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OPENING OF A 1,3-DIOXOLANE BY NUCLEOPHILIC ATTACK AT A KETAL METHYLENE[1]

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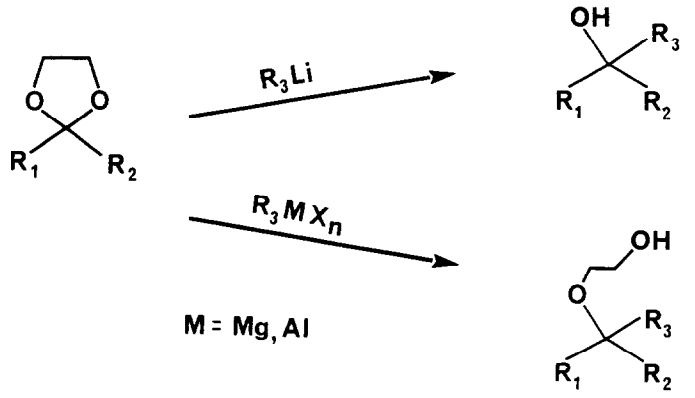
SUMMARY

A novel type of opening of an ethylene ketal has been observed in the reaction of 1 with alane $RAlMe_2$. The reaction is explained in terms of a nucleophilic attack on the ketal methylene synchronous with participation by one of the ketal oxygens in the opening of the epoxide function located across the 7-membered ring of 1.

While 1,3-dioxolanes (ethyleneketals) have been used as protective groups of ketones for decades, there have been numberous reports over the years of opening of such ketals by organometallic reagents.

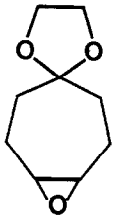


(Eqn. 1)

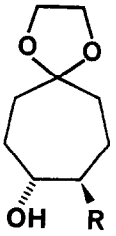
(Eqn. 2)

One type of such opening (Eqn. 1)[2,3] produces a tertiary alcohol and is believed to proceed via the free ketone, produced by proton abstraction from a ketal methylene.[3] The other reported type of nucleophilic opening of a cyclic ketal (Eqn. 2) takes place apparently in the presence of reagents that can function as Lewis acids, especially under conditions where they are not complexed by solvents.[4,5] We report here yet another type of ketal opening where nucleophilic attack is at a ketal methylene and is facilitated by one of the ketal oxygens spacial proximity to a developing positive charge elsewhere in the molecule.

During our synthetic efforts at preparing substituted cycloheptanols we became interested in opening epoxide 1[6] with acetylenic alanes. The alane reagent $RAlMe_2$ was prepared from the acetylene RH[8] according to the method of Fried[11] and then allowed to react with epoxide 1 (0.4 equiv.) in



1



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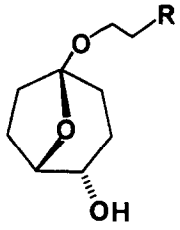

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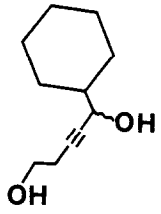

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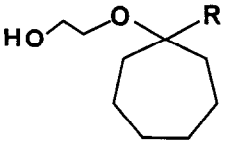

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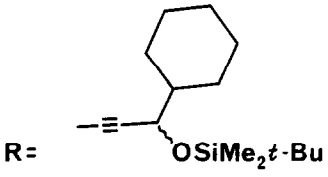

refluxing hexane-toluene mixture for 16 hrs. The crude, worked-up (stirring with aqu. NaOH) reaction mixture proved to consist of two major products and several minor by-products (TLC and GC-analyses). Column chromatography (silica gel; acetone-ether-methylene chloride-hexane 3:10:30:55) was employed to obtain the two major components in pure form. The more mobile material (28%) was the expected product 2.[12] The second major product was obtained in 10% yield and its spectral properties are in agreement with the assignment of structure 3. One outstanding signal in the ^{1}H-NMR of 3 is a sharp triplet of doublets δ 2.47. Further structural proof was obtained by the isolation of 4 (60%) from the hydrolytic cleavage of 3 (oxalic acid in refluxing 80% acetonitrile for 2 hrs). The formation of 3 from the reaction of 2 with alane $RAlMe_2$ is the result of a transannular process, the tendency for which can be readily seen upon examination of a molecular model of 2 (Figure A).

