Lewis Acid-induced Regio- and Stereo-selective Cyclisation of Epoxy-allylic Stannanes

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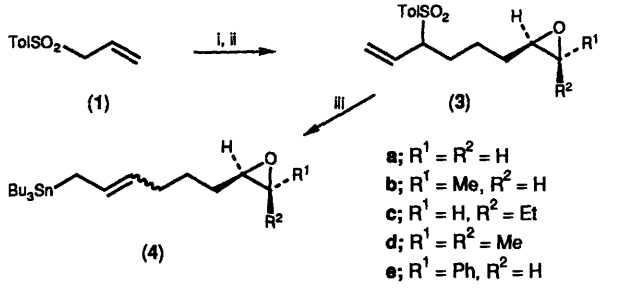
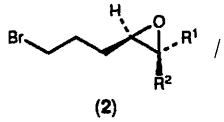
Lewis acid-induced cyclisation of epoxy-allylic stannanes to give carbocyclic alcohols has been studied. The regio- and stereo-selectivities shown in the reaction are discussed in terms of the effects of substituents on the epoxide rings and of the Lewis acids employed.

Intramolecular reactions of allylic metal compounds with an electrophilic centre provide useful methodology for construction of cyclic systems. Recently much interest has been devoted to regiochemically controlled intramolecular reactions of allylic silanes or stannanes with epoxides.[1] Most examples were concerned with substrates containing glycidyl alcohol, ether, or ester entities, which significantly affected the regioselectivities of the cyclisations by chelation with a Lewis acid. The stereochemistry of the above cyclisations allowed retention of the epoxide ring configuration in the cyclised products.[1h] Proctor and co-workers demonstrated that 1,2-epoxy-8-trimethylsilyloct-6-ene (*E*/*Z* ratio 1:4) was cyclised in the presence of $TiCl_4$ to afford 1-hydroxymethyl-2-vinylcyclopentane (*cis*/*trans* ratio 4:1) in 55% yield.[1c,f] But the stereochemical control of the reaction has not been well understood. We present here results for the regio- and stereoselective cyclisations of epoxy-allylic stannanes.

We examined the cyclisations of epoxy-allylic stannanes (**4**) having various substituents on the epoxide rings. They were prepared by alkylation of the allyl sulphone (**1**), followed by AIBN-initiated desulphono-stannylation[2] with tributyltin hydride in good yield in a *E*/*Z* ratio of *ca.* 4:1 (Scheme 1). The major *Z*-isomer (**4a**) could also be obtained by a modified procedure previously reported for the preparation of an epoxy-allylic silane[1c,f] using (iodomethyl)tributylstannane in a *E*/*Z* ratio of 22:78.



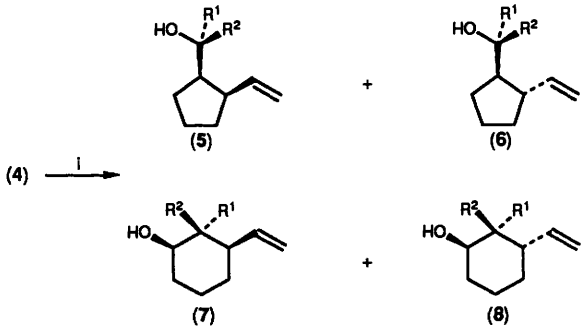
Scheme 1. *Reagents:* i, BuLi–HMPA/THF–Et_2O/−20 °C ii,  /−78 °C; iii, Bu_3SnH, AIBN/benzene.

Reactions of (**4**), carried out in CH_2Cl_2 in the presence of a Lewis acid ($TiCl_4$, $SnCl_4$, or Me_3SiOTf, 1 equiv.), were quenched after 30 min to afford a diastereoisomeric mixture of *exo*- and *endo*-cyclised products (**5**), (**6**), and (**7**) (Scheme 2). A further possible isomer (**8**) could not be detected in the product mixtures. The isomers were difficult to separate by conventional column chromatography on silica gel, but their regio- and

Table.

(4)	R^1	R^2	E/Z*	Lewis acid	Temp. (°C)	Yield (%)	(5)	(6)	(7)
a	H	H	77/23	$TiCl_4$	−78	100	74	26	—
a	H	H	77/23	$TiCl_4$	−20	90	63	36	—
a	H	H	77/23	$SnCl_4$	−78	21	11	89	—
a	H	H	77/23	TMSOTf	−78	81	74	26	—
a	H	H	22/78	$TiCl_4$	−78	84	76	24	—
b	Me	H	81/19	$TiCl_4$	−78	91	25	68	7
b	Me	H	81/19	TMSOTf	−78	94	25	62	13
c	H	Et	78/22	$TiCl_4$	−78	97	73	27	—
c	H	Et	78/22	TMSOTf	−78	78	79	21	—
d	Me	Me	78/22	$TiCl_4$	−78	90	—	2	98
d	Me	Me	78/22	TMSOTf	−78	69	—	28	72
e	Ph	H	79/21	$TiCl_4$	−78	100	—	3	97
e	Ph	H	79/21	TMSOTf	−78	95	—	3	97

* These ratios were determined from the integral ratio of the alkenic protons in the ^1H NMR spectra (400 MHz, $CDCl_3$), as follows; (**4a**) δ 5.18(*E*), 5.04 (*Z*); (**4b**) δ 5.19(*E*), 5.04(*Z*); (**4c**) δ 5.20(*E*), 5.05(*Z*); (**4d**) δ 5.21(*E*), 5.06(*Z*); (**4e**) δ 5.20(*E*), 5.06(*Z*).



