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Heterofullerenes

Synthesis of an Azahomoazafullerene $C_{59}N(NH)R$ and Gas-Phase Formation of the Diazafullerene $C_{58}N_2$**

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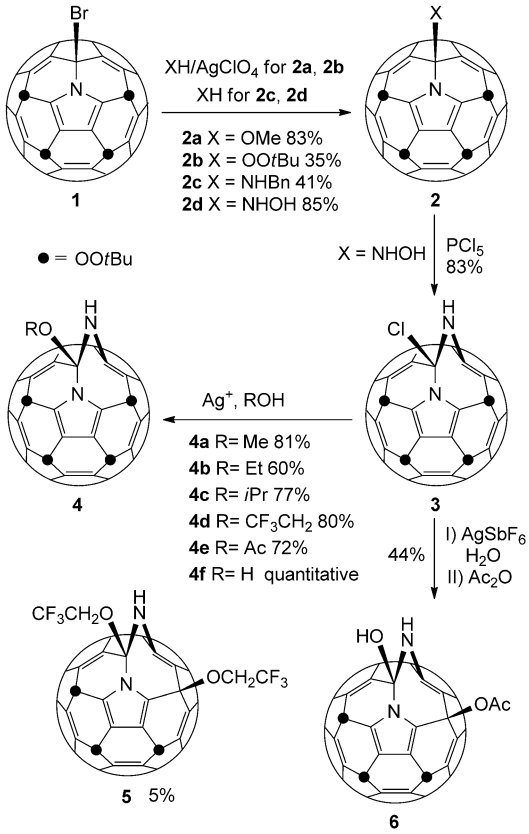
In comparison to the well-developed chemistry of fullerenes, investigations on heterofullerenes have been quite limited. So far, only monoazafullerenes have been prepared in macroscopic quantities. The aza(C_{60}-I_h)fullerene $C_{59}NR$ is the best-known azafullerene structure.[1] The aza(C_{70}-D_{5h})fullerene $C_{69}NR$ has also been prepared by an analogous method.[2] Further functionalization of the monoazafullerene has produced many well-defined azafullerene derivatives, in particular, $C_{59}NR$ derivatives with a single substituent attached.[3] A few multiadducts of the azafullerene $C_{59}N$ are also known,[4] and endohedral azafullerenes have been reported.[5] The cage structure of the azafullerene remains fully closed in all these compounds.

Skeleton modification of C_{60} has resulted in many novel fullerene derivatives.[6] The method used by Wudl and coworkers for the first preparation of an azafullerene is based on an open-cage precursor with a ketolactam orifice.[7] Open-cage fullerenes with a relatively large orifice can encapsulate various small molecules and noble gases.[8] Endohedral fullerenes containing H_2 ($H_2@C_{60}$[9]) and H_2O ($H_2O@C_{60}$[10]) were prepared by "molecular surgery". Inspired by these results, we investigated the skeleton modification of azafullerenes in an effort to prepare open-cage azafullerene and diazafullerene derivatives. Herein we report the preparation of azahomoazafullerenes $C_{59}N(NH)R$ as potential precursors to the diazafullerene $C_{58}N_2$ and the reaction of one azahomoazafullerene to give an open-cage azafullerene with a ketoimide moiety on the rim of the 15-membered orifice.

We previously reported a fullerene-peroxide-mediated method for the preparation of azafullerene derivatives such as **1**.[4c] To explore the skeleton modification of azafullerenes, we treated **1** with various nucleophiles, including hydroxylamine (Scheme 1). As expected, the bromine atom can be replaced effectively to form compounds **2a**–**d**. Treatment of the hydroxylamine adduct **2d** with PCl_5 afforded the azahomo



Scheme 1. Synthesis of azahomoazafullerenes.

derivative **3**. This step involves a Beckman-type rearrangement process, which is the same as the key step in the formation of **1**.[4c] The chlorine atom in **3** is slightly more reactive towards alcohol substitution than the bromine atom in **1** because the extra nitrogen atom increases the stability of the carbocation intermediate in the S_N1 reaction. Compounds **4a**–**f** were readily prepared by reactions similar to those used for the formation of **2**.

