Communications

(2,4,6-Triisopropylphenyl)selenium Bromide (TIPPSe-Br). An *in Situ*-Generated Reagent for Effecting Highly Selective Ring Closures of Homoallylic Alcohols to Substituted Tetrahydrofurans

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Ring closure reactions of homoallylic alcohols **1** can be effected by various electrophiles (E^+), which commonly include protons, Hg^{+2},[1] various sources of I^+,[2] and PhSeX (X = Cl, phthalimide).[3] Stereoselectivities of cyclizations vary widely depending upon substrate structure (Figure 1) as well as choices of E^+, temperature, and especially solvent.[3d,g] We now describe a new reagent for purposes of providing a general solution to tetrahydrofuran-forming processes of the 5-endo-trig-like type.[4] Moreover, in many cases, remarkably enhanced diastereoselectivities are to be expected relative to previously reported results.

The reagent (2,4,6-triisopropylphenyl)selenium bromide, **4**, derives from diselenide **3**. This precursor is a known, stable, orange-yellow solid (mp 101–103 °C),[5] prepared from commercially available 2,4,6-triisopropylbromobenzene (**2**)[6] *via* lithiation and subsequent treatment with selenium (Scheme 1). Dissolution of **3** in CH_2Cl_2 followed by cooling to −78° and dropwise addition of Br_2 (1 equiv) generates **4** which is immediately ready for use.

Introduction of a homoallylic alcohol of type **1a–d**[7] to *in situ*-generated **4** leads to rapid cyclization at −78°. Figure 2 contains examples illustrative of this methodology, results being summarized in Table 1, along with comparison data from the literature using either PhSeCl[3] or *N*-(phenylseleno)phthalimide (N-PSP).[3b] Most striking are the results obtained from *syn* or *anti E*-olefinic educts,

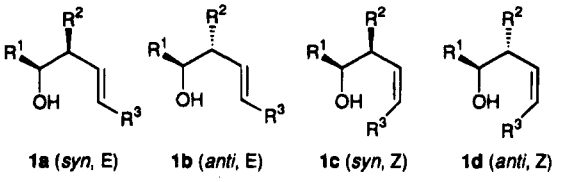


Figure 1.

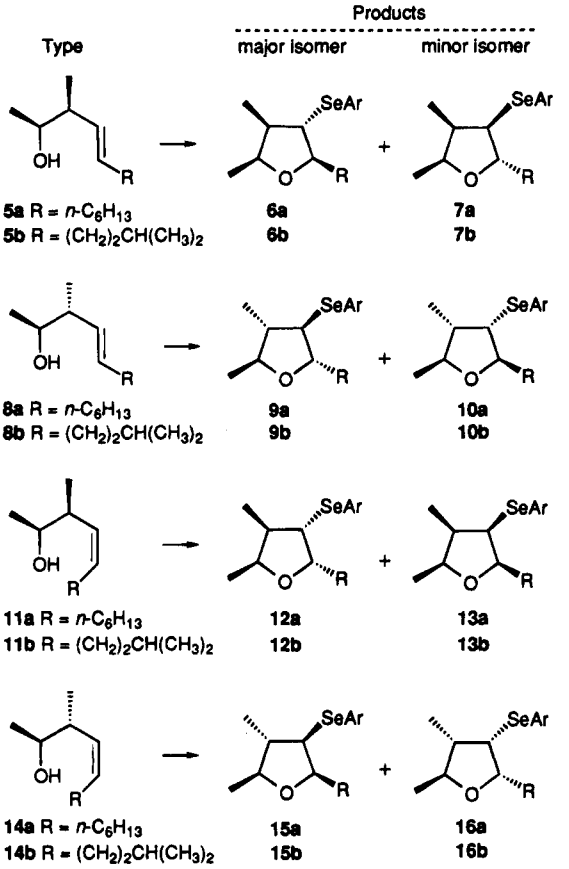
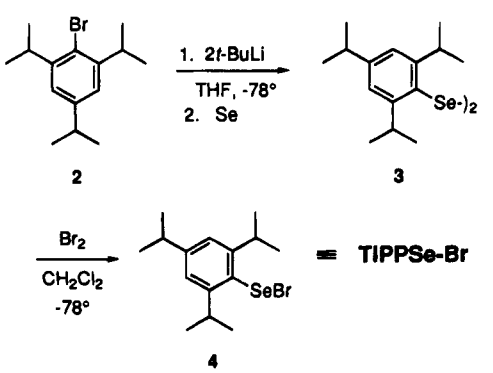


Figure 2. Educts and THF products from cyclizations of alcohols **5a,b**, **8a,b**, **11a,b**, and **14a,b**.

Scheme 1



where diastereoselectivities are enhanced by a factor of *ca.* 10–100 (entries for **1a**, **1b**).[8] Isolated yields are consistently high, and the product selenide can easily be reduced to the trisubstituted THF using *n*-Bu_3SnH in refluxing benzene (eq 1).[3b,9]

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(4) Baldwin, J. E. *J. Chem. Soc., Chem. Commun.* **1976**, 734.

(5) du Mont, W. W.; Martens, A.; Pohl, S.; Saak, W. *Inorg. Chem.* **1990**, *29*, 4848.

(6) Available from Lancaster Synthesis Inc., catalog no. 2230.

(7) Alkyl substrates of type **1a–d** were synthesized from openings of *cis*- and *trans*-2,3-epoxy butane *via* either lithiated 1-octyne or 5-methyl-1-hexyne, followed by subsequent reduction with Na in liquid NH_3 (to the *E*-isomer) or hydrozirconation (to the Z-isomer).

