

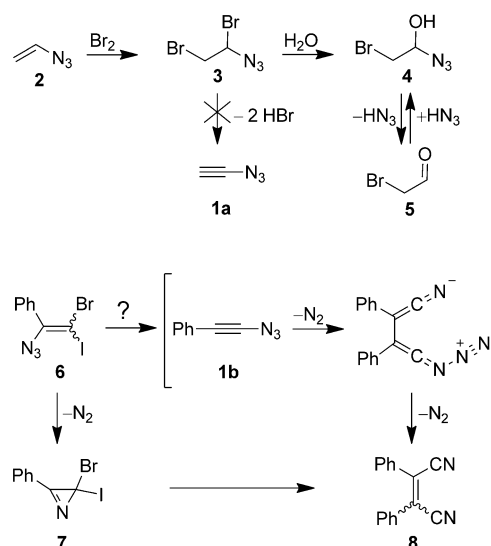
Ethynyl Azides

1-Azido-1-Alkynes: Synthesis and Spectroscopic Characterization of Azidoacetylene**

Klaus Banert,* René Arnold, Manfred Hagedorn, Philipp Thoss, and Alexander A. Auer*

Dedicated to Professor K. Barry Sharpless

In 1910, Forster and Newman had already studied the addition of bromine to vinyl azide (**2**) in an aqueous solution to prepare azidoacetylene (**1a**) by base-induced elimination of two molecules of hydrogen bromide (Scheme 1). However, owing to the explosion-like course of the addition reaction and the high sensitivity of the product **3** to hydrolysis, **3** could not be detected and aldehyde **5** was generated instead.^[1] A hundred years later, it was shown that the transformation **2** → **3** can be performed conveniently and quantitatively with bromine in organic solvents at low temperature. Careful hydrolysis of **3** led to an equilibrium mixture of α-azido alcohol **4** and aldehyde **5**,^[2] but all efforts to convert **3** into the alkyne **1a** were in vain. Since the 1950s, many groups have tried to generate 1-azido-1-alkynes, but these species have remained elusive even until today.^[3] Other attempts at preparing these compounds were also unsuccessful or yielded unwanted products.^[4] For example, the reactions of (phenylethynyl)sodium or alkyl-1-ynyl lithiums and aromatic sulfonyl azides exclusively led to 1,2,3-triazole derivatives instead of ethynyl azides.^[5] Furthermore, the transformation of azide **6** into the dinitriles **8**, a reaction that can be performed under a variety of conditions and in high yield, was postulated to proceed via the short-lived alkyne **1b** (Scheme 1).^[6] However, 2*H*-azirine **7** was also predicted to be an intermediate in the



Scheme 1. Some of numerous unsuccessful attempts to prepare ethynyl azides **1a** and **1b**.

transformation **6** → **8**.^[7] Recently, the highly unstable heterocycle **7** was photochemically prepared from **6** in 90% yield, characterized by its NMR data, and thermolyzed to give the nitriles **8**, nearly quantitatively.^[8]

