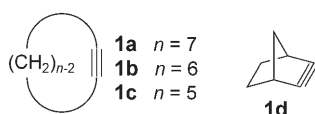


Strained Molecules

DOI: 10.1002/anie.200503124

 Bi-3*H*-diazirin-3-yls as Precursors of Highly Strained Cycloalkynes**

Mohammad Al-Omari, Klaus Banert,* and Manfred Hagedorn

 Several methods for the generation of highly strained non-isolable cycloalkynes, for example, **1a–c**, have been developed within the last decades (Scheme 1).^[1] These methods


Scheme 1.

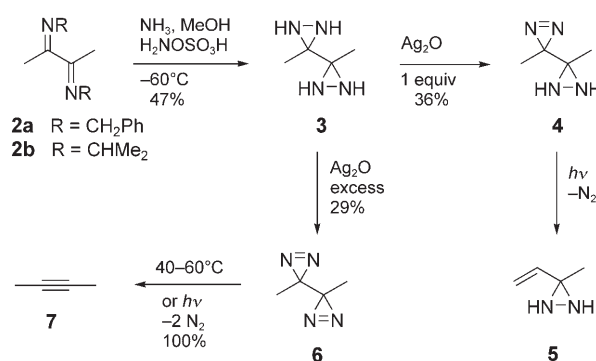
 typically rely on the use of metals, metal salts or complexes, organometallic compounds, strong bases, fluoride salts, or oxidizing reagents. High temperatures or irradiation of the starting material are sometimes also necessary. After their generation, the highly reactive cycloalkynes **1a–c** can be trapped by cycloaddition reactions. Norbornyne (**1d**)^[2–5] and related bicyclic compounds^[6] are the limiting cases of strained cyclic alkynes that be proved experimentally by trapping reactions.

 [*] Dr. M. Al-Omari, Prof. Dr. K. Banert, Dr. M. Hagedorn
 Lehrstuhl für Organische Chemie
 Technische Universität Chemnitz
 Strasse der Nationen 62, 09111 Chemnitz (Germany)
 Fax: (+49) 371-531-1839
 E-mail: klaus.banert@chemie.tu-chemnitz.de

[***] Strained Rings, Part 1. This research was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.

 Supporting information for this article is available on the WWW under <http://www.angewandte.org> or from the author.

 We now report on the isolable diazirine derivatives **6**, **12**, **13**, and **26**, which lead to the alkyne **7** and the short-lived cycloalkynes **1a**, **1b**, and **1d**, respectively, already at room temperature or slightly above without the need of other reagents and without formation of any side product except nitrogen. Originally, we planned to prepare the title compounds in order to investigate the possible valence isomerization yielding tetraazabenzenes. Analogous rearrangement reactions of bi-2*H*-azirin-2-yls to give diazabenzenes occur already at surprisingly low temperatures.^[7]

 We obtained bidiaziridin-3-yl **3** as a mixture of diastereomers (ca. 10:1) upon treatment of a solution of bisimine **2a**^[8] in anhydrous methanol with liquid ammonia and hydroxylamine-*O*-sulfonic acid (Scheme 2). If one assumes that N-


Scheme 2.

 bonded substituents (here H atoms) in a diaziridine ring always adopt a *trans* configuration,^[9] the formation of both a C_2 -symmetrical (*rac*, *R,R,R,R* and *S,S,S,S*) and an achiral (*meso*, *R,R,S,S*) stereoisomer should occur. Starting with **2b**,^[10] similar results were found. Although the workup is more convenient, the yield of **3** is significantly lower. Early attempts^[11] to prepare **3** from butane-2,3-dione were unsuccessful, and our own efforts to synthesize the bidiaziridines **3**, **9**, and **24** from the corresponding α -diketones, their dioximes, or α -iminoketones also failed.^[12] The structure of **3** was supported by the usual spectroscopic methods including ¹⁵N NMR data (Table 1) as well as by its oxidation to give the diazirine **4**. Reaction of **3** with an excess of freshly generated silver oxide afforded the isolable^[13] product **6**. This compound as well as the bi-3*H*-diazirin-3-yls described below slowly eliminated nitrogen at room temperature. They can be handled conveniently in solution and stored at -30°C for a long period. On warming or irradiation a solution of **6** in chloroform, the alkyne **7** was formed quantitatively. When this transformation was monitored by NMR spectroscopy, no intermediate could be observed. The mild conditions of the thermal reaction and the high yield of **7** may be the outcome of a cooperative effect between both 3*H*-diazirine units of **6**. When **6** was photolyzed in the presence of a great excess of hex-3-yne, exclusively alkyne **7** and thus no product of intermolecular carbene trapping results. However, product **5**, which was generated in only moderate yield (36% based on ¹H NMR) by irradiation of **4**, can be explained by insertion of a carbene into the neighboring C–H bond.

