h. Excess LAH was destroyed by addition of wet diethyl ether followed by aqueous HCl (0.5 N). The reaction was extracted with diethyl ether (3 × 70 mL). The organic layer was washed and dried over Na_2SO_4 (anhydrous) and concentrated under reduced pressure. Purification on a short silica gel column yielded a mixture of **6** and **7** (0.64 g, 77% yield). Medium-pressure chromatography using a Lobar column (Merck) eluted with hexane and increasing amounts of diethyl ether of a small sample yielded the two separated diols **6** and **7** in a ratio 1:3. The less polar was **6**: $[\alpha]^{25}_D$ -3.8° (*c* 6, $CHCl_3$) [lit.[5] $[\alpha]^{25}_D$ -5°]; ^1H NMR (80 MHz, $CDCl_3$) δ 0.77 (s, 3 H, $C_{19}H$), 0.84 (s, 3 H, $C_{18}H$), 0.93 (s, 3 H, $C_{20}H$), 1.09 (s, 3 H, $C_{17}H$), 1.32 (s, 3 H, $C_{16}H$), 5.09 (dd, 1 H, J = 11 and 1.5 Hz, $C_{15}H_c$), 5.27 (dd, 1 H, J = 18 and 1.5 Hz, $C_{15}H_t$), 6.02 (dd, 1 H, J = 18 and 11 Hz, $C_{14}H$). The more polar was **7**: $[\alpha]^{25}_D$ +5.0° (*c* 2, $CHCl_3$) [lit.[5] $[\alpha]^{25}_D$ +12°]; ^1H NMR (80 MHz, $CDCl_3$) δ 0.80 (s, 6 H, $C_{19}H$ and $C_{20}H$), 0.86 (s, 3 H, $C_{18}H$), 1.14 (s, 3 H, $C_{17}H$), 1.27 (s, 3 H, $C_{16}H$), 2.64 (br s, 2 H, OH), 5.02 (dd, 1 H, J = 11 and 1.5 Hz, $C_{15}H_c$), 5.23 (dd, 1 H, J = 18 and 1.5 Hz, $C_{15}H_t$), 6.00 (dd, 1 H, J = 18 and 11 Hz, $C_{14}H$).

The reaction was carried on with the remaining mixture.

Oxidation of 14(15)-Labdene-8,13-diols 6 and 7. To a solution of **6** and **7** (0.36 g, 1.2 mmol) in acetone (28 mL) at 20 °C a mixture of $KMnO_4$ (0.62 g) and $MgSO_4$ (0.53 g) was added for 30 min. The reaction was additionally stirred for 30 min. Filtration over a Celite pad and evaporation of the solvent at reduced pressure yielded crude **8** and **9** (0.330 g, 1.2 mmol, 100% yield). Thin-layer chromatography (3:7 diethyl ether/hexane) revealed superimposed spots with R_f 0.3, which would decompose producing a compound with R_f 0.9. Attempts to purify the reaction product by column chromatography would lead to more decomposition product. IR ν_{max}^{film} (cm^{-1}) 3400 (OH), 1720 (C=O); ^1H NMR (60 MHz, CCl_4) δ 0.80, 0.88, 1.08, 1.25, 1.33, 2.05 (methyl groups).