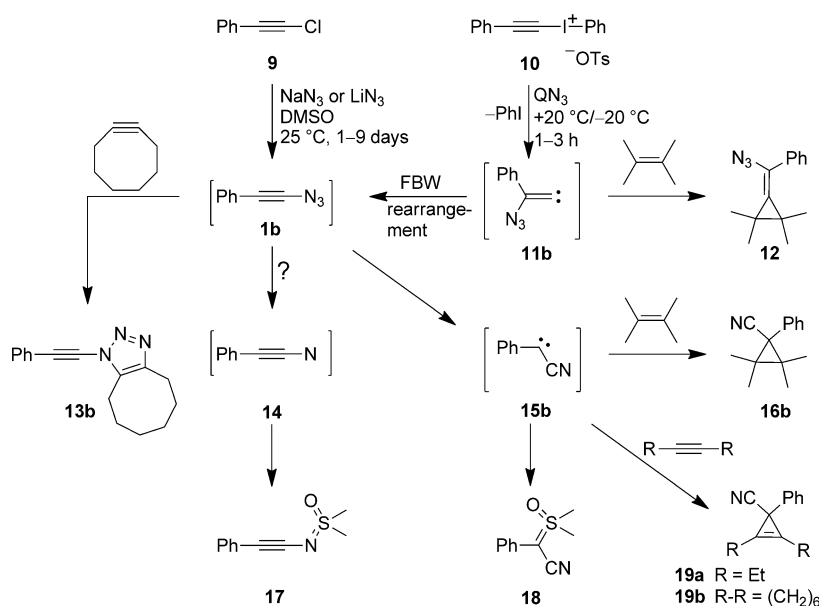
In 1983, Tanaka and Yamabe reported on the treatment of chloride **9** with sodium azide in dimethyl sulfoxide, a reaction that was claimed to afford in low yield (5–8%) the sulfoximine **17** and some other products but no dinitriles **8** (Scheme 2). The synthesis of **17** was rationalized to proceed through the formation of short-lived azide **1b** followed by loss of dinitrogen and trapping of the nitrene **14** by the solvent.^[9] When the experiment starting with **9** was repeated recently, it was shown that the actual product **18**, resulting from the reaction pathway via carbene **15b**, had been erroneously taken for **17**.^[8] Furthermore, previous ab initio studies demonstrated that ethynyl nitrenes such as **14** do not correspond to a local minimum of energy and that cleavage of dinitrogen from azide **1b** should generate carbene **15b**.^[10,11] Not only the carbene-interception product **18** but also the triazole **13b** was obtained when the reaction of **9** with lithium azide in dimethyl sulfoxide was performed in the presence of cyclooctyne.^[8] This heterocyclic product is currently the most plausible evidence for short-lived ethynyl azides. To the best of our knowledge, any spectroscopic proof for the existence of these azides is still missing.

[*] Prof. Dr. K. Banert, R. Arnold, Dr. M. Hagedorn, P. Thoss
Technische Universität Chemnitz, Organische Chemie
Strasse der Nationen 62, 09111 Chemnitz (Germany)
E-mail: klaus.banert@chemie.tu-chemnitz.de
Homepage: <http://www.tu-chemnitz.de/chemie/org/index.html>
Prof. Dr. A. A. Auer^[†]
Max-Planck-Institut für Eisenforschung GmbH
Max-Planck-Strasse 1, 40237 Düsseldorf (Germany)
E-mail: aaauer@gwdg.de

[†] New address: Max-Planck-Institut für Chemische Energiekonversion
Stiftstrasse 34–36, 45470 Mülheim an der Ruhr (Germany)

[**] We gratefully acknowledge financial support from the Deutsche Forschungsgemeinschaft (BA 903/12-1). We thank Dr. O. Jaurich (Mettler Toledo) and Dr. S. Hemeltjen (TU Chemnitz) for their help in the measurement of low-temperature IR spectra, as well as A. Käßner and Dr. A. Ihle for the realization of some experiments and assistance with preparing the manuscript. Dedicated to Professor K. Barry Sharpless, who inspired us to bring alkynes and azides together. Reactions of Unsaturated Azides, Part 30; for Part 29, see: K. Banert, C. Berndt, M. Hagedorn, H. Liu, T. Anacker, J. Friedrich, G. Rauhut, *Angew. Chem.* **2012**, 124, 4796–4800; *Angew. Chem. Int. Ed.* **2012**, 51, 4718–4721.

Supporting information for this article is available on the WWW under <http://dx.doi.org/10.1002/anie.201203626>.



Scheme 2. Generation of phenylethynyl azide (**1b**). QN₃ = hexadecyltributylphosphonium azide.

