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A New Class of Chiral Organogermanes Derived from C_2-Symmetric Dithiols: Synthesis, Characterization and Stereoselective Free Radical Reactions

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A new class of dithiostannanes and dithiogermanes have been prepared from 1,1′-binaphthyl-2,2′-dithiol and 3,3′-bis(trimethylsilyl)-1,1′-binaphtho-2,2′-dithiol. While reduction of 4-butyl-4-chloro-3,5-dithia-4-stanna-cyclohepta[2,1-*a*;3,4-*a*′]dinaphthalene to the corresponding tin hydride was unsuccessful, 4-*tert*-butyl-3,5-dithia-4-germa-cyclohepta[2,1-*a*;3,4-*a*′]dinaphthalene and 4-*tert*-butyl-2,6-bis(trimethylsilyl)-3,5-dithia-4-germa-cyclohepta[2,1-*a*;3,4-*a*′]dinaphthalene were obtained by reduction of the parent germanium chlorides with $NaBH_4$ and $LiBH_4$, respectively. Kinetic constants for hydrogen transfer to a primary alkyl radical were measured for both germanium hydrides. Reduction of α-halo carbonyl compounds by these germanium hydrides occurs with moderate ee values (up to 42%), while hydrogermylation of methyl methacrylate occurs with low selectivity (<3/1) for the former hydride but high selectivity (>10/1) for the latter.

Introduction

Stereoselectivity in reactions of acyclic radicals is a rapidly growing, yet still challenging field of radical chemistry.[1] One way in which stereoselectivity can be achieved is by use of chiral reagents that are analogues of the popular tin hydride and, to a lesser extent, silicon and germanium hydride reducing agents. Chiral, enantiomerically pure, tin and germanium hydrides are known,[2,3] but to this date only a few of them have been used for stereoselective free radical reactions.

To avoid possible racemization problems associated with metal hydrides possessing an asymmetric metal center, in 1996 we introduced the first chiral tin hydride derived from a C_2-symmetric binaphthyl ligand.[4] Since then, the groups of Metzger[5] and Schiesser[6] have synthesized more chiral tin hydrides based either on a C_2-symmetric substituent or chiral ligands and proven that they can indeed be used as stereoselective radical reducing agents (either alone or in conjunction with chiral Lewis acids)[7] with high ee values[6] (>90%).

We continued to elaborate on the C_2-symmetric derived metal hydrides by exploring different patterns of substitution in the C_2-symmetric ligand. We started by exploring the replacement of metal−carbon bonds with metal−sulfur bonds, and observing how this affects both the stability and the reactivity of the resulting metal hydrides. This eventually led us to synthesize a new class of chiral germanium hydrides as alternatives to the traditional tin hydrides, and a preliminary report on some of this work has appeared.[8] We now report the

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(1) (a) Sibi, M. P.; Porter, N. A. *Acc. Chem. Res.* **1999**, *32*, 163. (b) Curran, D. P.; Porter, N. A.; Giese, B. *Stereochemistry of Radical Reactions*; VCH: Weinheim, Germany, 1996. (c) Giese, B. *Angew. Chem., Int. Ed. Engl.* **1989**, *28*, 969.

(2) (a) Gielen, M. *Top. Curr. Chem.* **1982**, *104*, 57. (b) Vitale, C. A.; Podestá, J. C. *J. Chem. Soc., Perkin Trans. 1* **1996**, 2407 and references therein. (c) Schumann, H.; Wassermann, B. C.; Pickardt, J. *Organometallics* **1993**, *12*, 3051 and referenced cited therein. (d) Pratt, R. M.; Thomas, E. J. *J. Chem. Soc., Perkin Trans. 1* **1998**, 727 and referenced cited therein.

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(4) Nanni, D.; Curran, D. P. *Tetrahedron: Asymmetry* **1996**, *7*, 2417.

(5) (a) Schwarzkopf, K.; Blumenstein, M.; Hayen, A.; Metzger, J. O. *Eur. J. Org. Chem.* **1998**, 177. (b) Blumenstein, M.; Schwarzkopf, K.; Metzger, J. O. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 235. (c) Schwarzkopf, K.; Metzger, J. O.; Saak, W.; Pohl, S. *Chem. Ber./Recl.* **1997**, *130*, 1539.

(6) (a) For a recent review see: Schiesser C. H. *Aust. J. Chem.* **2001**, *54*, 89. (b) Schiesser C. H. *Aust. J. Chem.* **2001**, *54*, 199. (c) Dakternieks, D.; Dunn, K.; Perchyonok, V. T.; Schiesser, C. H. *Chem. Commun.* **1999**, 1665.

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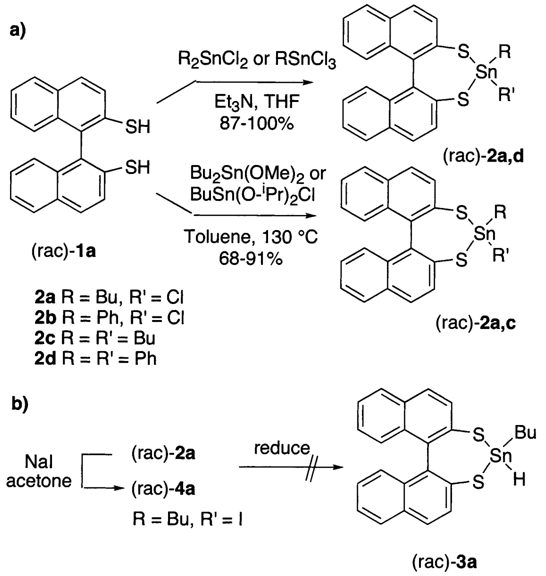
SCHEME 1. Synthesis of Dithiostannanes 2a−d



synthesis, detailed characterization, and reactivity data for these novel germanium hydrides.

