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SELECTIVE DEOXYGENATION OF α,α'-DIOXYGENATED 3-(2H)-FURANONES

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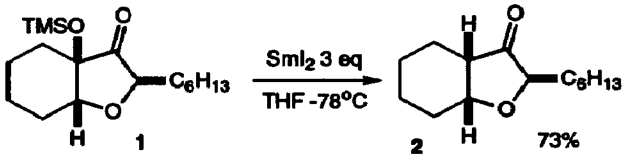
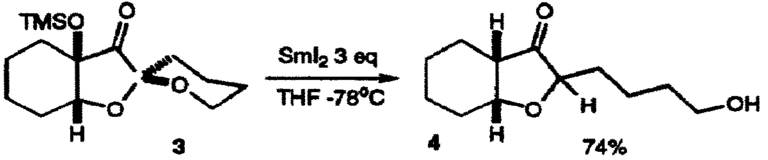
Summary Regioselective monodeoxygenation of α,α'-dioxygenated 3-(2H)-furanones has been achieved using samarium diiodide in the presence of excess ethylene glycol.

The applications of SmI_2 in organic synthesis are now widespread.[1] Since the initial report of this useful reagent by Kagan and co-workers[2], numerous groups have employed SmI_2 for the reductive removal of α–halo or α–oxygen substituents of carbonyl compounds, for pinacol couplings, and for the addition of ketyl radicals to double and triple bonds.[3] We have now explored the chemoselective deoxygenation of α,α'–3-(2H)-furanones by SmI_2 and report here a method for the selective removal of an α–acetoxy group in the presence of an α'-spirocyclic ketal. Deoxygenation reactions of α–oxygenated carbonyl compounds have been reported; however, selective deoxygenation of α,α'- disubstituted species has not been examined.[4]

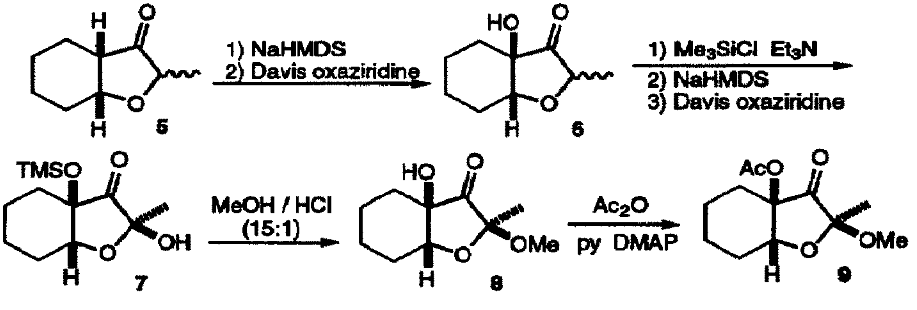
Attempted deoxygenation of a simple C4 oxygenated furanone 1[5] using 3 equivalents SmI_2 under the normal reaction conditions resulted in a 73% yield of the deoxygenated compound 2. Selective reduction of only the C4 oxygen in the presence of the endocyclic furanone oxygen can be readily explained by consideration of the relationship of the C4 C-O bond and the carbonyl CO pi bond. The C4 C-O bond is parallel to the pi system and, therefore, reduction is stereoelectronically favored for the exocyclic C4-O bond over the endocyclic furanone C2-O bond.[6] However, reaction of spirocyclic ketal furanone 3[5] under the same conditions resulted in reduction at both C2 and C4 leading to 4 in 74% yield. In this case, both the C4-O bond and the C2-O ketal (exocyclic) bond are favorably disposed for reduction in that both C-O bonds are aligned parallel with the CO pi system. Although the mechanism of the reduction of α–oxygenated ketones is not fully understood, we believed that the overreduction of