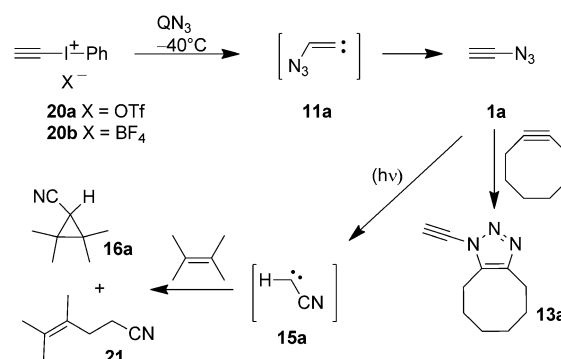
Herein, we show that 1-azidoalkynes can be synthesized more rapidly and under significantly milder reaction conditions when ethynyliodonium salts instead of 1-chloroacetylenes are treated with azide salts. Moreover, better yields of the trapping products are achieved, and it was possible to detect azidoacetylene (**1a**) for the first time by using IR and NMR spectroscopy. These results are strongly supported by quantum chemical calculations.

The conversion of **9** with sodium azide in dimethyl sulfoxide is very slow at ambient temperature and furnished only low yields of **18** (up to 10%) and **13b** (2–12%). Even slower reactions were observed when the polar solvent (DMSO or DMF) was diluted by the less-polar interception-reagent cyclooctyne.^[12] We assume that the nucleophilic substitution **9**→**1b** is a two-step addition–elimination process with attack of azide at the carbon atom that is connected to the chlorine atom. On the other hand, phenyliodonium salts, such as **10**,^[13] are well-known to react with azide at the other carbon atom to generate azidovinylidene intermediates such as **11b** after cleavage of iodobenzene.^[14] Proof for short-lived azidovinylidenes was presented by Stang and Kitamura, who analyzed the subsequent reactions, which led to insertion products.^[15]

When we treated the salt **10** with a highly soluble azide source such as QN₃^[16] (hexadecyltributylphosphonium azide) in the presence of 2,3-dimethyl-2-butene, not only the vinylidene-trapping product **12** (17% yield) but also the known^[17] cyanocyclopropane **16b** (29%) were isolated (Scheme 2). We explain the formation of **16b** through a Fritsch–Buttenberg–Wiechell-like rearrangement (FBW) of **11b**, cleavage of dinitrogen from resulting **1b**, and interception of carbene **15b**. After we had repeated the experiment with 3-hexyne instead of 2,3-dimethyl-2-butene, we found exclusively the 3-cyanocyclopropene **19a** (43%). Whereas general trapping of vinylidenes by olefins to produce

methylidenecyclopropanes is well-known,^[18] the analogous reaction with alkynes has seldom been investigated because the corresponding methylidenecyclopropanes are highly unstable and could only be characterized after interception by Diels–Alder reaction.^[19] Thus, it is not surprising that no methylidenecyclopropanes were detected from the reaction mixture of **10**, QN₃, and alkynes. On the other hand, treatment of **10** with QN₃ in the presence of ring-strained cyclooctyne instead of open-chain acetylenes afforded not only a small yield of **19b** (7%) but also the triazole **13b** (21%), which is the trapping product of azide **1b**.

These results encouraged us to also investigate the reaction of iodonium salts **20**^[20] with QN₃ (Scheme 3). We assume that the attack of azide at the terminal carbon atom of **20** will be more rapid than the analogous reaction of **10**. Furthermore, quantum chemical calculations,^[10] in which energy barriers for the cleavage of dinitro-



Scheme 3. Synthesis and reactions of azidoacetylene (**1a**). QN₃ = hexadecyltributylphosphonium azide.

gen were studied for different ethynyl azides, predicted an even greater stability of **1a** than that of **1b**, whereas azidoacetylenes with donor groups, such as amino or ethylsulfanyl, should cleave dinitrogen very easily.^[21–23]