Photolysis of 8 and 9. The ketones **8** and **9** (0.150 g, 0.54 mmol) in petroleum ether (20 mL) under Argon were irradiated in a quartz apparatus with a mercury lamp Phillips HLP 125 W. The temperature was maintained at 0 °C. The reaction was monitored by thin-layer chromatography revealing the formation of three products (R_f 0.6, 0.7 and 0.9; 3:7 diethyl ether/hexane). The solvent was evaporated at reduced pressure and the residue (149 mg) was purified by column chromatography eluted with diethyl ether/hexane (1:99). Compound with R_f 0.9 was the decomposition of the ketones. The second compound (R_f 0.7) was **1** (0.016 g, 13% yield): $[\alpha]^{25}_D$ -9.7° (*c* 0.7, $CHCl_3$); IR ν_{max}^{KBr} (cm^{-1}) 3400 (OH), 1630 (C=C), 900 (C=CH_2); ^1H NMR (100 MHz, $CDCl_3$) δ 0.87 (s, 3 H, $C_{14}H$), 0.89 (s, 3 H, $C_{13}H$), 1.26 (s, 3 H, $C_{15}H$), 1.38 (s, 3 H, $C_{12}H$), 4.87 (br s, 1 H, $C_{11}H$), 5.04 (br s, 1 H, $C_{11}H$); MS, *m/z* (relative intensity) 222 ($M^{\cdot+}$, 35), 204 (53), 129 (53), 95 (93), 69 (79), 43 (100). The more polar compound (R_f 0.6) **2** was very difficult to purify (0.013 g, 11% yield): $[\alpha]^{25}_D$ +22.5° (*c* 0.6, $CHCl_3$); IR ν_{max}^{film} (cm^{-1}) 3430 (OH), 1630 (C=C), 900 (C=CH_2); ^1H NMR (100 MHz, $CDCl_3$) δ 0.85 (s, 3 H, $C_{14}H$), 0.87 (s, 3 H, $C_{13}H$), 1.09 (s, 3 H, $C_{15}H$), 1.41 (s, 3 H, $C_{12}H$), 4.84 (br s, 1 H, $C_{11}H$), 5.22 (br s, 1 H, $C_{11}H$); MS, *m/z* (relative intensity) 222 ($M^{\cdot+}$, 65).

Oxidation of Methyl (5*R*,8*R*,9*S*,10*R*)-Labd-13-en-8-ol-15-oate (12). A mixture of $KMnO_4$ (0.31 g) and $MgSO_4$ (0.27 g) was added to a solution of **12**[7] (0.20 g, 0.6 mmol) in acetone (14 mL) at 20 °C. After being stirred for 1 h the reaction was filtered over Celite and a decolorizing carbon pad. The solvent was evaporated at reduced pressure, yielding **13** in 50% yield (0.09 g, 0.3 mmol): IR ν_{max}^{film} (cm^{-1}) 3400 (OH), 3010-2940 (C-H), 1710 (C=O); ^1H NMR (60 MHz, CCl_4) δ 0.83 (s, 6 H, $C_{19}H$ and $C_{20}H$), 0.87 (s, 3 H, $C_{18}H$), 1.10 (s, 3 H, $C_{17}H$), 2.05 (s, 3 H, $C_{16}H$).

Photolysis of 13. The ketone **13** (0.024 g, 0.8 mmol) in petroleum ether (20 mL) was submitted to photolysis as described above. Purification of the product on a silica gel column yielded **10** (0.004 g, 0.02 mmol, 21% yield): $[\alpha]^{25}_D$ +9° (*c* 2, $CHCl_3$); IR ν_{max}^{KBr} (cm^{-1}) 3400 (OH), 1630 (C=C), 900 (C=CH_2); ^1H NMR (100 MHz, $CDCl_3$) δ 0.85 (s, 3 H, $C_{14}H$), 0.87 (s, 3 H, $C_{13}H$), 1.25 (s, 3 H, $C_{15}H$), 1.38 (s, 3 H, $C_{12}H$), 4.82 (br s, 1 H, $C_{11}H$), 5.04 (br s, 1 H, $C_{11}H$). MS, *m/z* (relative intensity) 222 ($M^{\cdot+}$, 35), 204 (53), 185 (53), 95 (100).

