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# Tellurium-triggered formation of racemic and non-racemic allylic amines from aziridinemethanol derivatives

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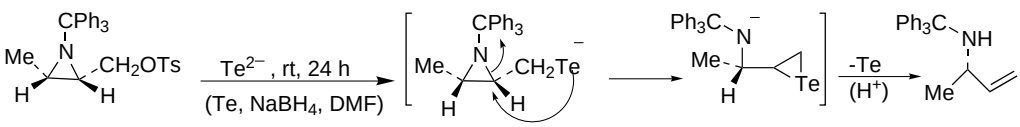
**Abstract**—Sharpless epoxidation, aminohydroxylation, and aziridination procedures provide substrates for the tellurium-triggered synthesis of racemic and non-racemic allylic amines under phase-transfer conditions. 

Allylic amines, particularly non-racemic examples, are useful synthetic intermediates because they embody both a reactive amine and an alkene functionality. They are used as antifungal agents,[1] and as precursors to α- and β-amino acids,[2] chiral terpenoid-based perfumes,[3] aminoepoxide intermediates for HIV protease inhibition,[4] β-hydroxy-γ-amino acids (renin inhibitors),[5] α-hydroxy-β-amino acids (immunopotentiators),[6] and peptide isosteres.[7]

The starting materials for the tellurium-triggered synthesis of allylic amines are allylic alcohols. These versatile intermediates have been used previously in the preparation of allylic amines by displacement reactions,[8] rearrangement reactions,[9] and by formation of π-allyl metal complexes followed by reaction with nitrogen nucleophiles.[10] Methods for the synthesis of allylic amines have been reviewed.[11]

Recent developments from the Sharpless group have provided easy access to racemic aziridinemethanol derivatives[12] and to non-racemic β-*N*-tosylamino-α-hydroxycarboxylic acid esters.[13] These latter compounds can be converted to aziridinemethanols, a class of compounds that comprised the starting materials for our previously reported synthesis of allylic amines via the intervention of telluride ions (exemplified in Scheme 1).[14] This earlier synthesis was unusual because the aziridine ring was readily opened by the nucleophilic telluride despite the lack of activation of the aziridine by an electron-withdrawing group on the nitrogen atom. Under the conditions used, electron-withdrawing substituents (e.g. *N*-tosyl) were actually unsatisfactory in yielding allylic amines with telluride ion, probably because the ring carbon atoms were attacked instead of the carbon atom of the alcohol tosylate. Nucleophilic opening of *N*-tosylaziridines is known to occur readily with organometallic reagents[15] and also internally analogous to the Payne rearrangement.[16] Since the convenient preparations of aziridinemethanols based on the chemistry described by Sharpless and co-workers yield *N*-tosyl derivatives, an adaptation of the telluride process to these previously recalcitrant molecules is desirable.

We find that under phase-transfer conditions the tellurium-triggered reaction works well with the electron-withdrawing *p*-toluenesulfonyl group on the nitrogen atom of the aziridine (Table 1).[17] Tellurium powder suspended in water (nitrogen atmosphere) is reduced with sodium borohydride or with rongalite (sodium hydroxymethanesulfinate dihydrate) under gentle heating (60°C) to give a purple to pink solution.[26] The aziridinemethanol derivative in toluene is added with a




**Scheme 1.** Previous allylic amine synthesis via tellurium.[14]

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phase-transfer catalyst (Adogen 464) to the aqueous solution of telluride cooled to room temperature. The reaction to produce the allylic amine occurs relatively rapidly as indicated by the formation of finely divided black tellurium. It is not necessary to purify the aziridinemethanol tosylates which are used directly in the telluride reaction. Only with the *N*-tosylaziridine derivative from cinnamyl alcohol did the tellurium process deviate from the mechanism of Scheme 1, yielding **3** instead of **2f** (Table 1). This behavior may be attributed to attack by the telluride ion at C-3 favored by phenyl stabilization of positive charge at that position caused by electron withdrawal by the *N*-tosyl group. However, the expected rearrangement occurs in our telluride-oxazolidinonemethanol procedure to give an analog of **2f** in which the *N*-tosyl group is replaced by *n*-hexyl.[27]

The precursors of the non-racemic aziridine tosylates (**1a**, **1b**) of Table 1 were derived, respectively, from aminodiols obtained via asymmetric epoxidation[28] followed by aminolysis with diphenylmethanamine, hydrogenolysis, and exhaustive tosylation (see Experimental)[14,18,19] or from ethyl crotonate via aminohydroxylation followed by reduction of the ester and exhaustive tosylation.[13] The racemic aziridine tosylates were prepared by aziridination of known allylic alcohols.[12]

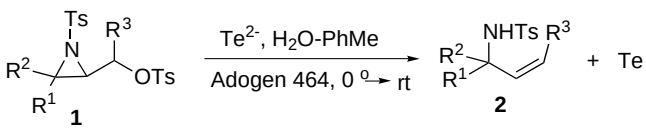
The conclusion is that the ready availability of both racemic and non-racemic aminodiols and racemic *N*-tosylaziridinemethanols enables a general synthesis of racemic and non-racemic allylic amines to be performed via a tellurium process under mild, phase-transfer conditions which allow easy isolation of product and easy recovery of tellurium which can be reused, thus avoiding the loss of a key reagent.