After treatment of the iodonium salt **20b** with QN₃ at –40 °C in the presence of 2,3-dimethyl-2-butene, we isolated the known^[24] cyclopropane **16a** (15% yield) and the insertion product **21** (7%), which obviously result from carbene **15a** (Scheme 3). We could not detect the corresponding azidomethylidenecyclopropane, which may form by the trapping of vinylidene **11a**. Thus, we assume that the isomerization **11a**→**1a** is more rapid than the FBW-like rearrangement **11b**→**1b**. When the reaction of **20a** with QN₃ was performed at –40 to –30 °C with cyclooctyne instead of 2,3-dimethyl-2-butene, we exclusively isolated the triazole **13a** (91%), which is a consequence of the 1,3-dipolar cycloaddition of azide **1a** to the cycloalkyne. Treatment of **20a** or **20b** with QN₃ in acetone, dichloromethane, or chloroform (–40 °C/30–120 min) in the

Table 1: Selected experimental and calculated spectroscopic data of azidoacetylene (**1a**) and [¹⁵N₃]-**1a**.^[a,b,c]

1a	IR (CHCl ₃ , −20 °C): ^[c]	$\tilde{\nu}$ = 3312 (m, C–H), 2188 (s, C≡C), 2148 (w), 2086 (s, N ₃), 1251 cm ^{−1} (w, N ₃)
	¹ H NMR ([D ₆]acetone):	δ = 3.38 (s) [δ = 3.7]
	¹³ C NMR ([D ₆]acetone):	δ = 55.81 (d, ¹ J = 265.5 Hz, CH), 72.25 (d, ² J = 58.3 Hz, CN ₃) [δ = 55.5 (¹ J = 259 Hz), 76.5 (² J = 59 Hz)]
	¹ H NMR (CD ₂ Cl ₂):	δ = 2.55 (s) [δ = 3.0]
	¹³ C NMR (CD ₂ Cl ₂):	δ = 54.52 (d, ¹ J = 262.8 Hz, CH) 71.94 (d, ² J = 57.5 Hz, CN ₃) [δ = 54.0 (¹ J = 259 Hz), 75.0 (² J = 59 Hz)]
[¹⁵ N ₃]- 1a	¹ H NMR (CD ₂ Cl ₂):	δ = 2.57 (dd, ⁴ J _{NH} = 1.7 Hz, ³ J _{NH} = 0.9 Hz)
	¹³ C NMR (CD ₂ Cl ₂):	δ = 54.31 (ddd, ¹ J _{CH} = 264.9 Hz, ² J _{CN} = 5.7 Hz, ³ J _{CN} = 2.9 Hz, CH), 71.69 (dd, ² J _{CH} = 58.8 Hz, ¹ J _{CN} = 15.4 Hz, CN ₃) [¹ J _{CN} = −17 Hz, ² J _{CNα} = 5.6 Hz, ² J _{CNβ} = 2.6 Hz]
	¹⁵ N NMR (CD ₂ Cl ₂):	δ = −314.6 (br d, ¹ J _{NN} = 15.5 Hz, N _{α}), −151.8 (d, ¹ J _{NN} = 7.4 Hz, N _{γ}), −139.9 (ddd, ¹ J _{NαNβ} = 15.5 Hz, ¹ J _{NβNγ} = 7.4 Hz, ⁴ J _{NH} = 1.7 Hz, N _{β}) [δ = 317.8 (¹ J _{NN} = −15.5 Hz, ³ J _{NH} = −0.8 Hz, N _{α}), −151.8 reference value (¹ J _{NN} = −6 Hz, N _{γ}), −133.8 (¹ J _{NαNβ} = −15.5 Hz, ¹ J _{NβNγ} = −6 Hz, ⁴ J _{NH} = 1.9 Hz, N _{β})]

