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LETTERS

A tellurium-triggered domino reaction for the synthesis of a 1-substituted-3-vinyl-1,3-dihydroisobenzofuran[1]

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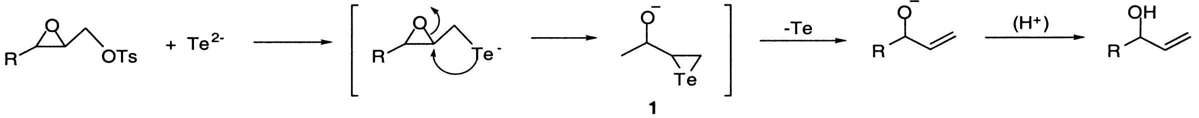
Abstract

Telluride ion reacts with an oxiranemethanol toluenesulfonate in toluene under phase-transfer conditions to give an allylic alkoxide anion that is trapped by addition to an adjacent α,β-unsaturated ester to yield a furan derivative. Use of a non-racemic oxiranemethanol tosylate gives two furan diastereomers in a ratio of 56:44. © 2000 Elsevier Science Ltd. All rights reserved.

Previously, a tellurium process has been applied to the conversion of both racemic and non-racemic epoxyalcohols, the latter being obtained by Sharpless–Katsuki asymmetric epoxidation, to racemic and non-racemic secondary and tertiary allylic alcohols (Scheme 1).[2] Elemental tellurium is relatively non-toxic.[3] It is reduced to telluride ions Te_n^{2-} ($n = 1,2,3$), which trigger the hypothetical reaction sequence shown in Scheme 1, which results in the formation of the desired product with the release of tellurium which can be reused. Still open is the question of whether the putative epitelluride intermediate (**1**) in Scheme 1 might be formed by a more-or-less simultaneous attack on two carbon atoms, displacing two leaving groups, the epoxide oxygen and the tosylate. The process may be performed under no-solvent or phase transfer conditions[4] and can be catalytic in tellurium.[5]



Scheme 1.

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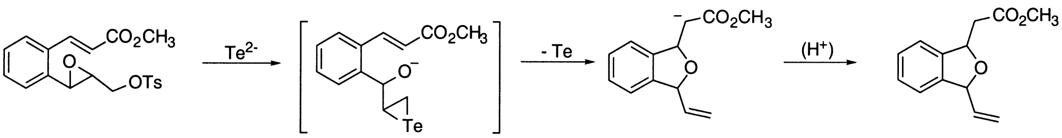
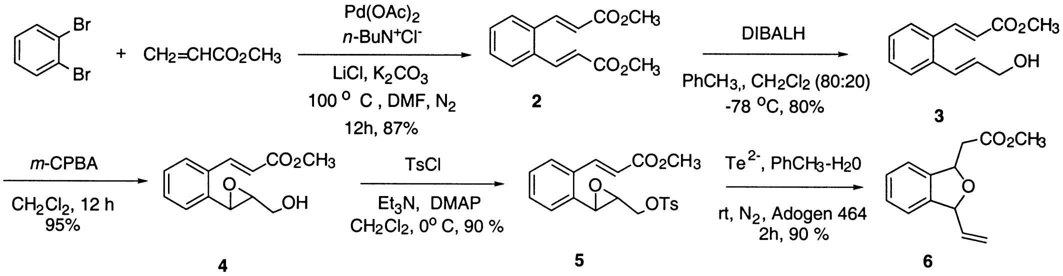
In our previous work exemplified in Scheme 1, the alkoxide ion from a ring-opening of the epoxide by telluride is trapped by protonation. If, however, the oxygen anion is generated in proximity to an electron-deficient group such as a Michael acceptor (Scheme 2), a heterocyclic ring is obtained. Intramolecular Michael-type additions of oxyanions to α,β-unsaturated esters have been previously observed.[6] Domino, tandem, or cascade reactions such as that shown in Scheme 2 are not uncommon in the synthesis of heterocyclic compounds and include Michael-type reactions.[7] They are especially useful in the one-step synthesis of complex molecules with excellent regio-, chemo-, diastereo- and enantioselectivity.[8,9]



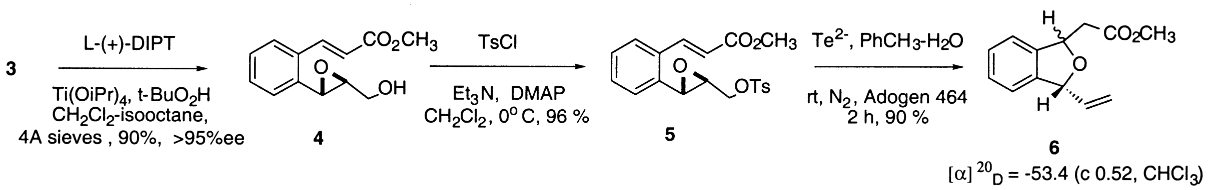
Scheme 2.

