2 reaction with vinyl-λ^3-iodane **4**, indicating greater activity of vinyl-λ^3-bromane **3** (see Scheme S3). Interestingly, S_N2V displacement of **3** with halide anions (Cl, Br, I) took place smoothly even at −78 °C (see Table S1).

Since no method for the synthesis of (*Z*)-vinyloxy oxosulfonium ylides **8** and sulfoximines **9** has been available to date, only our unique vinylic S_N2 strategy provides access to these compounds.

■ ASSOCIATED CONTENT

Supporting Information. Experimental details and supporting schemes, figures, and table. This material is available free of charge via the Internet at http://pubs.acs.org.

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