Prins Reaction Using Trioxane for Trisubstituted, *cis*-Fused Tetrahydropyrans

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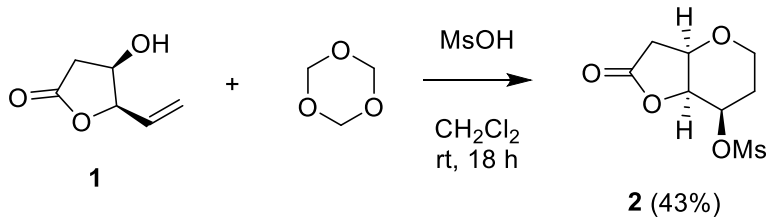
Keywords: Prins Reaction; Neuroactive Agents; 1,3,5–Trioxane; Stereoselective Reaction; *cis*–Fused Tetrahydropyran

Tetrahydropyrans are important class of compounds that occur as building blocks in many biologically active natural products.[1] The coupling of homoallylic alcohols with aldehyde in the presence of acid catalyst, known as Prins cyclization, has been reported to produce large number of tetrahydropyran derivatives.[2] Prins cyclization of 1,3,5–trioxane and homoallylic alcohol for *cis*-fused tetrahydropyrans was reported in 2010.[3] Encouraged by that work, we decided to employ Prins strategy using 1,3,5–trioxane as an equivalent for formaldehyde, for construction of the characteristic *cis*-fused tetrahydropyran motif that can be envisioned as a versatile precursor for analogs of dysiherbaine, the potent agonist for the kainate receptors.[4]

When homoallylic alcohol **1** was treated with two equiv of 1,3,5–trioxane and three equiv of methanesulfonic acid in dichloromethane at rt for 18 h, Prins cyclization proceeded smoothly to give corresponding *cis*-fused tetrahydropyran **2** in 43% yield. Extra one equiv of 1,3,5–trioxane and one equiv methanesulfonic acid were necessarily added to drive the reaction to completion. Structure of the *cis*-fused tetrahydropyran product was characterized using ^{1}H NMR spectroscopy.



1 **2** (43%)

1）U. Biermann, A. Lutzen, J. O. Metzger, *Eur. J. Org. Chem.* **2006**, 2631–2637. 2）B. V. S. Reddy, D. N. Chaya, J. S. Yadav, D. Chatterjee, A. C. Kunwar, *Tetrahedron Lett.* **2011**, *52*, 2961–2964. 3) J. S. Yadav, B. V. S. Reddy, A. P. Singh, D. N. Chaya, D. Chatterjee, A. C. Kunwar, *Tetrahedron Lett.* **2010**, *51*, 1475–1478. 4) M. Chiba, Y. Ishikawa, R. Sakai, M. Oikawa, *ACS Comb. Sci.* **2016**, *18*, 399–404.