of an α-proton inhibits further reaction, therefore no net reaction occurs. Although **4** possesses α-protons, stereoelectronic considerations suggest that the kinetic acidity of α-protons in the cation radical of **4** may be greatly reduced compared to those of **1** and **3** since the lone pair orbital on nitrogen atom should not be aligned parallel to the α C-H bond in the former. This alignment, which can occur readily for **1** and **3**, is indicated by MMX calculations to result in delocalization of the positive charge to the α C-H bonds and subsequently to enhanced kinetic acidity.[30-32] Perhaps of most significance in the present study is the finding that the reactive metastble products generated via the photoprocess (eq 2) are so cleanly converted via the subsequent "methylene shuttle" to **2** and **5**. The key is hydrolysis of the reactive iminium ion and efficient interception of the formaldehyde generated. Interestingly we find that irradiation of AQ and **1** or **3** in rigorously dry degassed benzene solution leads only to metastable products which return to starting materials in a dark reaction.[33]

Acknowledgment. We are grateful to the Department of Energy (Grant No. DE-FG02-86ER13504) for support of this research.

(30) Xu, W.; Mariano, P. S. *J. Am. Chem. Soc.* **1991**, *113*, 1431-1432.
(31) Lewis, F. J. *Acc. Chem. Res.* **1986**, *19*, 401-405.
(32) Nelsen, S. F.; Ippoliti, J. T. *J. Am. Chem. Soc.* **1986**, *108*, 4879-4881.
(33) Gan, H.; Whitten, D. G. To be published.

Unusual Reorganization Reactions of 3-Azabicyclo[3.3.1]nonanes

Nikolaus Risch,* Maria Langhals, Wolfgang Mikosch, Hartmut Bögge, and Achim Müller

Fakultät für Chemie der Universität Bielefeld Universitätsstrasse, D-4800 Bielefeld, Germany

Received July 19, 1991

Functionalized 3-azabicyclo[3.3.1]nonanes are studied intensively because of their pharmaceutical use[1] and their application as an important structure in the field of molecular recognition.[2] The basic step in our synthetic approach is a regiospecific Grob fragmentation of easily accessible 1-azaadamantane derivatives. We observe a surprising and fascinating self-organization of a key intermediate. The analysis of this remarkable reaction initiated a facile preparation of α-substituted 1-azaadamantanes, which may be of interest as concave bases.[3]

Refluxing a solution of the diketone **1**[4] (available from standard chemicals in two steps: methyl methacrylate, 3-pentanone, hexamethylenetetramine) for 12 h in thionyl chloride yields the derivative **2**. Specifically, only one of the carbonyl groups reacts and is dichlorinated. **2** can be isolated and characterized, but by application of special conditions during the workup [(1) aqueous ammonia, 25%; (2) methanol/NaOH; (3) concentrated hydrochloric acid], a Grob fragmentation[5] is induced. The chlorine axial to the carbocyclic ring (*exo*-chloride) probably acts as the leaving group.

The regiospecificity of this fragmentation is remarkable but not surprising. The α,β-unsaturated derivative **3** is isolated exclusively (TLC; NMR; 90% yield); the possible (alternative) fragmentation to the β,γ-unsaturated product is not observed.

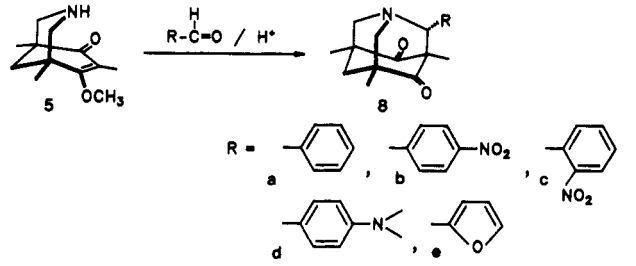
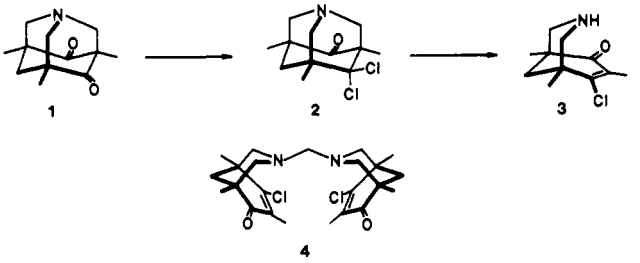
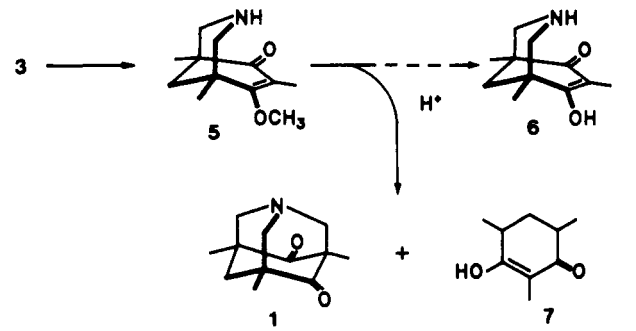