Table 1: Selected physical data of compounds **3**, **4**, **6**, **9**, **10**, **12**, **13**, **24**, and **26**.^[a]

3:^[b] White crystals; m.p. 149–151 °C (CH₃OH or CH₂Cl₂); major isomer: ¹H NMR ([D₆]DMSO): δ = 1.34 (s, 6H, CH₃), 2.36 (d, ³J = 8.1 Hz, 2H, NH), 2.58 ppm (d, ³J = 8.1 Hz, 2H, NH); ¹³C NMR ([D₆]DMSO): δ = 19.71 (q, CH₃), 56.51 ppm (s, C-3); ¹⁵N NMR ([D₂]MeNO₂, also as standard with δ = 0): δ = -314.8 (d, ¹J = 64 Hz), -308.9 ppm (d, ¹J = 62 Hz); minor isomer: ¹H NMR ([D₆]DMSO): δ = 1.31 (s), 2.42 ppm (br); ¹³C NMR ([D₆]DMSO): δ = 20.52 (q), 56.22 ppm (s).

4: Pale yellow crystals; m.p. = 56–58 °C; ¹H NMR ([D₆]DMSO): δ = 0.98 (s, 3H, CH₃), 1.13 (s, 3H, CH₃), 2.57 (d, ³J = 8.1 Hz, 1H, NH), 2.68 ppm (d, ³J = 8.1 Hz, 1H, NH); ¹³C NMR ([D₆]DMSO): δ = 15.28 (q, CH₃), 19.95 (q, CH₃), 28.04 (s, C-3), 54.45 ppm (s, C-3).

6: Brown oil; IR (C₆D₆): ν̄ = 2963, 2928, 1580, 1436, 1384, 1103 cm⁻¹; ¹H NMR (CDCl₃): δ = 0.85 ppm (s, CH₃); ¹³C NMR (CDCl₃): δ = 15.30 (q, CH₃), 26.55 ppm (s, C-3); ¹⁵N NMR (CDCl₃): δ = 69.7 ppm.

9:^[b] Yellow crystals; m.p. 120–125 °C (hexane/Et₂O); major isomer: ¹H NMR ([D₆]DMSO): δ = 1.50–1.85 (m, 10H, CH₂), 2.37 (d, ³J = 8.1 Hz, 2H, NH), 2.60 ppm (d, ³J = 8.1 Hz, 2H, NH); ¹³C NMR ([D₆]DMSO): δ = 23.59 (t), 26.69 (t), 34.10 (t), 59.09 ppm (s); minor isomer: ¹H NMR ([D₆]DMSO): δ = 1.50–1.85 (m, 10H, CH₂), 2.01 (d, ³J = 7.8 Hz, 2H, NH), 2.59 ppm (d, ³J = 7.8 Hz, 2H, NH); ¹³C NMR ([D₆]DMSO): δ = 25.26 (t), 29.26 (t), 35.75 (t), 57.92 ppm (s).