Compound **5** was isolated as a by-product from the reaction to form the trifluoroethyl derivative **4d**. The *tert*-butylperoxo group next to the enamine had also been replaced with a trifluoroethyl group in this by-product. The reaction between silver hexafluoroantimonate and **3** resulted

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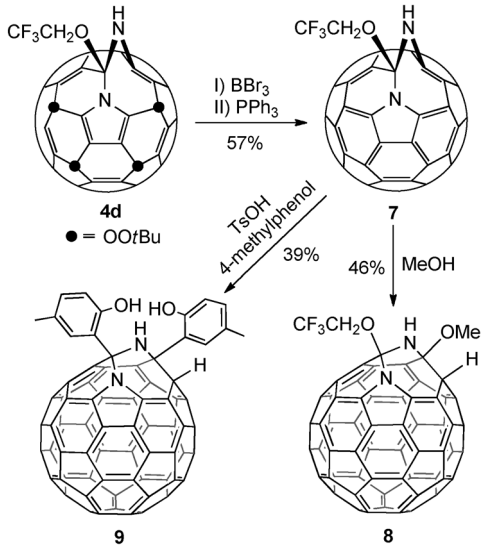
in replacement of the *tert*-butylperoxo group next to the enamine and the formation of compound **6**. This reaction is slightly different from that with silver trifluoroacetate, which gave **4f** quantitatively. Apparently, the electron-rich enamine can stabilize the carbocation resulting from the loss of the *tert*-butylperoxide ion. A similar enol-assisted S_N1 reaction was observed for an oxafulleroid derivative.[11]

The peroxo groups of compounds **4a–d** can be removed by treatment with BBr_3.[12] The yields are low (less than 20%), except for the formation of **7** (57%) from the trifluoroethoxy adduct **4d** (Scheme 2). To grow crystals, we kept compound **7**



Scheme 2. Reactions of azahomoazafullerenes. TsOH = *p*-toluenesulfonic acid.

in a benzene/methanol mixture. The methanol-addition product **8** was isolated after about 2 weeks. The lability of the enamine double bond in compound **7** is in agreement with the selective replacement of the *tert*-butylperoxo group in the formation of **5** and **6** (Scheme 1). To further explore the reactivity of the enamine, we treated **7** with 4-methylphenol in the presence of TsOH and obtained the product **9** of a double Friedel–Crafts reaction. The trifluoroethoxy group was also replaced under these conditions.

Spectroscopic data for the new compounds were in agreement with the structures depicted in Schemes 1 and 2. Compounds **2a–d** are analogous to the C_s-symmetric compound **1**, which was characterized previously by single-crystal X-ray structure analysis.[4c] Their ^1H and ^{13}C NMR spectra showed the expected number of signals, that is, two sets of signals for the four *tert*-butylperoxo groups and 31 signals for the carbon atoms of the fullerene skeleton. The spectra of compounds **3–9** indicated C_1 symmetry. The signal for the unique sp^3-hybridized carbon atom bound to the two nitrogen atoms appears at $\delta = 89.0$ ppm for the chloro derivative **3** and between $\delta = 94.4$ and 98.6 ppm for the oxygenated derivatives **4a–f**, **5**, and **6**. The equivalent carbon atom in compound **7** without the other four addends appears at slightly lower field ($\delta = 100.9$ ppm), probably owing to a decreased shielding effect. The ^{13}C NMR spectrum of compound **8** showed three signals for sp^3-hybridized cage carbon atoms at $\delta = 70.0$, 87.4, and 96.8 ppm, which are assignable to the carbon atoms connected to the H atom and the OMe and OCH_2CF_3 groups, respectively. The NMR spectra of **9** showed broad signals owing to restricted rotation of the aryl groups. The signal for the hydrogen-bound cage carbon atom of **9** appeared in the ^{13}C NMR spectrum at $\delta = 69.3$ ppm, which is very close to the equivalent signal for **8** ($\delta = 70.0$ ppm).

