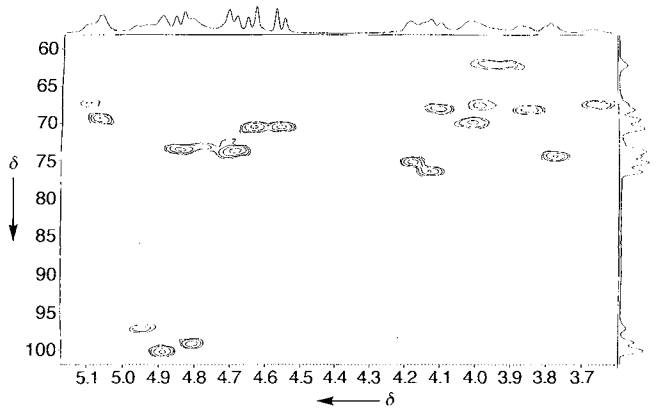

Figure 2. Diagnostic region of the $^{1}H-^{13}C$ HMQC NMR spectrum of **3**.

The spectra show that HR-MAS can be used for monitoring the solid-phase synthesis of oligosaccharides in a very sensitive fashion. Parenthetically, the measurements tend to confirm our earlier claim that solid-support coupling reactions—using properly protected 1,2-anhydro sugars (at least in this series)- are highly stereoselective, even more so than the solution-based couplings.[15] The original claim was based on the finding that no α-linked products could be found upon cleavage from the polymer and subsequent purification. Of course, arguments of this sort are subject to uncertainties as to whether other stereoisomers might have been inadvertently overlooked during the removal and purification sequence. The argument becomes more persuasive as one examines the "crude reaction mixture" bound to the solid phase. While the data we obtained cannot exclude adventitious overlapping of signals from small amounts of isomeric α-products, it certainly indicates a high degree of control of each coupling event conducted on the solid phase. We attribute this excellent β-stereoselectivity in this and related solid-state experiments[9, 10] to the relative diminution of effective solvation upon complexation of the oxirane by the zinc chloride promoter. Solvation forces can lend the anomeric oxiranyl donor oxonium-like qualities. A donor species, which is far advanced in the direction of a free oxonium ion, is likely to be responsible for the formation of small but significant amounts of α-glycosides from the solution-based α-epoxide donor.

In summary, the development of novel methodologies for the assembly of oligosaccharides on the solid support will undoubtedly benefit from this discerning "on-resin" analytical method. Chemists will be able to determine whether coupling has occurred and quickly estimate the specificity of the coupling step. Complete assignments can be made after the product is cleaved from the solid support and deprotected.

Experimental Section

All spectra were obtained on a Bruker DRX500 spectrometer, operating at 500.13 MHz (^{1}H) and 125.76 MHz (^{13}C), equipped with a 4 mm Bruker CCA HR-MAS probe. Trisaccharide **3** (20 mg at 0.54 mmol g^{-1} loading, 10.8 μmol) was loaded into a ceramic rotor, suspended in 30 μL $CDCl_3$, and spun at the magic angle at 3.5 KHz. ^{1}H NMR spectra were obtained with a Carr-Purcell-Meiboom-Gill pulse sequence [13]; 128 transients (1.64 s acquisition time, 0.5 s relaxation delay) were accumulated. The $^{13}C\{^{1}H\}$ spectrum was obtained in 2 h 10 min (3000 transients, 0.6 s acquisition time, 2 s relaxation delay). The phase-sensitive (TPPI) $^{1}H-^{13}C$ HMQC spectrum was obtained in 2 h (16 scans per 256 increments, 0.17 s acquisition time, 1.3 s relaxation delay) with a BIRD sequence to minimize resin signals [14]. Total time for ^{1}H, ^{13}C, and HMQC NMR experiments was 4 h 15 min.