[a] ¹H and ¹³C NMR spectra were recorded at −40 °C and 400 and 100.6 MHz, respectively. ¹⁵N NMR spectra were recorded at −60 °C and 40.5 MHz, and referenced to nitromethane (δ = 0). The sign of experimental *J* values was not determined. [b] All NMR data based on quantum chemical calculations are given in square brackets. In the case of the ¹H NMR and ¹³C NMR spectra, the reference of δ values is determined with the help of experimental and calculated chemical shifts of acetylene (see the Supporting Information). Calculated ¹⁵N NMR δ values were referenced to the experimental chemical shift of N _{γ} . All results have been obtained from all-electron calculations and are based on geometries that have been obtained at the CCSD(T)/cc-pVTZ level of theory. NMR chemical shifts have been calculated at the CCSD(T)/p3d2f level of theory including zero-point vibrational effects calculated at the MP2/cc-pVTZ (geometry and anharmonic force field) CCSD(T)/qz2p (chemical shifts) level of theory. Spin-spin coupling constants have been calculated at the CCSD/unc-cc-pVTZ level of theory including FC, SD, PSO and DSO contributions (FC and SD terms have been calculated using an unrelaxed UHF reference). [c] For IR data based on analytical CCSD(T)/cc-pVTZ normal mode calculations, see the Supporting Information.

absence of any trapping reagent led to solutions of **1a** after careful^[25] recondensation of the reaction mixtures under reduced pressure (yield approximately 40%, as determined by ¹H NMR spectroscopy). ¹⁵N-labeled azidoacetylene ([¹⁵N₃]-**1a**) was also synthesized using Q¹⁵N₃^[16,26] and **20a**.

We characterized **1a** using IR, ¹H NMR, ¹³C NMR, and ¹⁵N NMR spectroscopy, which provided conclusive proof of the structure (Table 1). These data, especially the δ and *J* values from the NMR spectra were compared with the corresponding values resulting from quantum chemical calculations at the coupled-cluster level of theory. Experimental and calculated data for acetylene were included for the referencing of the chemical shifts in the case of calculated ¹H NMR and ¹³C NMR spectra. Generally, good agreement between the measured and the theoretical data was found. The upfield shift for the signal corresponding to the C–H carbon (δ ca. 55) indicates that the azido group acts as a π donor, through which **1a** becomes an electron-rich alkyne. The coupling constants ¹J(¹³C,¹H) and ²J(¹³C,¹H) of **1a** are significantly larger than those of acetylene. This is typical for terminal alkynes with oxygen or nitrogen donor substituents.^[27] The IR spectrum of **1a** shows expected bands corresponding to C–H, C≡C, asymmetric N₃, and symmetric N₃ stretching modes. However, the high extinction of the C≡C stretching vibration is as strong as the azide band; this finding is remarkable and possibly results from coupling of vibration modes.

Azidoacetylene (**1a**) decomposed with a half-life period of approximately 17 hours in dichloromethane at −30 °C. Nevertheless, it can be reacted intermolecularly, for example, with cyclooctyne to furnish **13a** (35% yield based on precursor **20a**). When a cold solution of **1a** in dichloro-

methane was warmed to ambient temperature in the presence of 2,3-dimethyl-2-butene, the expected compounds **16a** (44%) and **21** (27%) were formed. The same products were also found with 35% and 15% yield, respectively, after irradiation of a solution of **1a** in dichloromethane for 3 hours at −60 °C.

In summary, we have characterized the first ethynyl azide by IR, ¹H NMR, ¹³C NMR, and ¹⁵N NMR spectroscopy. After 102 years of unsuccessful attempts, not only have the azide adducts, for example, the cycloadducts **13** and the cyanocarbene-trapping products **16**, **18**, **19**, and **21**, been observed but also the parent azide itself has been characterized. Currently, we are investigating whether the properties of azidoacetylene (**1a**) as an electron-rich alkyne can be utilized for electrophilic addition or cycloaddition reactions at the C≡C bond.

