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Neighbouring Group Assisted Sulfonamide Cleavage of Sharpless Aminols under Acetonation Conditions

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Abstract: It is accidentally observed that N-Ts cleavage and simultaneous protection of resulting free amino group as acetonide with the adjacent hydroxy group is achieved in one pot. Neighbouring carboxylic ester group is essential for this transformation.

Preparation of secondary amines from primary amines is generally achieved via aryl sulfonamides, however the N-aryl cleavage is more complicated and hence has several limitations. The prototype N-tosyl groups are cleaved using sodium in liquid NH_3,[1] refluxing in HBr[1] and sodium naphthalenide[2] which are harsh reagents. Relatively mild procedures have been reported in literature recently viz., SmI_2,[3] Bu_3SnH-AIBN,[4] and Mg-MeOH.[5] Similarly some modifications are achieved on the aryl group of sulphone for easy removal such as 4-methoxybenzenesulfonyl (Mbs)[6] and 2,2,5,7,8-pentamethylchromane-6-sulfonyl and heteroarene-2-sulfonyl groups.[3] The recent advent of asymmetric aminohydroxylation by Sharpless *et al*[7] especially when chloramine-T is the amino source[7a] has demanded milder procedures for the N-Ts cleavage as none of the reported procedures are compatible especially when substrates are racemization prone and sensitive functionalities are present. While working on Sharpless asymmetric aminohydroxylation reaction on conjugated esters, for the synthesis of Abbott Aminodiol [(2S,3R,4S)-2-amino-1-cyclohexyl-6-methyl heptane-3,4-diol] a part structure of Renin inhibitor Zankiren,[8] we observed a hitherto unnoticed and anchimerically assisted N-tosyl cleavage, the results being presented herein (equation 1).

Initially, methyl-4-cyclohexyl-2-E-butenonate (Table 1, entry 1) was aminohydroxylated using chloramine-T and $(DHQ)_2$ PHAL[7a] to obtain the N-tosyl alcohol 1a, $[\alpha]_D$=-8° (c=1.1 in $CHCl_3$). For operational

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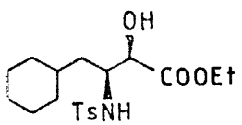
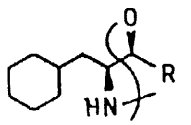
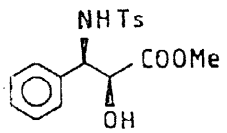
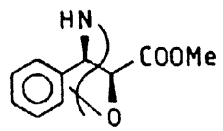
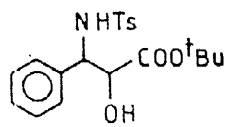
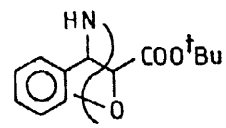
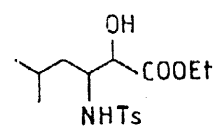
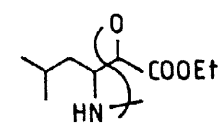
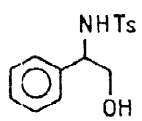
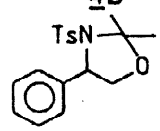
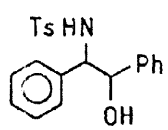
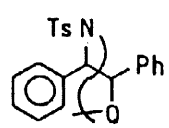
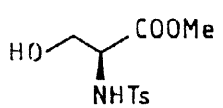
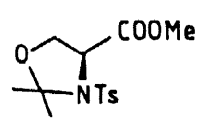
Table 1 Deprotection-acetonation of Sharpless Aminols

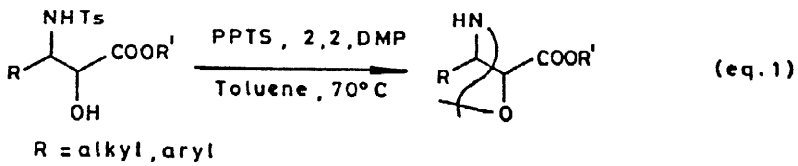
Entry	Starting material[a]	Product	Yield (%)[b]
1	 1a	 1b R = COOEt	76
2	 2a	 2b	80
3	 3a	 3b	74
4	 4a	 4b	72
5	 5a	 5b	82
6	 6a	 6b	90
7	 7a	 7b	78

a. Absolute stereochemical representation for racemic substrates is not mentioned.

b. Yields based on isolation of homogeneous and pure products after column chromatography.

simplicity, the N-tosyl aminol (1a) was subjected to acetonation (PPTS (10 mol %), 2,2-dimethoxypropane, Toluene, 70°C, 4h), however to our utmost surprise, we observed a very clean formation of acetonide with concomitant loss of tosyl group. This being a most unexpected, but most desirable transformation

prompted us study and generalize the reaction conditions. Accordingly Sharpless aminohydroxylated methyl cinnamate (2a) (precursor of the Taxol side chain), t-butyl cinnamate (3a) and ethyl-5-methyl-hexen-2-oate (4a) were acetonated while simultaneously cleaving the N-tosyl group. However, when the tosyl aminohydroxylated styrene (5a) was attempted for the said transformation, a clean acetonide formation was observed but the N-tosyl group was unaffected. This rather unexpected result led us to believe that the carboxyl ester functionality is anchimerically assisting the cleavage process.