Results and Discussion

Synthesis and Characterization. The tin hydride that we had previously synthesized (4,5-dihydro-4-methyl-3*H*-dinaphtho[2,1-*c*:1′,2′-*e*]stannepin)[4] suffered from partial cleavage of the benzylic carbon−tin bond in solution at room temperature. To strengthen the bond to tin, we decided to replace the benzylic $-CH_2-$ groups with sulfur atoms, by using 1,1′-binaphthyl-2,2′-dithiol **1a**[9] as the starting template. Racemic 1,1′-binaphthyl-2,2′-dithiol **1a** reacted smoothly with 1.1 equiv of R_2SnCl_2 or $RSnCl_3$ (R = Bu or Ph) in the presence of triethylamine to afford compounds **2a**−**d** in excellent yields (Scheme 1a). Alternatively, treatment of **1a** with butyl(chloro)tin diisopropoxide [Bu(Cl)Sn(O*i*-Pr)$_2$] or dibutyltin dimethoxide [$Bu_2Sn(OMe)_2$] in toluene at 130 °C with azeotropic removal of the alcohol also produced good yields of **2a** and **2c** (Scheme 1a). All these new organotin compounds were fully characterized and are stable both as solids and in solution in the air, indicating that the tin−sulfur bond is hydrolytically stable.[10] Butyltin chloride **2a** formed colorless crystals suitable for X-ray crystal structure analysis (see Supporting Information).

The appearance of the ^{1}H NMR spectrum of **2a** depended on concentration and temperature of the sample. Several spectra recorded from different samples of **2a** showed different aromatic patterns. Initially, in some spectra the 12 aromatic protons were all different from each other, as expected since the molecule is not C_2-symmetric. In other spectra, the six protons on one naphthyl unit were magnetically equivalent to the corresponding protons on the other naphthyl unit, as if the molecule were C_2-symmetric. In particular, the two most upfield diastereotopic protons appeared either as two clearly defined doublets at 6.89 (J = 8.4 Hz) and 6.96 ppm (J = 8.4 Hz) or as one broad doublet at 6.93 ppm (J = 8.2 Hz) (Figure 1, patterns A and C, respectively). Other spectra showed intermediate patterns, where the two doublets had coalesced into one very broad singlet (Figure 1, pattern B). It was found that 0.02 M samples in $CDCl_3$ at room temperature reproducibly showed the aromatic pattern B. Maintaining this concentration, the resonances further coalesced into pattern C at $T > 40$ °C and decoalesced into pattern A at $T < 0$ °C. Conversely, at room temperature, the spectrum varied from pattern C to pattern A as the concentration of the sample was decreased from 0.5 to 0.0008 M.

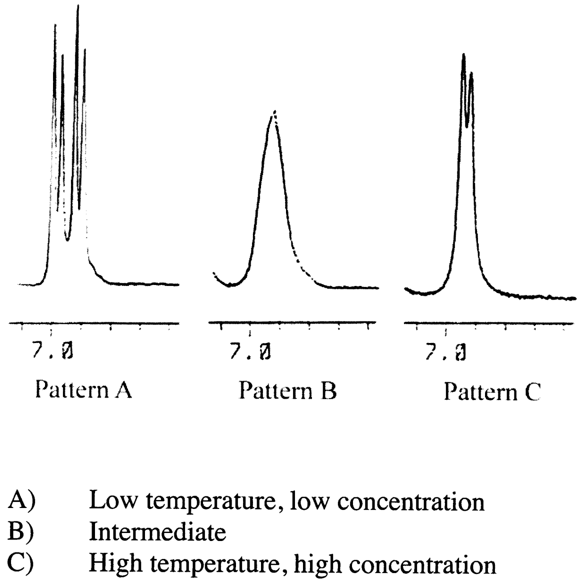


FIGURE 1. Representative ^{1}H NMR resonances of **2a** under different conditions.

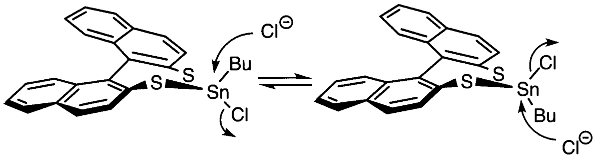


FIGURE 2. Postulated dynamic chlorine exchange at the tin center in **2a**.

We postulated that this behavior could be due to small amounts of free chloride ions in solution that promote a dynamic exchange of the chlorine ligands on tin, probably through a pentacoordinated symmetric tin species as shown in Figure 2. It is known that pentacoordinated tin species have a trigonal-bipyramid arrangement.[11]

To test this hypothesis, a small crystal of $AgBF_4$ was added to a 0.02 M NMR sample of **2a** (pattern B) to trap the free chloride ions. The aromatic region of the spectrum became non-C_2-symmetric (pattern A). When a small crystal of Bu_4NCl was added to that same sample, the aromatic region simplified into the C_2-symmetric pattern (pattern C). Apparently, at high dilution or low temperature the process of chlorine exchange is slow relative to the NMR time scale, therefore, the non-C_2-

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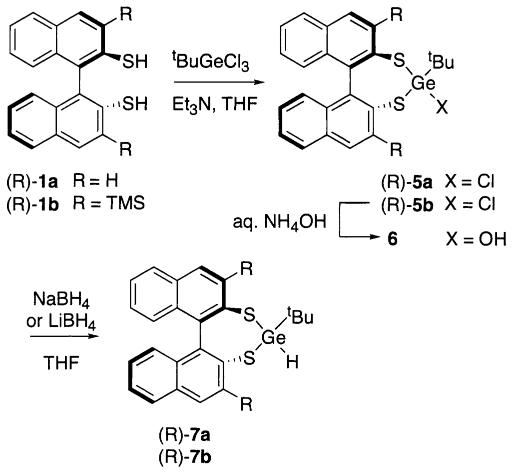
[9] Fabbri, D.; Delogu, G.; De Lucchi, O. *J. Org. Chem.* **1993**, *58*, 1748.

