In conclusion, this method represents a novel, efficient and selective synthesis of (*Z*)-vinyl bromides through a simple addition.[12] The ability to obtain both *trans*- and *cis*-haloalkylation of alkynes is synthetically useful as well as mechanistically intriguing. Current work is focused on further elucidation of the mechanism and expansion of the scope of the reaction.

Received: July 2, 1999 [Z13668]
Revised: October 4, 1999

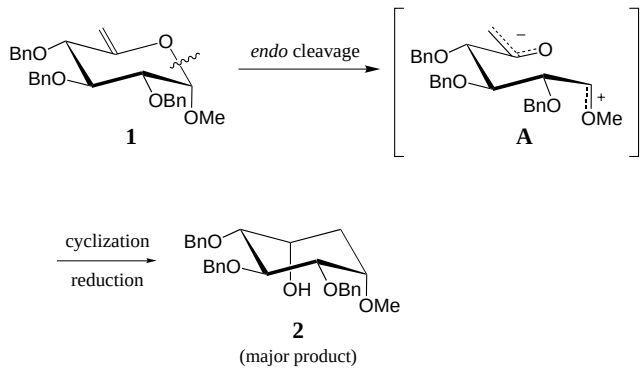
[1] For examples see: *Comprehensive Organometallic Chemistry II*, *Vol. 12* (Eds.: E. W. Abel, F. G. A. Stone, G. Wilkinson, L. S. Hegedus), Pergamon, Oxford, **1995**; N. A. Saccomano in *Comprehensive Organic Synthesis*, *Vol. 1* (Eds.: B. M. Trost, I. Fleming, S. L. Schreiber), Pergamon, Oxford, **1991**, pp. 193–201.
[2] Some examples: S. H. Pine, *Org. React.* **1994**, *43*, 1; D. A. Ager, *Org. React.* **1990**, *38*, 1; B. E. Maryanoff, A. B. Reitz, *Chem. Rev.* **1989**, *89*, 863.
[3] D. S. Matteson, *Tetrahedron* **1989**, *45*, 1859.
[4] E. Takada, S. Hara, A. Suzuki, *Tetrahedron Lett.* **1993**, *34*, 7067.
[5] B. M. Trost, *Angew. Chem.* **1995**, *107*, 285; *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 259.
[6] B. M. Trost, A. B. Pinkerton, *J. Am. Chem. Soc.* **1999**, *121*, 1988.
[7] For previous use of this catalyst in our group see: B. M. Trost, A. Indolese, T. J. J. Müller, B. Treptow, *J. Am. Chem. Soc.* **1995**, *117*, 615; B. M. Trost, T. J. J. Müller, J. Martinez, *J. Am. Chem. Soc.* **1995**, *117*, 1888; B. M. Trost, M. Portnoy, H. Kurihara, *J. Am. Chem. Soc.* **1997**, *119*, 836.
[8] T. P. Gill, K. R. Mann, *Organometallics* **1982**, *1*, 485.
[9] All new compounds have been characterized spectroscopically, and elemental composition has been established by combustion analysis or high resolution mass spectrometry; see Supporting Information.
[10] For several examples of *cis*-halometalations see: H. Dietl, H. Reinheimer, J. Moffatt, P. M. Maitlis, *J. Am. Chem. Soc.* **1970**, *92*, 2276; K. Kaneda, T. Uchiyama, Y. Fujiwara, T. Imanaka, S. Teranishi, *J. Org. Chem.* **1979**, *44*, 55; R. Hua, S. Shimada, M. Tanaka, *J. Am. Chem. Soc.* **1998**, *120*, 12365.
[11] For a *trans*-chloroalkylation see: Z. Wang, X. Lu, *Chem. Commun.* **1996**, 535. For a stoichiometric *cis*-chlororuthenation of acetylenedicarboxylates see: P. R. Holland, B. Howard, R. J. Mawby, *J. Chem. Soc. Dalton Trans.* **1983**, 231.
[12] M. Hulce, M. J. Chapdelaine in *Comprehensive Organic Synthesis*, *Vol. 4* (Eds.: B. M. Trost, I. Fleming, M. F. Semmelhack), Pergamon, Oxford, **1991**, pp. 279–287.