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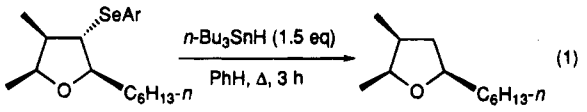
Table 1. Cyclizations of Homoallylic Alcohols of Types 1a–1d Using Reagent 4 in CH_2Cl_2 at −78 °C

		isomeric products[b,c]		yield	ratio[e]	
type	alcohol[a]	major	minor	(%)[d]	this work	lit.[3b]
1a	**5a**	**6a**	**7a**	86	49:1	1.2:1
(*syn*, E)	**5b**	**6b**	**7b**	82	109:1[f]	
1b	**8a**	**9a**	**10a**	85	>49:1	4:1
(*anti*, E)	**8b**	**9b**	**10b**	85	52:1	
1c	**11a**	**12a**	**13a**	82	24:1	32:1
(*syn*, Z)	**11b**	**12b**	**13b**	75	5:1	
1d	**14a**	**15a**	**16a**	86	19:1	1:0[g]
(*anti*, Z)	**14b**	**15b**	**16b**	87	25:1	

[a] Prepared according to ref 7. [b] All new compounds were fully characterized by IR, NMR, MS, and HRMS data. [c] SeAr = SeC_6H_2-2,4,6-(*i*-Pr)$_3$. [d] Isolated, chromatographically purified materials. [e] Determined by capillary GC using an H/P GCMS. [f] Ratio obtained at −95°; at −78 °C, the ratio was 58:1. [g] See ref 12.



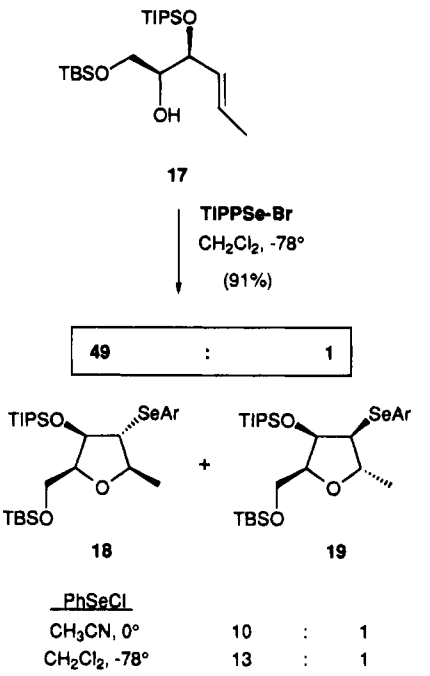
(1)

Reagent **4** can also find application to cyclizations of heteroatom-substituted cases, as with silyloxy derivative **17** (Scheme 2).[10] Thus, while PhSeCl in either CH_2Cl_2 or CH_3CN afforded THFs **18** and **19** in ratios of 13:1 and 10:1, respectively, the corresponding closure with TIPPSe-Br gave the expected products to the extent of 49:1 (91% isolated yield).

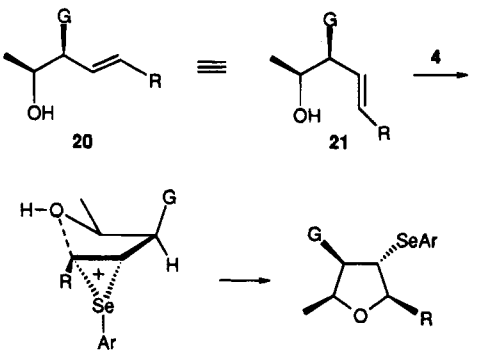
The enhanced selectivity realized using TIPPSe-Br is presumably a reflection of increased steric demands in the approach of **4** to the π-bond, preferentially occurring away from the allylic (alkyl or silyloxy) substituent (G, Scheme 3). Although extended conformations of educts **1a–d** are likely in the ground state,[11] obligatory C–C bond rotation (*e.g.*, in **20** to **21**) arrives at the precursor orientation for cyclization, followed by selenenium ion formation and net *trans* addition to afford the major THF product observed.

In conclusion, the reagent TIPPSe-Br, **4**, has been found to convert homoallylic alcohols to substituted tetrahydrofurans with excellent control at the newly generated stereogenic centers. Further extensions and applications of this methodology will be reported in due course.

Scheme 2



Scheme 3



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Supplementary Material Available: Spectral data for diselenide **3**, all major products in Table 1 and eq 1, and product **18** (18 pages).

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(8) Reactions of **5a** were screened based on the number of equivalents of **4** used. The following results were obtained: 2.1 equiv (86%, 49:1 ratio); 1.58 equiv (80%, 57:1 ratio); 1.05 equiv (75%, 53:1 ratio). We conclude, therefore, that only a slight excess of **4** is needed and that the ratio of products is independent of [**4**].

(9) Stereochemical assignments follow from comparison data on deselenated material (*e.g.*, eq 1) provided by Dr. E. Mihelich.[3b]

(10) The selectivity in this case was sensitive to the nature of the OH protecting group. With a benzyl instead of a TIPS ether, a 1.2:1 ratio of products was obtained.

(11) Hoffmann., R. W., *Chem. Rev.* **1989**, *89*, 1841.

(12) This reaction was carefully repeated under the literature conditions and analyzed by GCMS. In our hands, the ratio is actually 38:1, as expected, rather than the stereospecificity reported.[3b]