The Halogenolysis of Organoboranes

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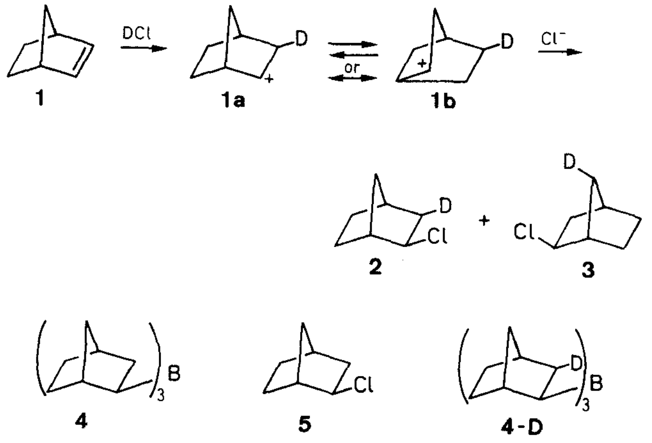
Transmercuration of tri-*exo*-2-norbornylborane followed by chlorinolysis of the resultant organoborane is a low yield ($\leq$ 5 %) method of producing *exo*-2-norbornyl chloride. The primary source of this low yield is the inefficient transmercuration of the sterically restricted organoborane. Yields of alkyl halide are substantially higher (up to 63 %) when the organoborane undergoes direct chlorinolysis promoted by boron trichloride. Even higher yields (approaching 80 %) are obtained when brominolysis of the organoborane is carried out. Controls suggest that at least part of the reason for the higher yield with bromine is due to the greater stability of the product under the reaction conditions. Despite the general retention aspects (*exo*-borane gives largely *exo*-halide) of these halogenolyses, deuterium labeling studies show that these reactions are accompanied by substantial Wagner–Meerwein rearrangement, very possibly due to boron trihalide induced rearrangement of the norbornyl halide product.

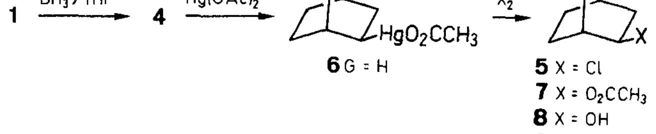
Hydroboration is one of the most well known organic reactions. An important advantage of hydroboration is the ability to readily convert alkenes to organoboranes, which in turn can be readily converted to other compounds such as alcohols and amines.[1] A reaction that is much less straightforward is the conversion of organoboranes to halides. Although there are a number of reports of halogenolyses of organoboranes,[2] many of these suffer from one or more of the following: low yields, inefficient use of all three alkyl groups of the organoborane, and ill-defined mechanisms.

Sometime ago we[3] and others[4] were interested in the mechanism of addition of hydrogen chloride to norbornene, a reaction mediated by carbocations. It is known that such electrophilic additions to norbornene give products showing substantial Wagner–Meerwein rearrangement. Thus, addition (Scheme 1) of deuterium chloride (DCl) to norbornene (**1**) is known to give (via **1a** and **1b**) both **2** and **3**. Since hydroboration is well known in the norbornane system,[5] the conversion of organoboranes such as the tri-*exo*-compound **4** to halides such as *exo*-2-norbornyl chloride **5** was of synthetic and stereochemical interest, not only to determine whether *exo*-borane **4** gave only *exo*-halide **5**, but to also identify conditions under which *cis*-*exo*-deuterated borane, **4-D**, could be converted to only *cis*-*exo*-deuterated chloride **2**, in the absence of Wagner–Meerwein isomer **3**.