The starting material **2** (Scheme 3) is obtained by way of a double Heck reaction with methyl acrylate on *o*-dibromobenzene.[10,11] Selective reduction of one ester group of **2** (Scheme 3) by diisobutylaluminum hydride (DIBALH) (2 equiv.) is easiest on a small-scale, and over-reduction to the insoluble bis-allylic alcohol can be minimized by use of a mixture of toluene and dichloromethane (80/20) at –78°C. The carbon–carbon double bond of the allylic alcohol is epoxidized selectively with *m*-chloroperoxybenzoic acid (*m*-CPBA). Conversion of the epoxyalcohol to its tosylate and reaction with telluride ions under phase-transfer conditions gave the dihydroisobenzofuran. Certain dihydrobenzo [*c*] furans are said to have medicinal uses.[12]



Scheme 3.

Sharpless–Katsuki asymmetric epoxidation of allylic alcohol **3** and subsequent conversion of the optically active epoxyalcohol to the dihydroisobenzofuran (Scheme 4) results in a mixture of two diastereomers of **6** in a 56:44 ratio according to the proton NMR spectrum which shows two non-equivalent methyl groups. Other similar non-equivalencies in the proton spectra indicate nearly equal amounts of the two diastereomers. The ^{13}C NMR spectrum (126 MHz) shows slightly unequal doublings for the two aliphatic carbon atoms of the dihydrofuran ring and for the two CH_2 groups (one alkene and one aliphatic). Thus, the effect of the chiral center introduced by asymmetric epoxidation is not very great in selecting one face of the acrylate carbon–carbon double bond over the other in the formation of the isobenzofuran derivative.



Scheme 4.

Relatively low diastereoselectivity has been observed in domino reactions involving addition of lithium benzyl (trimethylsilyl) amide without Lewis acid additives to α,β-unsaturated esters[13] although a single diastereomer was reported for the reactions of **2**,[11] and high stereocontrol was observed in non-domino Michael reactions of arylmenthyl crotonates when good π-stacking can occur between the aryl group of the crotonate ester and the carbon–carbon double bond.[14]

Experimental procedure: An aqueous suspension (3 mL) of Te powder (101 mg, 0.790 mmol) was heated (60°C) for 2 h under argon with rongalite ($HOCH_2SO_2Na{\cdot}2H_2O$) (0.280 g, 3.27 mmol) and NaOH (0.0950 g, 2.37 mmol). The original black suspension of Te was transformed into a deep red–purple solution containing telluride ions (Te_n^{2-}). The solution was cooled to room temperature and the quaternary ammonium phase transfer catalyst Adogen 464 (20 mg) in toluene (1 mL) and the tosylate of (2*S*,3*S*)-**4** (0.243 g, 0.680 mmol) in toluene (4 mL) were added.[15] Black elemental Te began to precipitate after about 15 min. The mixture was stirred for 2 h, and the layers were allowed to separate. Air was bubbled through the mixture to facilitate oxidation of excess telluride ions. The toluene layer was removed, dried ($MgSO_4$), and filtered through a pipet of silica gel to remove Te° followed by evaporation of the solvent to give the nearly pure isobenzohydrofuran **6** (0.133 g, 0.610 mmol, 90%) $[\alpha]_D^{20} = -53.4$ (*c* 0.52, $CHCl_3$): ^1H NMR (500 MHz) δ 2.81 (9-line multiplet, 2H), 3.74 (s, 0.44H), 3.75 (s, 0.56H), 5.22 (ddd, J = 9.1, 1.1, 1.1 Hz, 0.49H), 5.26 (ddd, J = 8.8, 1.1, 1.1 Hz, 0.51H), 5.43 (ddd, J = 17, 1.5, 1.1 Hz, 0.56H), 5.41 (ddd, J = 17, 1.5, 1.1 Hz, 0.44H), 5.56 (br d, 0.5H), 5.65 (br m, 1H), 5.74 (br td, 0.5H), 5.91 (m, 1H), 7.10–7.30 (m, 4H). ^{13}C NMR (126 MHz) 42.3, 43.0, 52.5, 80.3, 80.4, 85.4, 85.7, 117.5, 117.6, 121.8, 121.9, 122.6, 128.6, 128.7, 138.3, 139.0, 141.3, 171.9. HRMS (FAB): calcd for $C_{13}H_{14}O_3Na$ (M+Na): 241.0841; found: 241.0842.

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15. Compound (2*S*,3*S*)-**4** was obtained in greater than 95% ee as indicated by comparison of the ^{1}H NMR spectrum of the α-methoxy-α(trifluoromethyl)phenylacetate ester with that of racemic **4**.