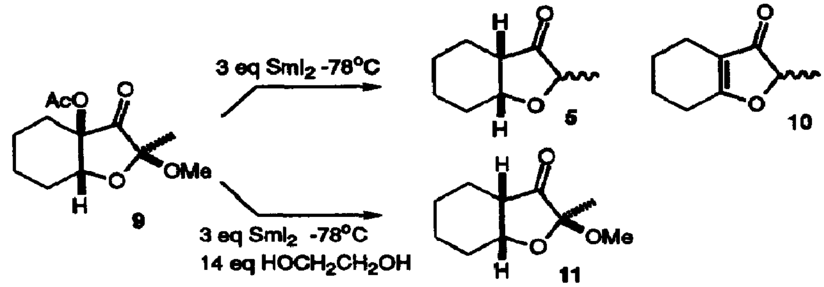
the spirocyclic ketal was potentially related to the Lewis acidity of the Sm (III) produced in the reaction. Holton and Williams[6a] reported that a novel rearrangement promoted by Sm (III) could be obviated by the addition of Et_3N to the reaction mixture. An earlier report by Inanaga and co-workers[7] described the SmI_2 monodeoxgenation of a tartrate ester using several alcohol additives. Hanessian and co-workers[8] have also described the SmI_2 deoxygenation of highly oxygenated carbohydrate derived lactones in the presence of ethylene glycol and HMPA. We chose to examine the reduction of a C2 methoxy C4 acetoxy disubstituted furanone derivative by SmI_2 in the presence of several additives as an attempt to achieve regioselective reduction at C4 without reduction at C2.



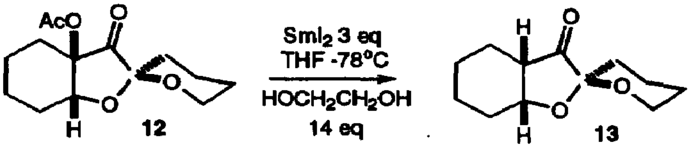
Furanone **5** was prepared from cyclohexanone according to the literature[9] procedure. Regiospecific oxidation of the C4 enolate using the Davis oxaziridine[10] provided the C4 hydroxy furanone **6**[11] as a single diastereomer in 80% yield. After protection of the alcohol as the TMS ether, oxidation at C2 was then accomplished by the same sequence (83%) providing the α,α'-dioxygenated furanone **7** as a 9:1 mixture of isomers (GC) at C2. Methanolysis provided the C2 methoxy C4 hydroxy furanone **8** (99%) as a 13:1 mixture of isomers. The stereochemistry of **8** was assigned by correlation of ^{13}C NMR data with earlier studies.[5] The C4 hydroxy was then protected as the acetate **9** in an effort to differentiate the C4 oxygen as a leaving group over the C2 methoxy group. However, it is important to note that Molander and Hahn[12] had previously shown that α–methoxy ketones are easily reduced with SmI_2. The reduction of furanone **9** with SmI_2 under the conditions employed for the reduction of **1** (above) resulted in complete reduction of both C2 and C4 to provide the simple furanone **5**. Reaction of **9** with 3 eq SmI_2 (in THF or CH_3CN) in the presence of MeOH at -78°C or RT lead to overreduction, producing furanone **5**, and formation of enone **10** (mechanism unknown) in up to 35% yield. Addition of Et_3N[6a] to the reaction mixture completely suppressed the reduction providing only recovered starting material (>85% material balance). Ethylene glycol[7] proved to be the additive of choice for selective reduction. Optimization of the reaction conditions for the conversion of **9** to **11** required the addition of 14 eq of ethylene glycol and 3 eq of SmI_2 in THF at -78°C.[13] Attempts



to reduce the number of equivalents of samarium diiodide required for the reduction were not



successful. We have found that the reduction reaction is more reproducible if the SmI_2 solution is not transferred via syringe from the flask it was prepared in to a second flask for the reduction. The presence of samarium metal (remaining from the preparation of the reagent) appears to be crucial for the observed regioselective reduction. To adjust the stoichiometry of the reaction an appropriate aliquot of the SmI_2 solution was removed from the flask prior to the addition of the reduction substrate. Formation of the SmI_2 reagent at lower concentrations than 0.084 M was problematic in our hands (due to reaction with adventitious oxygen). The differentially protected spirocyclic ketal furanone **12** (C4 acetoxy) was then prepared from the corresponding C4 alcohol[5] and subjected to the optimized reaction conditions. The desired deoxygenated furanone **13** was obtained in 68% isolated yield.