[10] (a) *Chemistry of Tin*, 2nd ed.; Smith, P. J., Ed.; Blackie: London, UK, 1997. (b) Davies, A. G. *Organotin Chemistry*; VCH: Weinheim, Germany, 1997.

[11] (a) Shibata, I.; Suwa, T.; Baba, A. *Main Group Met. Chem.* **2001**, *24*, 637. (b) Pereyre, M.; Quintard, J.-M.; Rahm, A. *Tin in Organic Synthesis*; Butterworth: London, UK, 1987.

SCHEME 2. Synthesis of Dithiogermanes 7a and 7b and Germanium Hydroxide 6



symmetric pattern is observed. At high concentration or temperature, the rate of chloride exchange increases and the peaks of the diastereotopic aromatic protons coalesce.

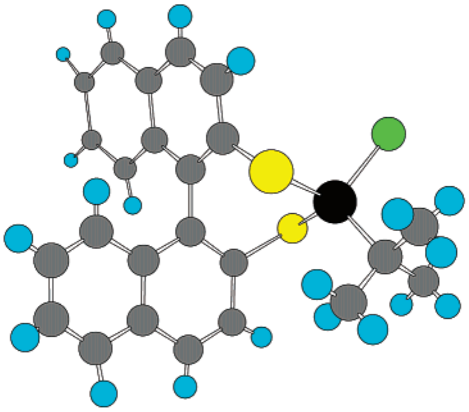
A facile exchange of electronegative ligands such as Cl and S between several organotin mercaptoesters has also been observed by other groups.[12] We viewed the mobility of the chloro atom attached to tin in **2a** as a promising feature for further manipulation of this functionality.[13]

Unfortunately, all efforts to reduce (*rac*)-**2a** to the corresponding tin hydride (*rac*)-**3a** failed. Mild reducing agents (Bu_3SnH, Ph_3SnH, AlH_3, $NaBH_4$) returned unreacted starting material, while stronger reducing agents ($LiAlH_4$, DIBAL) induced cleavage of the sulfur−tin bond to give back dithiol **1a**. The chloride **2a** was easily converted into the iodide **4a** by treatment with NaI in acetone, but attempted reduction of the Sn−I bond was once again unsuccessful (Scheme 1b).[14]

To strengthen the bond to sulfur we next turned our attention to the nuclear substitution of tin by germanium. Although trialkylgermanium hydrides are poorer hydrogen donors than their corresponding tin hydrides,[15] there is reason to expect that the thio substituents could have an activating effect on the hydrogen donor ability of germanium hydrides.[16]

As with its tin counterpart, the reaction between **1a** and commercially available *tert*-butyl germanium trichloride proceeded very smoothly over 1 h at room temperature in THF as shown in Scheme 2 (the scheme shows syntheses of one enantiomer, but the other enantiomer and racemic samples were also made by the same route). Dilution of the reaction mixture with diethyl ether and filtration consistently afforded 95−100% yield of clean product **5a** as a white solid. The germanium chloride **5a** was very stable both as a solid and in solution, being only prone to hydrolysis on silica gel. Colorless crystals suitable for X-ray analysis were obtained from chloroform (Figure 3a).

a) Germanium chloride 5a



b) Germanium chloride 5b

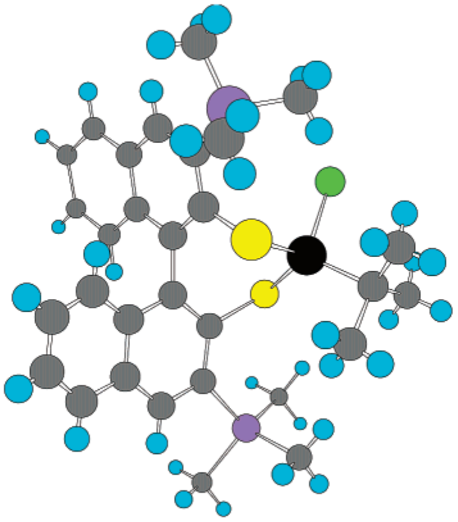


FIGURE 3. X-ray crystal structures of germanium chlorides **5a** (a) and **5b** (b).

To evaluate the effect of bulky substituents on the ortho positions of the binaphthyl unit, we also prepared 3,3′-bis(trimethylsilyl)-1,1′-binaphtho-2,2′-dithiol **1b**.[17] This was reacted with *tert*-butyl germanium chloride and triethylamine in THF at room temperature to afford crude **5b** in quantitative yield. Due to the steric demand of the ortho TMS groups, this reaction was slower than that for the nonsilylated dithiol **1a**, and was completed in about 2 h (Scheme 2). Germanium chloride **5b** was

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(12) (a) Burley, J. W.; Hutton, R. E.; Dworkin, R. D.; Hutton, R. E. *J. Organomet. Chem.* **1985**, *284*, 171. (b) Blunden, S. J.; Hobbs, L. A.; Smith, P. J.; Davies, A. G.; Teo, S. B. *J. Organomet. Chem.* **1985**, *282*, 9. (c) Burley, J. W.; Dworkin. R. D. *J. Vinyl Technol.* **1986**, *8*, 15.