(eq. 1)

Other Sharpless aminols, wherein ester functionality is absent, responded to acetonation without tosyl loss. These include aminol of stilbene (6a) and N-tosyl serine methyl ester (7a). For substrate 7a, wherein the NH-Ts is α to ester functionality resisted the tosyl loss which is rather unexpected.

In conclusion, it is pertinent to mention that, the mild reaction procedure described herein opens more avenues for the Sharpless asymmetric aminohydroxylation protocol.[9,10]

Typical Experimental Procedure:

To compound **2a** (349mg, 1 mmol) in dry Toluene (10 ml) was added 2,2-dimethoxypropane (2 ml, ~15 mmol) under N_2 atmosphere followed by catalytic PPTS (70 mg). The reaction mixture was stirred at 70°C for 6h, cooled to room temperature, then the solids were filtered off and the solution evaporated. The crude product was chromatographed on silica gel (60-120 mesh) using Hexane : Ethyl acetate (98:2) mixture as eluent to get the product **2b** in 80% yield.

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Reference and Notes:

1. Roemmele, R.C.; Rapoport, H. *J. Org. Chem.* **1988**, *53*, 2367-2371 and references cited therein.
2. Ji, S.; Gortler, L.B.; Waring, A.; Battisti, A.; Bank, S.; Closson, W.D.; Wriede, P. *J. Am. Chem. Soc.* **1967**, *89*, 5311-5312.

3. a) Vedejs, E.; Lin, S. *J. Org. Chem.* **1994**, *59*, 1602-1603 ; b) Goulaouic Dubois, C.; Guggisberg, A.; Hesse, M. *J. Org. Chem.* **1995**, *60*, 5969-5972; c) Goulaouic Dubois, C.; Guggisberg, A.; Hesse, M. *Tetrahedron*, **1995**, *51*, 12573-12582 ; d) Vedejs, E.; Lin, S.; Klapars, A.; Wang, J. *J. Am. Chem. Soc.* **1996**, *118*, 9796-9797 ; e) Knowles, H.; Parsons, A.F.; Pettifer, R.M. *Synlett*, **1997**, 271-272.
4. Parsons, A.F.; Pettifer, R.M. *Tetrahedron Lett.*, **1996**, *37*, 1667-1670.
5. Nyasse, B.; Grehn, L.; Ragnarsson, U. *J. Chem. Soc. Chem. Comm.*, **1997**, 1017-1018.
6. Nishimura, O.; Fujino, M. *Chem. Pharm, Bull.*, **1976**, *24*, 1568-1575.
7. a) Li, Guigen.; Chang, H-T.; Sharpless, K.B. *Angew. Chem. Int. Ed. Engl.*, **1996**, *35*, 451-454; b) Rudolph, J. Sennhenn, P.C.; Vlaar, P.; Sharpless, K.B. *Angew. Chem.*, **1996**, *35*, 2810-2813 ; c) Li, G.; Angert, H.H.; Sharpless, K.B. *Angew. Chem.*, **1996**, *35*, 2813-2816.
8. Kleinhert, H.D.; Rosenberg, S.H.; Baker, W.R.; Stein, H.H.; Kinghofer, V.; Barlow, J.; Spina, K.; Polakowski, J.; Kover, P.; Cohen, J.; Dennisen, J. *Science*, **1992**, *257*, 1940-1943.
9. The details pertaining to synthesis of Abbott Aminodiol, Zankiren and analogues will be published later.
10. Selected ^{1}H NMR data for compound **1b** and **2b**.

1b : ^{1}H NMR (200 MHz, $CDCl_3$) : δ = 4.1-4.3 (m, 3H, C*H*$_2$-ester, C*H*-NH-), 4.0 (1H, d, J=8.3Hz C*H*-O-), 1.1-1.8 (m, 13H, C$_7$*H*$_{13}$), 1.45 (s, 6H, ->C(C*H*$_3$)$_2$), 1.3 (t, 3H, J=8.3Hz, C*H*$_3$-ester). **2b**: ^{1}H NMR (200 MHz, $CDCl_3$) : δ = 7.30-7.51 (m, 5H, *H*-Ar), 5.15 (d, 1H, J=6.6Hz, C*H*-NH-), 4.3 (d, 1H, J=6.6Hz, C*H*-O-), 3.75 (s, 3H, OC*H*$_3$), 1.58 (s, 3H), 1.60 (s, 3H).

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