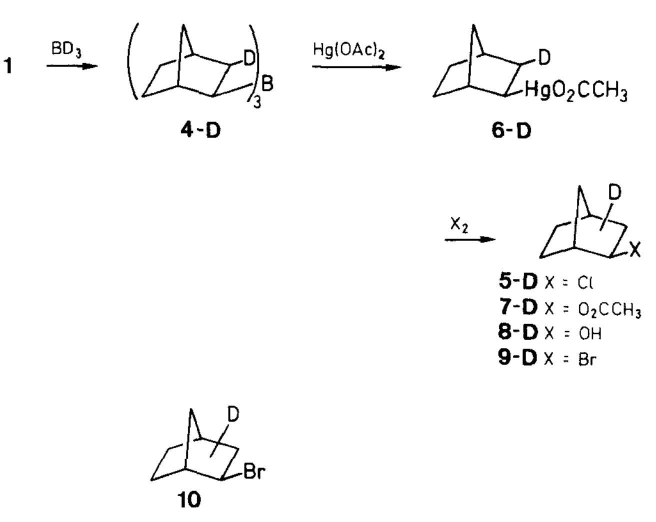


Scheme 1

Tufariello[6] reported that terminal alkenes after hydroboration could be converted to primary organomercurials by treatment with mercury(II) compounds, and the resulting organomercurials could in turn be halogenolyzed to bromides (by reactions with well-defined mechanisms[7]). This suggested the route to halides shown in Scheme 2 (with BD_3 addition: Scheme 2-D). Since Tufariello had only modest success with an internal alkene (which gave only low yields of secondary organomercurial), we felt a broad-based study of these reactions was in order; we were, however, never able to carry out Scheme 2 in more than 5 % yield. Controls indicated that the hydroboration, as expected,[1] occurred in high yield. Jensen's studies[7] clearly indicate that halogenolysis of organomercurials should proceed in high yield. Thus, our study focused on modifications of the second step. Despite a large number of experiments in which we changed reaction solvent and the identity of the mercury compound used, we were never able to improve this step. Analysis of the norbornyl chloride from Scheme 2-D showed 89.4 % D incorporation and roughly equal amounts of **2** and **3**.[8]



Scheme 2



Scheme 2-D

Only when boron trichloride was used to promote halogenolysis of organoborane (Scheme 3) were we able to produce norbornyl chloride **5** in reasonable (30–63 %) yield (Table 1). The mechanism likely involves Lewis acid

Table 1. Chlorinolysis of tri-*exo*-2-Norbornylborane[a]

BCl_3[b]	Temp., °C (Time, h)[c]	Yield of **5** (%)
0.1	−70 (1), 0 (2), 25 (96)	43
0.3	−70 (1), 0 (2), 25 (96)	46
0.5	−70 (1), 0 (2), 25 (96)	30
0.1	−70 (6), 0 (1), 25 (46)	38
0.1	−70 (24), 0 (1), 25 (46)	31
0.1	−70 (1), 0 (1), 25 (46)	43
0.1	−70 (1), 0 (6), 25 (46)	50
0.1	−70 (1), 0 (24), 25 (46)	40
0.1	0 (6), 25 (46)	63
0.1	0 (6), 25 (24)	63
0.1	−70 (1), 0 (6), 25 (46)	50

[a] The stoichiometry is three mole equivalents of chlorine for every mole of organoborane. All reactions were run in CH_2Cl_2.

[b] Mole equivalents of BCl_3 per mole of organoborane.

[c] For example, in the first run the reagents were subjected successively to temperatures of −70 °C, 0 °C and 25 °C for the noted times.

interactions of boron trihalide as described in Scheme 4. We cannot exclude a modification of this mechanism in which a free norbornyl anion **11** is generated, as this anion should be electrophilically trapped largely on the *exo*-side to form chloride **5**. Of interest is the fact that we obtained largely (90 + %) *exo*-chloride. The minor amount of *endo*-product (detected by GC-MS) could be formed in the second rather than the first step (at least 99.5% *exo*-hydroboration of norbornene has been reported[5]), although we cannot exclude the possibility that boron trichloride induces *exo-endo* equilibration of product chloride. When deuterium-labeled compounds were used (Scheme 3-D), the final chloride product contained substantial amounts of both **2** and **3**. At this point it is unclear whether the Wagner–Meerwein scrambling was part of Scheme 3-D (likely step 2) or whether only *cis-exo* labeled product **2** was formed which subsequently was converted to a **2**/**3** mixture by reaction of the chloro group with boron trichloride (Scheme 5). The fact that (to our knowledge) *cis*-3-deuterio-2-*exo*-norbornenyl chloride **2** has never been made stereochemically pure prevents us from carrying out the important control study of examining this compound's ability to undergo Wagner–Meerwein reaction under the conditions of our halogenolysis reactions.