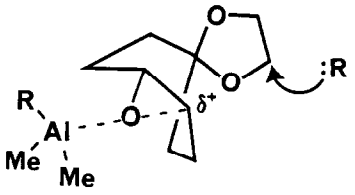

Figure A

When we subjected the ethylene ketal of cycloheptanone to the alane $RAlMe_2$ in refluxing hexane-toluene we were able to isolate only one product (63%) to which we assigne structure 5. This finding is comparable to the known ketal openings by Grignard reagents already mentioned.[4,5]

In conclusion, our discovery of a novel type of nucleophilic ring cleavage of an ethyleneketal is one more indication of the limitations of ethyleneketals as protective groups.

REFERENCES AND FOOTNOTES

1) Contribution No. 662 from the Institute of Organic Chemistry.

2) Holland, H.L.; Jahangir, *Tetrahydron Lett., 1983, 24,* 1577-1580.

3) Ho, T.-L., *Synthetic Comm., 1983, 13(9),* 769-772.

4) Mallory, R.A.; Rovinski, S., Kohen, F.; Scheer, I., *J. Org. Chem., 1967, 32(5),* 1417-22 and references therein.

5) Karaev, S.F.; Shikhiev, I.A; Khabibova, A.K.; *Azerb. Khim. Zh., 1977, (2),* 61-4. C.A. 87:151726p; Orlova, S.E.; Atavin, A.S; Trofimov, B.A.; Vyalykh, E.P., *Khim. Atsetilena, 1968,* 252-5. C.A. 72:111388p.

6) Epoxide 1 was prepared from 4-cycloheptenone[7] in two steps. The ketone was converted into the ketal under standard conditions and the epoxidation was carried out with MCPA in methylene chloride.

7) Wilson, S.R.; Wiesler, D.P., *Synthetic Comm., 1980, 10(4),* 339-343.

8) For the preparation of RH the addition of acetylene to an aldehyde as described for cinnamaldehyde[9] was applied to cyclohexylcarboxaldehyde. The resulting 1-cyclohexyl-2-propyn-1-ol was O-silylated by the method of Evans;[10] product bp 70-71°/0.5 mm.

9) *Org. Syntheses, Coll. Vol. IV,* 792 (1962), John Wiley & Sons, New York.

10) Evans, D.A.; Crawford, T.C.; Thomas, R.C.; Walker, J.A., *J. Org. Chem., 1976, 41/25,* 3947-3952.

11) Fried, J.; Lin C.-H.; Ford, S.H., *Tetrahedron Lett., 1969, 18,* 1379-1381.

12) 1 ^{1}H-NMR ($CDCl_3$) δ 1.5-2.15 (m, cycloheptyl methylenes), 3.07 (m, epoxide methines), 3.91 (s, ketal methylenes); MS *m/e* 171 (MH^+).

2 ^{1}H-NMR ($CDCl_3$) δ 2.67 (m, C<u>H</u>-C≡), 3.7-3.85 (m, ketal methylenes), 4.03 (d, J = 6.3 Hz, SiOC<u>H</u>C≡), 4.36 (m, C<u>H</u>OH); MS *m/e* 440 (MNH_4^+).

3 ^{1}H-NMR ($CDCl_3$) δ 2.47 (td, J = 7.4, 1.8 Hz, C<u>H$_2$</u>C≡), 3.6-3.8 (m, OC<u>H$_2$</u>), 3.89 (m, C<u>H</u>OH), 4.04 (dd, J = 6.3, 1.8 Hz, SiOC<u>H</u>C≡), 4.22 (br. S C<u>H</u>OC); MS *m/e* 440 (MNH_4^+), 279 (RCH_2CH_2).

4 ^{1}H-NMR ($CDCl_3$) δ 0.95-1.9 (m, cyclohexyl), 2.48 (td, J = 6.0, 2.0 Hz, C<u>H$_2$</u>C≡), 3.72 (t, J = 6.0 Hz, HOC<u>H$_2$</u>), 4.13 (dd, J = 6.0, 2.0 Hz) C<u>H</u>OH); MS *m/e* 181 (M-H).

5 ^{1}H-NMR ($CDCl_3$) δ 3.66 (m, C<u>H$_2$</u>OC), 3.71 (m, HOC<u>H$_2$</u>), 4.12 (d, J = 6.2, SiOC<u>H</u>); MS *m/e* 426 (MNH_4^+).

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