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CHEMO- AND REGIOSELECTIVE REDUCTION OF α,β-EPOXY KETONES TO β-HYDROXY KETONES BY SODIUM HYDROGENTELLURIDE

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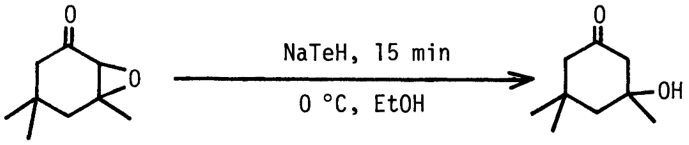
α,β-Epoxy ketones were chemo- and regioselectively reduced to β-hydroxy ketones by sodium hydrogentelluride in good yields.

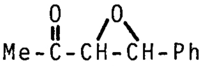
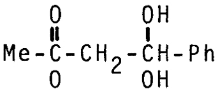
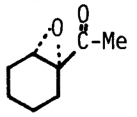
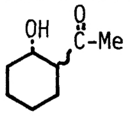
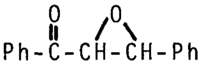
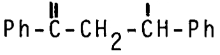
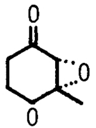
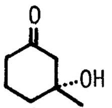
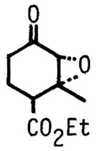
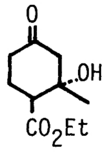
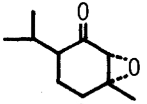
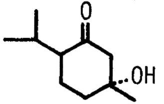
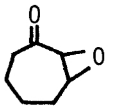
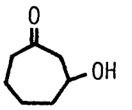
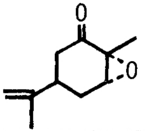
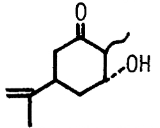
In recent years, the application of tellurium in organic syntheses has significantly increased.[1)] Among these, sodium hydrogentelluride (NaTeH),[2)] which is readily prepared *in situ* from tellurium and sodium borohydride ($NaBH_4$), has been used for several chemoselective reductions.[3)] Particularly interesting is its high reactivity towards the reductive removal of electronegative α-substituents of ketones and acids; and its reluctance to reduction of simple aldehydes and ketones.[4)] Herein we disclose the results of our new procedure for chemo- and regioselective reduction of α,β-epoxy ketones to β-hydroxy ketones through the use of NaTeH.



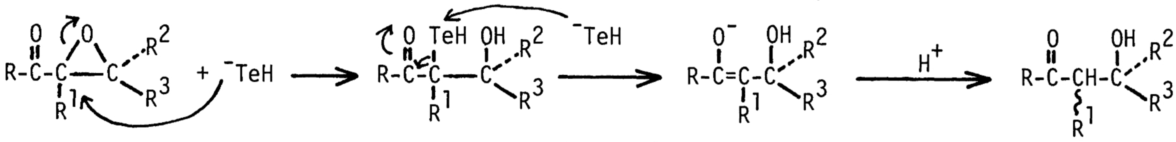
The method involves just the treatment of α,β-epoxy ketones with NaTeH at 0 °C for a short time. The typical experimental procedure is exemplified by the synthesis of 3-hydroxy-3,5,5-trimethylcyclohexanone from isophorone oxide. A solution of isophorone oxide (0.616 g, 4 mmol) in ethanol (4 mL) was added at 0 °C under argon atmosphere to a solution of NaTeH,[2)] prepared *in situ* from tellurium (1.3 g, 10 mmol) and $NaBH_4$ (0.9 g). An instantaneous reaction occurred and the color of the reaction mixture changed to deep black. After 15 min, water (50 mL) was added, and the resulting mixture was left open to air with stirring at 0 °C. The solution became clear after 1 h with the deposition of tellurium powder. It was then filtered through Celite 545 and the filtrate was extracted with CH_2Cl_2. The extracts were washed with water, dried over Na_2SO_4, and evaporated to give crystalline solid, which was recrystallized from hexane to give 3-hydroxy-3,5,5-trimethylcyclohexanone (0.518 g, 83%; mp 79-79.5 °C). Some representative examples were given in Table 1. In most cases, the reductive opening of oxirane ring took place regioselectively at α-position; and neither the reduction of keto group nor the further dehydration of β-hydroxy ketones were observed. While single isomers were produced from α,β-epoxy ketones possessing no α-alkyl substituents, isomeric mixtures at α-carbon were obtained from α,β-epoxy ketones possessing α-alkyl substituents. NaTeH is a specific reducing reagent for activated epoxides, and thus reduces α,β-epoxy ester 1 to the corresponding β-hydroxy ester in 90% yield, but does not reduce at all trans-stilbene oxide or epoxy alcohol 2.

Although the mechanism of this reduction has not been studied yet, the stereochemical results

Table 1. Reduction of α,β-epoxy ketones to β-hydroxy ketones by NaTeH.

Reactant	Product	Yield/%[a]	Reactant	Product	Yield/%[a]
	 $\mathrm{Me{-}\overset{O}{\overset{\|}{C}}{-}CH_2{-}\overset{OH}{\overset{|}{C}H}{-}Ph}$	89			89[c]
	 $\mathrm{Ph{-}\overset{O}{\overset{\|}{C}}{-}CH_2{-}\overset{OH}{\overset{|}{C}H}{-}Ph}$	91			
		75			72
		96			74
		80[b]			

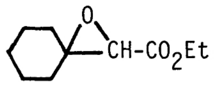
[a] Isolated yields. [b] 4:1 Mixture. (-)-Carvone was formed in 16% yield. [c] 2:1 Mixture.



Scheme 1.

noted above can be explained in terms of the mechanism shown in Scheme 1.

The present reaction is particularly suited for the preparation of alicyclic β-hydroxy ketones, and has significant synthetic importance in connection with the synthesis of cardiac-active steroids,[5] periplogenin and strophanthidin, and the conversion of prostaglandins PGA_2 into PGE_2 and $PGF_{2\alpha}$.[6] The application of this procedure to biologically important natural products as well as the detailed mechanistic study are now in progress.



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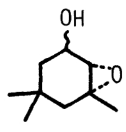

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