(13) The ability of **2a** to reduce alkyl halides under catalytic conditions ($NaCNBH_3$/t-BuOH/benzene/AIBN) was tested in the reduction of bromoadamantane. Gas chromatographic analysis of the reaction mixture after 1 h at 80 °C showed 99% yield of adamantane (using naphthalene as internal standard). Sodium cyanoborohydride alone does not reduce bromoadamantane under these conditions, therefore an organotin hydride formed in situ is probably the active reducing agent.

(14) Attempts to synthesize **3a** directly by reaction of dithiol **1a** with $BuSnH_3$ in benzene at 80 °C also failed, although the same reaction between **1a** and Bu_2SnH_2 successfully afforded clean **2c**.

(15) (a) Chatgilialoglu, C.; Newcomb, M. *Adv. Organomet. Chem.* **1999**, *44*, 67. (b) Chatgilialoglu, C.; Ballestri, M.; Escudié, J.; Phailhous, I. *Organometallics* **1999**, *18*, 2395. (c) Chatgilialoglu, C. *Acc. Chem. Res.* **1992**, *25*, 188.

(16) Chatgilialoglu, C.; Guerra, M.; Guerrini, A.; Seconi, G.; Clark, K. B.; Griller, D.; Kanabus-Kaminska, J.; Martinho-Simões, J. A. *J. Org. Chem.* **1992**, *57*, 2427.

(17) Cossu, S.; De Lucchi, O.; Fabbri, D.; Valle, G.; Painter, G. F.; Smith R. A. J. *Tetrahedron* **1997**, *53*, 6073.

obtained as a white solid, very stable to air and moisture. Recrystallization from hexanes gave colorless crystals suitable for X-ray crystallography (Figure 3b).

Analysis of the crystal structures of **5a** and **5b** shows that the germanium atom has a distorted tetrahedral geometry with angles between the *tert*-butyl group and S(2) significantly larger than 109° (117° and 118°, respectively) to accommodate the steric bulk of the *tert*-butyl group, at the expense of the angles between the chlorine and S(2) which are significantly smaller (101° and 99°, respectively). As a result of the steric strain imposed by the seven-membered ring, angles between the two aromatic carbons at the binaphthyl junction are slightly larger than 120°. The dihedral angle between the four aromatic carbons of the ring increases from 76° in **5a** to 86° in **5b**, to relieve the steric repulsion between the *tert*-butyl group and the ortho TMS groups. Furthermore, in **5b**, angles at the ortho carbons (bonded to the TMS groups) are considerably larger than 120° as a result of this steric repulsion (125° and 126°). The seven-membered ring also has a distorted conformation, with bond angles about S(1) and S(2) being different, and the difference being larger in **5b** than in **5a** (95° and 104° vs 100° and 97°, respectively). Bond lengths of 2.18 and 2.19−2.21 Å for the Ge−Cl and Ge−S bonds are within normal ranges.[18]

Although stable in the solid state, **5b** was found to be prone to partial hydrolysis in solution or on silica gel to give the germanium hydroxide **6**. The latter was also independently prepared by treatment of **5b** with an aqueous solution of ammonium hydroxide in ether (Scheme 2). The white solid obtained in quantitative yield was recrystallized from hexanes and fully characterized, including by X-ray crystallography (see Supporting Information).

For the reduction of chloride **5a** to hydride **7a**, we screened some mild reducing agents (AlH_3, Bu_3SnH, Ph_3SnH, $NaCNBH_3$, $NaBH_4$) and found that sodium borohydride was the best choice, although the reaction conditions had to be carefully controlled. Thus, **5a** was treated with sodium borohydride in THF at room temperature, and the desired germanium hydride **7a** was obtained as the major product. The yield of **7a** was dependent on the reaction time, and dithiol **1a** formed upon prolonged stirring so it was important to stop the reaction as soon as the starting material had reacted completely (typically about 1 h and 40 min). In reaction scales larger than 1 mmol, 2−10% of dithiol **1a** was usually found as a byproduct, together with variable amounts of another unidentified byproduct (2−10%). Short column chromatography was effective in removing most of the impurities of the crude product, but at the expense of 30−40% material loss.

The most reliable method to obtain **7a** in purity ≥90% and good yield was to run the reaction on a small scale (0.3−0.5 mmol). After completion and standard extractive workup, the dithiol byproduct was removed by washing the organic layer with an aqueous solution of sodium carbonate (pH 11.5−12). The germanium hydride **7a** was obtained from the organic layer with a dithiol content of less than 2% molar and 2−5% of other impurities (as judged by ^1H NMR analysis), and was normally used as such. If higher purity was needed, a small sample of **7a** was first filtered through a silica gel plug, then dissolved in diethyl ether and washed with aqueous base. Alternatively, the crude hydride was purified by semipreparative chiral HPLC and obtained in ≥98% purity.