We have now shown that highly chemoselective reduction of α,α'-dioxygenated 3-(2H)-furanones can be effected using SmI_2 in the presence of ethylene glycol. The ethylene glycol may serve to reduce the Lewis acidity of the reaction medium; however, the exact nature of the role of additives in SmI_2 reductions is not known.[1,7,8,14] Our study indicates that careful selection of reaction conditions can result in a considerable degree of chemoselectivity in SmI_2 deoxygenation reactions.

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References and Footnotes

1. For reviews of SmI_2 chemistry, see: Molander, G.A. *Chem. Rev.* **1992**, *92*, 29-68; Soderquist, J.A. *Aldrichim. Acta* **1991**, *24*, 15-23.
2. Girard, P.; Namy, J.L.; Kagan, H.B. *J. Am. Chem. Soc.* **1980**, *102*, 2693-2698.

3. For examples of recent reports, see: Enholm, E.J.; Jiang, S.; Abboud, K. *J. Org. Chem.* **1993**, *58*, 4061-4069; Lebrun, A.; Namy, J-L.; Kagan, H.B. *Tetrahedron Lett.* **1993**, *34*, 2311-2314; Gillmann, T. *Tetrahedron Lett.* **1993**, *34*, 607-610.

4. A low valent V (II) reagent has been reported to selectively cleave an acetoxy group over an acetal protected α–oxygen substituent: Inokuchi, T.; Kawafuchi, H,; Torii, S. *Chem. Lett.* **1992**, 1895-1896.

5. Linderman, R.J.; Viviani, F.G.; Kwochka, W.R. *Tetrahedron Lett.*, **1992**, *33*, 3571-3574.

6. (a) Holton, R.A.; Williams, A.D. *J. Org. Chem.* **1988**, *53*, 5981-5983. (b) White, J.D.; Somers, T.C. *J. Am. Chem. Soc.* **1987**, *109*, 4424-4426.

7. Kusada, K.; Inanaga, J.; Yamaguchi, M. *Tetrahedron Lett.* **1989**, *30*, 2945-2948.

8. Hanessian, S.; Girard, C.; Chiara, J.L. *Tetrahedron Lett.* **1992**, *33*, 573-576.

9. Dolmazon, R.; Gelin, S. *J. Heterocyclic. Chem.* **1982**, *19*, 117-121.

10. Davis, F.A,; Sheppard, A.C.; Chen, B.-C.; Haque, M.S. *J. Am. Chem. Soc.* **1990**, *112*, 6679-6690.

11. All new compounds were fully characterized by NMR and combustion analysis.

12. Molander, G.A.; Hahn, G. *J. Org. Chem.* **1986**, *51*, 1135-1138.

13. Experimental: A 0.084 M solution of SmI_2 was prepared by adding a THF solution (2.5 mL) of diiodoethane (0.176 g, 0.63 mmol) to a slurry of Sm metal (0.101 g, 0.67 mmol) in 5.0 mL THF at RT under an atmosphere of Ar. For reduction on an 0.106 mmol scale, 3.8 mL of the 0.084 M SmI_2 solution was removed by syringe. The remaining dark blue SmI_2 solution was then cooled to -78°C and distilled ethylene glycol (83 µL, 1.48 mmol, 14 eq) was added. A THF solution (1.5 mL) of the furanone (0.106 mmol) was then added dropwise and the resulting mixture stirred at -78°C for 15 min. The reaction mixture was then diluted with 10 mL ether and exposed to air (at -78°C) for 5 min. Saturated aqueous K_2CO_3 (10 mL) was then added and the reaction mixture then allowed to warm to RT. The layers were separated and the aqueous phase was extracted with ether (2 x 25 mL). The combined organic phases were dried over Mg_2SO_4. The reduced furanone was purified by chromatography on florisil using 4:1, petroleum ether:ether as eluent.

14. For a recent study on additive effects in reactions of samarium diiodide, see: Hasegawa, E.; Curran, D.P. *J. Org. Chem.* **1993**, *58*, 5008-5010.

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