Figure 1. Synthesis of α-substituted 1-azaadamantanediones **8a-e** from **5** (only one of two possible enantiomers is shown).



3 is an interesting and versatile synthetic building block. The NMR data verify the chair conformation of the piperidine part of the bicycle. The ^4J (W) couplings observed are in good agreement with the depicted rigid conformation of **3** and help to establish the geometry of the molecular cleft in products of this type. This is of interest, because special derivatives may be useful in the field of molecular recognition.[6] For example, modified workup of the above reaction (80% aqueous ethanol, triethylamine) yields the dimer **4**, exclusively. Other dimers are easily available, too. **3** is not only a secondary amine (nucleophile) but also a vinylogous acid chloride (diminished reactivity, probably because of the geometry of the compound). The cooperation of both functional groups establishes a variety of chemical applications.[6] Treatment of **3** with CH_3O^- yields the vinylogous ester **5** (addition-elimination reaction), which we planned to hydrolyze for generating the reactive bicycle **6**. While **3** is surprisingly stable toward acids, the ester **5** immediately reacts with hydrochloric acid at room temperature. The vinylogous acid **6**, however, is not the product; the diketone **1** is isolated instead. This results from



a remarkable and surprising self-organization, probably of the intermediate **6** in acidic medium (retro-Mannich/Mannich reaction). The optimized yield of this reaction does not exceed 62%.[7]

(1) Del Campo, C.; Martinez, E.; Trigo, G. G. *Helv. Chim. Acta* **1984**, *67*, 1291. Ruenitz, P. C.; Mokler, C. M. *J. Med. Chem.* **1977**, *20*, 1668. Thompson, M. D.; Smith, G. S.; Berlin, K. D.; Holt, E. M.; Scherlag, B. J.; v. d. Helm, D.; Muchmore, S. W.; Fidelis, K. A. *J. Med. Chem.* **1987**, *30*, 780.
(2) Marshall, L.; Parris, K.; Rebek, J. J., Jr.; Luis, S. V.; Burguete, M. I. *J. Am. Chem. Soc.* **1988**, *110*, 424.
(3) Lüning, U. *Liebigs Ann. Chem.* **1987**, 949. Lüning, U.; Müller, M. *Liebigs Ann. Chem.* **1989**, 367.
(4) Risch, N. *Chem. Ber.* **1985**, *118*, 4073. Billerbeck, U. Dissertation, University of Bielefeld, 1988.
(5) Grob, C. A. *Angew. Chem., Int. Ed. Engl.* **1969**, *8*, 535. Grob, C. A.; Bolleter, M.; Kunz, W. *Angew. Chem., Int. Ed. Engl.* **1980**, *19*, 1977.
(6) Rebek, J. J., Jr.; *Angew. Chem., Int. Ed. Engl.* **1990**, *29*, 245. Langhals, M. Dissertation, University of Bielefeld, 1990. Unlike the interesting derivatives of Kemp's acid, *several* sites of **3** are functionalized. ^{13}C NMR data of **3** (75 MHz, $CDCl_3$): δ 13.22 (q), 21.32 (q), 24.79 (q), 40.52 (s), 40.56 (s), 47.40 (t), 50.96 (t), 53.84 (t), 136.87 (s), 157.65 (s), 200.20 (s). The total assignment of the ^1H NMR data (300 MHz) succeeds by conventional methods and analysis of the COSY spectra.