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Superacid-Catalyzed Isomerization of *endo*- to *exo*-Trimethylenenorbornane (Tetrahydrodicyclopentadiene) and to Adamantane[1]

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One of the most significant developments of hydrocarbon chemistry in our time is that of diamondoid cage hydrocarbons, i.e. adamantane and its homologues. Adamantane was first isolated from petroleum by Landa in 1933,[2a] and its structure was confirmed by Prelog's synthesis in 1941.[2b] The single most important discovery that allowed the field to blossom to its present scope and significance was, however, Schleyer's finding of the aluminum trichloride catalyzed isomerization of *endo*-trimethylenenorbornane to adamantane.[3] Schleyer was studying the isomerization of the endo to the exo isomer, when he observed that in the reaction, upon workup, a white crystalline solid also formed that he realized was adamantane. During the facile isomerization of *endo*- to *exo*-trimethylenenorbornane, giving 90% exo isomer, 10% adamantane was obtained in solvent-free $AlCl_3$ sludge system at elevated temperature.[3b,4] Yield of adamantane could not be improved in the same system starting with the exo isomer. Investigations of ways to maximize the yield of adamantane gave a maximum yield of 18.8% using a large excess of $AlBr_3$ with *sec*-butyl bromide as promotor and HBr as cocatalyst.[5] A nearly quantitative yield of the exo isomer was obtained when endo-trimethylenenorbornane was isomerized with $AlCl_3$ in methylcyclohexane solvent. The rearrangement was also brought about with concentrated H_2SO_4. The equilibrium mixture contains 99% exo and 1% endo compound.

Since Schleyer's observation[3b] that concentrated H_2SO_4 readily isomerizes *endo*- to *exo*-trimethylenenorbornane, no systematic report of the use of other strong acid systems in the isomerization appeared. The transformation must involve several energetically unfavorable carbocationic intermediates. A free energy difference of about 3 kcal/mol has to be overcome to reach, after a long reaction at room temperature using H_2SO_4, thermodynamic equilibrium and to obtain 99.6% exo isomer. The amount of acid required is high (more than 1 equiv with respect to hydrocarbon).

Schleyer's discovery of the aluminum halide catalyzed rearrangement of *endo*- and *exo*-trimethylenenorbornane to adamantane prompted extensive further studies.[6,7]

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Table I. Isomerization of *endo*- to *exo*-Trimethylenenorbornane

acid systems	acid to endo (molar ratio)	solvent	temp, °C	time, h	*exo*-trimethylene-norbornane (% yield)[a]
CF_3SO_3H	1:2	Freon-113	rt	20	99.8
	1:1	CCl_4	rt	24	99.2
	5:1		0–rt	20	95.4
FSO_3H	1:2	C_6H_{12}	rt	20	99.6
$CF_3SO_3H + SbF_5$ (1:1)	1:80	C_6H_{12}	0–rt	20	98.3
	1:80	Freon-113	0–rt	16	98.5
	1:10	Freon-113	0	3/4	96.0
	1:3	Freon-113	0	1/4	98.3
$CF_3SO_3H + B(OSO_2CF_3)_3$ (2:1)	1:80	Freon-113	0–rt	15	94.0
$FSO_3H + SbF_5$ (1:1)	1:80	Freon-113	0–rt	15	98.0
$HF + SbF_5$ (1:1)	1:51	C_6H_{12}	0–rt	15	98.6
Nafion-H	1:3 (by wt)		~170	200	91.0
	1:1 (by wt)		~170	40	72.6
	2:1 (by wt)		~170	20	59.0
SbF_5–graphite	1:1	Freon-113	rt	22	98.2
	2:1	Freon-113	rt	22	92.8

[a] In isolated product.

Aluminum trichloride catalyzed isomerization, however, represents substantial difficulties as relatively large amount of catalyst (or sludge) must be used under harsh conditions, and fragmentation process and other side reactions produce many byproducts. Several attempts were made to further improve the isomerization.

The use of $HF–BF_3$ was reported to give a 30% yield of adamantane, with the disadvantage of the corrosive nature of the system and working under pressure.[8] Yields of adamantane as high as 40% could be realized by using an $HCl–AlCl_3$ system under high hydrogen pressure (40 atm).[9] Gas-phase isomerization of *endo*-trimethylenenorbornane over aluminosilicate catalyst[10] at high temperature (450–475 °C) yields 6–13% of adamantane along with a substantial number of acyclic, alicyclic, and aromatic byproducts.

