

1376, 1245, 1227, 1204, 1168, 1106, 986, 902  $\text{cm}^{-1}$ ;  
 $^1\text{H-NMR}$  (200 MHz,  $\text{CDCl}_3$ ):  $\delta$  2.05-1.45 (m, 6H, methylene envelope), 1.40 (s, 3H, C5 methyl), 1.28 (s, 3H, endo methyl), 1.15 (s, 3H, exo methyl), 1.14 (s, 3H, C1 methyl);  
 $^{13}\text{C NMR}$  ( $\text{CDCl}_3$ ): 105.6 (C5), 82.5 (2 $\times$ C, C1 and C7), 33.4, 31.7, 26.9, 25.9, 21.1, 20.6, 18.2.

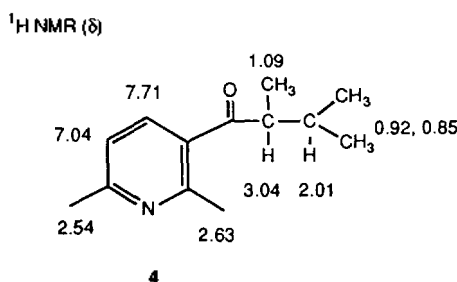


Figure 1.

### Study on the Rearrangement Reaction of Bicyclic Ketal with Aluminum Iodide

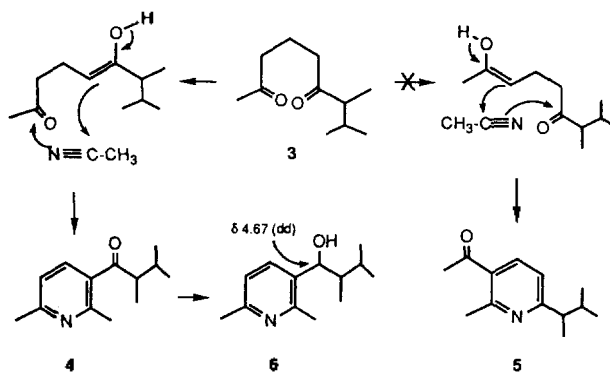
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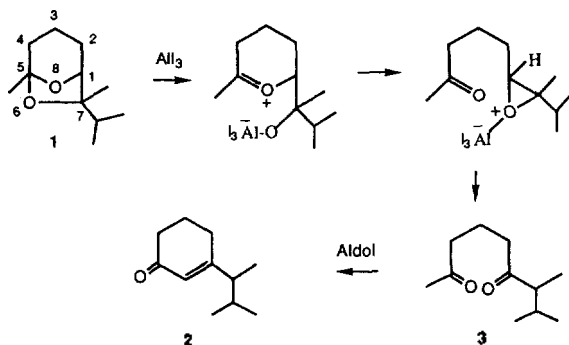
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Scheme 2.

Aluminum iodide prepared from aluminum foil and iodine has been known as easily accessible and versatile ether-cleaving reagent by Bhatt *et al.*<sup>1</sup> In the course of our continuing research into the bicyclic ketals in the 6,8-dioxabicyclo[3.2.1]octane series, we applied this reagent in our system and found interesting results. We report herein the novel ketal rearrangement reaction with aluminum iodide in acetonitrile to give cyclohexenone and pyridine derivatives.

In the fragmentation reaction of bicyclic ketal **1** with aluminum iodide in acetonitrile, we found two products in a ratio of about 5 : 1. The major product had higher mobility on TLC (silica gel, hexane/ether, 7 : 3). The structure of the minor product **2** (9% isolated yield) was readily identified from analysis of spectral data.<sup>2</sup> HRMS required a formula of  $\text{C}_{11}\text{H}_{18}\text{O}$  (Found: 166.1359, requires *M*, 166.1358). The IR (thin film) spectrum gave a strong signal at  $1669\text{ cm}^{-1}$ , indicative of an enone. Relevant proton and carbon NMR spectral data are provided for the structure **2**. A mechanism to account for formation of the cyclohexenone product is relatively straightforward (Scheme 1). Initial attack of the Lewis acid on O-6 has been suggested in prior fragmentation reactions.<sup>3,4</sup>



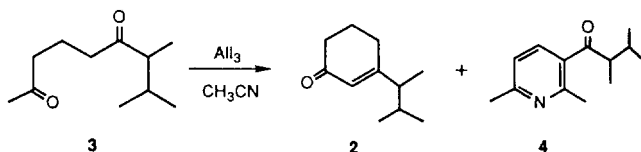
Scheme 1.

The 1,5-diketone intermediate **3** seems to be critical for formation of the cyclohexenone via the aldol condensation.