10:^[b] Brown solid; m.p. 152–154 °C; IR (KBr): ν̄ = 3427, 3178, 2946, 2923, 2863, 2366, 1652, 1399, 1201, 855 cm⁻¹; ¹H NMR ([D₆]DMSO): δ = 1.62 (brs, 8H, CH₂), 2.23 (d, ³J = 7.8 Hz, 2H, NH), 2.63 ppm (d, ³J = 7.8 Hz, 2H, NH); ¹³C NMR ([D₆]DMSO): δ = 24.14 (t), 33.79 (t), 58.06 ppm (s).

12: Brown oil; ¹H NMR (CDCl₃): δ = 1.30 (m, 4H, CH₂), 1.70–1.86 ppm (m, 6H, CH₂); ¹³C NMR (CDCl₃): δ = 24.43 (t), 29.91 (s, C-3/C-4), 30.29 (t, C-9), 32.84 ppm (t).

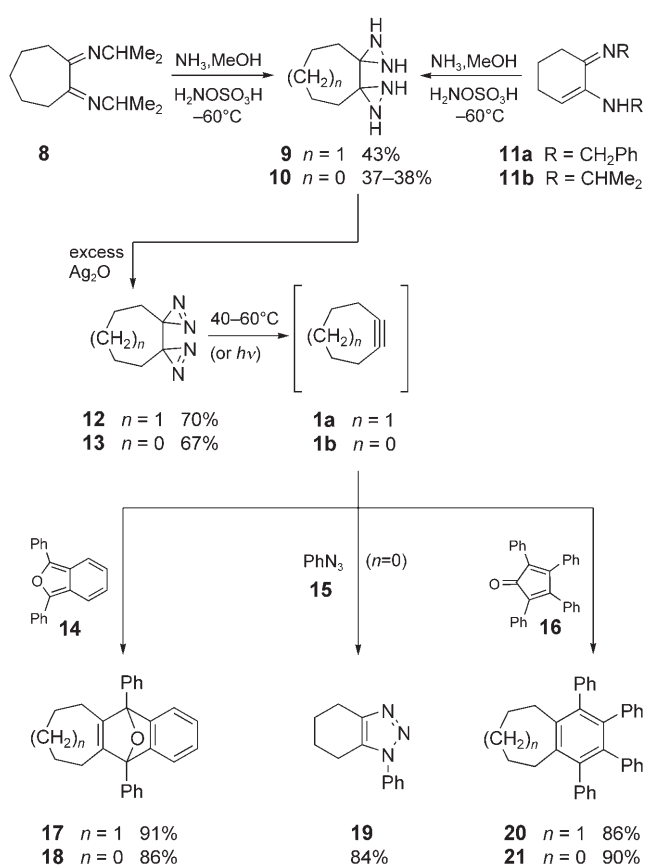
13: Brown oil; ¹H NMR (CDCl₃): δ = 1.36 (m, 4H, CH₂), 1.86 ppm (m, 4H, CH₂); ¹³C NMR (CDCl₃): δ = 23.72 (t), 27.99 (s), 30.68 ppm (t).

24:^[b] Yellow oil; IR (CDCl₃): ν̄ = 3176, 3124, 2970, 2878, 1670, 1591, 1406, 1125 cm⁻¹; ¹H NMR (CDCl₃): δ = 1.05–2.55 (m), 2.60–3.80 ppm (m); ¹³C NMR (CDCl₃): δ = 23.51 (t), 24.95 (t), 34.77 (t), 43.00 (d), 43.20 (d), 64.34 (s), 64.79 ppm (s).

26: Brown oil; ¹H NMR (CDCl₃): δ = 1.50 (m, 2H, 7-H/10-H), 1.54 (dt, ²J = 9.9 Hz, ⁴J = 1.8 Hz, 1H, 11_{syn}-H), 1.75 (m, 2H), 2.02 (m, 2H), 2.37 ppm (dm, ²J = 9.9 Hz, 1H, 11_{anti}-H); ¹³C NMR (CDCl₃): δ = 24.53 (t, C-8/C-9), 37.28 (t, C-11), 37.88 (s, C-3/C-4), 40.19 ppm (d, C-7/C-10).