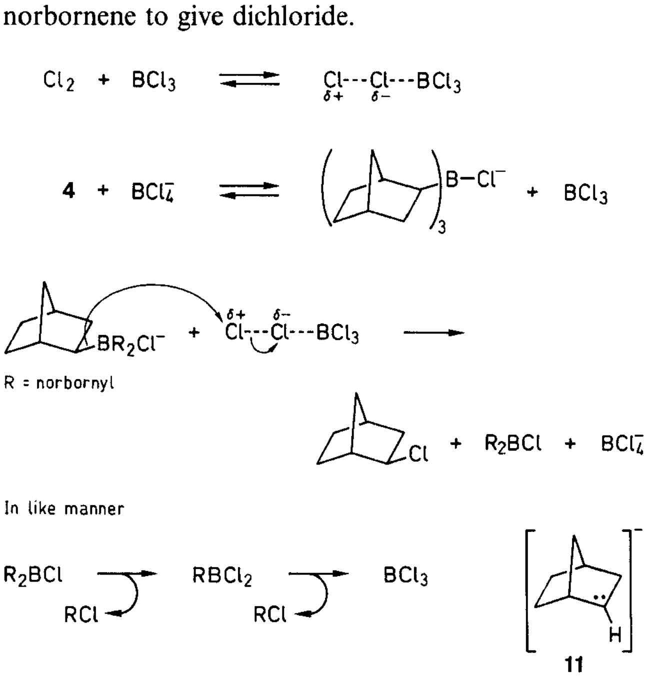
$$\mathbf{1} \xrightarrow{BH_3/THF} \mathbf{4} \xrightarrow{Cl_2/BCl_3} \mathbf{5}$$

Scheme 3

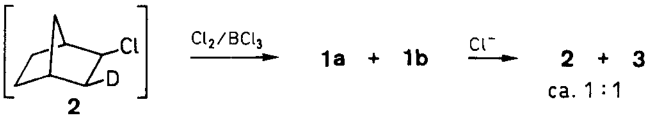
$$\mathbf{1} \xrightarrow{BD_3/THF} \mathbf{4\text{-}D} \xrightarrow{Cl_2/BCl_3} \mathbf{5\text{-}D(2+3)}$$

Scheme 3-D

The next phase of our research focused on our desire to find conditions for maximizing the yield, while minimizing rearrangement. We thus carried out this reaction with variations in stoichiometry and reaction temperatures (Table 1). The boron trichloride stoichiometry was varied over 0.1–0.5 equivalents; the best yield here (46%) was obtained with 0.3 moles of boron trichloride. In one run, the product was found by ^1H NMR to be 90% *exo*/10% *endo* (by integration of the proton geminal to halogen); the latter product requires consideration of the *endo*-chloride formation processes discussed above. Longer times at room temperature resulted in lower yields (31–38%) and longer times at 0 °C resulted in a better yield (50% at 6 hours). Stirring at room temperature is likely ineffective in promoting chlorinolysis due to loss of boron trichloride gas at this higher temperature. The highest yield (63%) occurred when the reagents were combined at 0 °C for 1 hour, and then stirred at 0 °C for 6 hours followed by 24 hours at room temperature. When samples of norbornyl chloride were subjected to control conditions (see Table 1), some consumption of the monohalide was observed; GC-MS analysis showed that dichloronorbornanes had formed. Both the control experiment and boron trichloride induced chlorinolysis of organoborane experiments gave rise to similar product compositions (GC-MS). Clearly there is a delicate balance between the rate of norbornyl halide formation vs. conditions needed to minimize Wagner–Meerwein rearrangement and norbornyl chloride consumption. It seems reasonable to expect that the route to dichloride involves boron trichloride induced conversion of the monochloride to the norbornyl cation, proton loss to form norbornene, and addition of molecular chlorine to the so-formed norbornene to give dichloride.



Scheme 4



Scheme 5

A similar reaction study has been done for brominolysis (Table 2). Norbornyl bromide yields in the 60–76%

Table 2. Brominolysis of tri-*exo*-2-Norbornylborane[a]

BBr_3[b]	Temp., °C (Time, h)[c]	Yield of **9** (%)
0.1	0 (1), 25 (96)	61[d]
0.3	0 (1), 25 (96)	66[d]
0.5	0 (1), 25 (96)	76[d]
0.7	0 (1), 25 (96)	74[d]
1.0	0 (1), 25 (96)	62[d]
0.1	0 (6), 25 (24)	63[d]
0.5	0 (24), 25 (24)	106[d,e]
0.1	0 (2), 25 (96)	81.1[f]
0.25	0 (2), 25 (96)	63.8[f]
0.50	0 (2), 25 (96)	61.5[f]
1.0	25 (96)	103[e,f]

[a] The stoichiometry is three mole equivalents of bromine for every mole of organoborane.