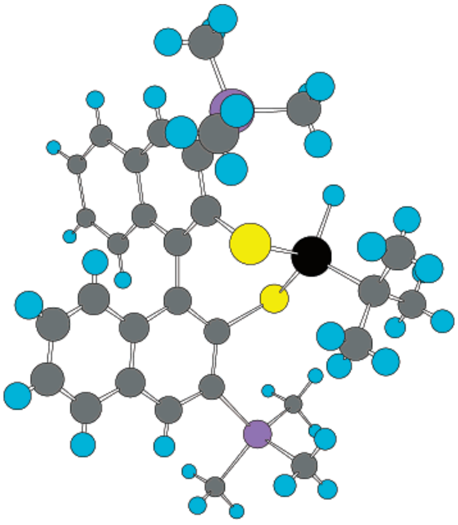

FIGURE 4. X-ray crystal structure of germanium hydride **7b**.

On the other hand, treatment of **5b** with sodium borohydride in THF at room temperature or at reflux did produce some of the desired germanium hydride **7b**, but the reaction was not clean, as reduction of the Ge−S bonds competed with reduction of the Ge−Cl bond. The smaller and more powerful lithium borohydride proved to be much more effective at room temperature or below for the reduction of **5b**, although some formation of dithiol **1b** was still observed. The hydroxide **6** was also reduced effectively by lithium borohydride but provided a lower hydride-to-dithiol ratio.[19] Thus, we focused on optimizing the reduction of the chloride **5b** (Scheme 2).

To minimize formation of byproducts it was best to carry out the reaction at low temperature. Thus, a solution of **5b** and an excess of lithium borohydride (20 equiv) in THF was kept at −8 °C for 5 days, after which the reaction mixture was worked up with a dilute solution of ammonium chloride. The residue usually contained less than 15% of combined dithiol and germanium dihydride byproduct.[20] After recrystallization from hexanes, germanium hydride **7b** was obtained with a purity of ≥95% in 65−80% yield. The crystals obtained were suitable for X-ray crystal structure analysis (Figure 4). As observed in **5b**, angles at S(1) and S(2) are significantly different (93° vs 105°), the aromatic carbons at the binaphthyl junction have angles larger than 120° and the TMS groups are pushed back from the *tert*-butyl group, with angles at the ortho carbons of 126° and 127°. The dihedral angle between the four aromatic carbons of the seven-membered ring is also large (84.6°).

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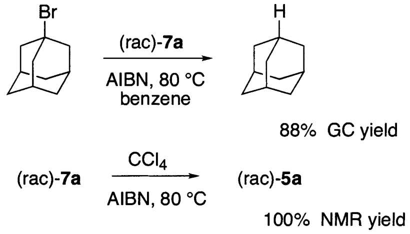
(18) Baines, K. M.; Stibbs, G. W. *Coord. Chem. Rev.* **1995**, *145*, 157−200.

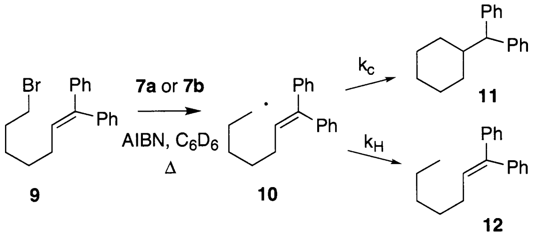
(19) Gualtieri, G. Ph.D. Thesis, University of Pittsburgh, 2000.

(20) The byproduct found in the crude reaction mixture is believed to be the C_2-symmetric dithiogermanium dihydride, as judged by the singlet at 5.7 ppm (2H) in the ^1H NMR spectrum, which correlate with a singlet at 0.57 ppm (18H). This byproduct, probably the result of β-elimination at the germanium center with loss of isobutene, was never isolated and fully characterized, but it was found in small amounts in almost every reaction condition employed.

SCHEME 3. Radical Chain Reduction with 7a



SCHEME 4. Competition Kinetic Experiments with Radical Clock 9



This hydride proved to be remarkably stable as a solid and could be stored for long periods of time in closed containers without any precautions. In solution, it is somewhat sensitive to air and moisture, but oxidation or hydrolysis are quite slow, so handling of this product is very simple and practical.

Rate Constant Measurements. The reactivity of **7a** as a radical chain reducing agent was first tested for two simple substrates, bromoadamantane and carbon tetrachloride, at 80 °C and with AIBN as radical initiator (Scheme 3). In both cases the reaction proceeded smoothly to give high yields of the reduced products. In the reduction of bromoadamantane, 88% yield of adamantane was calculated by GC with dodecane as internal standard. With carbon tetrachloride, proof of reduction was obtained by comparing the proton NMR spectrum of the resulting germanium chloride with that of an authentic sample of **5a**. A quantitative yield of **5a** was obtained by ^{1}H NMR with 1,3,5-trimethoxybenzene as internal standard.

To learn more about the intrinsic reactivity of **7a** and **7b**, we measured the kinetic constants for hydrogen transfer from both hydrides to a primary alkyl radical using a calibrated radical clock (Scheme 4).[21] From the ratio of cyclized/reduced products (**11**/**12**) and knowing k_c,[22] the kinetic constant for hydrogen transfer can be calculated from the appropriate equations (see Supporting Information).[23]

The kinetic measurements were carried out by mixing 1 equiv of the 7-bromo-1,1-diphenyl-1-heptene **9** with 2−3 equiv of **7a** or **7b** and a catalytic amount of AIBN in deuterated benzene in a sealed tube. The resulting mixture was then heated at the appropriate temperature (80−83 °C) for 4−11 h. After removal of the solvent, an internal standard was added and the yields and ratios of cyclized/reduced products (**11**/**12**) were obtained from ^{1}H NMR analysis. The data for these experiments are summarized in Table 1.