[a] ¹H NMR: 300 MHz; ¹³C NMR: 75 MHz; ¹⁵N NMR: 30 MHz. [b] The bidiaziridines **3**, **9**, **10**, and **24** were treated with an excess of PhNCO to yield urea derivatives which were completely characterized (including combustion analyses).

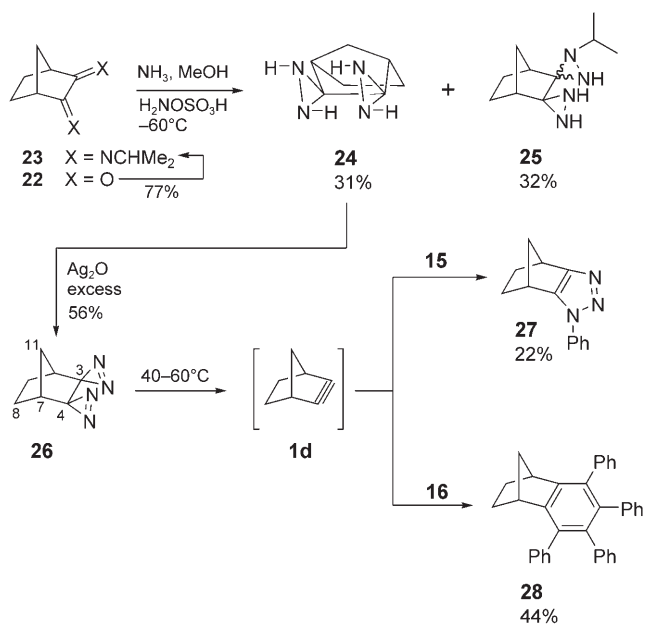
The spirocyclic diaziridines **9** and **10** were accessible from the bisimines **8**^[14] and **11a**^[14] or **11b**,^[15] respectively. The spectroscopic data of **9** (Table 1) point to a mixture of diastereomers (ca. 9:5). The isolable title compounds **12** and **13**, which function as precursors of cycloheptyne (**1a**) and cyclohexyne (**1b**), were obtained by oxidation of **9** and **10**, respectively. When **12** or **13** were warmed in the presence of the reaction partners **14**, **15**, or **16**, the trapping products of cycloalkynes **17–21**^[16] were formed in excellent yields (Scheme 3). Similar results were achieved on irradiation of precursors **12** or **13** in the presence of **14** or **16**. Lower yields of



Scheme 3.

20 (25–35%) were obtained when trapping reagent **16** was added *after* photolysis of **12** at low temperature (–90 °C in CD₂Cl₂ or –120 °C in CD₂ClF).

The bisimine **23**, which is easily accessible from diketone **22**, can also be transformed into bidiaziridines. After workup



Scheme 4.

by chromatography (neutral alumina), we isolated the desired product **24** and also the isopropyl derivative **25**. Based on the ^{13}C NMR data (Table 1) and supposing that both H-N-N-H units have a *trans* arrangement, we assume either an all-*R* configuration (see Scheme 4) or an all-*S* configuration for the four nitrogen atoms of **24**. Oxidation of **24** afforded the norbornyne precursor **26**. Thermolysis of the latter compound in the presence of **15** led to cycloadduct **27**, whereas **28**^[17] was formed in the presence of **16**.

This clean and reagent-free generation of highly strained cycloalkynes from bi-3*H*-diazirin-3-yls, which occurs under very mild reaction conditions, could lead to new applications for these compounds.

Received: September 2, 2005

Keywords: cycloaddition · cycloalkynes · reactive intermediates · spiro compounds · strained molecules

- A. Krebs, *Chem. Ber.* **1961**, *94*, 3260–3275; f) R. Breslow, L. J. Altman, A. Krebs, E. Mohacsi, I. Murata, R. A. Peterson, J. Posner, *J. Am. Chem. Soc.* **1965**, *87*, 1326–1331; g) F. G. Willey, *Angew. Chem.* **1964**, *76*, 144; *Angew. Chem. Int. Ed. Engl.* **1964**, *3*, 138.
 [17] Alternative synthesis of **28**: D. W. Macomber, A. G. Verma, R. D. Rogers, *Organometallics* **1988**, *7*, 1241–1253.