Received: May 10, 2012

Published online: July 6, 2012

Keywords: carbenes · ethynyl azides · NMR spectroscopy · quantum chemistry · reaction mechanisms

- [1] M. O. Forster, S. H. Newman, *J. Chem. Soc.* **1910**, 97, 2570–2579.
- [2] K. Banert, C. Berndt, S. Firdous, M. Hagedorn, Y.-H. Joo, T. Rüffer, H. Lang, *Angew. Chem.* **2010**, 122, 10404–10407; *Angew. Chem. Int. Ed.* **2010**, 49, 10206–10209.
- [3] Reviews on ethynyl azides: a) K. Banert in *Organic Azides—Syntheses and Applications* (Eds.: S. Bräse, K. Banert), Wiley, Chichester, **2010**, pp. 115–166; b) K. Banert in *Houben-Weyl, Science of Synthesis*, 5th ed., Vol. 24 (Ed.: A. de Meijere), Thieme, Stuttgart, **2006**, pp. 1061–1072; c) K. I. Booker-Milburn in *Comprehensive Organic Functional Group Transformations*,

- Vol. 2 (Eds.: A. R. Katritzky, O. Meth-Cohn, C. W. Rees), Pergamon, Oxford, **1995**, pp. 1054–1055; d) G. Himbert in *Houben-Weyl*, 4th ed., Vol. E15 (Eds.: H. Kropf, E. Schaumann), Thieme, Stuttgart, **1993**, p. 3455.
- [4] a) J. H. Boyer, C. H. Mack, N. Goebel, L. R. Morgan, Jr., *J. Org. Chem.* **1958**, 23, 1051–1053; b) J. H. Boyer, R. Selvarajan, *Tetrahedron Lett.* **1969**, 10, 47–50; c) V. A. Garibina, A. A. Leonov, A. V. Dogadina, B. I. Ionin, A. A. Petrov, *J. Gen. Chem. USSR (Engl. Transl.)* **1985**, 55, 1771–1781.
- [5] a) R. Helwig, M. Hanack, *Chem. Ber.* **1985**, 118, 1008–1021; b) E. Robson, J. M. Tedder, B. Webster, *J. Chem. Soc.* **1963**, 1863–1865; c) M. E. Meza-Aviña, M. K. Patel, C. B. Lee, T. J. Dietz, M. P. Croatt, *Org. Lett.* **2011**, 13, 2984–2987.
- [6] J. H. Boyer, R. Selvarajan, *J. Am. Chem. Soc.* **1969**, 91, 6122–6126.
- [7] A. Hassner, R. J. Isbister, *J. Am. Chem. Soc.* **1969**, 91, 6126–6128.
- [8] K. Banert, M. Hagedorn, J. Wutke, P. Ecorchard, D. Schaarschmidt, H. Lang, *Chem. Commun.* **2010**, 46, 4058–4060.
- [9] a) R. Tanaka, K. Yamabe, *J. Chem. Soc. Chem. Commun.* **1983**, 329–330; b) K. Yamabe, R. Tanaka, *Sasebo Kogyo Koto Senmon Gakko Kenkyu Hokoku* **1985**, 22, 119–123 [*Chem. Abstr.* **1987**, 106, 49680t].
- [10] E. Prochnow, A. A. Auer, K. Banert, *J. Phys. Chem. A* **2007**, 111, 9945–9951.
- [11] For other quantum chemical calculations to characterize ethynyl azides, see: a) P. Politzer, P. Lane, P. Sjöberg, M. E. Grice, H. Shechter, *Struct. Chem.* **1995**, 6, 217–223; b) A. V. Golovin, V. V. Takhistov, *J. Mol. Struct.* **2004**, 701, 57–91.
- [12] Synthesis of cyclooctyne: L. F. Tietze, T. Eicher, *Reaktionen und Synthesen im Organisch-Chemischen Praktikum und Forschungslaboratorium*, 2nd ed., Thieme, Stuttgart, **1991**, p. 40.
- [13] A. J. Margida, G. F. Koser, *J. Org. Chem.* **1984**, 49, 4703–4706.
- [14] For reviews, see: a) P. J. Stang, V. V. Zhdankin, *Chem. Rev.* **1996**, 96, 1123–1178; b) V. V. Zhdankin, P. J. Stang, *Tetrahedron* **1998**, 54, 10927–10966; c) V. V. Zhdankin, P. J. Stang, *Chem. Rev.* **2008**, 108, 5299–5358; d) P. J. Stang, *J. Org. Chem.* **2003**, 68, 2997–3008; e) W. Kirmse, *Angew. Chem.* **1997**, 109, 1212–1218; *Angew. Chem. Int. Ed. Engl.* **1997**, 36, 1164–1170.