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Novel Carbocyclic Ring Closure of Hex-5-enopyranosides

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Carbohydrates have been used as starting materials for the synthesis of an extensive range of enantiomerically pure noncarbohydrate natural products and related substances.[1] The intramolecular ring closure of carbohydrates to form carbocyclic compounds is an attractive transformation, which offers direct access to highly functionalized cyclohexane derivatives. In this

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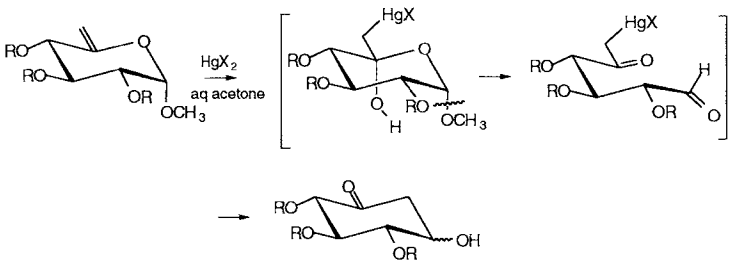
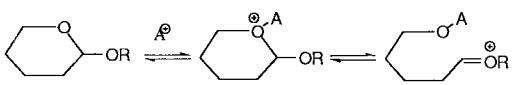
ring-closure reaction a carbanionic center (C6) usually attacks the electrophilic carbonyl center (C1). An early example is the Grosheintz–Fischer synthesis[2] of deoxy nitroinositols from 6-deoxy-6-nitrohexoses.

In 1979 Ferrier reported the convenient conversion of an easily available hex-5-enopyranoside into a highly functionalized cyclohexane derivative in the presence of mercury(II) chloride.[3] Hydroxymercuration of the vinyl ether moiety of a hex-5-enopyranoside gives an unstable hemiacetal, which loses methanol to generate a critical dicarbonyl intermediate (Scheme 1). This species then undergoes an aldol-like intramolecular cyclization to form a substituted cyclohexane. Mechanistic and stereochemical studies[4] as well as modified reaction conditions[5] have been published. Highly functionalized cyclohexane derivatives are of major significance for several groups of natural products. This remarkable rearrangement—the Ferrier-II reaction[6]—has provided a practical route to a large variety of bioactive substances such as aminocyclitols, pseudosugars, and inositols.[7] A basic feature of the Ferrier-II reaction is the loss of alcohol, for example methanol (Scheme 1), and generation of an electrophilic aldehyde, which is necessary for the aldol reaction.

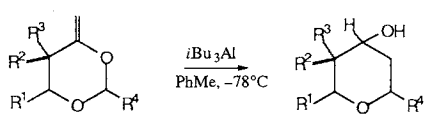


Scheme 1. Proposed mechanism for the Ferrier-II reaction [7].

We now report an alternative, direct conversion of hex-5-enopyranosides into highly functionalized cyclohexane derivatives without cleavage of the glycosidic bond. The discovery of this novel carbohydrate rearrangement is a result of a logical deduction from two independent facts: 1) Acyclic products of the selective cleavage of the ring carbon–oxygen bond of glycopyranosides have occasionally been observed[8] upon treatment with suitable electrophilic species (Scheme 2). 2) Hex-5-enopyranosides are vinyl acetals with a vinyl ether subunit as part of an acetal moiety. Among the various reactions known for vinyl acetals,[9] the triisobutylaluminum-assisted reductive rearrangement provides an elegant entry to substituted cyclobutanes,[10] cyclopropanes,[11] tetrahydrofurans,[12] and tetrahydropyrans[13] (Scheme 3).

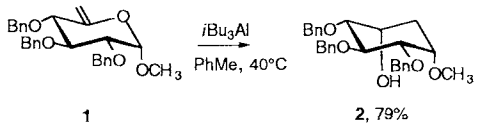


Scheme 2. *Endo* activation in glycoside cleavage.



Scheme 3. Stereocontrolled Petasis synthesis [13] of substituted tetrahydropyrans from substituted vinyl acetals.

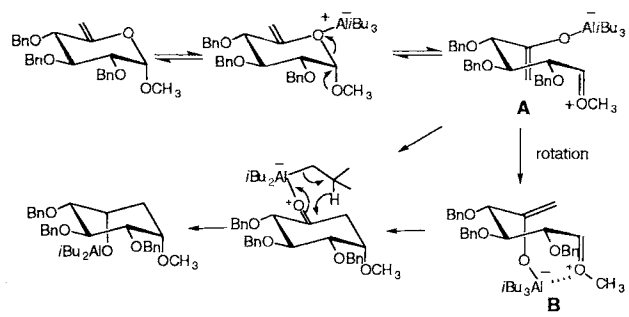
As predicted, the reaction of the known carbohydrate vinyl acetal **1**[14] with four equivalents of triisobutylaluminum (TIBAl) at 40 °C resulted in the transposition of an oxygen atom on the ring with the exocyclic carbon atom (Scheme 4).