Single crystals of compound **9** were obtained by slow evaporation of a solution in CS_2/PhH/MeCN. The structure showed that the fullerene single bonds around the amino bridge are longer and the double bonds are shorter than those on the other hemisphere of the cage (Figure 1). The distance

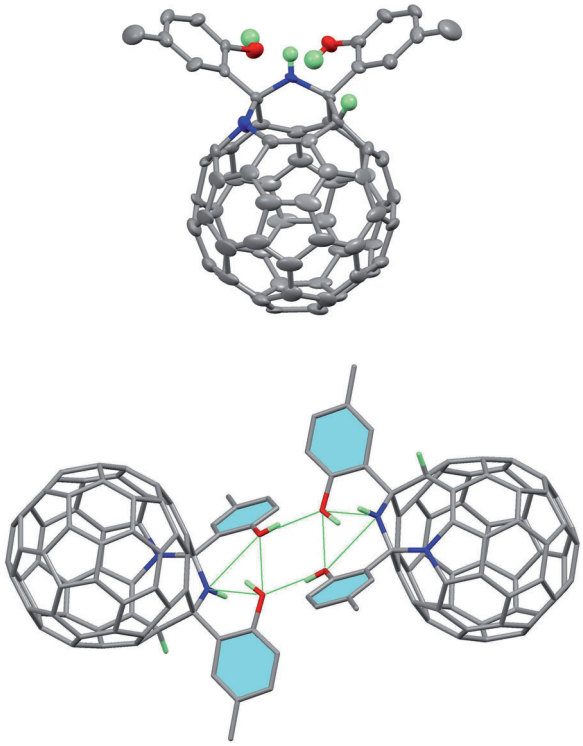


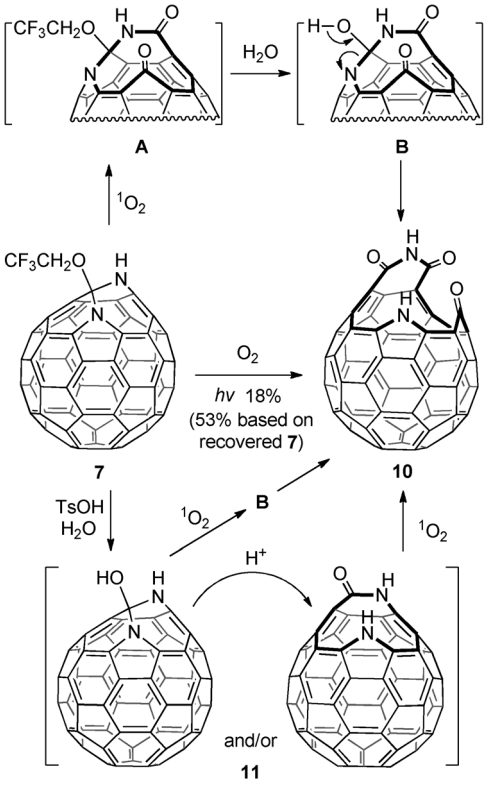
Figure 1. Structure of **9** as determined by single-crystal X-ray diffraction, with thermal ellipsoids drawn at 50% probability (C gray, N blue, O red, H green). For clarity, hydrogen atoms on the aryl groups are not shown.

between the two bridgehead carbon atoms of the amino bridge is 2.539 Å, which confirms the open structure. The two single bonds between the aryl groups and the cage are the longest C–C bonds in the molecule (1.544 and 1.550 Å). There is strong intra- and intermolecular hydrogen bonding between the amino and the hydroxy groups. The network of hydrogen bonds forms dimeric structures between pairs of enantiomers in the crystal.[13] The distances of the two intermolecular H bonds O–H···O are the same at 2.794 Å. The intramolecular H bonds N–H···O and O–H···O range from 2.694 to 3.026 Å. In agreement with the broad signals in the NMR spectra, a space-filling model indicates that the rotation of the aryl groups is hindered by an interaction

between the OH and NH groups. The fullerenyl H atom also affects the rotation of the neighboring aryl group.

The formation of compounds **8** and **9** indicates that the reactivity of the NH-enamine double bond in compound **7** is much enhanced relative to that of the other double bonds of the cage. Similar results have been reported previously. The reaction between C_{60} and excess [(trimethylsilyl)ethoxy]-methyl azide afforded a diazafulleroid (diazahomofullerene) with high regioselectivity.[14] Methano-bridged [5,6] open fulleroids (homofullerenes) also undergo selective Diels–Alder and epoxidation reactions at the bridgehead double bond.[15] The enhanced reactivity of the enamine is mainly due to misalignment of the p orbitals in the bridgehead anti-Bredt double bond.