Carbocyclic Ring Closure of Unsaturated S-, Se-, and C-Aryl Glycosides

Matthieu Sollogoub, Jean-Maurice Mallet, and Pierre Sinaÿ*

The glycoside-to-carbocycle transformation[1] provides an attractive route for the synthesis of functionalized carbocycle derivatives from readily available sugar precursors. Usually these transformations rely on the cleavage of the glycosidic acetal functionality to liberate the reactive carbonyl group that undergoes carbocyclization.[1b] The disadvantage of these approaches is the loss of the aglycon. Furthermore it is impossible to apply this method to sugars bearing unusual aglycons, particularly C-glycosides, where no acetal functionality is present. Herein, we report the first direct transformation of hex-5-eno S-, Se-, and C-glycosides into carbocycles with retention of the aglycon.

We reported that hex-5-enopyranosides such as **1** undergo reductive rearrangement with triisobutylaluminum (TIBAL) to afford highly substituted cyclohexane derivatives such as **2**,[2] where both the aglycon moiety and anomeric configuration are retained[3] (Scheme 1). The key step in this transformation is the *endo* cleavage of the glycosidic bond to give a stabilized carbocationic intermediate **A**, which then recyclizes and undergoes reduction to afford the observed major product **2**.



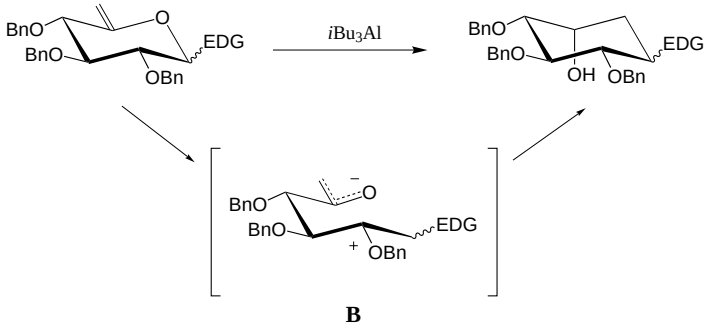
Scheme 1. The key step of the TIBAL-promoted rearrangement: *endo*-glycosidic cleavage (the detailed mechanism of this process is not known). Bn = benzyl.

We assumed that it should be possible to replace the methoxy group by other electron-donating groups that would stabilize the analogous carbocationic intermediate **B** and therefore promote *endo* cleavage (Scheme 2). However, when the known C-glucoside **3**[4] was treated with five equivalents of TIBAL at 50 °C, we failed to observe the desired carbocycle

[*] Prof. P. Sinaÿ, Dr. M. Sollogoub, Dr. J.-M. Mallet
Département de Chimie
Associé au CNRS, Ecole Normale Supérieure
24 rue Lhomond, 75231 Paris cedex 05 (France)
Fax: (+33) 1-44-32-33-97
E-mail: pierre.sinay@ens.fr

Supporting information for this article is available on the WWW under http://www.wiley-vch.de/home/angewandte/ or from the author.

  0044-8249/00/11202-0370 $ 17.50+.50/0

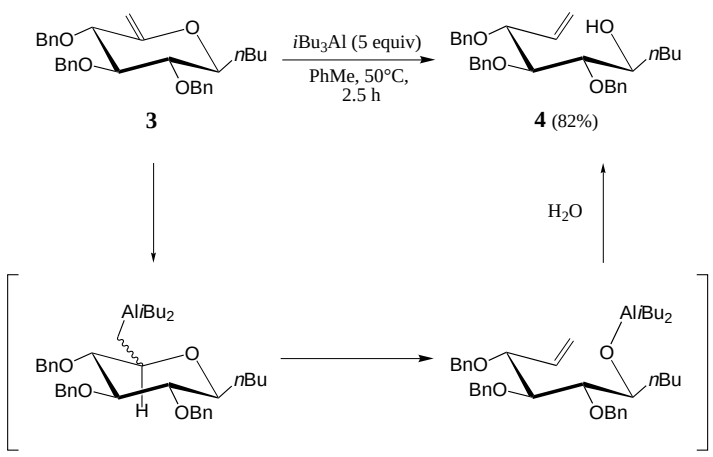


Scheme 2. Putative mechanism for the general sugar-to-carbocycle rearrangement promoted by TIBAL. EDG = electron-donating group.