[b] Mole equivalents of BBr_3 per mole of organoborane.

[c] For example, in the first run the reagents were subjected successively to temperatures of 0 °C, and then 25 °C, for the noted times.

[d] Solvent: CH_2Cl_2.

[e] CONTROL.

[f] Solvent: benzene/CCl_4.

range were obtained. Unlike the chloride, norbornyl bromide is stable under halogenolysis conditions (control entry, Table 2). Norbornyl bromide product was found (^1H NMR) to be 93% *exo*/7% *endo*.

In summary, our results indicate that these halogenolyses are useful reactions. With care in the selection of reaction conditions, both reactions occur with the conversion of the better part of all three alkyl groups to alkyl halide, a result that has not always been obtained in earlier studies.[2] We are continuing to study these reactions by detailed examination of the fate of deuterium label under brominolysis conditions and by extending the scope of this reaction to iodination.

All reagents were reagent grade chemicals purchased from Aldrich Chemical Co., unless otherwise stated. BCl_3 was obtained from Aldrich as a complex with CH_2Cl_2 in CH_2Cl_2 solvent. IR spectra were obtained from a Perkin-Elmer 1310 spectrometer. Liquid samples were run neat. NMR spectra were obtained from PE R-20 (60 MHz), Nicolet NT-200 (200 MHz), and GE QE 300 (300 MHz) spectrometers. $CDCl_3$ was used as the solvent and TMS as internal standard. GC-MS analyses were carried out on a Hewlett-Packard 5995 instrument with a fused silica capillary column at 120 °C.

Preparation of *exo*-Norbornyl Chloride (5) by Boron Trichloride Promoted Chlorinolysis of tri-*exo*-2-Norbornylborane (4); General Procedure:

A 100 mL three-necked flask is equipped with a reflux condenser topped by a $CaCl_2$ drying-tube, a gas dispersion tube, a thermometer and a magnetic stirring bar. All glass is predried in an oven and cooled after assembly with a steam of dry deoxygenated N_2 admitted through the gas dispersion tube. Dry deoxygenated N_2 is prepared by passing N_2 through a series of traps containing, in order, Fieser's solution (alkaline sodium anthraquinone beta-sulfonate and $Na_2S_2O_4$[9]) to absorb O_2, an empty trap, conc. H_2SO_4 to absorb H_2O, and finally anhydr. KOH for H_2O and acid absorption.

In a typical experiment crude **4** (7 g, 22.2 mmol) prepared by the hydroboration method described below) in CH_2Cl_2 (33 mL) as well as an additional charge of CH_2Cl_2 (30 mL) were added through the thermometer port. This solution was cooled to − 65 °C with a Dewar flask containing a dry ice/*i*-PrOH mixture. The N_2 line was disconnected, the thermometer removed, and Cl_2 gas was added through the gas dispersion tube as monitored by a calibrated F-1100 flow meter (Gilmont Instruments Incorporated). Then BCl_3-CH_2Cl_2 (2.3 mL, 1.0 M solution in CH_2Cl_2) was added with a syringe. This induced a slow generation of a greenish-yellow color. The solution was successively stirred at − 65 °C, 0 °C, and r. t. (Table 1). During the 0 °C time the solution first became colorless, then light yellow. During the r. t. stirring, the solution became brownish yellow. Methylene chloride was removed by a rotary evaporator and a crude yield was determined by weighing. Analysis by GC-MS allowed for determination of the yield of pure norbornyl chloride (yields, see Table 1). The norbornyl chloride could be recovered by vacuum distillation as described under the section on the preparation of an authentic sample. The identity of the norbornyl chloride obtained in this way was established by GC-MS coinjection, IR, and NMR. All results indicated that the sample was identical to the authentic sample whose production is described below. ^1H NMR analysis allowed for *exo*/*endo* composition determination by integrating the area under the signal for the proton on the carbon bearing the chlorine (at $\delta = 3.90$ for *exo*-norbornyl chloride and at $\delta = 4.25$ for *endo*-norbornyl chloride).