Scheme 2. *Reagents:* i, Lewis acid/CH_2Cl_2.

diastereo-isomeric ratio could be determined from the integral ratio of the alkenic protons in their ^1H NMR spectra (see Table). Configurations of the *exo*-cyclised products (**5**) and (**6**) were deduced from conformational analysis using the NMR shift reagent, Eu(FOD)$_3$. For *endo*-cyclised products (**7**), proton–proton *J* couplings assisted the assignments.

We found that catalytic amounts of Lewis acids were insufficient for completion of the reactions even with Me_3SiOTf which was known to catalyze the reactions of allylsilane with carbonyl and acetal groups.[3] Reactions with $TiCl_4$ and Me_3SiOTf resulted in much higher yields than previous results for the allylic silane-mediated reaction.[1c,f] BF_3·OEt_2 and $Cl_2Ti(OPr^i)_2$ were also efficient promoters for the cyclisations, but their stereoselectivities were lower. A $SnCl_4$-induced reaction gave many undesirable by-products which were detected by TLC. Such complex behaviour is probably a result of exchange between tributyl and trichlorostannyl groups and the involvement of reaction paths differed from those employing other Lewis acids.

Higher regioselectivities were observed with substituents which stabilize a cationic centre in the epoxy group induced by a chelation with a Lewis acid. However, in the case of (**4b**) and (**4c**), which have two electrically equivalent reaction sites, the *exo*-cyclisations occurred selectively. The regioselectivities increased as a function of the acidity of the Lewis acid; the reaction with $TiCl_4$ resulted in slightly higher selectivities than with Me_3SiOTf in the reaction of (**4b**) and (**4d**).

The stereoselectivities of the *exo*-cyclisations were significantly influenced by the substrate structure, Lewis acid employed, and reaction temperature. In the case of (**4a**), the $SnCl_4$-induced reaction afforded mainly *trans* isomer (**6a**) in low yield. In contrast, in the presence of $TiCl_4$ at −78 °C, *cis* (**5a**) and *trans* (**6a**) isomers were formed in a ratio 74:26 ~ 76:24, independent of the *E*/*Z* configuration of the substrate (**4a**): the selectivity dropped at higher temperature. A *trans* substituent at a terminal position of the epoxides preferentially directed the reaction to give the *trans* products (**6**).

In the *endo* cyclisation, only *cis* isomers were formed: As in earlier work,[1h] the epoxide ring configurations in (**4b**), (**4c**), and (**4e**) were retained in the cyclisations as a result of rear attack of the allylic stannane entity on the C–O bond.

Experimental

Titanium Tetrachloride-induced Reaction of trans-*7,8-Epoxy-1-tributylstannylnon-2-ene* (**4b**).—To a solution of (**4b**) (215 mg, 0.5 mmol) in dry dichloromethane (20 ml) at −78 °C was added slowly a 0.2M solution of titanium tetrachloride in dichloromethane (2.5 ml, 0.5 mmol). The mixture was stirred (30 min) at the same temperature under nitrogen and saturated aqueous $NaHCO_3$ (5 ml) was added; the mixture was then allowed to reach room temperature. The organic layer was separated, washed with 10% aqueous NH_3 and brine, dried ($MgSO_4$), and evaporated. The residue was flash chromatographed on silica gel [elution, hexane–diethyl ether (3:1)] to give an isomeric mixture of the cyclised products (**5b**), (**6b**), and (**7b**) (64 mg, 91%) in a ratio of 25:68:7 [Found: $(M - H)^+$, 141.1264. $C_9H_{17}O$ requires *M* + H, 141.1277; Found: $(M + OH)^+$, 123.1167. C_9H_{15} requires *M* − OH, 123.1172]; ν_{max}(film) 3 280(OH) and 1 640 cm^{-1} (C=C); δ_H(400 MHz, $CDCl_3$): (**5b**) 1.19 (3 H, d, *J*, 8.6 Hz, Me), 1.2–1.9 (8 H, m), 2.58 (1 H, m, 2-H), 3.74 (1 H, quintet, *J* 6.5 Hz, C*H*OH), 4.94 (1 H, dd, *J* 10.1 and 2.1 Hz, vinyl H), 5.02 (1 H, dd, *J* 17.0 and 2.1 Hz, vinyl H), 5.85 (1 H, ddd, *J* 17.0, 10.1, and 9.3 Hz, vinyl H); (**6b**) 1.19 (3 H, d, *J* 8.6 Hz, Me), 1.2–1.9 (8 H, m), 2.29 (1 H, m, 2-H), 3.80 (1 H, dq, *J* 4.4 and 6.5 Hz, C*H*OH), 4.94 (1 H, dd, *J* 10.1 and 2.1 Hz, vinyl H), 5.02 (1 H, dd, *J* 17.0 and 2.1 Hz, vinyl H), and 5.76 (1 H, ddd, *J* 17.0, 10.1, and 9.3 Hz, vinyl H); (**7b**) 1.00 (3 H, d, *J* 6.5 Hz, Me), 1.2–1.9 (8 H, m), 1.97 (1 H, m, 3-H), 3.18 (1 H, dt, *J* 4.1 and 9.9 Hz, 1-H), 4.96 (1 H, dd, *J* 9.9 and 2.2 Hz, vinyl H), 5.03 (1 H, dd, *J* 16.9 and 2.2 Hz, vinyl H), and 5.60 (1 H, ddd, *J* 16.9, 9.9, and 8.8 Hz, vinyl H).

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