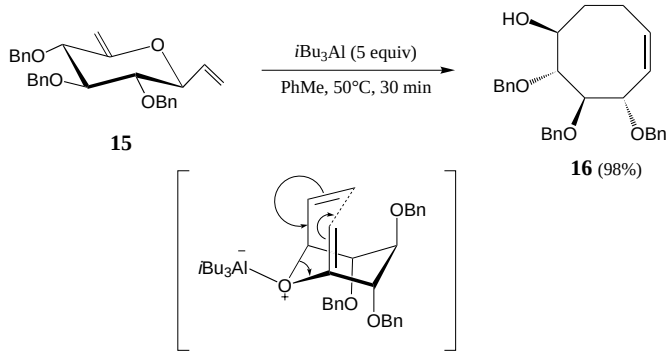
and instead isolated the known open-chain product **4**[4] in 82% yield (Scheme 3, the physical and spectroscopic data of the rearrangement products are given in the Supporting Information). Product **4** is the result of an overall reductive cleavage of the endocyclic C5–O bond, a reaction which has already been described for simple enol ethers.[5] An hydroalumination–elimination mechanism, as shown in Scheme 3, may explain this process.

In light of this observation we proposed that only stronger stabilization of the carbenium intermediate **B** (Scheme 2) would kinetically favor *endo* cleavage and subsequent rearrangement over competitive hydroalumination–elimination. Indeed, reaction of the C-phenyl glycoside **5**[6] resulted in the desired cyclohexane **6** (35%) along with the open-chain byproduct **7** (35%; Scheme 4). The increased electron-donating ability of the *para*-methoxyphenyl group in **8**[7] further biased the reaction towards rearrangement, and the desired carbocycles **9** and **10** were isolated in 85% yield as a 4:1 mixture along with only 10% of the open-chain product **11**. Finally, reaction of the trimethoxyphenyl derivative **12**[8] afforded exclusively the carbocyclization products **13** and **14** in 95% yield as an inseparable mixture (3:2); no traces of the open-chain product were detected.

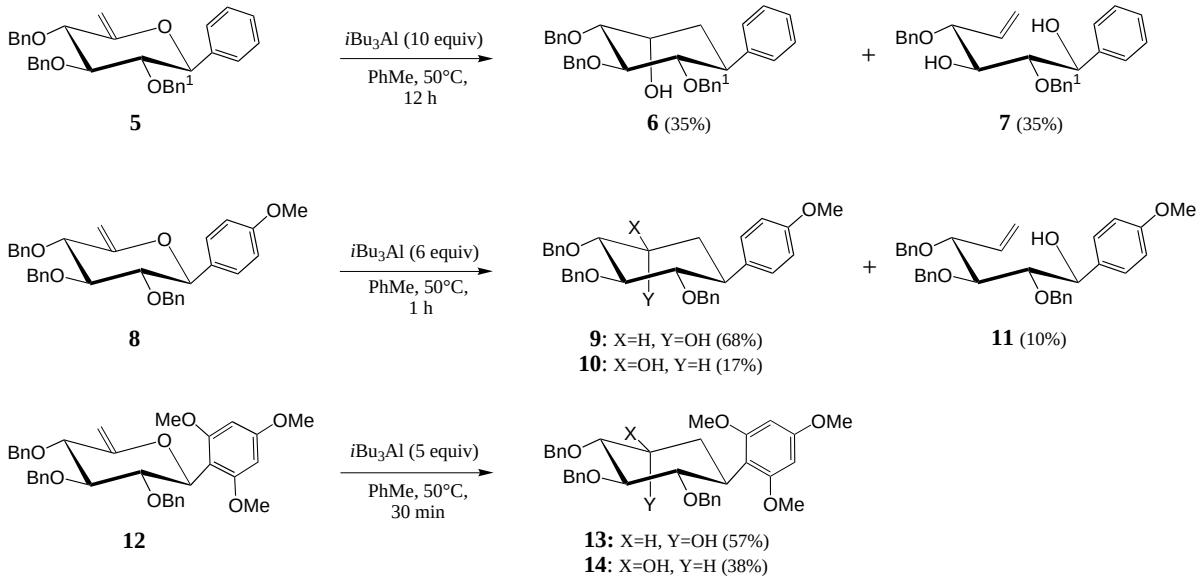
In the case of the C-vinyl glycoside **15**,[9] no six-membered ring was observed as a product of carbocyclization. Instead Claisen rearrangement catalyzed by TIBAL[10] afforded cyclooctene **16** in 98% yield (Scheme 5). Thiem and Wershkun



Scheme 3. Formation of **4** by a postulated hydroalumination–elimination mechanism.