Labeled chloride was prepared according to Scheme 3 using labeled borane, **4-D**, produced by one of two methods: deuteroboration was carried out by a procedure like that described above for hydroboration except $LiAlD_4$ (Alfa, 99% D) in THF was treated with $BF_3 \cdot Et_2O$ to produce deuteroborane which was carried by a dry N_2 stream into a THF solution of norbornene to form **4-D**. Alternatively, BD_3–THF complex (commercially available from Aldrich Chemical Co.) was used to carry out the formation of **4-D**.

Preparation of *exo*-Norbornyl Bromide (9) by Boron Tribromide Promoted Brominolysis of tri-*exo*-2-Norbornylborane (4); General Procedure:

A 200 mL three-necked flask was equipped with a reflux condenser topped by a $CaCl_2$ drying-tube, a thermometer and a magnetic stirring bar. All glass was predried in an oven and cooled after assembly with a stream of dry deoxygenated N_2 (see above) admitted through a hyperdermic needle in a septum on one neck.

In a typical experiment crude **4** (7 g, 22.2 mmol) (prepared by the hydroboration method described below) in CH_2Cl_2 (33 mL) as well as an additional charge of CH_2Cl_2 (35 mL) were added through the thermometer port. This solution was cooled to 0 °C with an ice-water bath. The N_2 line was disconnected, the thermometer removed, and Br_2 (10.66 g, 66.6 mmol) was added through the thermometer port. Then BCl_3 (2.2 mL) was added with a syringe through the septum. This induced a red-brown solution color. The solution was successively stirred at 0 °C and r. t. (Table 2). The final red-brown solution was added to H_2O (25 mL), filtered, and the separated organic layer was washed with sat. aq $NaHCO_3$ (25 mL), 25% aq sodium bisulfite solution and finally with H_2O (25 mL). This brown solution was dried (Na_2SO_4) and the CH_2Cl_2 was removed by simple distillation. The crude *exo*-norbornyl bromide produced in this way was weighed and subjected to GC-MS analysis resulting in the yields listed in Table 2. The identity of the norbornyl bromide obtained in this way was established by GC-MS coinjection, IR, and ^1H NMR. All results indicated that the sample was identical to the authentic sample whose production is described below.

Preparation of Authentic Samples of *exo*-Norbornyl Chloride (5) and Bromide (9):

Both compounds were prepared by essentially the same procedure as those reported in the literature. Authentic **5** was prepared by the addition of HCl to norbornene as described by Schmerling[10] and by Wilcox.[11] Fractional distillation (43–45.5 °C at aspirator pressure) gave chloride whose spectra proved identical to literature spectra. The refractive index was $n_D^{26} = 1.4808$ (corrected was $n_D^{20} = 1.4813$). Lit.[10,12] $n_D^{20} = 1.4823$, $n_D^{25} = 1.4842$. The chemical shift of the *endo* proton (α to Cl) was $\delta = 3.90$, and the *exo*, $\delta = 4.25$. Authentic **9** was prepared by the addition of hydrobromic acid to norbornene as described by Roberts.[13] Fractional distillation (64–66 °C at aspirator pressure) gave bromide whose spectra proved identical to literature spectra.[13] The refractive index was $n_D^{26} = 1.5105$ (corrected was $n_D^{20} = 1.5110$). Lit.[13] $n_D^{25} = 1.5126$.

Preparation of tri-*exo*-2-Norbornylborane (4) by Hydroboration of Norbornene (1):

This procedure was a modified form of the one reported by Lane[2] and Kawakami.[5] A 250-mL flask was equipped with a reflux condenser ($CaCl_2$ drying tube), thermometer, magnetic stirring bar and a pressure-equalizing dropping funnel. All glassware was preheated overnight, assembled and dried with a stream of dry deoxygenated N_2 (see above) introduced by a syringe needle through a septum on the dropping funnel. The reaction flask was charged at r.t. with **1** (18.8 g, 0.2 mol) and dry THF (10 mL). The system was flushed again with N_2 and the colorless homogeneous solution was cooled with stirring in an ice bath to 5–10°C. Then 1.0 M borane–THF complex in THF (80 mL, 0.067 mol plus 20% excess) was added to the dropping funnel with a syringe and this was slowly added dropwise to the norbornene solution. The resulting colorless homogeneous mixture was allowed to warm to 20–30°C and stirred for 2.5 h. The mixture was again cooled to 5–10°C (ice bath) and excess hydrides were destroyed by careful addition of distilled H_2O (3 mL). This cold solution was stirred for 10 min and allowed to warm to r.t. THF was removed under reduced pressure resulting in a white waxy substance (20–21 g, ca. 100% crude yield). This product was stored under N_2 with refrigeration in a vessel wrapped with aluminum foil.