Singlet oxygen can also add to the enamine double bond of azahomofullerenes (azafulleroids) to form open-cage fullerene derivatives, as shown by Wudl and co-workers.[7] The present azahomoazafullerene exhibits similar reactivity. Irradiation of **7** with a blue-diode light strip in the presence of oxygen (bubbled through the mixture) afforded compound **10** (Scheme 3). The ^{1}H NMR spectrum of **10** showed two singlets at $\delta = 9.79$ and 10.03 ppm for the two NH groups. Its ^{13}C NMR spectrum contained one signal for a carbonyl carbon atom at $\delta = 190.96$ ppm and two amide signals at $\delta =$ 167.82 and 162.46 ppm. There was no signal in the range $\delta =$ 0–122 ppm, which indicated the absence of an sp^3-hybridized carbon atom in the fullerene skeleton. The structure of the ketoimide **10** with a 15-membered orifice is reminiscent of that of the diketoimide open-cage fullerene derivative synthesized by Hachiya and Kabe by the double singlet



Scheme 3. Formation of an open-cage azafullerene.

oxygenation of an azahomofullerene.[16] The replacement of the pyrrole NH group in **10** with a carbonyl group would result in the parent skeleton of the open-cage derivative described by Hachiya and Kabe.

The formation of the ketoimide **10** may involve the formation of an intermediate **A**, followed by hydrolysis of the trifluoroethoxy group to form **B**. The driving force for the ring-expansion rearrangement of **B** to form **10** should mainly be the release of ring strain. The presence of the 11-membered orifice in **B** is crucial for the ring expansion. The same moiety in the hydroxy derivatives **4f** and **6** is quite stable and does not undergo such a ring-opening rearrangement. There is no carbonyl signal in the ^{13}C NMR spectra of **4f** and **6**.

An alternative route for the formation of **10** is the hydrolysis of **7** by residual water as the first step, followed by oxygenation/ring expansion or ring expansion/oxygenation. To test this possibility, we irradiated the solution of **7** with a blue-diode light strip as before, but without bubbling oxygen through the solution. Compound **7** was relatively stable under these conditions, and the formation of **10** was very slow: much slower than when oxygen was bubbled through the solution. This result indicates that the photochemical conditions do not induce the hydrolysis of **7** and is in agreement with the observation that under neutral conditions, methanol could not replace the trifluoroethoxy group in **7** (as shown in the formation of **8**, Scheme 2). To further explore the hydrolysis of compound **7**, we treated a solution of **7** in chlorobenzene with TsOH and obtained a scarcely soluble product **11**, which was converted into compound **10** under the photochemical conditions used for the conversion of **7** into **10**. These results indicate that the major route to **10** under the photochemical conditions involves oxygenation to form **A** as the first step, which is also the rate-limiting step.

Full characterization of product **11** formed by the hydrolysis of **7** was difficult because of its low solubility. Both structures shown for **11** in Scheme 3 are possible under the conditions for acid-catalyzed hydrolysis. The MALDI-TOF mass spectrum of the crude product **11** with α-cyano-4-hydroxycinnamic acid (CCA) as the matrix showed a signal corresponding to the hydrolyzed product $C_{59}N_2OH^+$ as the base peak (Figure 2). The other peak at m/z 725 corresponds to the diazafullerene $C_{58}N_2H^+$. This diazafullerene species could form under the MALDI-TOF conditions by decarbonylation of the amide moiety. It is unlikely that product **11** contains the diazafullerene, since TLC analysis showed that the product has high polarity. In the preparation of the azafullerene **1**, decarbonylation of the amide moiety was achieved by column chromatography on silica gel or basic alumina.[4c,12]

Various isomers have been predicted for the diazafullerene $C_{58}N_2$.[17] The signal observed in this study is most likely due to the isomer with an N–N moiety at the 6,6-junction. Hirsch and co-workers[18] studied the preparation of $C_{58}N_2$ through the intramolecular addition of an azide to the monoazafullerene $C_{59}NR$ and observed signals due to a mixture of $C_{59}N$ and $C_{58}N_2$; the latter species accounted for up to 20% of the mixture according to FAB mass spectra.[18b] In contrast to the synthetic method described herein, the method