Scheme 5. TIBAL-catalyzed Claisen rearrangement of the C-vinyl glycoside **15**.

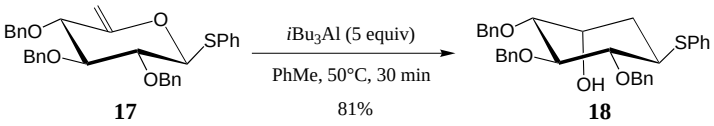


Scheme 4. TIBAL-promoted rearrangement of **5**, **8**, and **12**. Increasing electron-donating ability of the substituent at C1 favors carbocyclization over reductive cleavage of the endocyclic C5–O bond.

  0044-8249/00/11202-0371 $ 17.50+.50/0

applied the thermal variant of this reaction to sugars under more forcing conditions.[11]

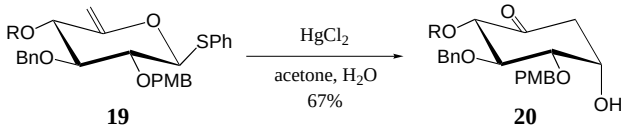
The reaction of the thiophenyl substrate **17**[12] with five equivalents of TIBAL at 50 °C also gave the desired carbocycle **18** in 81 % yield (Scheme 6). In contrast, the Ferrier-II[13] reaction has been applied[14] to the thiophenyl derivative **19** to



17 **18**

Scheme 6. Application of the TIBAL-promoted rearrangement to a thiophenyl glucoside.

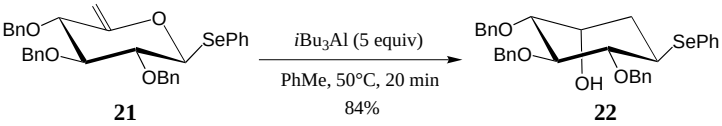
give the hydroxy ketone **20** (i.e., with loss of the thiophenyl moiety, Scheme 7). However, in our case the sulfur atom stabilizes the carbenium intermediate (**B**, EDG = SPh in Scheme 2) to afford the cyclohexane with retention of the thiophenyl functionality, as predicted. This example illustrates the fundamental difference between the TIBAL-promoted rearrangement and the Ferrier-II reaction.



19 **20**

Scheme 7. Application of the Ferrier-II rearrangement to a thiophenyl glucoside.[14] PMB = *para*-methoxybenzyl; R = substituted monosaccharide.

Similarly, the same conditions were applied to the selenophenyl glucoside **21**,[15] which was converted into the cyclohexane **22** (84 %; Scheme 8).



21 **22**

Scheme 8. Application of the TIBAL-promoted rearrangement to a selenophenyl glucoside.

In conclusion we have demonstrated that the TIBAL-promoted rearrangement of unsaturated glycosides (5-hex-enopyranosides) into carbocycles is generally applicable to carbohydrates, provided the aglycon is sufficiently electron donating in nature (O-, S-, Se-, and C-glycosides). We are currently exploring further suitable systems known to stabilize cations and also the wider application of this rearrangement in non-carbohydrate systems.

Experimental Section

TIBAL (0.9 mL, 0.9 mmol, 1M in toluene) was added to a stirred solution of **12** (100 mg, 0.17 mmol) in anhydrous toluene (1 mL) at room temperature under argon. The reaction mixture was heated at 50 °C for 30 min, when TLC (EtOAc/cyclohexane 3/7) indicated no starting material ($R_f = 0.5$) and a major product ($R_f = 0.3$). The mixture was cooled to room temperature, and water (2 mL) was added. The mixture was extracted with EtOAc (3 × 10 mL) and washed with water (10 mL). Combined extracts were dried ($MgSO_4$) and filtered, and the solvent was removed in vacuo. The residue was purified by flash chromatography (eluent, EtOAc/cyclohexane 3/7) to afford an inseparable mixture of the two isomers **13** and **14** as an oil (95 mg, 95 %).