0002-7863/91/1513-9411$02.50/0

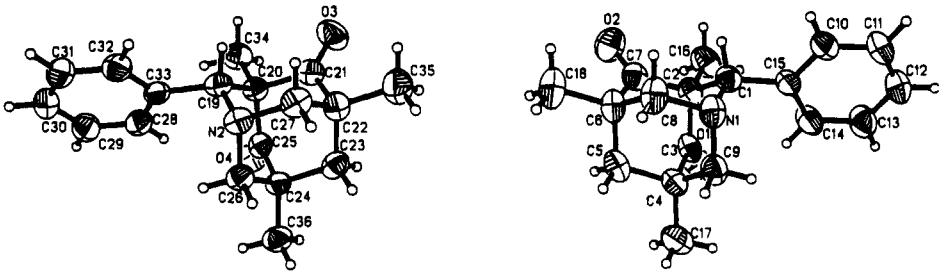


Figure 2. Part of the crystal structure of **8a** (asymmetric unit); selected distances (pm): N1–C1 146.2 (3), N1–C8 145.8 (3), N1–C9 145.2 (3), O1–C3 121.5 (3), O2–C7 121.1 (3), C1–C2 159.0 (3), C1–C15 152.0 (3), C2–C7 153.8 (3), C2–C16 151.5 (4), C3–C4 150.1 (3), C4–C5 153.6 (3), C4–C9 154.4 (3), C4–C17 151.9 (4), C5–C6 153.0 (3), C6–C7 150.0 (4), C6–C8 154.4 (3), C6–C18 152.7 (3), C10–C11 137.9 (4), C10–C15 138.2 (3), C11–C12 137.4 (4), C12–C13 136.4 (4), C13–C14 138.8 (4), C14–C15 139.5 (3). The values for the second molecule do not significantly deviate from these data.

These facts support the conclusion that the unstable aza bicycle **6** is partly degraded in the complex reaction system, generating formaldehyde equivalents, which enable the reorganization toward the thermodynamically more stable heterotricyclic adamantane system.

We used this result for preparative purposes. Adding formaldehyde analogues (in excess) to the reaction mixture stops the degradation and establishes a simple route to α-substituted 1-azaadamantanes **8** (Figure 1).[8] We consider compounds **8** to be valuable products for further investigations. The overall reaction sequence cuts off a one-carbon unit from the tricycle and replaces this by variable CHR groups. This results in a remarkable arylation of a saturated tertiary amine within three steps.

Figure 2 shows the result of the X-ray analysis of **8a** and confirms the interpretations of the spectroscopic data.[9] Furthermore, it is obvious that one or two more α-substituents are necessary for the development of good model systems for concave bases.[3]

The azaadamantane **8a** crystallizes in the monoclinic space group $P2_1/c$ [a = 1490.0 (5) pm, b = 1478.1 (6) pm, c = 1360.9 (8) pm, β = 91.12 (4)°, V = 2999 (2) × 10^6 pm^3, Z = 8, d_{calcd} = 1.255 g/cm^3]. The structure was refined to $R > 0.048$ and R_w = 0.050 for 3394 independent reflections [$F > 4\sigma(F)$]. Figure 2 shows the two enantiomeric molecules of **8a**, which are found in the asymmetric unit of the monoclinic cell. The bonding parameters of **8a** are in good agreement with literature data: The C4–C9 bond distance, for example, is well comparable to the distance of a normal single bond [154.1 (3) pm][10] and the value found in adamantane [153.6 (5) pm].[11] N–C and C–C (phenyl) distances are also normal. The C–C bonds, which are neighbors of *one* C–O bond [e.g., C6–C7 = 150.0 (4) pm], do not deviate from literature data [150.0 (2) pm].[10] The carbon atom in the neighborhood of two C–O bonds, however, shows two elongated C–C(CO) bonds [C2–C3 = 151.3 (3) pm, C2–C7 = 153.8 (3) pm], a strongly elongated C–C (ring) bond [C2–C1 = 159.0 (3) pm], and a slightly shortened C–C(Me) bond [C2–C16 = 151.5 (4) pm]. The deformation of the tricyclic system induced by the incorporation of the phenyl ring is quite small.

Acknowledgment. We thank the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie for their financial support.

Registry No. 1, 136947-01-8; **2**, 136947-02-9; **3**, 136911-70-1; **4**, 136911-71-2; **5**, 136911-72-3; **8a**, 136911-73-4; **8b**, 136911-74-5; **8c**, 136911-75-6; **8d**, 136911-76-7; **8e**, 136911-77-8; benzaldehyde, 100-52-7; 4-nitrobenzaldehyde, 555-16-8; 2-nitrobenzaldehyde, 552-89-6; 4-(dimethylamino)benzaldehyde, 100-10-7; 2-furaldehyde, 98-01-1.