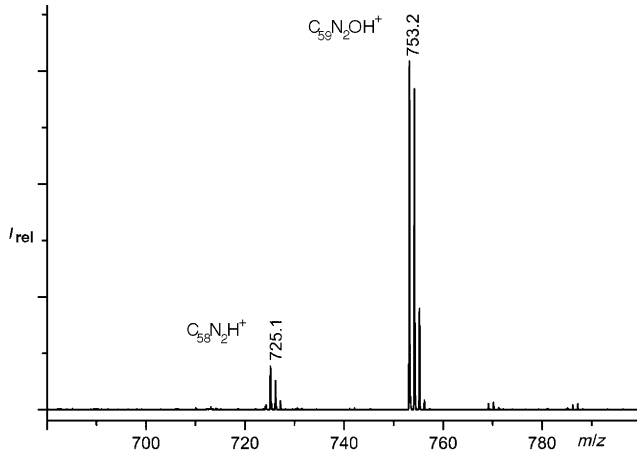


Figure 2. MALDI-TOF mass spectrum of **11**.

described by Hirsch and co-workers is designed to form a diazafullerene isomer with the two nitrogen atoms well apart from one another.

In summary, azahomoazafullerene derivatives have been prepared through the addition of hydroxylamine to azafullerene and a subsequent Beckman-type rearrangement. The enamine double bond in the azahomoazafullerene undergoes addition reactions readily because of its anti-Bredt nature. An open-cage azafullerene has been prepared through the addition of singlet oxygen to an azahomoazafullerene and a ring-opening rearrangement. An azahomoazafullerene was also converted into the diazafullerene $C_{58}N_2$ under the conditions of MALDI-TOF mass spectroscopy. Further studies are under way to prepare the diazafullerene $C_{58}N_2$ and related heterofullerenes in macroscopic quantities.

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[1] a) J. C. Hummelen, B. Knight, J. Pavlovich, R. González, F. Wudl, *Science* **1995**, *269*, 1554; b) M. Keshavarzk, R. González, R. G. Hicks, G. Srdanov, V. I. Srdanov, T. G. Collins, J. C. Hummelen, C. Bellavia-Lund, J. Pavlovich, F. Wudl, K. Holczer, *Nature* **1996**, *383*, 147.

[2] B. Nuber, A. Hirsch, *Chem. Commun.* **1996**, 1421.

[3] a) O. Vostrowsky, A. Hirsch, *Chem. Rev.* **2006**, *106*, 5191; b) J. C. Hummelen, C. Bellavia-Lund, F. Wudl, *Top. Curr. Chem.* **1999**, *199*, 93.

[4] a) U. Reuther, A. Hirsch, *Chem. Commun.* **1998**, 1401; b) F. Hauke, A. Hirsch, *Chem. Commun.* **2001**, 1316; c) G. H. Zhang, S. H. Huang, Z. Xiao, Q. Chen, L. B. Gan, Z. M. Wang, *J. Am. Chem. Soc.* **2008**, *130*, 12614; d) N. B. Shustova, I. V. Kuvychko, A. A. Popov, M. von Delius, L. Dunsch, O. P. Anderson, A. Hirsch, S. H. Strauss, O. V. Boltalina, *Angew. Chem.* **2011**, *123*, 5651; *Angew. Chem. Int. Ed.* **2011**, *50*, 5537; e) R. Neubauer, F. W. Heinemann, F. Hampel, Y. Rubin, A. Hirsch, *Angew. Chem.* **2012**, *124*, 11892; *Angew. Chem. Int. Ed.* **2012**, *51*, 11722.

[5] a) T. M. Zuo, L. S. Xu, C. M. Beavers, M. M. Olmstead, W. J. Fu, T. D. Crawford, A. L. Balch, H. C. Dorn, *J. Am. Chem. Soc.* **2008**, *130*, 12992; b) S. Stevenson, Y. Ling, C. E. Coumbe, M. A. Mackey, B. S. Confait, J. P. Phillips, H. C. Dorn, Y. Zhang, *J. Am. Chem. Soc.* **2009**, *131*, 17780; c) W. J. Fu, J. Y. Zhang, T. Fuhrer, H. Champion, K. Furukawa, T. Kato, J. E. Mahaney, B. G. Burke, K. A. Williams, K. Walker, C. Dixon, J. C. Ge, C. Y. Shu, K. Harich, H. C. Dorn, *J. Am. Chem. Soc.* **2011**, *133*, 9741.