Received: July 8, 1999 [Z13694]

[1] a) R. J. Ferrier, S. Middleton, *Chem. Rev.* **1993**, *93*, 2779 – 2831; b) P. Sinaÿ, P. Dalko, *Angew. Chem.* **1999**, *111*, 819 – 823; *Angew. Chem. Int. Ed.* **1999**, *38*, 773 – 776.

[2] S. K. Das, J.-M. Mallet, P. Sinaÿ, *Angew. Chem.* **1997**, *109*, 513 – 516; *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 493 – 496.

[3] We successfully applied this methodology for the direct synthesis of disaccharide mimetics by replacing the aglycon methoxy group with monosaccharide substituents: A. J. Pearce, M. Sollogoub, J.-M. Mallet, P. Sinaÿ, *Eur. J. Org. Chem.* **1999**, 2103 – 2117.

[4] D. Rouzaud, *Thèse de troisième cycle*, Université Paris-Sud Orsay (France), **1985**.

[5] P. Pino, P. Lorenzi, *J. Org. Chem.* **1966**, *31*, 329 – 331.

[6] Prepared according to Scheme 9 from the known (2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)benzene; see C. D. Hurd, R. P. Holysz, *J. Am. Chem. Soc.* **1950**, *72*, 1732 – 1735.

[7] Prepared according to Scheme 9 from the known (2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)anisol; see P. Allevi, M. Anastasia, P. Ciuffreda, A. Fiecchi, A. Scala, *J. Chem. Soc. Chem. Commun.* **1987**, *16*, 1245 – 1246.

[8] Prepared according to Scheme 9 from the known 2,4,6-trimethoxy-2-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)benzene; see R. A. Eade, H.-P. Pham, *Aust. J. Chem.* **1979**, *32*, 2483 – 2493.

[9] Prepared by debenzoylation and subsequent benzylation of the benzoylated compound.[11]

[10] L. A. Paquette, D. Friedrich, R. D. Rogers, *J. Org. Chem.* **1991**, *56*, 3841 – 3849.

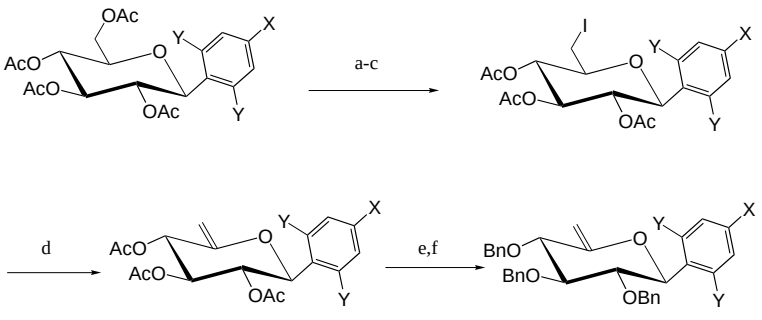
[11] B. Wershkun, J. Thiem, *Angew. Chem.* **1997**, *109*, 2905 – 2906; *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 2793 – 2794.

[12] Prepared according to literature procedures[2] from the known phenyl 2,3,4-tri-*O*-benzyl-1-thio-β-D-glucopyranoside; see P. J. Pfaffli, S. Hixson, L. Anderson, *Carbohydr. Res.* **1972**, *23*, 195 – 206.

[13] R. J. Ferrier, *J. Chem. Soc. Perkin Trans. 1* **1979**, 1455 – 1458.

[14] N. Sakairi, M. Hayashida, A. Amano, H. Kuzuhara, *J. Chem. Soc. Perkin Trans. 1* **1990**, 1301 – 1313.

[15] Prepared according to literature procedures[2] from the known phenyl 2,3,4-tri-*O*-benzyl-1-seleno-β-D-glucopyranoside; see E. Perrin, PhD thesis, Université Pierre et Marie Curie Paris 6 (France), **1996**.



5: X=Y=H
8: X=OMe, Y=H
12: X=Y=OMe

Scheme 9. Preparation of unsaturated C-aryl glucosides. Reagents: a) MeONa, MeOH; b) I_2, PPh_3, DMF; c) Ac_2O, pyridine; d) 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU), THF, reflux; e) MeONa, MeOH; f) BnBr, NaH, DMF.

  0044-8249/00/11202-0372 $ 17.50+.50/0