Available online at www.sciencedirect.com
ScienceDirect
Tetrahedron Letters 49 (2008) 4063–4066
Tetrahedron Letters

Click chemistry with fullerene derivatives

Julien Iehl [a], Rossimiriam Pereira de Freitas [b], Jean-François Nierengarten [a,*]

[a] *Laboratoire de Chimie des Matériaux Moléculaires (UMR 7509), Université Louis Pasteur, Ecole Européenne de Chimie, Polymères et Matériaux, 25 rue Becquerel, 67087 Strasbourg Cedex 2, France*
[b] *Universidade Federal de Minas Gerais, Departamento de Química, Av. Antônio Carlos, 6627, 31270901 Belo Horizonte, MG, Brazil*

Received 19 March 2008; accepted 9 April 2008
Available online 12 April 2008

Abstract

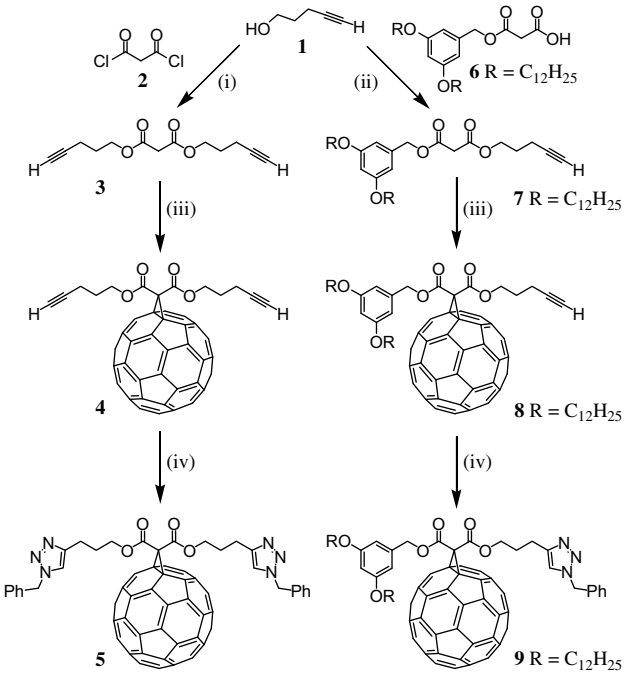
C_{60} derivatives bearing either terminal alkyne or azide functional groups have been prepared and used as building blocks under the copper-mediated Huisgen 1,3-dipolar cycloaddition conditions leading to 1,2,3-triazole derivatives.

The recent developments in the functionalization of fullerenes allow the easy preparation of C_{60} derivatives,[1] and the electronic properties such as facile multiple reducibility, optical non-linearity, or efficient photosensitization that are characteristic of the parent fullerene are maintained for most of the C_{60} derivatives.[2] As far as synthesis is concerned, most of the fullerene derivatives reported to date have been prepared by the direct functionalization of C_{60} in the final step. In contrast, the use of fullerene building blocks in multi-step synthesis has been much scarcely considered. This is mainly associated with the chemical reactivity of the fullerene moiety. Effectively, C_{60} derivatives react readily with nucleophiles and are reactive 2π component in cycloadditions.[1] Thus the range of reactions that can be used for the further transformations of fullerene derivatives appears to be quite limited. As a part of our research program on fullerene derivatives, we have decided to evaluate the potential of click reactions[3] to functionalize fullerene derivatives. Such chemistry appears to be an attractive tool for fullerene chemistry as click reactions are modular, tolerant to a wide range of functional groups, and high yielding. In this Letter, we now report on the copper-mediated Huisgen 1,3-dipolar cycloaddition of azides and alkynes[4] starting from fullerene building blocks. To this end, we have prepared C_{60} derivatives bearing either terminal alkyne or azide functional groups allowing their further transformation under the copper-mediated Huisgen 1,3-dipolar cycloaddition conditions. Whereas this click reaction has proven to be powerful for a large variety of building blocks,[5] its compatibility with fullerene derivatives is not obvious as organic azide undergoes [3+2] cycloadditions to the [6,6] double bonds of fullerenes.[6] However, reaction of C_{60} with azides requires in most cases elevated temperature.[6] The copper-mediated Huisgen 1,3-dipolar cycloaddition of azides and alkynes being carried out at room temperature, the reaction of C_{60} with azides should not significantly compete with the cycloaddition leading to the desired 1,2,3-triazole derivatives.