McKervey et al.[11] reported subsequently an improved isomerization in the gas phase over chlorinated platinum–alumina catalyst and obtained up to 60% adamantane. During the course of reaction the catalyst suffers increasing deactivation.

In preceding work we reported[12] that the superacid-catalyzed isomerization of *endo*-trimethylenenorbornane to adamantane with anhydrous fluoroantimonic acid at a temperature of 100 °C gives a 47% yield of adamantane. More recently we found[13] an improved yield of 65% by using the novel $B(OSO_2CF_3)_3–HSO_3CF_3$ superacid system.

We now report our more detailed studies of the isomerization of *endo*- to *exo*-trimethylenenorbornane and subsequently to adamantane by various superacids (including solid superacids).

Results and Discussion

All the liquid superacid systems used in the present investigation (Table I) converted in different solvents [CCl_4, Freon-113 (1,1,2-trichloro-1,2,2-trifluoroethane), cyclohexane] *endo*-trimethylenebornornane to its exo isomer in almost quantitative yield with comparable reaction times. Whereas, in the case of the very strong conjugate Brønsted–Lewis superacids, extremely low acid to hydrocarbon ratios can bring about the thermodynamic equilibrium of nearly complete conversion to *exo*-trimethylenenorbornane, a relatively high acid to hydrocarbon ratio is required with less acidic CF_3SO_3H and FSO_3H. In control reactions of these acids with different solvents, no interaction was observed under the reaction conditions employed. After the completion of the reaction the heavier acid layer was allowed to settle at the bottom of the reaction flask, thus enabling easy separation and reuse. Solvent-free CF_3SO_3H even in relatively high acid to hydrocarbon ratio (5:1) and $CF_3SO_3H–B(OSO_2CF_3)_3$ in extremely low acid to hydrocarbon ratio gave ≤5% adamantane. All other systems gave <2% of adamantane.

Although the solid superacid Nafion-H, a perfluorinated resin, has been used in some hydrocarbon transformation, its use in the isomerization of trimethylenenorbornane has not been reported. We found that the endo to exo isomerization can be brought about by Nafion-H. The process is slow below 100 °C at relatively low acid to hydrocarbon ratio (by weight). A 50% conversion could be obtained only by carrying out the isomerization for 1 week at <100 °C. High yields of *exo*-trimethylenenorbornane could be, however, obtained at 170 °C still needing prolonged reaction times. Formation of adamantane is also observed with this solid superacid system. An increase in the acid to hydrocarbon ratio (by weight) increases adamantane formation to 18–28%.

In order to further improve the endo ⇄ exo isomerization over a solid superacid catalyst, intercalated SbF_5–graphite was used as the catalyst. This system turned out to be as active as liquid trifluoromethanesulfonic acid in case of a 1:1 acid to hydrocarbon molar ratio. A further increase of the ratio also led to 7% adamantane formation.

Use of liquid superacid systems with higher acid to hydrocarbon ratios led the isomerization of both *endo*- and *exo*-trimethylenenorbornane to adamantane in very high yields. Of all the superacid systems used in this investigation, the highest yield of adamantane was obtained with neat $CF_3SO_3H–SbF_5$ and $CF_3SO_3H–B(OSO_2CF_3)_3$ (yields reached 94–98%). In the solvent-free neat acid systems it was observed that solid *endo*-trimethylenenorbornane was, in the initial stage of reaction, slowly taken up into the acid, forming a homogeneous solution in which subsequently adamantane was formed. To our knowledge, no

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Table II. Isomerization of *endo*- and *exo*-Trimethylenenorbornane to Adamantane