TABLE 1. Determination of the Kinetic Constant for Hydrogen Transfer from 7a and 7b to a Primary Alkyl Radical

run	hydride	(*rac*)-**1a** (mol %)	[**7**]	[**9**]	**11**/**12**	T (°C)	$10^7 k_{H(T)}$ (M^{-1} s^{-1})
1	(*rac*)-**7a**	1.5	0.15	0.05	1.38	83	2.8
2	(*rac*)-**7a**	1.5	0.10	0.05	0.73	83	2.5
3	(*rac*)-**7a**	3[a]	0.10	0.05	0.85	83	2.9
4	(*rac*)-**7a**	6[a]	0.10	0.05	0.87	83	3.0
5	(*rac*)-**7a**	6[a]	0.10	0.05	1.06	83	3.7
6	(*rac*)-**7b**	0	0.08	0.04	0.37	80	1.4
7	(*rac*)-**7b**	0	0.16	0.08	0.61	80	1.2
8	(*rac*)-**7b**	0	0.21	0.11	0.89	80	1.4

[a] Extra dithiol **1a** added by doping.

Since the sample of **7a** used for these reactions was contaminated by 1.5% molar of dithiol **1a**, we were concerned that the dithiol could act as a polarity-reversal catalyst, thus competing with the germanium hydride for hydrogen transfer to the intermediate carbon radical. This well-known phenomenon has been exploited in the radical hydrosilylation of alkenes with silicon hydrides.[24] To check if thiol catalysis existed, we ran some of the kinetic experiments doping the reaction mixture with additional amounts of dithiol **1a** (3% and 6% molar, entries 3−5). We anticipated observing a difference in the calculated rate constants if the thiol was acting as a catalyst.

As can be seen from Table 1, the range of values obtained for the kinetic constant of **7a** at increasing amounts of added **1a** fluctuates only within experimental error (entries 1−5). Therefore, it appears that the presence of up to 12% molar of −SH groups does not significantly interfere with the rate of hydrogen abstraction by the primary radical **10** from the germanium hydride. The average kinetic constant obtained for **7a** ($k_{H(83)} = 3.0 \times 10^7$ M^{-1} s^{-1}) shows that this hydride is an even better hydrogen donor than Bu_3SnH, for which $k_{H(83)} = 6.8 \times 10^6$ M^{-1} s^{-1}.[21]

For germanium hydride **7b** the kinetic constant was calculated as the average of three runs (entries 6−8, $k_{H(80)} = 1.4 \times 10^7$ M^{-1} s^{-1}). The value obtained shows that **7b** is a roughly 2-fold slower hydrogen donor than **7a**, probably due to the bulky trimethylsilyl substituents on the binaphthyl unit. Considering the beneficial effect that sulfur ligands have on the hydrogen donor ability of silicon hydrides,[16] it is not surprising that a similar trend is observed for germanium hydrides.

Stereoselectivity of Free-Radical Transformations. Given the good stability of these novel germanium hydrides and their favorable kinetic constants as radical chain propagating agents, we next tested them as enantioselective radical reducing agents for the reduction of racemic 3-iodo-3-methoxymethyl-2-chromanone **13** and methyl 2-bromo-2-phenyl-3,3-dimethylbutanoate **15** (Scheme 5 and Table 2). Both enantiomers of **1a** were prepared by resolution of (*rac*)-**1a** according to the procedure reported by De Lucchi and co-workers,[25] thereby granting access to enantiopure **7a** and **7b**.

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SCHEME 5. Reduction of α-Halo Carbonyl Compounds 13 and 15 with 7a and 7b

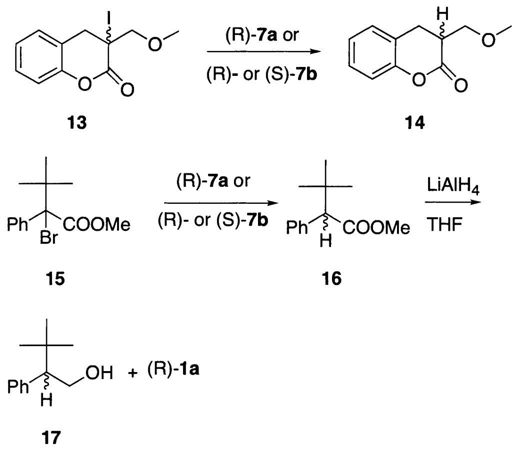
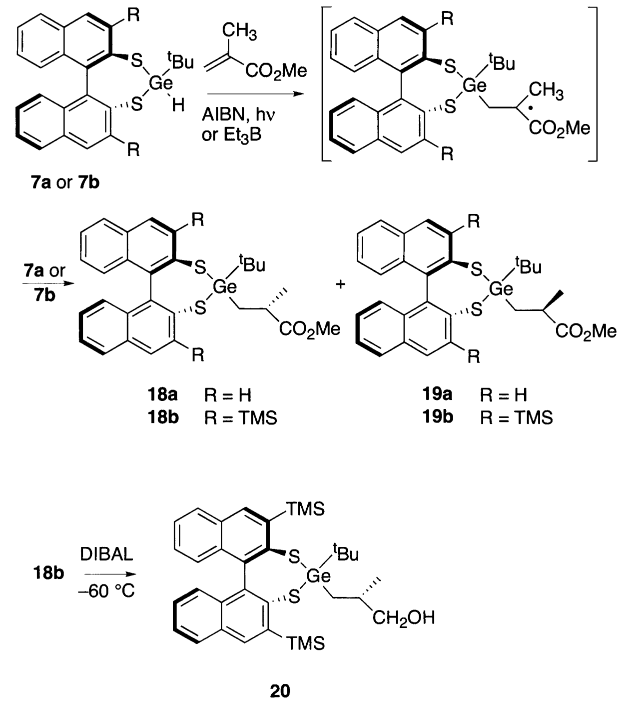


