THE DOUBLE REDUCTION OF CYCLIC BENZO-FUSED SULFONAMIDES

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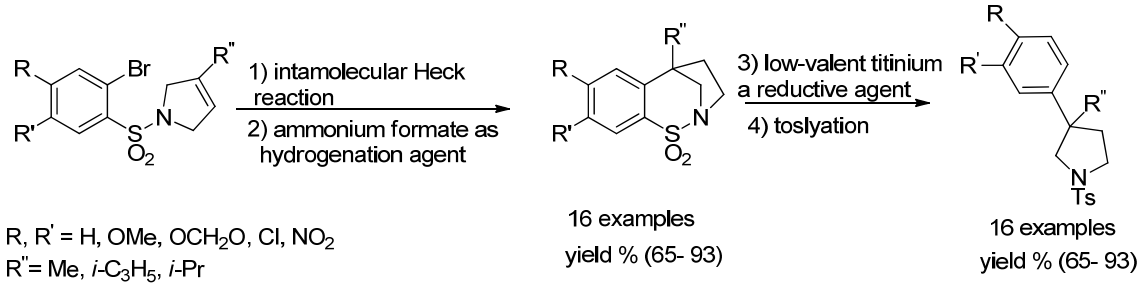
In this work we describe the straight-forward synthesis of a range of saturated benzo-fused cyclic sulfonamides. As shown in the Scheme below this was achieved using a new reductive intramolecular Heck reaction sequence which employs ammonium formate as the hydrogen source and utilises the palladium catalyst for two distinct chemical processes (the Heck reaction and the subsequent alkene reduction).[1] The range of compounds thus prepared were then subjected to a low-valent titanium species formed *in situ* from Ti(O*i*-Pr)$_4$ and Mg.[2] Typically, this method excised the sulfonyl functionality and produced the corresponding aryl substituted cyclic amines in reasonable to excellent yield. As shown in the Scheme below following this process both the C-S and N-S bonds undergo reductive cleavage.[3]

Notably, using the new low-valent titanium method the loss of substituents on the aromatic ring does not occur. This contrasts with the same type of reaction process performed under dissolved metal conditions (Li-NH_3). And the usefulness of this method was demonstrated with the synthesis of mesembrane.



Conditions and reagent; 1) $Pd(OAc)_2$ (10 mol%),PPh_3 (20 mol%), K_2CO_3,DMF, 110 °C, 15 h
2) NH_4CHO_2 (55 equiv.),80 °C, 18 h; 3) Mg (powder) Ti(*Oi*-Pr)$_4$,Me_3SiCl.THF, 80-100 °C, 15 h, Argon;
4) TsCl, Et_3N, DCM, 0 °C, 15 h;

[1] A. Khalifa, L. Conway, K. Geoghegan and P. Evans, *Tetrahedron Lett*., **2017**, *58*, 4559-4562

[2] N. Shohji, T. Kawaji and S. Okamoto, *Org. Lett*., **2011**, *13*, 2626-2629.

[3] A. Khalifa and P. Evans, *J. Org. Chem*., doi: 10.1021/acs.joc.8b02827.