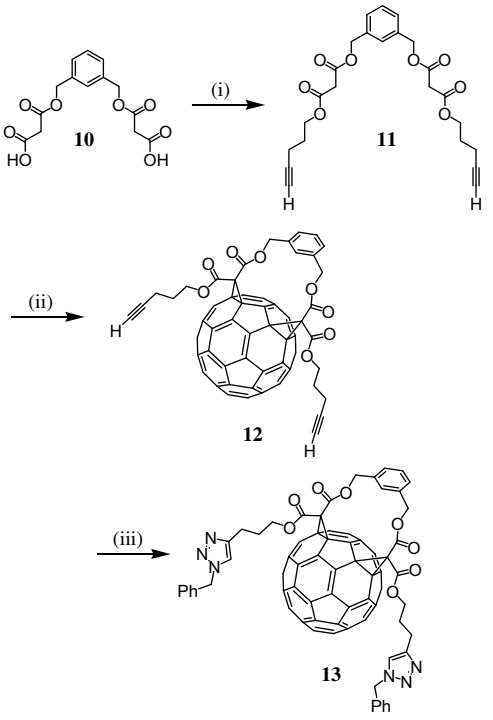
The first series of click reactions have been performed from fullerene derivatives functionalized with terminal alkyne groups. The preparation of alkyne **4** is depicted in Scheme 1. Reaction of malonyl dichloride (**2**) with 5-pentyn-1-ol (**1**) in the presence of pyridine afforded malonate **3** in 71% yield. The reaction of C_{60} with compound **3**, iodine and 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) under Bingel conditions[7] then gave methanofullerene **4** in 44% yield. The 1,3-dipolar cycloaddition of compound **4** with benzyl azide was then attempted under different conditions. The best results were obtained when a mixture of **4** (1 equiv), benzyl azide (3 equiv), $CuSO_4{\cdot}5H_2O$ (0.1 equiv) and sodium ascorbate (0.3 equiv) in CH_2Cl_2/H_2O was

* Corresponding author. Tel.: +33 390 242764; fax: +33 390 242774.
E-mail address: nierengarten@chimie.u-strasbg.fr (J.-F. Nierengarten).

0040-4039/$ - see front matter © 2008 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetlet.2008.04.064



Scheme 1. Reagents and conditions: (i) CH_2Cl_2, pyridine, rt (71%); (ii) DCC, DMAP, HOBt, CH_2Cl_2, 0 °C to rt (59%); (iii) C_{60}, DBU, I_2, PhMe, rt (**4**: 44%, **8**: 31%); (iv) Benzyl azide, $CuSO_4{\cdot}5H_2O$, sodium ascorbate, CH_2Cl_2/H_2O, rt (**5**: 48%, **9**: 80%).



Scheme 2. Reagents and conditions: (i) 4-pentyn-1-ol, DCC, DMAP, HOBt, CH_2Cl_2, 0 °C to rt (58%); (ii) C_{60}, DBU, I_2, PhMe, rt (44%); (iii) Benzyl azide, $CuSO_4{\cdot}5H_2O$, sodium ascorbate, CH_2Cl_2/H_2O, rt (70%).

