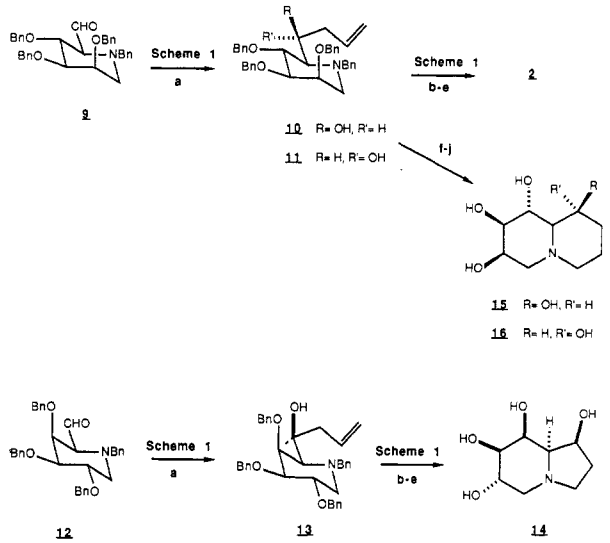
Scheme II[a]



[a] (f) acetic anhydride, pyridine; (g) borane–dimethyl sulfide, THF; (h) MsCl, Na_2CO_3, CH_2Cl_2; (i) H_2, Pd/C, 3:1 EtOH/CH_3OH; (j) K_2CO_3, 3:1 CH_3OH/H_2O.

and **16** as shown in Scheme II. The ^1H NMR spectrum of **15** showed a 1.8-Hz coupling of the C-1 proton to the adjacent cis hydrogen at the ring fusion, trans coupling in isomer **16** resulting in a coupling constant of 8.9 Hz.

6-Epicastanospermine, recently isolated from seeds of the Australian tree *Castanospermum australe*, had been assigned the absolute configuration shown in **2** by analogy with **1**.[3b] Although spectra and chromatographic properties of natural and synthetic **2** were identical, chiroptical measurements revealed them to be enantiomeric structures. Thus the natural (dextrorotatory) form of **2** must correspond to L-mannose in its hydroxyl group configuration, which helps to explain why (+)-**2** was a weak inhibitor of α-mannosidase.[1b] Unfortunately (−)-**2** was an even poorer inhibitor when tested against jackbean α-mannosidase. We conclude that structure–activity relationships in castanospermine and its congeners are far more subtle than has been suggested in the biochemical literature.

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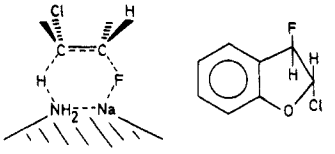
Unusual Regiospecificity in Syn Elimination from *trans*-2-Chloro-3-fluoro-2,3-dihydrobenzofuran Promoted by Complex Base[1]

Summary: Elimination from *trans*-2-chloro-3-fluoro-2,3-dihydrobenzofuran induced by $NaNH_2$–NaO-*t*-Bu in THF results in syn dehydrofluorination to the exclusion of β-aryl-activated syn dehydrochlorination.

Sir: In 1979, we reported[2] a most unusual regiospecificity in syn eliminations from *trans*-1-fluoro-2-halocyclohexanes induced by a mixture of $NaNH_2$–NaO-*t*-Bu in THF ("complex base"[3]). Thus, both *trans*-1-bromo-2-fluorocyclohexane and *trans*-1-chloro-2-fluorocyclohexane gave dehydrofluorination products exclusively.[2] Such reversal of the normal leaving group element effect ordering of I > Br > Cl ≫ F[4] was ascribed to special interactions between the fluoro leaving group and the base counterion in the syn-elimination transition-state **1**. Subsequently, it was demonstrated that preferential loss of the "normally poorer" halogen leaving group in such syn eliminations disappears in the presence of 15-crown-5.[5] Complexation of Na^+ by the crown ether prohibits the special leaving group–Na^+ interactions shown in **1**.



1 **2**

To further probe the propensities for competitive syn dehydrochlorination and syn dehydrofluorination in elimination reactions induced by complex base, we prepared a sample of *trans*-2-chloro-3-fluoro-2,3-dihydrobenzofuran[6] (**2**). Baciocchi and co-workers[7] observed only 3-fluorobenzofuran, the product of β-aryl-activated syn dehydrochlorination, in reactions of **2** with EtOK–EtOH, *t*-BuOK–*t*-BuOH, and *t*-BuOK–*t*-BuOH in the presence of 18-crown-6.

Compound **2** (2.9 mmol) was added to a magnetically stirred heterogeneous mixture of $NaNH_2$ (4.3 mmol) and in situ generated NaO-*t*-Bu (4.3 mmol) in 10 mL of THF at room temperature under nitrogen.[5] After 1 min, a sample was removed and quenched by injection into a solution of THF–H_2O (9:1) which contained *o*-xylene as an internal standard. Analysis by GC and GC/MS showed complete conversioin of **2** into 2-chlorobenzofuran (>97% yield), the product of syn dehydrofluroination. With complex base, there is a striking reversal of the elimination regiospecificity from that reported for more ordinary base–solvent combinations. Thus the special transition-state interactions depicted in **1** are shown to produce exclusive syn dehydrofluorination even when a competitive syn dehydrochlorination process would have been facilitated by a β-aryl-activating group.

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