Scheme 4. Typical example of the novel carbohydrate transposition.

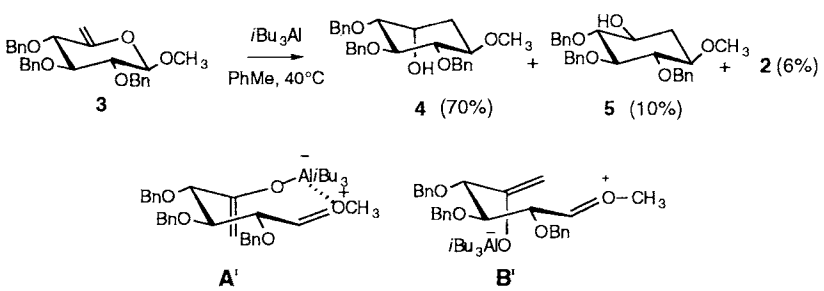
The only isolated product of the reaction (79%) was the secondary alcohol **2**, which was formed by the subsequent stereoselective reduction of the carbonyl group by TIBAl. Starting material (20%) was also recovered.

Although a detailed mechanism for the formation of **2** is still a matter of speculation (Scheme 5), the reaction is presumably initiated[13] by the coordination of the aluminum atom of TIBAl with the endocyclic enolic oxygen atom. This *endo* activation is followed by a ring opening step with the generation of the zwitterionic aluminum enolate intermediate **A**. Assuming that **A** retains its geometry on the time scale of the reaction, it may then undergo direct cyclization through a twist form,[15] thus keeping the anomeric stereochemical "memory". Alternatively, a rotation would give the intermediate **B**, which could then undergo cyclization through a chair-like six-membered ring. In this case, the electrostatic attraction between the positively charged oxygen and the negatively charged aluminum unit would hold the enolate in proximity to the C–O π bond (tight ion pair), which nicely explains the observed stereochemical outcome. In both cases the intramolecular aldol condensation goes through the favored[16] 6-*exo*-trig process. The final reduction of the keto group with TIBAl leads exclusively to the alcohol **2** by intramolecular hydrogen delivery from the less hindered β side.



Scheme 5. Probable mechanism of the transposition. Bn = benzyl.

Reaction of the vinyl acetal **3** under the same reaction conditions provided the three secondary alcohols **4** in 70%, **5** in 10%, and **2** in 6% yield (Scheme 6, physical and spectroscopic data



Scheme 6. Application of the transposition to a β-glucoside.

Table 1. Physical and spectroscopic data for **2**, **4**, **5**, **7**–**9**, **11**, **12**, and **14** [a].

2: $[\alpha]_D^{20} = -9$ ($c = 0.8$ in $CHCl_3$); ^1H NMR (250 MHz, $CDCl_3$): $\delta = 7.3$–7.1 (m, 15H, arom. H), 4.85–4.6 (m, 6H, 3 -CH_2Ph), 4.09 (t, 1H, $J(2,3) = 9.3$, $J(3,4) = 9.3$ Hz, H-3), 3.98 (dddd, 1H, $J(5,OH) = 9.5$, $J(4,5) = 3.3$, $J(5,6e) = 3.8$, $J(5,6a) = 2.0$ Hz, H-5), 3.6 (ddd, 1H, $J(1,2) = 2.9$, $J(1,6a) = 2.0$, $J(1,6e) = 3.8$ Hz, H-1), 3.55 (d, 1H, OH), 3.45 (s, 3H, OMe), 3.33 (dd, 1H, H-2), 3.29 (dd, 1H, H-4), 2.2 (dt, 1H, $J(6a,6e) = 15.0$ Hz, H-6e), 1.25 (dt, 1H, H-6a).