TABLE 2. Reductions of Racemic Iodide 13 and Bromide 15 with Germanium Hydrides 7a and 7b

entry	substrate	hydride	*T* (°C)	initiator	product	yield (%)[a]	ee (%)
1	**13**	(*R*)-**7a**	−78	Et_3B/Ar	**14**	97	20 (*R*)
2	**13**	(*R*)-**7a**	−78	AIBN/*hν*	**14**	96	26 (*R*)
3	**13**	(*R*)-**7b**	−78	Et_3B/Ar	**14**	70[b]	41 (*S*)
4	**13**	(*S*)-**7b**	−78	Et_3B/O_2	**14**	41[b]	40 (*R*)
5	**15**	(*R*)-**7a**	−78	Et_3B/Ar	**16**	79	22 (*S*)[c]
6	**15**	(*R*)-**7a**	−78	Et_3B/O_2	**16**	94	27 (*S*)[c]
7	**15**	(*R*)-**7a**	−78	AIBN/*hν*	**16**	80	29 (*S*)[c,d]
8	**15**	(*R*)-**7b**	−25	Et_3B/Ar	**16**	54[b]	32 (*R*)
9	**15**	(*S*)-**7b**	−60	Et_3B/Ar	**16**	34[e]	42 (*S*)[f]

[a] By proton NMR analysis unless otherwise indicated. [b] Isolated yield. [c] Enantiomeric excess calculated for the alcohol **17**. [d] This reaction was repeated in identical conditions and gave 87% yield and 20% ee. [e] Conversion of starting material incomplete. [f] This reaction was repeated in identical conditions and gave 37% yield and 41% ee.

SCHEME 6. Hydrogermylation of Methyl Methacrylate with (*rac*)- and (*R*)-7a,b



In a typical run, the radical initiator (AIBN or Et_3B) was added to a solution of the iodide **13** or bromide **15** (1 equiv) and the germanium hydride (2 equiv) in toluene at the appropriate temperature. If needed, additional triethylborane was added in several portions, until the starting material had reacted completely. When TLC analysis showed complete consumption of starting material, the reaction mixture was concentrated, and *p*-dimethoxybenzene was added as internal standard to determine the yield of product by proton NMR spectroscopy. The crude product was then purified by column chromatography and analyzed by chiral HPLC to obtain the enantiomeric excess.

In the particular case of the reduction of bromide **15** by **7a**, isolation of pure **16** from the reaction mixture proved rather cumbersome due to partial hydrolysis on silica gel of the excess germanium hydride and the byproduct germanium bromide. We found that reduction of the crude reaction mixture with LAH produced the alcohol **17** and dithiol **1a**, which were easily separated through a silica gel plug. Therefore, the enantiomeric excesses for these reductions were obtained for the alcohol **17**, rather than the ester **16**.

Reduction of both halides with (*R*)-**7a** proceeded well with either AIBN or Et_3B as initiator and the reduced products were obtained in high yields but low ee values (20−29%, Table 2, entries 1,2 and 5−7).[26] With **7b**, the ee of **14** increased to 41% (Table 2, entries 3 and 4), although initiation with AIBN was not effective. The reduction of **15** with **7b** at −25 °C gave slightly better ee than was obtained with **7a** at −78 °C for the same substrate (Table 2, compare entry 8 with entries 5−7). At −60 °C, the reaction became very slow, therefore it was stopped after 2 days at incomplete conversion. In this case, the ee increased further to 42% (Table 2, entry 9). As expected, opposite enantiomers of **7b** afforded opposite enantiomers of reduced products (Table 2, entries 3,4 and 8,9). The absolute configurations of the reduced products were assigned by comparing their α_D to the literature values.

Introduction of the ortho TMS groups on the binaphthyl ring of the hydride resulted not only in higher enantiomeric excesses of the reduced substrates **14** and **16** but also in a reversal of the selectivity. The same enantiomers of **7a** and **7b** afforded preferentially opposite enantiomers of the reduced products (Table 2, entries 2,3 and 7,8).

To investigate diastereoselective transformations with both racemic and enantiopure **7a** and **7b**, we next studied the hydrogermylation reactions of methyl methacrylate, which give diastereomeric products **18a**/**19a** and **18b**/**19b** (Scheme 6).

Methyl methacrylate (1.2−2 equiv), AIBN, and the germanium hydride (1 equiv) dissolved in toluene (ben-

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(25) De Lucchi, O.; Fabbri, D.; Delogu, G. *J. Org. Chem.* **1995**, *60*, 6599.

(26) To verify whether any of the observed ee values could be ascribable to traces of (*R*)-**1a** present in the reaction mixtures, we ran a series of control experiments in which **15** was reduced with Bu_3SnH in the presence of variable amounts of (*R*)-**1a** (from 0.1 up to 1 equiv). In all cases, the reduced product **16** was obtained as racemic, indicating that if **1a** takes part in the hydrogen abstraction step it does so without any stereoselectivity. This is expected since the structure of **1a** is not as rigid and sterically demanding as that of **7a**.

