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A New One-Step Method for Oxaadamantane Synthesis

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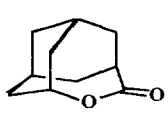
Abstract: Oxidation of 2-methyl-2-hydroxyadamantane by trifluoroperacetic acid in trifluoroacetic acid gives oxaadamantane and *exo*-2-oxaadamantane-4-ol in a good yield. Other 2-hydroxyadamantane derivatives do not undergo this transformation. An oxidative cleavage and subsequent cyclization mechanism is proposed.

Oxaadamantane **6** and its derivatives have represented ongoing synthetic challenges at a time when these compounds have an increased interest for chemists and biologists. The literature indicates the most well-elaborated approach to oxaadamantane synthesis to be the transanular cyclization of bicyclo[3.3.1]nonane derivatives [1] in strongly acidic media. However, these methods are far from convenient as the bicyclo[3.3.1]nonane precursors are not readily available. The current approach was based upon our previous study of the oxidative cleavage of adamantanes with trifluoroperacetic acid.[2] The key for the oxaadamantane synthesis was to direct the oxidative process specifically to the C2-position of adamantane. We introduced the hydroxyl group in the C2-position of adamantane to make it more vulnerable to peracid oxidation. The reactions of 2-hydroxyadamantane (**2**), 2-phenyl-2-hydroxyadamantane (**3**) and 2-methyl-2-hydroxyadamantane (**4**) with trifluoroperacetic acid have been studied.



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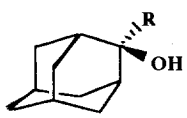
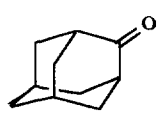


R = H(**2**), Ph(**3**), CH_3(**4**)



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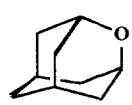

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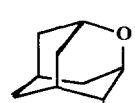
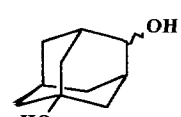


7 OH



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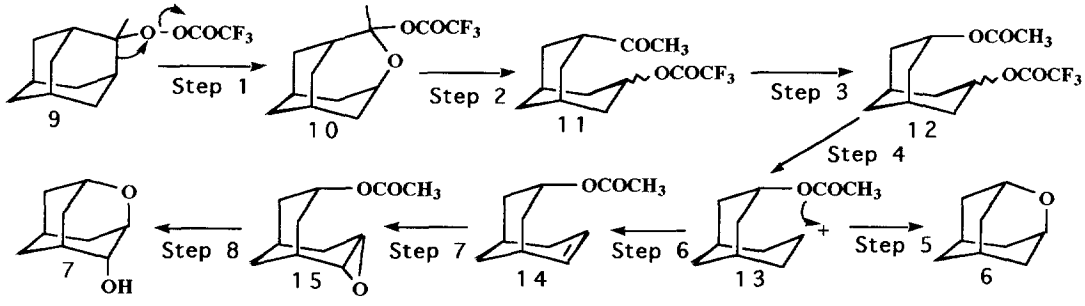
The reaction conditions were identical to those of the previously described cleavage process [2] : ([CF_3CO_3H/ CF_3COOH = 2/3; CF_3COOOH/[substrate] = 8; t = 20-40 ^oC, τ = 1–2 hours). It was observed that the oxidation of compound **3** proceeded through the successive formation of oxoadamantane **5** and lactone **1**. The oxidation of **2** gave a mixture of lactone **1** and 1,4-dihydroxyadamantane (**8**) in the ratio of 1:4. No other products were found when the oxidation was performed in the range of temperatures from 20 - 50 ^oC. In contrast to these relatively uninteresting products, the oxidation of 2-methyl-2-hydroxyadamantane (**4**) provided more exciting results. GC-MS analysis of the reaction mixture (t = 20 ^oC, τ = 1 hour)provided the following constituent distribution: oxaadamantane **6** - 56%, *exo*-2-hydroxy-4-oxaadamantane (**7**) - 40%, lactone **1** - 4%.

The reaction mixture was easily separated on silica. Oxaadamantanes **6** and **7** have been previously described [1,3] and the physical properties (i.e. melting points, IR-, NMR-spectra) were a perfect match. The GC-analysis of the oxidation products from compound **4** over time resulted in the paralleled accumulation of products **6** and **7**. Oxaadamantane **6** was found to be quite stable under the oxidative conditions and does not form any **7.** Therefore, **6** should not be considered as an intermediate for the formation of compound **7**. The loss of two carbon atoms from **4** indicates that onium rearrangement for the peroxy intermediate **9** is proceeding within the adamantane structure. The selective reactivity of **4** to generate oxaadamantane results from the relatively low migratory aptitude of the methyl group in **9** and leads to the Criegee rearrangement within the adamantane skeleton. The isolation of 4% of the lactone **1** in the reaction mixture demonstrates a 24-fold lower migratory aptitude of CH_3-group compared to the C1-C2 σ–bond in the adamantane skeleton. Based on our results it is possible to state the relative migratory aptitude of R-group in the reaction conditions: Ph > H > **C1-C2-bond of adamantane** >> CH_3. The underlined R-group presents a new member of the relative migratory aptitude scale.[4] The overall mechanistic scheme can be summarized by the following: **Step 1** - Criegee rearrangement of **9** to **10**; **Step 2** - acidic cleavage of **10** to **11**; **Step 3** - Baeyer-Villiger oxidation of **11** to **12**; **Step 4** - parallel acidic cyclization of **13** to **6** and elimination of **13** to **14**; **Step 5** - epoxidation of **14** to **15**; **Step 6** - acidic cyclization of **15** to **7**.



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REFERENCES AND NOTES

1. Stetter, H.; Schwartz, E. F. *Chem. Ber.*, **1968**, 101, 2464; Averina, N. V.; Zefirov, N. S. *J. Chem. Soc. Chem. Communs.*, **1973**, *6*, 197; Krasutsky, P. A.; Ambrosienko, H. V.; Rodionov, V. N.; Yurchenko, A. G.; Parnes, Z. N.; Bolestova, G. I. *Russian J. Org. Chem.*, **1985**, *21*, 1465.
2. Krasutsky, P. A.; Baula, O. P.; Yurchenko, A. G. *Russian J. Org. Chem .*, **1994**, *30*, 370.
3. Subramanian, R.; Fort R. C.; *J. Org. Chem.*, **1984**, *49*, 2891.
4. R.Hiat in D.Swern. *Organic Peroxides;* Wiley: New York. **1971**, Vol.2, 65; Lee, J.B.; Leff, B.C.; *Quart. Rev.* **1967**, *21*, 429; Olah G. A.; Parker D. G.; and Yoneda N. *Angew. Chem. Int. Ed. Engl.* **1978**, *17*, 913.

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