4: Syrup, $[\alpha]_D^{20} = +8$ ($c = 1.7$ in $CHCl_3$); ^1H NMR (250 MHz, $CDCl_3$): $\delta = 7.3$ (15H, arom. H), 4.8–4.55 (m, 6H, 3 -CH_2Ph), 4.05 (dddd, 1H, $J(4,5) = 3.1$, $J(5,6a) = 2.0$, $J(5,6e) = 4.4$, $J(5,OH) = 1.6$ Hz, H-5), 3.73 (t, 1H, $J(2,3) = 9.3$, $J(3,4) = 9.3$ Hz, H-3), 3.60 (ddd, 1H, $J(1,2) = 9.1$, $J(1,6a) = 12.0$, $J(1,6e) = 4.4$ Hz, H-1), 3.4 (s, 3H, OMe), 3.36 (dd, 1H, H-4), 3.30 (dd, 1H, H-2), 2.28 (dt, 1H, $J(6a,6e) = 14.0$ Hz, H-6e), 1.2 (ddd, 1H, H-6a).

5: White solid, m.p. = 95 °C; $[\alpha]_D^{20} = +35$ ($c = 0.7$ in $CHCl_3$); ^1H NMR (250 MHz, $CDCl_3$): $\delta = 7.3$–7.15 (s, 15H, arom. H), 5.0–4.6 (m, 6H, 3 -CH_2Ph), 3.5–3.1 (m, 5H, ring protons), 3.4 (s, 3H, OMe), 2.29 (dt, 1H, $J(1,6e) = 4.0$, $J(5,6e) = 4.0$, $J(6a,6e) = 12.0$ Hz, H-6e), 1.3 (ddd, 1H, $J(1,6a) = 12.0$, $J(5,6a) = 12.0$ Hz, H-6a).

7: White solid, m.p. = 70 °C; $[\alpha]_D^{20} = -3$ ($c = 0.95$ in $CHCl_3$); ^1H NMR (250 MHz, $CDCl_3$): $\delta = 7.2$ (m, 20H, arom. H), 4.9–4.5 (m, 8H, 4 -CH_2Ph), 4.01 (m, 1H, H-5), 3.85 (ddd, 1H, $J(1,2) = 9.4$, $J(1,6a) = 11.3$, $J(1,6e) = 4.3$ Hz, H-1), 3.75 (t, 1H, $J(2,3) = 9.4$, $J(3,4) = 9.4$ Hz, H-3), 3.4 (t, 1H, H-2) 3.4 (dd, 1H, H-4), 2.42 (bs, OH), 2.28 (dt, 1H, $J(5,6e) = 4.3$, $J(6a,6e) = 13.7$ Hz, H-6e), 1.30 (dd, 1H, $J(5,6a) = 4.0$ Hz, H-6a).

8: White solid, m.p. = 121 °C; $[\alpha]_D^{20} = +25$ ($c = 0.95$ in $CHCl_3$); ^1H NMR ($CDCl_3$, 250 MHz): $\delta = 7.2$ (m, 20H, arom. H), 4.92–4.55 (m, 8H, 4 -CH_2Ph), 3.55–3.34 (m, 4H, ring protons), 3.23 (t, 1H, $J = 9.0$ Hz), 2.28 (ddd, 1H, $J = 11.5$, $J = 4.2$, $J = 4.2$ Hz, H-6e), 1.37 (ddd, 1H, J(all) = 11.5 Hz, H-6a).

9: Syrup, $[\alpha]_D^{20} = +20$ ($c = 0.9$ in $CHCl_3$); ^1H NMR (250 MHz, $CDCl_3$): $\delta = 7.3$–7.1 (20H, arom. H), 4.9–4.5 (m, 8H, 4 -CH_2Ph), 4.1 (t, 1H, $J(2,3) = 9.2$, $J(3,4) = 9.2$ Hz, H-3), 4.0 (m, 1H, H-5), 3.9 (m, 1H, H-1), 3.7 (d, 1H, $J(5,OH) = 9.4$ Hz, OH), 3.32 (dd, 1H, $J(1,2) = 2.8$ Hz, H-2), 3.3 (dd, 1H, $J(4,5) = 3.4$ Hz, H-4), 2.2 (dt, 1H, $J(1,6e) = 3.9$, $J(5,6e) = 3.9$, $J(6a,6e) = 15.0$ Hz, H-6e), 1.3 (dt, 1H, $J(1,6a) = 2.0$, $J(5,6a) = 2.0$ Hz, H-6a).