TABLE 3. Hydrogermylation of Methyl Methacrylate with Germanium Hydrides 7a and 7b

entry	hydride	*T* (°C)	products	yield (%)[a]	ratio
1	(*rac*)-**7a**	25	(*rac*)-**18a**/**19a**	57	1.8:1[b]
2	(*rac*)-**7a**	−78	(*rac*)-**18a**/**19a**	77	1.7:1[b]
3	(*R*)-**7a**	−78	(*R*)-**18a**/**19a**	61	3:1[b]
4	(*rac*)-**7b**	25	(*rac*)-**18b**/**19b**	61	11:1[c]
5	(*R*)-**7b**	25	(*R*)-**18b**/**19b**	56[d]	15:1[c]
6	(*rac*)-**7b**	−20	(*rac*)-**18b**/**19b**	63	14:1[c]
7	(*R*)-**7b**	−20	(*R*)-**18b**/**19b**	55[d]	25:1[c]
8	(*rac*)-**7b**	−60	(*rac*)-**18b**/**19b**	54	18:1[c]

[a] Isolated yield of mixture unless otherwise indicated. [b] By proton NMR analysis. [c] By HPLC analysis. [d] Isolated yield of **18b**.

zene for reactions at room temperature) were placed in a sealed tube purged with argon. The mixture was irradiated with a 450-W medium-pressure mercury lamp and stirred at the appropriate temperature until TLC analysis showed complete consumption of the germanium hydride. In the reactions with Et_3B, 1.5 equiv of methyl methacrylate was used, and triethylborane was added to a solution of the reactants at the appropriate temperature. At −60 °C, the reaction with **7b** became sluggish and addition of more triethylborane was necessary to drive it to completion. The crude mixture was concentrated under reduced pressure and analyzed either by proton NMR spectroscopy or by analytical HPLC to obtain the ratio of products.[27] Then, the product was purified by column chromatography or preparative HPLC to afford the adducts **18a**/**19a** and **18b**/**19b**. The yields and diastereomeric ratios obtained from this series of experiments are summarized in Table 3.

In the reactions run with racemic **7a**, isolated yields of combined **18a**/**19a** were moderate (57−77%) but the diastereomer ratio was low (1.7:1) and independent of the reaction temperature (virtually no change from −78 °C to room temperature, Table 3, entries 1 and 2). When enantiomerically pure germanium hydride was used, the diastereomer ratio increased to 3:1 (Table 3, entry 3). The minor isomer **19a** was isolated by column chromatography and the X-ray crystal structure was solved to assign the relative configuration, which was found to be (*R*,*S*) (see Supporting Information).

The diastereoselectivity of the hydrogermylation was considerably higher when the more sterically biased hydride **7b** was used as a racemate (Table 3, 11:1, entry 4), and increased further at lower temperature to 18:1 (Table 3, entries 6 and 8). Also in this case, there was a slight increase in selectivity in reactions run with enantiomerically pure (*R*)-**7b** as opposed to racemic **7b** (Table 3, compare entries 4 and 6 with entries 5 and 7). The major and minor products **18b**/**19b** were isolated either as a mixture by column chromatography or separately by semipreparative HPLC. Isolated yields of combined **18b** and **19b** were generally moderate (54−63%), although they were not optimized. While the major product **18b** was very stable, the minor isomer **19b** was found to be unstable in $CDCl_3$ solution, decomposing rather quickly into an unidentified yellow byproduct. However, the minor isomer was characterized by NMR spectroscopy in CD_2Cl_2 or benzene-d_6 solutions.

We were unable to obtain crystals of either diastereomer **18b** or **19b**; however, reduction of the major adduct **18b** with DIBAL at −60 °C afforded the corresponding alcohol **20**, which was recrystallized from hexanes and found to have the (*R*,*R*) relative configuration by X-ray crystallography (see Supporting Information).

The stereoselectivity of the hydrogermylation reactions with **7a** and **7b** follows the same course, yielding the (*R*,*R*)-diastereomer as the major product in both cases. Since in the reduction of halides **13** and **15** the same enantiomers of **7a** and **7b** afforded opposite enantioenriched products, this result suggests that in the hydrogermylation it is the Ge atom β to the radical center that dictates the stereochemical outcome of the hydrogen abstraction step. The approaching germanium hydride has a secondary effect, and enhances the selectivity if it is of the same (*R*) configuration (matched pair). Comparison of the results with racemic and enantiopure hydrides also supports this hypothesis and indicates that the difference in energy between the matched and the mismatched pairs is not very large.

Conclusions

We have synthesized the first chiral enantiomerically pure germanium hydrides **7a**,**b** containing a C_2-symmetric binaphthyl substituent and two germanium−sulfur bonds. Although care is required in the last part of the synthesis, the hydrides are very stable as solids and can be conveniently handled without any special precautions.

The kinetic constants for hydrogen transfer from **7a**,**b** to primary alkyl radicals are 2−4 times higher than that of tributyltin hydride, indicating that the two Ge−S bonds significantly enhance the hydrogen donor ability of the germanium hydrides. These new germanium hydrides are effective free-radical chain hydrogen transfer agents.

As anticipated, the introduction of bulky TMS groups on the ortho positions of the binaphthyl units resulted in enhanced selectivity and decreased reactivity of the germanium hydride. High diastereoselectivity was obtained in the hydrogermylation of methyl methacrylate with (*R*)-**7b**.

To the best of our knowledge this is the first application of chiral germanium hydrides in stereoselective radical chain reactions. The synthesis of **7a** and **7b** should serve as a starting point for the design and synthesis of improved tin, germanium, or silicon hydrides of this type.

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Supporting Information Available: Complete experimental details, copies of the ^1H and ^{13}C NMR spectra of all the compounds, and crystallographic details. This material is available free of charge via the Internet at http://pubs.acs.org.

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(27) The **18a** to **19a** ratios were determined by proton NMR spectroscopy, by integration of the $-OCH_3$ resonances.