Preparation of Deuterium Labeled *exo*-Norbornyl Chloride (5-D) by Transmercuration followed by Chlorinolysis of tri-*exo*-[[3-^{2}H]-2-Norbornylborane] (4-D, Scheme 2-D):

Deuteroboration was carried out by a procedure like that described above for hydroboration except $LiAlD_4$ (Alfa, 99% D) in THF was treated with $BF_3 \cdot Et_2O$ to produce deuteroborane which was carried by a dry N_2 stream into a THF solution of norbornene. Solvent was removed and product **4-D** (3 g, 0.01 mol) was dissolved in dioxane (50 mL). To this was added $Hg(OAc)_2$ (9.6 g) and this mixture was allowed to reflux for 24 h. The dioxane was removed with a rotatory evaporator and pyridine (50 mL) was added to the reaction vessel. The pyridine solution was cooled to −30°C. Cl_2 gas (94.3 g, 0.06 mol, a two-fold excess) was admitted to the solution through a frit over 30 min maintaining a temperature of no higher than −30°C. The mixture was allowed to warm to r.t. and Et_2O (50 mL) was added. This solution was cooled in an ice bath while conc. HCl (100 mL) was added to neutralize the pyridine. The resulting acidic solution was washed with Et_2O (3 × 100 mL), and the combined Et_2O extracts were washed with conc. HCl (25 mL), followed by H_2O (2 × 25 mL). The Et_2O solution was dried ($CaCl_2$) and the solvent was removed (rotatory evaporator). The residue was distilled at 0.5 Torr (Hg manometer) and the distillate was collected in an acetone/dry-ice cooled receiver. GC analysis of this distillate showed a yield (based on norbornene) of 0.7% (0.028 g, 2×10^{-4} mol) of labelled *exo*-norbornyl chloride, 5.9% (0.096 g) of labelled *exo*-norborneol and 17.6% (0.285 g) of labelled *exo*-norbornyl acetate. Mass spectral analysis (molecular ion analysis) showed 89.4% deuterium incorporation. ^{1}H NMR analysis (60 MHz) of the proton alpha to the chlorine indicated that it appeared to be comprised of roughly equal contributions of the doublet of doublets expected for *cis-exo* labeled chloride **2** and the apparent triplet expected for Wagner–Meerwein rearranged isomer **3**; the latter is expected to be identical in appearance to the signal expected for the unlabelled chloride **5**.[3]

When the same reaction was done using unlabelled compounds (Scheme 2), only 1–5% yields were realized, despite the use of a wide range of solvents (THF, dioxane, pyridine, diglyme, DMSO, with dioxane giving the highest yield). Moreover changing from $Hg(OAc)_2$ to $Hg(NO_3)_2$ did not enhance the yield. Extensive reflux during transmercuration also did not improve the yield.

Controls (treatment of the product of hydroboration with Br_2 showing negligibly small amounts of unreacted norbornene, and oxidation of the organoborane to *exo*-2-norborneol in 90% + yield[1]) indicated that the hydroboration occurred in virtually quantitative yield.

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Jensen, F.R.; Rickborn, B. *Electrophilic Substitution of Organomercurials*; McGraw-Hill: N.Y., 1968.

(8) In view of the well known *syn-exo* stereochemistry of deuteroboration[5] and the fact that we used retention conditions[7] for the chlorinolysis step, it seemed likely that the Wagner–Meerwein scrambling occurred in step 2 of Scheme 2. An interesting aside is the fact that Scheme 2-D resulted in a higher yield of *exo*-acetate **7** and *exo*-alcohol (**8**, easily formed from **7** in the H_2O work-up) than chloride (**5-D**, less than 1% yield).

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