11: White solid, m.p. = 117 °C; $[\alpha]_D^{20} = +3$ ($c = 1$ in $CHCl_3$); ^1H NMR (250 MHz, C_6D_6): $\delta = 7.3$–6.9 (m, 15H, arom. H), 4.8–4.32 (m, 6H, 3 -CH_2Ph), 3.95 (t, 1H, $J(1,2) = 8.7$, $J(2,3) = 8.7$ Hz, H-2), 3.73 (dd, 1H, H-3), 3.55 (m, 1H, H-5), 3.48 (ddd, 1H, $J(1,6a) = 10.7$, $J(1,6e) = 4.0$ Hz, H-1), 3.42 (m, 1H, H-4), 3.2 (s, 3H, OMe), 1.86 (ddd, 1H, $J(5,6a) = 2.9$, $J(6a,6e) = 13.5$ Hz, H-6a), 1.72 (ddd, 1H, $J(5,6e) = 4.0$ Hz, H-6e).

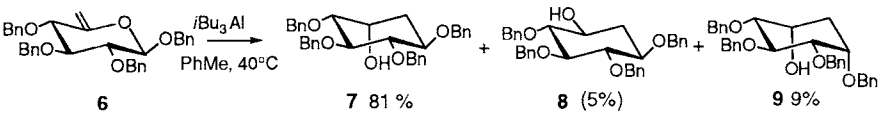
12: White solid, m.p. = 97 °C; $[\alpha]_D^{20} = +17$ ($c = 0.8$ in $CHCl_3$); ^1H NMR (250 MHz, $CDCl_3$): $\delta = 7.3$ (m, 15H, arom. H), 5.09, 4.55 (2d, 2H, $J = 12.5$ Hz, -CH_2Ph), 4.8 (s, 2H, -CH_2Ph), 4.70 (ABq, 2H, $J = 11.9$ Hz, -CH_2Ph), 3.85 (dd, 1H, $J(3,4) = 2.4$, $J(4,5) = 1.5$ Hz, H-4), 3.79 (t, 1H, $J(1,2) = 9.0$, $J(2,3) = 9.0$ Hz, H-2), 3.47 (ddd, 1H, $J(5,6a) = 11.8$, $J(5,6e) = 5.0$ Hz, H-5), 3.4 (s, 3H, OMe), 3.32 (dd, 1H, H-3), 3.10 (ddd, 1H, $J(1,6a) = 11.8$, $J(1,6e) = 5.0$ Hz, H-1), 2.1 (s, 1H, OH), 2.05 (ddd, $J(6a,6e) = 11.8$ Hz, H-6e), 1.67 (ddd, 1H, H-6a).

14: Syrup, $[\alpha]_D^{20} = -20$ ($c = 1.0$ in $CHCl_3$); ^1H NMR (250 MHz, $CDCl_3$): $\delta = 7.2$ (m, 15H, arom. H), 4.7–4.4 (m, 6H, 3 -CH_2Ph), 3.95 (dddd, 1H, $J(4,5) = 4.0$, $J(5,6a) = 8.0$, $J(5,6e) = 4.0$, $J(5,OH) = 9.6$ Hz, H-5), 3.75 (dd, 1H, $J(2,3) = 6.0$, $J(3,4) = 2.7$ Hz, H-3), 3.62 (dd, 1H, $J(1,2) = 7.8$ Hz, H-2), 3.62 (dd, 1H, H-4), 3.50 (ddd, 1H, $J(1,6e) = 8.0$, $J(1,6a) = 4.0$ Hz, H-1), 3.32 (s, 3H, OMe), 2.35 (d, 1H, OH), 2.01 (dt, 1H, $J(6a,6e) = 13.0$ Hz, H-6e), 1.65 (ddd, 1H, H-6a).

[a] All compounds gave correct elemental analyses.