Supplementary Material Available: Tables of positional parameters, bond lengths and angles, anisotropic thermal parameters, and hydrogen positions of **8a** (9 pages). Ordering information is given on any current masthead page.

(7) The yields and the analysis of the products show that three parts of **5** reorganize to two parts of the diketone **1** and one part of the cyclohexanedione **7**.

(8) Preparation of **8a**: 4 mL of concentrated hydrochloric acid is added dropwise to a mixture of 0.48 g (2.25 mmol) of **5** and 1.1 g (10.5 mmol) of benzaldehyde. The mixture is stirred at room temperature for 12 h. With ice cooling, ammonia (25% aqueous solution) is slowly added until an alkaline pH is obtained. Elution with dichloromethane is followed by washing of the organic layer with dilute ammonia. The organic layers are dried with Na_2SO_4 and concentrated under reduced pressure. Unreacted benzaldehyde and **8a** are separated by column chromatography (silica gel, CH_2Cl_2/acetone, 10:1). **8a** is isolated as colorless crystals (0.45 g, 1.6 mmol, 72%, mp 131 °C).

(9) The X-ray data will be helpful in future investigations to get information about the interactions between the 1,3-dicarbonyl system and the nitrogen lone pair. The pK_a values of compounds of type **1** are in the region of 3.5–4, which is remarkably low.

(10) *International Tables for X-Ray Crystallography*; Kynoch: Birmingham, 1968, (Vol. 3).

(11) Donohue, J.; Goodman, S. H. *Acta Crystallgr.* **1967**, *22*, 352.

2,3-Dioxa-5,7-bicyclo[2.2.2]octadiene (Benzene 1,4-*endo*-Peroxide)

Taehee Noh and Nien-chu C. Yang*,†

Department of Chemistry, University of Chicago
Chicago, Illinois 60637

Received July 31, 1991
Revised Manuscript Received September 26, 1991

Energy-rich endoperoxides of aromatic hydrocarbons are of both synthetic and theoretical interest.[1-9] Benzene 1,4-*endo*-peroxide (2,3-dioxa-5,7-bicyclo[2.2.2]octadiene **1**), the simplest and most energetic member of this series, is not yet known. We have developed a convenient synthesis of *cis,anti*-dibenzene **2**,[10] which is a reactive substrate in Diels–Alder addition,[11,12] and its adducts

† Dedicated to Professor George H. Büchi on the occasion of his 70th birthday.

(1) For a review, see: Balci, M. *Chem. Rev.* **1981**, *81*, 91–108.
(2) Kearns, D. R. *J. Am. Chem. Soc.* **1969**, *91*, 6554–6563.
(3) Adam, W.; Balci, M. *J. Am. Chem. Soc.* **1979**, *101*, 7542–7547.
(4) Schäfer-Ridder, M.; Brocker, U.; Vogel, E. *Angew. Chem., Int. Ed. Engl.* **1976**, *15*, 228–229.
(5) Wasserman, H. H.; Scheffer, J. R. *J. Am. Chem. Soc.* **1967**, *89*, 3073–3075. Wasserman, H. H.; Scheffer, J. R.; Cooper, J. L. *J. Am. Chem. Soc.* **1972**, *94*, 4991–4996.
(6) Turro, N. J.; Chow, M.-F.; Rigaudy, J. *J. Am. Chem. Soc.* **1979**, *101*, 1300–1302.
(7) Schmidt, R.; Schaffner, K.; Trost, W.; Brauer, H.-D. *J. Phys. Chem.* **1984**, *88*, 956–958.
(8) Rigaudy, J.; Defoin, A.; Baranne-Lafont, J. *Angew. Chem., Int. Ed. Engl.* **1979**, *18*, 413–415.
(9) Hou, S.-Y.; Dupuy, C. G.; McAuliffe, M. J.; Hrovat, D. A.; Eisenthal, K. B. *J. Am. Chem. Soc.* **1981**, *103*, 6982–6983. See also: Schmidt, R.; Brauer, H.-D.; Rigaudy, J. *J. Photochem.* **1986**, *34*, 197–208.
(10) Yang, N. C.; Noh, T.; Gan, H.; Halfon, S.; Hrnjez, B. J. *J. Am. Chem. Soc.* **1988**, *110*, 5919–5920.
(11) Berson, J. A.; Davis, R. F. *J. Am. Chem. Soc.* **1972**, *94*, 3658–3659.

0002-7863/91/1513-9412$02.50/0