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A Convenient Deoxygenation of α,β-Epoxy Ketones to Enones

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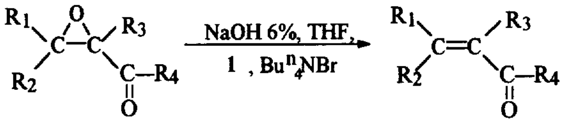
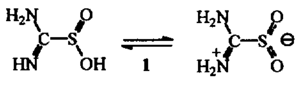
Abstract: A new and efficient methodology for the deoxygenation of α,β-epoxy ketones to enones has been developed, using aminoiminomethanesulfinic acid (thiourea dioxide) as the reducing agent under phase transfer conditions. The epoxides of mesityl oxide, isophorone, (-)-carvone, (+)-6-methyl-carvone, (+)-6-ethyl-carvone and (-)-myrtenal, were converted into their respectives enones in good to excellent yields. © 1997, Elsevier Science Ltd. All rights reserved.

Deoxygenation of epoxides is a valuable synthetic transformation which can be achieved in one or more steps, resulting in complete retention, inversion, or loss of stereochemistry of the starting epoxide.[1] Methods for epoxide deoxygenation have been reviewed in detail,[2] but to our knowledge very few reagents have been reported for the deoxygenation of α,β-epoxy ketones into the corresponding α,β-enones. These include $CrCl_2$ and $Cr(OAc)_2$,[3] sodium cyclopentadienyldicarbonylferrate,[4] $Fe(CO)_5$,[5] dimethyl diazomalonate[6] and P_2I_4.[7]

In this communication, we describe an efficient deoxygenation of α,β-epoxy ketones to enones, with aminoiminomethanesulfinic acid (thiourea dioxide, TDO **1**) in THF/alkaline medium and using tetra-n-butyl ammonium bromide as the phase transfer catalyst.





TDO 1 [8] is easily prepared by the oxidation of thiourea with hydrogen peroxide, and has been widely used as a strong reducing agent for inorganic metal ions.[9]

However, its application in organic synthesis is rather limited and very few synthetic transformations have been performed with this reagent. The use of TDO for the reduction of aromatic nitro, azoxy, azo and hydrazo compounds as well as of quinones, was first described by Gore in 1954.[10] Reduction of ketones by **1** has been reported[11,12] although in this case the role of TDO as the reducing agent was questioned by Caputo et al.[13] Borgogno, Colonna, and Fornasier[14] have utilized TDO to reduce sulphimines and disulfides to the corresponding sulfides and thiols in a two phase system using hexadecyltributylphosphonium bromide as the phase transfer catalyst. Drabowicz and Mikolajczyk[15] employed **1** in the presence of iodine to reduce sulfoxides to sulfides. Lang et al.[16] have reported the synthesis of sulfides, selenides and tellurides from the corresponding disulfides, diselenides and ditellurides under phase transfer catalysis.

In connection with a related study on the epoxidation and subsequent ring opening reactions of monoterpene enones, we studied the generation[16] of nucleophiles in the presence of TDO, and discovered the facile reduction of the epoxides back to the corresponding enones. The present communication describes a general study of this interesting reduction using six readily available model epoxides.

The epoxides **8-13** of mesityl oxide **2**, isophorone **3**, (-)-carvone **4**, (+)-6-methyl-carvone **5**, (+)-6-ethyl-carvone **6** and (-)-myrtenal **7**, were prepared in standard conditions[17] with 30% H_2O_2 and 6N NaOH. The yields of isolated epoxides are normally over 80%, with the exception of **8** probably due to its high volatility.

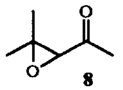
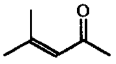
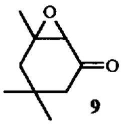
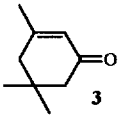
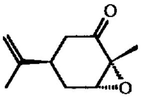
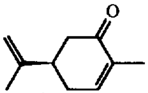
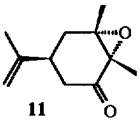
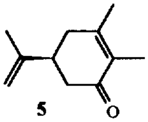
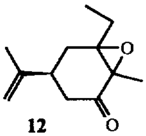
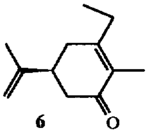
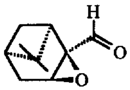
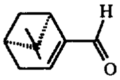
The α,β-epoxy ketones were reduced as described in the typical procedure below, furnishing the enones **2** to **7** as shown in Table I. The yields vary from 70 to 95%, with the exception of mesityl oxide (40%) probably due to its high volatility, and the reduction accommodates highly substituted and sterically hindered epoxides, even proximate with the aldehyde function. The facility for preparing TDO **1**, coupled with the ease of the reduction reaction, makes this procedure highly competitive with the previous methodologies.

Typical procedure for the deoxygenation of α,β-epoxy ketones.

To a solution of TDO **1** (216 mg; 2 mmol) and Bu^n_4NBr (5 mg) in 6% aqueous sodium hydroxide (3 mL), is added a solution of the α,β-epoxy ketone (1.5 mmol) in THF (3 mL). The two-phase system is vigorously stirred at room temperature, or under reflux, for the time indicated in Table I. The phases are separated and the aqueous layer is extracted with Et_2O (3x20 mL). The organic phase is washed with water (3x20 mL) and dried with $MgSO_4$. The solvent is evaporated and the residue is chromatographed on silica gel, eluting with hexane-EtOAc (90:10). The enones were obtained in the yields shown in Table I.

TDO **1** is easily prepared[8] by oxidation of thiourea with cold aqueous 15% H_2O_2 , with stirring for one hour, filtration and washing with ice-water, followed by crystallization from hot ethanol.

Table I. Reduction of α,β-Epoxy Ketones With Thiourea Dioxide **1**.

Entry	Substrate	Product	Reaction time (h)	Yield^{c}	$[\alpha]_D^{23}$	^{1}H NMR, δ (ppm)
1	 **8**	 **2**	0.2^{a}	40	-	1.90 (br. s, 3H); 2.20 (s, 6H); 6.10 (m, 1H).
2	 **9**	 **3**	1.0^{a} 0.5^{b}	89 95	-	0.95 (s, 6H); 1.95 (br. s, 4H); 5.85 (br. s, 1H).
3	 **10**	 **4**	1.0^{a} 0.5^{b}	85 89	+60.03° (neat) +61.0° (lit.)[17a]	1.80 (br. s, 6H); 2.30-2.60 (m, 5H); 4.75 (m, 2H); 6.75 (m, 1H).
4	 **11**	 **5**	1.0^{a} 0.5^{b}	88 92	+102.8° (neat) +103.5° (lit.)[18]	1.75 (br. s, 6H); 1.95 (s, 3H); 2.10-2.85 (m, 5H); 4.75 (br. s, 2H).
5	 **12**	 **6**	1.5^{a}	91	-	1.05 (t, 3H, J = 7.8 Hz); 1.75 (br. s, 6H); 2.00-2.40 (m, 7H); 4.75 (sl, 2H).
6	 **13**	 **7**	36^{a}	70	-14.8° (neat) -15.0° (lit.)[17a]	0.80 (s, 3H); 1.50 (s, 3H); 2.20-3.05 (m, 6H); 6.90 (m, 1H); 9.60 (s, 1H).

[a] reaction carried out at room temperature.

[b] reaction carried out at reflux (50°C).

[c] yield of the chromatographed product.

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