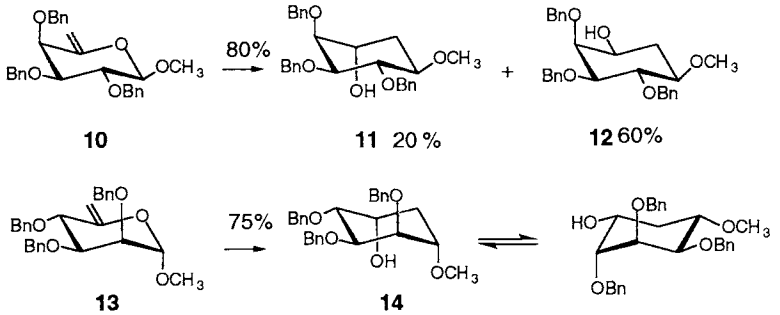
are given in Table 1). Interestingly, **4** and **5** (that is, 80% of the products) retain the stereochemical information of the anomeric center. Again, this reaction may proceed through the ion pair **A′** or the intermediate **B′**. Therefore, a distinctive feature of this entry to highly functionalized cyclohexanes is the retention of the anomeric stereochemical information in the starting glucoside. This is in sharp contrast to the Ferrier-II reaction, where the reaction inherently requires an *exo* cleavage to eject the aglycon.

In the same manner, the benzyl glucoside **6** was converted into the alcohol **7** (83%); isomers **8** (5%) and **9** (9%) were also isolated as minor products. Compound **7** has recently been prepared in racemic form from *myo*-inositol (Scheme 7).[17]



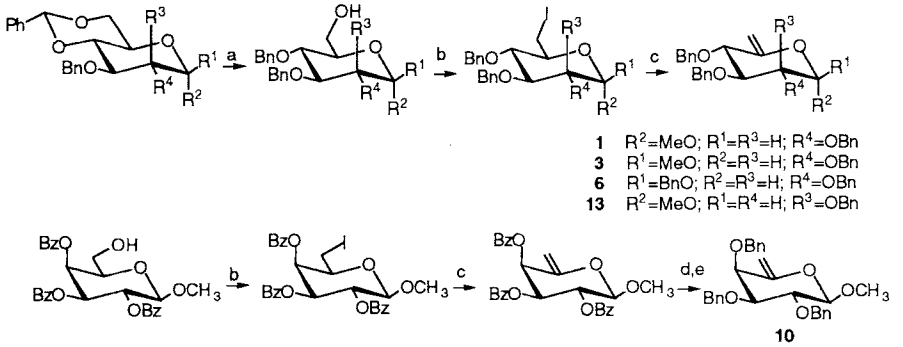
Scheme 7. An expedient synthesis of an optically active protected monodeoxygenated derivative of *myo*-inositol.

Finally, the same conditions were applied to vinyl acetals **10** and **13** (Scheme 8), which are derived from methyl β-D-galactopyranoside and methyl α-D-mannopyranoside, respectively (Scheme 9). In the case of **10**, the axially oriented benzyloxy group at C4 probably hinders reduction from the β side; compound **12** is the major product (60%).



Scheme 8. Application of the transposition to a β-galactoside and an α-mannoside.

In conclusion, we have developed a novel, stereoselective access to substituted cyclohexane derivatives, starting from hex-5-enopyranosides. A distinctive feature of the reaction is the retention of the anomeric stereochemical information. An extension to disaccharides and oligosaccharides is therefore attractive. It would also provide an expedient and stereoselective entry to pseudo disaccharides and oligosaccharides,[18] which are compounds of potential biological interest.[19]



Scheme 9. Preparation of the hex-5-enopyranosides: a) $LiAlH_4$, $AlCl_3$, CH_2Cl_2, ether, 30 °C (80%); b) I_2, Ph_3P, imidazole, toluene, 70 °C (80%); c) DBU, THF, reflux (75%); d) MeONa, MeOH, RT; e) BnBr, NaH, DMF, RT (80%); Bz = benzoyl, DBU = 1,8-diazabicyclo[5.4.0]undec-7-ene.