acid systems	acid to substrate (molar ratio)	solvent	temp, °C	time, h	% yield: *exo*-trimethylenenorbornane	% yield: adamantane[d]
$CF_3SO_3H + SbF_5$ (1:1)	1:1 (endo)[a,b]		0–rt	10	0.4	95.4
			0–rt	7	0.1	98.0
	1:1 (exo)[a]		0–rt	12		94.0
	1:1 (endo)[c]	Freon	0–rt	16	41.0	50.0
		Freon	0–rt	50	30.0	64.3
	1:3 (exo)[c]		0–rt	16	28.3	58.2
			0–rt	50	27.0	68.0
$CF_3SO_3H + B(OSO_2CF_3)_3$ (1:1)	1:1 (endo)		0–rt	12		98.0
$FSO_3H + SbF_5$ (1:1)	1:3 (endo)[c]		0–rt	18	59.5	38.0
$HF + SbF_5$ (1:1)	1:1 (endo)[c]		0–rt	18	71.0	16.0
	1:1 (exo)[c]		0–rt	18	66.0	20.0
$HF + BF_3$ (800 psi)	10:1 (endo)		100	6	67.0	32.0
	20:1 (endo)		100	5	67.0	33.0
$CF_3SO_3H + HF + BF_3$ (1:1) (500 psi)	10:1 (endo)[b]		100	7	66.0	32.7
	5:1 (endo)		rt	7	27.0	27.0

[a] An unidentified product (y) was obtained: 3–6% in CF_3SO_3H–SbF_5; <2% in FSO_3H–SbF_5. [b] 1-Adamantanol was identified (<2%). [c] An unidentified product (x) was obtained: 6–13% in CF_3SO_3H–SbF_5; ~1% in FSO_3H–SbF_5; 13–14% in HF–SbF_5. [d] Yield of isolated adamantane.

comparable high yields of adamantane were ever reported with any other acid catalyst system. Use of solvents as well as lower acid to hydrocarbon ratios significantly decreased the yield of adamantane. The nearly quantitative yield of adamantane obtained is attributed to the fact that in the acid layer the carbocation equilibrium is that of nearly 100% 1-adamantyl cation. The nonoxidizing nature of the used superacid system help to avoid byproduct formation. Magic acid (FSO_3H–SbF_5) although has an even higher acidity[14] but gives lower yields of adamantane with side products due to its oxidizing nature.

For comparison we also studied other superacid systems. The yield of adamantane with HF–SbF_5 under the mild conditions employed in the present investigation was lower than that obtained under more forcing conditions reported previously.[11] Attempts to improve the yield of adamantane by increasing the acid to hydrocarbon ratio in both HF–SbF_5 and FSO_3H–SbF_5 systems resulted in more complex reaction mixtures than in case of CF_3SO_3H–SbF_5.

The patent literature[7] reports a 30% yield of adamantane with HF–BF_3 as isomerizing catalyst. We also reinvestigated this reaction and found that the yield remained the same even at more elevated temperatures and with much higher acid to hydrocarbon ratios. The ternary $CF_3SO_3H/HF/BF_3$ acid system under varying reaction conditions also did not improve the yield of adamantane further.

In conclusion, the isomerization of *endo* to *exo*-trimethylenenorbornane takes place nearly quantitatively with a variety of liquid and solid superacid catalysts under mild conditions. Subsequent isomerization to adamantane can be achieved in 20–98% yield depending on the strength of the acid system, reaction temperature, time conditions, and particularly acid to hydrocarbon ratio. In the former isomerization with low acid to hydrocarbon ratios equilibrium of the neutral hydrocarbons gives a nearly quantitative yield of the exo product. The adamantane isomerization due to its complex nature is best achieved under conditions where the related carbocation equilibrium can be achieved, i.e. with high superacid to hydrocarbon ratios. As the 1-adamantyl cation is the most stable C_{10} carbocation, the adamantane isomerization can be consequently nearly quantitative.

Experimental Section

Trifluoromethanesulfonic (triflic) acid (3M Co.) and fluorosulfuric acid (Allied) were freshly distilled under dry nitrogen prior to their use. *endo*-Trimethylenenorbornane was available from Aldrich, and *exo*-trimethylenenorbornane was prepared according to Schleyer's procedure.[3b] Antimony pentafluoride in graphite (50%) was purchased from Alfa. The CF_3SO_3H–$B(OSO_2CF_3)_3$ system was prepared according our previous procedure.[13] Other Lewis-conjugated superacids were prepared by Vortex mixing of appropriate ratios of protic acid with Lewis acid at low temperature. Nafion-H was generated from Nafion-K resin (DuPont) by stirring in 25% nitric acid.[15] GC analysis was carried out on a Varian Model 3700 gas chromatograph equipped with a capillary column and an on-line automatic integrator.