- [1] Reviews: a) H. Hopf, *Classics in Hydrocarbon Chemistry*, Wiley-VCH, Weinheim, **2000**, chap. 8.2; b) R. Gleiter, R. Merger in *Modern Acetylenic Chemistry*, (Eds.: P. J. Stang, F. Diederich), VCH, Weinheim, **1995**, pp. 285–319; c) H. Meier in *Advances in Strain in Organic Chemistry, Vol. 1* (Ed.: B. Halton), JAI, London, **1991**, pp. 215–272; d) A. Krebs, J. Wilke, *Top. Curr. Chem.* **1983**, *109*, 189–233.
 [2] D. W. Laird, J. C. Gilbert, *J. Am. Chem. Soc.* **2001**, *123*, 6704–6705.
 [3] In early attempts to generate **1d**,^[4] trapping by means of a Diels–Alder reaction was not successful (see Ref. [5]).
 [4] a) P. G. Gassman, I. Gennick, *J. Am. Chem. Soc.* **1980**, *102*, 6863–6864; b) P. G. Gassman, I. Gennick, *J. Org. Chem.* **1980**, *45*, 5211–5213.
 [5] H. Hart, S. Shamouilian, Y. Takehira, *J. Org. Chem.* **1981**, *46*, 4427–4432, see footnote [27].
 [6] T. Kitamura, M. Kotani, T. Yokoyama, Y. Fujiwara, K. Hori, *J. Org. Chem.* **1999**, *64*, 680–681.
 [7] K. Banert, F. Köhler, *Angew. Chem.* **2001**, *113*, 173–176; *Angew. Chem. Int. Ed.* **2001**, *40*, 174–177.
 [8] H. Bock, H. tom Dieck, *Chem. Ber.* **1967**, *100*, 228–246.
 [9] A. Mannschreck, W. Seitz, *Angew. Chem.* **1969**, *81*, 224; *Angew. Chem. Int. Ed. Engl.* **1969**, *8*, 212.
 [10] H. tom Dieck, K.-D. Franz, W. Majunke, *Z. Naturforsch. B* **1975**, *30*, 922–925.
 [11] E. Schmitz, C. Hörig, C. Gründemann, *Chem. Ber.* **1967**, *100*, 2093–2100.
 [12] Reviews on the synthesis of diaziridines and diazirines: a) E. Schmitz in *Comprehensive Heterocyclic Chemistry, Vol. 7* (Ed.: W. Lwowski), Pergamon, Oxford, **1984**, pp. 195–236; b) R. G. Kostyanovsky, R. Murugan, M. Sutharchanadevi in *Comprehensive Heterocyclic Chemistry II, Vol. 1A* (Ed.: A. Padwa), Pergamon, New York, **1996**, pp. 347–364.
 [13] Caution should be exercised during isolation of diazirines which may be explosive. However, our bidiazirinyls did not explode even when samples were hit with a hammer.
 [14] Compounds **8** and **11a** can be prepared easily from the corresponding α -diketones and primary amines.
 [15] R. van Asselt, C. J. Elsevier, W. J. J. Smeets, A. L. Spek, R. Benedix, *Recl. Trav. Chim. Pays-Bas* **1994**, *113*, 88–98.
 [16] a) G. Wittig, R. Pohlke, *Chem. Ber.* **1961**, *94*, 3276–3286; b) G. Wittig, P. Fritze, *Angew. Chem.* **1966**, *78*, 905; *Angew. Chem. Int. Ed. Engl.* **1966**, *5*, 846; c) K. L. Erickson, J. Wolinsky, *J. Am. Chem. Soc.* **1965**, *87*, 1142–1143; d) T. Harada, K. Iwazaki, T. Otani, A. Oku, *J. Org. Chem.* **1998**, *63*, 9007–9012; e) G. Wittig,