Experimental Section

A 1 M solution of triisobutylaluminum in toluene (1.8 mL, 1.8 mmol) was added to **1** (200 mg, 0.45 mmol) in freshly distilled, dry toluene (15 ml) at 0 °C. The reaction mixture was then stirred at 40 °C for 6 h. After completion of the reaction, excess triisobutylaluminum was quenched with ice-cold water. The reaction mixture was filtered, and the organic phase separated. The water layer was extracted twice with ethyl acetate. The combined organic fractions were dried ($MgSO_4$) and concentrated, and the residue subjected to flash chromatography (eluent: cyclohexane/ethyl acetate 2/1) to give **2** as a syrup(158 mg, 79%).

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Transition Metal Germylene Complexes as Hydrogenation Catalysts: The Synthesis of a Rare Bis(amino)germane**

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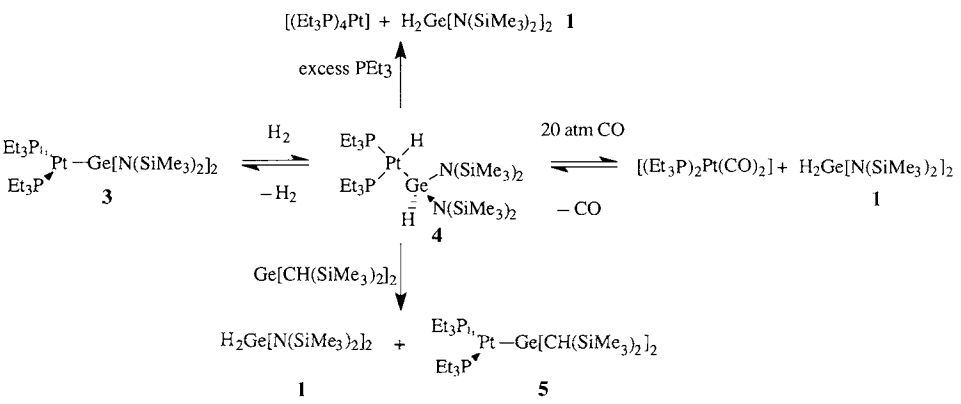
Molecules in which germanium is bound to both hydrogen and nitrogen are surprisingly rare.[1] Of the known examples, namely, H_3GeN_3,[2] H_3GeNCS,[3] H_3GeNCO,[3] $(H_3Ge)_3N$,[4] $F_3CN{=}GeH_2$,[5] $H_3GeN{=}C{=}NGeH_3$,[6] and $Ph_2(H)GeNR_2$,[7] the first three complexes contain pseudohalogen ligands and thus resemble the well-established halogermanes. The fourth example, $(H_3Ge)_3N$, is widely known to exhibit delocalized π bonding and enhanced Ge–N bond strength, whereas $Ph_2(H)GeNR_2$ is unstable and readily disproportionates to Ph_2GeH_2 and $Ph_2Ge(NR_2)_2$. Other than $(H_3Ge)_3N$, we are not aware of any aminogermanes of stoichiometry $HGe(NR_2)_3$, $H_2Ge(NR_2)_2$, or H_3GeNR_2 previously reported. In fact, amino groups are commonly employed as leaving groups when germanes are formed by hydrogenation reactions, which makes the easily accessible complexes of general stoichiometry $Cl_xGe(NR_2)_y$ unsuitable as precursors to aminogermanes.[8] Standard approaches for making aminogermanes, which involve reagents such as $LiAlH_4$ and $NaBH_4$, typically result in amine formation. Recently, we have synthesized $H_2Ge[N(SiMe_3)_2]_2$ (**1**) and $H_2Ge[CH(SiMe_3)_2]_2$ (**2**) by both stoichiometric and catalytic routes using well-defined, three-coordinate, Group 10 metal germylene complexes of general stoichiometry $[(R_3P)_2MGeR'_2]$.[9] The three-coordinate catalysts are similar to compounds previously reported by Lappert and co-workers.[10] In addition, we have found that Ni^0 complexes such as $[Ni(cod)_2]$ (cod = 1,5-cyclooctadiene) can serve as catalyst precursors, even in the absence of phosphane.

The initially discovered routes to **1** and **2** made use of **3** and **4**, as summarized in Scheme 1:[11] Treatment of a benzene



Scheme 1. Synthetic route to **1**.

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