General Method of Isomerization of *endo*- to *exo*-Trimethylenenorbornane and to Adamantane. Isomerization of *endo*- to *exo*-trimethylenenorbornane was carried out by treating *endo*-trimethylenebornornane [usually 5 g (36.8 mmol)] with various acid systems in different solvents either at 0 °C or at room temperature under dry argon (Table I).

The isomerization reaction to adamantane was carried out by mixing the acids with either the *endo*- or the *exo*-trimethylenenorbornane [usually 5 g (36.8 mmol)] under varying conditions as shown in Table II. Experiments in solvent-free acids were carried out as follows: 3.0 g (22.0 mmol) of *endo*- (or *exo*-) trimethylenenorbornane was placed into a Schlenk flask and cooled to 0 °C. Subsequently 22.0 mmol of the corresponding superacids [16.6 g of CF_3SO_3H–$B(OSO_2CF_3)_3$, 8.1 g of CF_3SO_3H–SbF_5] was added under dry argon. The flask was evacuated and then allowed to continue at room temperature for the specified time (Table II).

Reactions with Nafion-H were carried out by adding Nafion-H to the *endo*-trimethylenenorbornane (8 g, 58.8 mmol) at its melting point and heating the reaction mixture to about 170 °C for different lengths of time (Table I). The reaction flask was connected to a cold finger to collect any adamantane that sublimes.

Reactions with HF–BF_3 were carried out in a stainless-steel autoclave by adding HF to a known amount of the endo compound (5 g, 36.8 mmol) at −30 °C and then closing the autoclave and heating it to about 100 °C under BF_3 pressure (800 psi).

All reactions were worked up with ice–bicarbonate quenching followed by methylene chloride extraction. exo-Trimethylenenorbornane was distilled at 184 °C (lit.[3] 185 °C). Adamantane was isolated by precipitation from *n*-pentane.

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Registry No. F_3CSO_3H, 1493-13-6; FSO_3H, 7789-21-1; SbF_5, 7783-70-2; $B(OSO_2CF_3)_3$, 64371-01-3; HF, 7664-39-3; BF_3, 7637-07-2; Nafion-14, 63937-00-8; graphite, 7782-42-5; *endo*-trimethylenenorbornane, 2825-83-4; *exo*-trimethylenenorbornane, 2825-82-3; adamantane, 281-23-2.

In Situ Opening of Epoxy Alcohols: A Convenient Alternative to the Isolation of Unstable Epoxy Alcohols

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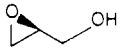
The synthetic utility of the titanium-catalyzed asymmetric epoxidation has been demonstrated by numerous applications of the reaction to the synthesis of enantiomerically pure compounds.[1] However, successful applications of the original epoxidation procedure have been elusive for small epoxy alcohols, especially those bearing a terminal epoxy group, among which glycidol (1) and 2-methylglycidol (2) are of particular importance as chiral



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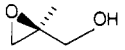

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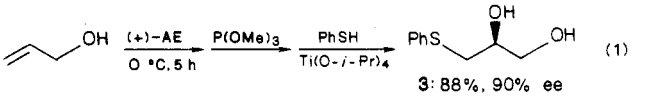
building blocks.[2] The problems often cited in the production of these epoxy alcohols are their propensity for undergoing ring-opening reactions and their water solubility. Although recent developments in the catalytic version of the process[3] and the nonaqueous workup procedure[4] have made it possible to obtain these epoxy alcohols in good yield and high enantiomeric purity,[5] difficulties are still encountered during workup, distillation, and storage.