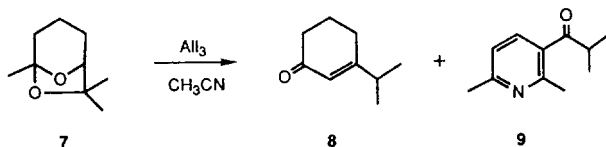
The structure of the major product (46%) was much difficult to assign. The proton NMR indicated five methyl peaks. Three doublets appeared at  $\delta$  1.09,  $\delta$  0.92 and  $\delta$  0.85, and two highly deshielded singlets were observed at  $\delta$  2.63 and  $\delta$  2.54. Two complex methine signals were found at  $\delta$  2.01 and  $\delta$  3.04. These two protons are coupled with one another. Irradiation of the  $\delta$  3.04 signal frequency collapsed the  $\delta$  1.09 doublet while irradiation of the  $\delta$  2.01 signal gave two singlets at  $\delta$  0.92 and  $\delta$  0.85. The proton NMR spectrum also exhibited two highly deshielded aromatic protons at  $\delta$  7.71 and  $\delta$  7.04. These two protons are coupled, with  $J=8$  Hz. The carbon NMR spectrum revealed 13 signals for carbon. There were four highly deshielded singlets ( $\delta$  207.3,  $\delta$  159.9,  $\delta$  157.2 and  $\delta$  121.2), 4 doublets ( $\delta$  30.2,  $\delta$  50.0,  $\delta$  119.9 and  $\delta$  135.7), and 5 quartets ( $\delta$  12.5,  $\delta$  18.4,  $\delta$  21.4,  $\delta$  23.9 and  $\delta$  24.4). The UV spectrum (EtOH) contained maxima at 274 nm ( $\epsilon$  4140) and 239 nm ( $\epsilon$  6640). HRMS required a formula of  $\text{C}_{13}\text{H}_{19}\text{NO}$  (Found: 205.1472, requires *M*, 205.1466). The two highly-deshielded adjacent protons ( $\delta$  7.71 and  $\delta$  7.04) are useful clue to the final assembly of the pieces. This suggested the structure **4** for the major product (Figure 1), which has been synthesized in different way.<sup>5</sup>

The origin of the two new carbon atoms and the nitrogen must be the acetonitrile. Based on our isolation of the diketone intermediate **3**,<sup>6</sup> we suggest that the formation of the pyridine compound arises from insertion of the acetonitrile by way of an enol intermediate. An alternative insertion mode can be imagined to give **5** (Scheme 2). This structure **5** was readily eliminated by reduction of the carbonyl group to an alcohol **6**. The carbinol proton at  $\delta$  4.67 was observed as a doublet of doublets confirming **4** as its precursor.

The role of the diketone **3** as an intermediate for both



Scheme 3.



Scheme 4.

products, **2** and **4**, was testified by subjecting it to reaction conditions and confirmed to give expected results (Scheme 3). The reaction has also been carried out on the ketal, 5,7,7-trimethyl-6,8-dioxabicyclo[3.2.1]octane (**7**) as shown in Scheme 4. Here the cyclohexenone product **8** was obtained in 11% yield and the pyridine **9** in 48%, respectively.

In a typical experiment, to a 25 ml 2-necked flask was added 22 mg of dry aluminum foil and 0.10 g of iodine, in acetonitrile (3 ml). After 3 hr at reflux the iodine color had discharged and 0.10 g of **1** was added. The reaction was allowed to reflux. After reflux for 18 hr the reaction mixture was cooled and poured into 20 ml of water. The aqueous mixture was extracted with ether, washed with 5% NaOH and then 10% sodium thiosulfate. After drying over anhydrous  $\text{MgSO}_4$ , then chromatographed ([GLC: 10% OV-

17, 11'  $\times$  1/4"; two products in a GLC ratio of 1 : 5]; [TLC and Flash chromatography, silica gel, hexane/ether (7 : 3)]. From this reaction was isolated 50 mg (46%) of a less polar product ( $R_f=0.35$ ) and 8 mg (9%) of a more polar product ( $R_f=0.25$ ). The structures of the products were determined by spectroscopic means, as described.

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## References

- Bhatt, M. V.; Babu, J. R. *Tetrahedron Lett.* **1984**, 25, 3497.
- Spectral data of **2**. (9%)  $^1\text{H-NMR}$  (200 MHz,  $\text{CDCl}_3$ ):  $\delta$  5.84 (1H, br s), 2.36 (1H, m), 2.24 (2H, t,  $J=6$  Hz), 2.02-1.88 (4H, m), 1.65 (1H, m), 1.04 (3H, d,  $J=7$  Hz), 0.88 (3H, d,  $J=7$  Hz), 0.83 (3H, d,  $J=7$  Hz);  $^{13}\text{C-NMR}$  ( $\text{CDCl}_3$ ):  $\delta$  199.9 (s), 170.7 (s), 125.8 (d), 48.8 (d), 37.7 (t), 31.1 (d), 27.4 (t), 22.9 (t), 21.6 (q), 19.5 (q), 15.8 (q); IR (neat): 2941, 1669, 1456, 1376, 1245, 890, 731  $\text{cm}^{-1}$ ; MS ( $m/z$ ): 166 ( $M^-$ ), 151, 148, 124 (base), 109, 96, 81, 67, 55, 41; HRMS (Found: 166.1359.  $\text{C}_{11}\text{H}_{18}\text{O}$  requires  $M$ , 166.1358).
- Bjorklund, M.; Jun, J.-G.; Mundy, B. P. *Tetrahedron Lett.* **1985**, 26, 3895.
- Kim, S. H.; Jun, J.-G. *Bull. Korean Chem. Soc.* **1993**, 14, 319.
- Jun, J.-G.; Ha, T. H.; Kim, D.-W. *Tetrahedron Lett.* **1994**, 35, 1235.
- Jun, J.-G.; Suh, S.; Shin, D. G. *J. Chem. Soc. Perkin Trans. 1* **1989**, 1349.