### Experimental tellurium procedure for (*R*)-2a

(2*R*,3*R*)-3-(α-Phenylbenzylamino)-1,2-hexanediol $[\alpha]_D^{20} = -20.0$ ($CHCl_3$, $c = 1.5$), lit[14] $[\alpha]_D^{20} = -24.2$ ($CHCl_3$, $c = 4.4$), prepared in 65% yield by reaction of diphenylmethylamine with (2*S*,3*S*)-3-*n*-propyl-2-oxiranemethanol, as described by Pericàs and Riera,[18] was converted to (2*R*,3*R*)-3-amino-1,2-hexanediol $[\alpha]_D^{20} = +9.3$ ($CHCl_3$, $c = 1.5$) by reduction with $H_2$-Pd.[18]

The aminodiol (0.387 g, 2.90 mmol) in $CH_2Cl_2$ (10 mL) at 0°C was treated with *p*-toluenesulfonyl chloride (2.21 g, 11.6 mmol), 4-*N*,*N*-dimethylaminopyridine (0.008 g), and triethylamine (4.83 mL). The reaction mixture was stirred at room temperature for 32 h, water (2 mL) was added, and the phases were separated. The aqueous phase was extracted with $CH_2Cl_2$ (10 mL), and the combined organic phases were dried ($MgSO_4$), concentrated, and chromatographed (silica gel, ethyl acetate:hexane, 15:85) to give the crude aziridine derivative, 1-(*N*-4-methylbenzenesulfonyl)-2-aziridinemethyl *p*-toluenesulfonate, (2*S*,3*R*)-**1a** (0.920 g, 2.18 mmol, 75%) [$^1$H NMR ($CDCl_3$) $\delta$ 7.82 (d, $J = 8.2$ Hz, 2H), 7.72 (d, $J = 8.1$ Hz, 2H), 7.32 (m, 4H), 4.07 (m, 2H), 2.90 (m, 1H), 2.72 (m, 1H), 2.42 (s, 6H), 1.58–1.42 (m, 2H), 1.26 (m, 2H), 0.85 (t, $J = 7.4$ Hz, 3H); $^{13}$C NMR ($CDCl_3$) $\delta$ 147.0, 144.2, 137.1, 132.3, 130.0, 129.6, 127.8, 127.3, 68.2, 47.5, 45.2, 31.0, 21.7, 21.5, 20.3, 13.5]. The aziridine tosylate (0.700 g, 1.65 mmol) without further purification was treated with sodium telluride [prepared by reduction of a suspension of tellurium powder (0.42 g, 3.3 mmol) with aqueous $NaBH_4$ (0.25 g, 6.6 mmol) at 60°C for 2 h under argon and cooled to room temperature] under phase-transfer conditions [toluene, 0.2 M in aziridine, Adogen 464 (0.1 g)]. Black elemental tellurium began to precipitate even at 0°C after about 15 min. The toluene–water mixture was stirred for 3 h and the toluene layer was removed, dried ($MgSO_4$), filtered through a pipette of silica gel to remove tellurium, and evaporated to give 4-methyl-*N*-(1-propyl-2-propenyl)benzenesulfonamide[20] (*R*)-**2a** (0.288 g, 1.21 mmol, 74%) as a colorless oil: $[\alpha]_D^{20} = -3.5$ ($CHCl_3$, $c = 2.0$); $^1$H NMR ($CDCl_3$) $\delta$ 7.79 (d, $J = 8.1$ Hz, 2H), 7.21 (d, $J = 8.1$ Hz, 2H), 5.67 (m, 1H), 5.06 (d, $J = 17.1$ Hz, 1H), 5.0 (d, $J = 11.2$ Hz, 1H), 4.75 (d, $J = 7.7$ Hz, 1H), 3.80 (m, 1H), 2.42 (s, 3H), 1.58–1.42 (m, 2H), 1.27 (dt, $J = 14.0$, 7.2 Hz), 0.86 (t, $J = 7.2$ Hz, 3H). $^{13}$C NMR ($CDCl_3$) 144.2, 137.1, 137.0, 129.6, 127.2, 115.5, 56.0, 37.5, 21.2, 19.0, 13.3. HRMS (FAB, $M^+$+H) calcd for $C_{13}H_{19}NO_2S$+H 254.1216. Found 254.1207.

**Table 1.** *N*-Tosylallylic amines from *N*-tosylaziridinemethanol tosylates




| | $R^1$ | $R^2$ | $R^3$ | | % Yield |
|---|---|---|---|---|---|
| (2*S*,3*R*)-**1a**[14,18,19] | *n*-Pr | H | H | (*R*)-**2a**[20,21a] | 74 |
| (2*S*,3*S*)-**1b**[13] | H | Me | H | (*S*)-**2b**[22] | 81 |
| **1c** | Me | Me | H | **2c**[21] | 85 |
| **1d** | $BnOCH_2$ | H | H | **2d**[23] | 88 |
| **1e** | H | -$(CH_2)_3$- | -$(CH_2)_3$- | **2e**[20,21,24] | 95 |
| **1f** | Ph | H | H | **2f** | 0[a] |

[a] The product is (*E*)-PhCH=CHCH$_2$NHTs[25] (**3**) (80%).

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