Since the synthetic utility of such epoxy alcohols is largely due to their facile ring-opening reactions with nucleophiles, it appeared advantageous to exploit this reactivity by opening the terminal epoxide group in situ without isolation of the unstable epoxy alcohol. Although many of the nucleophiles that are known to open epoxy alcohols might be considered for such an in situ opening process, we initially chose to examine those nucleophiles that had been successfully used in the Ti-mediated epoxy alcohol opening reaction.[6] This was done in order to avoid any potential complication due to the titanium alkoxides already present in the reaction mixture. Regioselectivity is not a problem at all in this case because the C-3 position, which is electronically favored in attack by nucleophiles, is also a terminal center. Instead, the major concerns here are the synthetic utility and practical convenience in handling the ring-opened products (diols). Accordingly, our investigations were limited to such nucleophiles as thiols, secondary amines, and phenols.

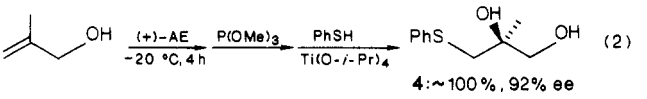
Benzenethiol, which was one of the most reactive nucleophiles among those studied in the Ti-mediated epoxy alcohol opening reaction, was found to readily open glycidol under in situ conditions (eq 1, where AE = 5 mol % Ti(O-*i*-Pr)$_4$, 6 mol % (+)- or (−)-DIPT, 2 equiv cumene hydroperoxide, 3-Å powdered sieves). Thus, after the cat-



(1)

3: 88%, 90% ee

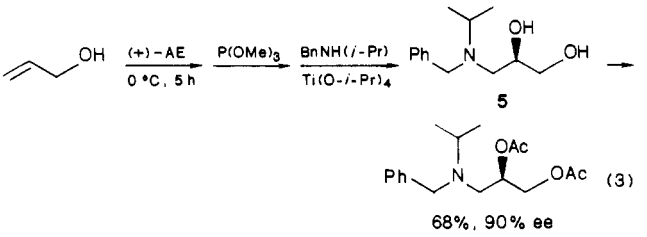
alytic asymmetric epoxidation was complete, the excess hydroperoxide was reduced with trimethyl phosphite. The reaction mixture was then treated with benzenethiol in the presence of 1 equiv of Ti(O-*i*-Pr)$_4$. Aqueous acidic workup was followed by chromatography to yield the thiophenyl diol **3** in 88% yield and ca. 90% ee. A similar procedure was employed with methallyl alcohol as substrate to yield the diol **4** in a quantitative yield and 92% ee (eq 2). The synthetic utility of the product phenylthio diols has been demonstrated in the literature.[7]



(2)

4: ~100%, 92% ee

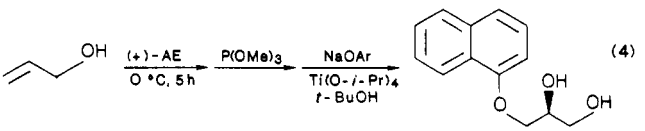
Secondary amines also opened glycidol in situ. When *N*-isopropylbenzylamine was used as nucleophile, the opening product was isolated, after peracetylation, in 68% yield (eq 3).



(3)

68%, 90% ee

Although phenols are not generally effective as nucleophiles in the Ti-mediated epoxy alcohol opening reaction, the high reactivity of glycidol and the practical importance of the opening products (aryl ether diols) as synthetic intermediates in the preparation of β-adrenergic blocking agents prompted us to investigate the in situ opening with phenols. As a result, it was found that addition of *t*-BuOH as a cosolvent was essential to promote the ring-opening reaction. Thus, after catalytic epoxidation of allyl alcohol and reduction of the excess hydroperoxide, the reaction mixture was treated with sodium 1-naphthoxide in *t*-BuOH in the presence of 1 equiv of Ti(O-*i*-Pr)$_4$. The opening product **6** was isolated by crystallization in 54% overall yield (eq 4). Synthesis of propranolol via this sequence has already been reported.[8]



(4)

6: 54%, 90% ee

The in situ opening process described above, which takes advantage of the reactivity of the terminal epoxide group of glycidol and 2-methylglycidol, not only allows easier

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