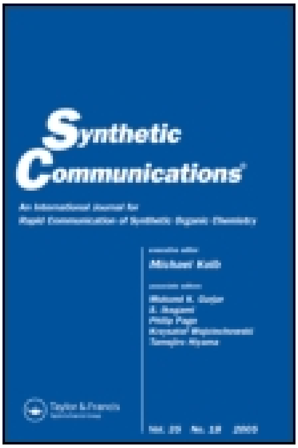


Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry
Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/lsyc20

A Facile One-Step Synthesis of 2,4-Adamantanedione

Michael M. Bobek [a] & Udo H. Brinker [a]
[a] Institut für Organische Chemie, Universität Wien, Währinger Str. 38, A-1090, Wien, Austria

To cite this article: Michael M. Bobek & Udo H. Brinker (1999) A Facile One-Step Synthesis of 2,4-Adamantanedione, Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry, 29:18, 3221-3225, DOI: 10.1080/00397919908085947

To link to this article: http://dx.doi.org/10.1080/00397919908085947

SYNTHETIC COMMUNICATIONS, 29(18), 3221-3225 (1999)

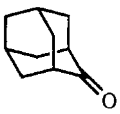
A FACILE ONE-STEP SYNTHESIS OF 2,4-ADAMANTANEDIONE

Michael M. Bobek and Udo H. Brinker*

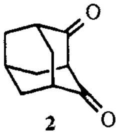
Institut für Organische Chemie, Universität Wien
Währinger Str. 38, A-1090 Wien, Austria

ABSTRACT: 2,4-Adamantanedione (**2**) can be synthesized in one step by direct oxidation of adamantanone with a pyridine-chromium trioxide complex in acetic anhydride in 54% isolated yield.

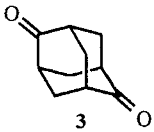
2,4-Adamantanedione (**2**) and related compounds possess a variety of useful applications. They show, for instance, antiviral activity.[1] Hence, the synthesis of substituted adamantanes continues to be a significant endeavour and has stimulated great interest among many chemists over the past decades.[2] **2** was prepared in a four-step synthesis[3] starting with adamantanone (**1**). This laborious procedure involves oxidation of **1** with H_2O_2/SeO_2 in *tert.*-butanol, a π-route cyclization[4] *via* acetolysis with H_2SO_4/Ac_2O,[5] followed by hydrolysis with aq. NaOH affording 4-hydroxy-2-adamantanone. This precursor can be readily oxidized to compound **2** according to well-known procedures.[6]



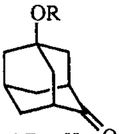
1



2



3



4 R = H
5 R = Ac

---

* To whom correspondence should be addressed.

www.dekker.com

The chromium-based oxidation of adamantanone in acetic anhydride has been reported three times; however, each experiment yielded different results. The original procedure gave a mixture of **5** (36%), **3** (20%) and small amounts of **4**.[7] **2** was not found. The formation of predominant product **5** was confirmed by Adcock and Zhang,[8] although they were not able to isolate more than trace amounts of **3**. Meanwhile, when Gilbert[9] repeated this reaction, he was able to isolate **2**, but only in 20% yield. In search of a simple method to prepare adamantanediones, we studied the oxidation of adamantanone (**1**) under various conditions.

We found that the oxidation of adamantanone is sensitive to the solvent used. No reaction[10] occurred in *tert.*-butanol, pyridine and acetone/sulfuric acid, whereas **4** is formed as the predominant product in acetic acid.[11] In acetic anhydride we found **2** to be the predominant product together with **3**, **4** and **5**, thus confirming the results of Gilbert.[9]

The addition of up to one equivalent of pyridine increases the overall yield of products. Upon addition of two equivalents of pyridine, however, the reaction is retarded, as is the case with sodium acetate or oxalic acid.[12] Therefore, by using a pyridine-chromium trioxide complex in acetic anhydride, compound **2** was prepared in 54% yield in a simple one-step reaction.[13] In addition, small amounts of **3** and **4**, easily separable by column chromatography, were formed. Trace amounts of **5** in less than one percent could also be detected.