[6] a) M. Murata, Y. Murata, K. Komatsu, *Chem. Commun.* **2008**, 6083; b) G. C. Vougioukalakis, M. M. Roubelakis, M. Orfanopoulos, *Chem. Soc. Rev.* **2010**, *39*, 817; c) L. B. Gan, D. Z. Yang, Q. Y. Zhang, H. Huang, *Adv. Mater.* **2010**, *22*, 1498.

[7] J. C. Hummelen, M. Prato, F. Wudl, *J. Am. Chem. Soc.* **1995**, *117*, 7003.

[8] a) Y. Rubin, T. Jarrosson, G. W. Wang, M. D. Bartberger, K. N. Houk, G. Schick, M. Saunders, R. J. Cross, *Angew. Chem.* **2001**, *113*, 1591; *Angew. Chem. Int. Ed.* **2001**, *40*, 1543; b) Y. Murata, M. Murata, K. Komatsu, *J. Am. Chem. Soc.* **2003**, *125*, 7152; c) S.-i. Iwamatsu, S. Murata, *Synlett* **2005**, 2117; d) Z. Xiao, J. Y. Yao, D. Z. Yang, F. D. Wang, S. H. Huang, L. B. Gan, Z. S. Jia, Z. P. Jiang, X. B. Yang, B. Zheng, G. Yuan, S. W. Zhang, Z. M. Wang, *J. Am. Chem. Soc.* **2007**, *129*, 16149; e) Q. Y. Zhang, T. Pankewitz, S. M. Liu, W. Klopper, L. B. Gan, *Angew. Chem.* **2010**, *122*, 10131; *Angew. Chem. Int. Ed.* **2010**, *49*, 9935; f) Y. M. Yu, L. J. Shi, D. Z. Yang, L. B. Gan, *Chem. Sci.* **2013**, *4*, 814.

[9] K. Komatsu, M. Murata, Y. Murata, *Science* **2005**, *307*, 238.

[10] K. Kurotobi, Y. Murata, *Science* **2011**, *333*, 613.

[11] F. D. Wang, Z. Xiao, L. B. Gan, Z. S. Jia, Z. P. Jiang, S. W. Zhang, B. Zheng, G. Yuan, *Org. Lett.* **2007**, *9*, 1741.

[12] a) N. N. Xin, H. Huang, J. X. Zhang, Z. F. Dai, L. B. Gan, *Angew. Chem.* **2012**, *124*, 6267; *Angew. Chem. Int. Ed.* **2012**, *51*, 6163; b) N. N. Xin, X. B. Yang, Z. S. Zhou, J. X. Zhang, S. X. Zhang, L. B. Gan, *J. Org. Chem.* **2013**, *78*, 1157.

[13] For a head-to-tail and back-to-back dimer of an open-cage fullerene derivative, see: S. M. Liu, Q. Y. Zhang, Y. M. Yu, L. B. Gan, *Org. Lett.* **2012**, *14*, 4002.

[14] T. Grösser, M. Prato, V. Lucchini, A. Hirsch, F. Wudl, *Angew. Chem.* **1995**, *107*, 1462; *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 1343.

[15] a) N. Ikuma, Y. Susami, T. Oshima, *Eur. J. Org. Chem.* **2011**, 6452; b) N. Ikuma, S. Sumioka, H. Asahara, T. Oshima, *Tetrahedron Lett.* **2012**, *53*, 3581.

[16] H. Hachiya, Y. Kabe, *Chem. Lett.* **2009**, *38*, 372.

[17] a) Z. F. Chen, K. Q. Ma, Y. M. Pan, X. Z. Zhao, A. Q. Tang, J. K. Feng, *J. Chem. Soc. Faraday Trans.* **1998**, *94*, 2269; b) S. Ostrowski, M. H. Jamroz, J. E. Rode, J. C. Dobrowolski, *J. Phys. Chem. A* **2012**, *116*, 631, and references therein.

[18] a) U. Reuther, A. Hirsch, *Carbon* **2000**, *38*, 1539; b) M. von Delius, F. Hauke, A. Hirsch, *Eur. J. Org. Chem.* **2008**, 4109.