Tetrahedron Letters, Vol.31, No.37, pp 5301-5302, 1990
Printed in Great Britain

0040-4039/90 \$3.00 + .00
Pergamon Press plc

MECHANISTIC ASPECTS OF A NOVEL 1,2-3,4 REDUCTIVE-FRAGMENTATION THAT ESTABLISHES FOUR STEREOCENTERS IN A SINGLE STEP

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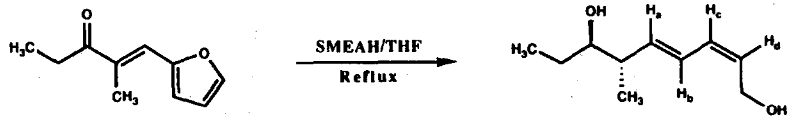
Abstract: Reduction of a β-furanyl unsaturated ketone with $LiAlH_4$, $LiAlD_4$ or sodium bis(methoxyethoxy)aluminum hydride (SMEAH) results in a novel reductive-fragmentation in which four elements of stereochemistry are established in a single step.

In the previous communication, we demonstrated the general nature of 1,2- 3,4 reductions on unsaturated ketones frequently encountered in organic synthesis.[1] In this letter we would like to present another aspect of this reduction process that is noteworthly. SMEAH reduction of enone **1** (3 equiv/THF) afforded a 9:1 mixture of the diastereomeric diene-diols **2** (major diastereomer shown) in 54% yield.[2] Reduction of **1** with $LiAlD_4$ afforded the trideuterio diene **3**. 1,2-Delivery of the first two deuterides was consistent with the 1,2-3,4 reduction process detailed in the previous letter while the introduction of the final deuteride suggested the intermediacy of an aldehydic species. Reduction of **1** with SMEAH followed by a DCl/D_2O quench afforded the mono-deuterio adduct **4**,further suggesting the presence of an organoaluminate species.



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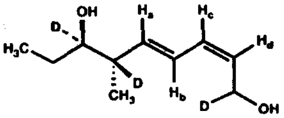

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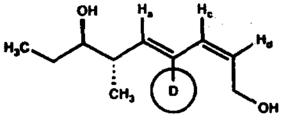
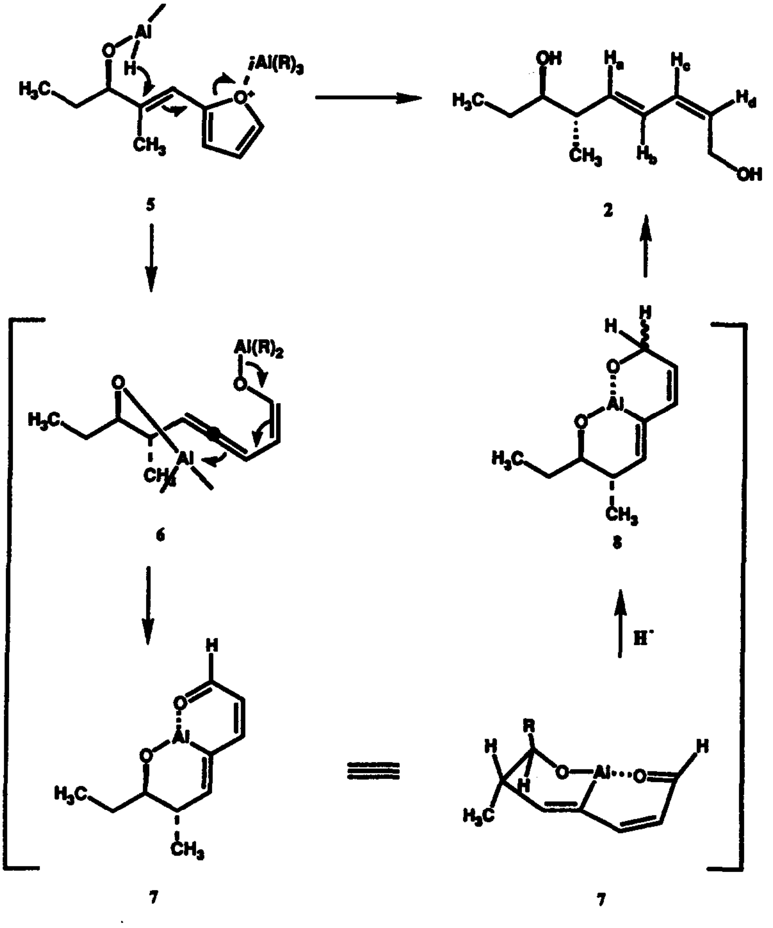


4

A plausible mechanism to explain these results is illustrated in the scheme. Intramolecular hydroalumination of **5** is followed by furan ring opening to yield the allene aldolate **6**. Intermediate **6** undergoes an intramolecular collapse to yield the vinylogous aldolate intermediate **7**[3]. In the next step (**7** → **8**), the aldehyde present in **7** undergoes a hydride reduction to yield **8**. Protonation of **8** then affords the observed product **2**. This mechanism is consistent with our labeling studies.

This is an interesting transformation that creates four elements of stereochemistry from an easily accessible unsaturated system. This type of functionality is common amoung many natural products. In light of the isomeric purity and our understanding of stereocontrol with respect to 1,2-3,4 reductions, this reaction should find application in organic synthesis.



Acknowledgement: We would like to thank our colleagues in Physical and Analytical Chemistry for spectral and analytical data and Mary Ferriell for the preparation of this manuscript.

References and Notes

1. See previous paper in this issue. 2. Physical and analytical data (IR, UV, high resolution MS) were consistant with assigned structures (^{1}H-NMR, CDCl$_3$, δ 6.38 (H$_b$, dd, J = 14.83 and 11.11 Hz), 6.08 (H$_e$, dt, J = 11.09 and 11.06), 5.78 (H$_a$, dd,.J = 14.83 and 8.07), 5.54 (H$_d$, dt, J = 11.06 and 7.02), 4.30 (2H, dd, J = 1.23, 7.02), 3.36 (1H, m), 2.31 (1H, m), 1.56 (2H, m), 1.05 (3H, d, J = 6.45), 0.96 (3H, t, J = 7.83), ^{13}C-NMR (CDCl$_3$, PPM) 138.2, 130.7, 128.4, 126.2, 76.5, 58.7, 42.8, 27.2, 16.8, 10.0. Full details will be forthcoming in the full report on this aspect of 1,2-3,4 reductions. 3. For examples of such organoaluminum intermediates see: Corey, E. J., Tetrahedron Letters (1971) 1821; Keck, G. E.; Webb, R. R.; Tetrahedron Letters (1982) 3051. 4. For a review on the synthesis of E,Z dienes see: Normant, J. F., in "Modern Synthetic Methods", Vol. 3 (1983), Scheffold, R., Ed.; John Wiley & Sons, New York, NY, p. 139. 5. Using high field NMR we could not detect any E,E diene.

(Received in USA 31 May 1990)