At -5°C and room temperature the product ratios are almost identical (Table), whereas at 35-40 °C the product ratio is shifted in favor of the title compound. Unfortunately, elevated temperatures also cause a significant loss of recoverable material. This can be attributed to C-C fragmentation and oxidation.[14] These products can no longer be extracted from the aqueous phase during workup. An increase of reaction time decreases the amount of starting material recovered and does not improve the yield of 2,4-adamantanedione (**2**).

Table

Temperature dependence of the product distribution

Temperature °C	Recovered material	Time (hours)	Unreacted material	**2**	**3**	**4**
-5	99%	16	73%	25%	<1%	3%[a]
35-40	57%	16	18%	28%	2%	<1%[a]
20	82%	16	29%	38%	4%	6%[b]

a. Ratios determined by GC

b. Isolated yields. Difference between recovered material and products due to losses during chromatography.

EXPERIMENTAL:

4 g (40 mmol) of CrO_3 are placed in a 100 mL round-bottom flask equipped with a drying tube and a magnetic stirrer. 40 mL of distilled acetic anhydride and 3.1 mL (39 mmol) of pyridine are added in an ice bath and the mixture is stirred in the ice bath for 90 minutes. 1 g (6.67 mmol) of adamantanone, dissolved in 30 mL of acetic anhydride, is added slowly to the cooled solution with a dropping funnel. The mixture is allowed to warm to room temperature and is stirred for 16 hours. The reaction is quenched by careful addition of 160 mL of saturated Na_2CO_3 solution and the aqueous phase is extracted three times with 40 mL of hexanes/diethyl ether (2:1) to remove starting material (260 mg). The products are extracted with six portions of CH_2Cl_2 (50 mL each).[15] The dichloromethane extracts are evaporated, the residue transferred to a sintered funnel and triturated with five portions of ether (50 mL each). After evaporation, the crude products are chromatographed over 30 g of silica gel (hexanes/ethyl acetate 7:3) to yield 30 mg of **1**, 420 mg (54%) **2** (mp: 284°C)[16], 42 mg (5.2%) **3**[17] and 67 mg (8.5%) **4**.[7,18]

ACKNOWLEDGEMENT:

We are indebted to the Fonds zur Förderung der wissenschaftlichen Forschung in Österreich (project P 12533-CHE) for financial support.

REFERENCES AND NOTES:

1 Chen, C. S. H.; Shen, D.-M.; Wentzek, S. E. PCT Int. Appl. WO 94 28.885; **1994**; *Chem. Abstr.* **1995**, *122*; 239227.

2 Shvekhgeimer, G. A. *Chem. Heterocycl. Comp.* **1997**, *33*, 367.

3 Shen, D.-M. U.S. Patent 5.298.666; **1994**; *Chem. Abstr.* **1994**, *120*; 322827.

4 Faulkner, D.; McKervey, M. A. *J. Chem. Soc.* **1971**, 3906.

5 In the absence of acetic anhydride yields suffer significantly. Also see Ref. 4 and 9.

6 Wiberg, K. B. "Oxidation in Organic Chemistry, Part A." Academic Press New York, **1965**.

7 Morat, C.; Rassat, A. *Tetrahedron Lett.* **1979**, *45*, 4409.

8 Adcock, J. L.; Zhang, H. *J. Org. Chem.* **1996**, *61*, 1975.

9 Gilbert, E. E. *Synth. Commun.* **1985**, *15*, 53.

10 >95% starting material recovered.

11 Srivastava, S.; le Noble, *W. Synth. Commun.* **1984**, *14*, 65.

12 <12% conversion.

13 Pyridinium-chlorochromate oxidation in the same medium afforded a variety of chlorinated products in addition to **2**, **3** and **4**.

14 Müller, P.; Blanc, J. *Helv. Chim. Acta* **1979**, *62*, 1980.

15 Alternatively, continuous extraction with ether could be performed.

16 Duddeck, H.; Wiskamp, V.; Rosenbaum, D. *J. Org. Chem.* **1981**, *46*, 5332.

17 Surya Prakash, G. K.; Krishnamurthy, V. V.; Arvanaghi, M.; Olah, G. A. *J. Org. Chem.* **1985,** *50,* 3985.

18 Yields based on consumed adamantanone. Analytical data in agreement with Ref. 7, 16 and 17.

Accepted 12/01/98