- [15] T. Kitamura, P. J. Stang, *Tetrahedron Lett.* **1988**, 29, 1887–1890.
- [16] K. Banert, *Synthesis* **2007**, 3431–3446.
- [17] R. A. Moss, G. Kmiecik-Ławrynowicz, D. P. Cox, *Synth. Commun.* **1984**, 14, 21–25.
- [18] a) D. P. Fox, P. J. Stang, Y. Apeloig, M. Karni, *J. Am. Chem. Soc.* **1986**, 108, 750–756; b) M. Ochiai, T. Sueda, K. Uemura, Y. Masaki, *J. Org. Chem.* **1995**, 60, 2624–2626; c) H.-Y. Lee, Y.-H. Lee, *Synlett* **2001**, 1656–1658.
- [19] P. J. Stang, M. G. Mangum, *J. Am. Chem. Soc.* **1975**, 97, 3856.
- [20] a) T. Kitamura, M. H. Morshed, S. Tsukada, Y. Miyazaki, N. Iguchi, D. Inoue, *J. Org. Chem.* **2011**, 76, 8117–8120; b) M. Ochiai, T. Ito, Y. Takaoka, Y. Masaki, M. Kunishima, S. Tani, Y. Nagao, *J. Chem. Soc. Chem. Commun.* **1990**, 118–119; c) P. J. Stang, A. M. Arif, C. M. Crittall, *Angew. Chem.* **1990**, 102, 307–308; *Angew. Chem. Int. Ed. Engl.* **1990**, 29, 287–288.
- [21] In the light of this ab initio study, it seems unrealistic to utilize 1-azido-2-dimethylaminoethyne as a hypergolic fuel for hypergolic bipropellant mixtures.^[22] Moreover, the report^[23] on the synthesis and isolation of (ethylsulfanyl)ethynyl azide is highly questionable. In this case, it has also been shown that the presented NMR data are incompatible with the structure,^[10] and several attempts to reproduce the generation of the latter azide were unsuccessful.^[3a,8]
- [22] D. Sengupta (CFD Research Corporation, AL), US 2008/0202655A1, **2008** [*Chem. Abstr.* **2008**, 149, 310772].
- [23] a) S. G. D'yachkova, E. A. Nikitina, N. K. Gusarova, M. L. Al'pert, B. A. Trofimov, *Russ. Chem. Bull.* **2001**, 50, 751–752; b) S. G. D'yachkova, E. A. Nikitina, N. K. Gusarova, A. I. Albanov, B. A. Trofimov, *Russ. J. Gen. Chem. (Engl. Transl.)* **2003**, 73, 782–785.
- [24] a) J. Martel, J. Tessier, J.-P. Demoute (Roussel Uclaf), FR 2479192, A1 19811002, **1981** [*Chem. Abstr.* **1982**, 96, 85115]; b) R. A. Moss, F. Zheng, K. Krogh-Jespersen, *Org. Lett.* **2001**, 3, 1439–1442.
- [25] **Caution!** The azide **1a** is a highly volatile and explosive compound that can be safely used in cold solution. However, recondensation under reduced pressure can lead to an explosion (protective shield). The explosive properties of **1a** are similar to those of diazomethane. For potential hazards in handling hydrazoic acid and organic azides, see: T. Keicher, S. Löbbecke in *Organic Azides: Syntheses and Applications* (Eds.: S. Bräse, K. Banert), Wiley, Chichester, **2010**, pp. 3–27.
- [26] K. Banert, J. Lehmann, H. Quast, G. Meichsner, D. Regnat, B. Seiferling, *J. Chem. Soc. Perkin Trans. 2* **2002**, 126–134.
- [27] A. Sebald, B. Wrackmeyer, *Spectrochim. Acta Part A* **1981**, 37, 365–368.