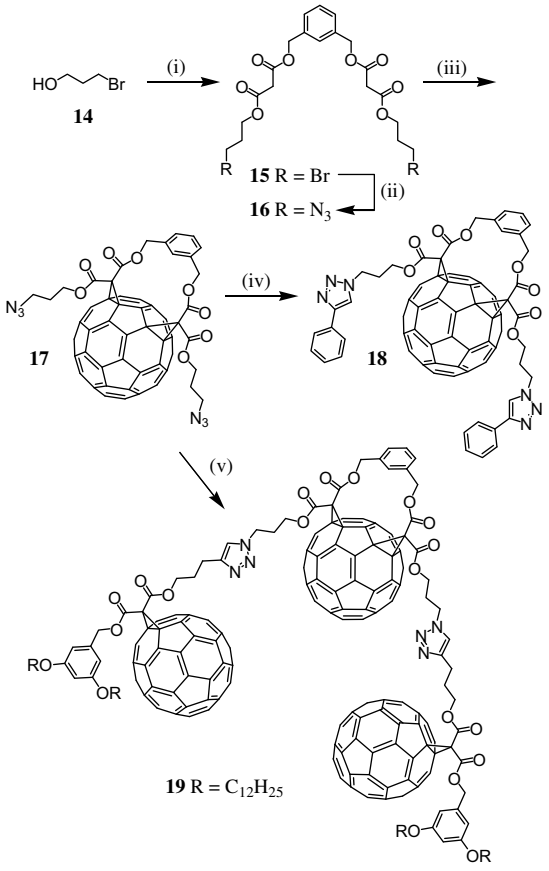
vigorously stirred at room temperature for 96 h. Under optimized conditions, compound **5** was obtained in a moderate yield (48%). Actually, the solubility of compound **4** is quite low and all the starting material did not dissolve under the copper-mediated Huisgen reaction conditions. Thus, the reaction was slow and side reactions, most probably cycloaddition of benzyl azides to the fullerene core, were observed. This prompted us to prepare a methanofullerene-alkyne derivative bearing a 3,5-didodecyloxybenzyl group to prevent solubility problems. *N*,*N*′-dicyclohexylcarbodiimide (DCC)-mediated esterification of **1** with carboxylic acid **6**[8] yielded malonate **7**. Subsequent treatment with C_{60}, iodine and DBU afforded methanofullerene **8**. Owing to the good solubility of alkyne **8**, the reaction of compound **8** with benzyl azide in the presence of $CuSO_4{\cdot}5H_2O$ and sodium ascorbate in CH_2Cl_2/H_2O could be achieved under optimized concentration conditions. Compound **9** was thus obtained in a good yield (80%),[9] thus showing that the reactivity of the fullerene moiety with organic azides plays only a minor role under copper-mediated Huisgen 1,3-dipolar cycloaddition conditions.

To further decrease the reactivity of the C_{60} moiety toward the azide reagents in the click reactions, we have decided to prepare a fullerene bis-adduct bearing two terminal alkyne groups. It is well known that the reactivity of the fullerene unit is decreased by increasing the number of substituents on the carbon cage.[10] The synthesis of building block **12** is depicted in Scheme 2. Treatment of diacid **10** with alcohol **1** and DCC in the presence of 4-dimethylaminopyridine (DMAP) and 1-hydroxybenzotriazole (HOBt) gave bis-malonate **11** in 58% yield. Fullerene derivative **12** was then prepared by taking advantage of the versatile regioselective reaction developed in the group of Diederich,[11] which led to macrocyclic bis-adducts of C_{60} by a cyclization reaction at the C sphere with bis-malonate derivatives in a double Bingel[7] cyclopropanation. Reaction of **11** with C_{60}, I_2, and DBU in toluene at room temperature afforded the desired cyclization product **12** in 44% yield. The relative position of the two cyclopropane rings in **12** on the C_{60} core has been determined based on the molecular symmetry (C_s) deduced from the ^1H and ^{13}C NMR spectra. It is also well established that the 1,3-phenylenebis(methylene)-tethered bis-malonates produce regioselectively the C_s symmetrical *cis*-2 addition pattern at C_{60}.[12] Reaction of **12** with benzyl azide under the conditions optimized for the preparation of compound **9** gave bis-1,2,3-triazole **13** in 70% yield.[13] When compared to the preparation of compound **5** from methanofullerene **4**, the increased yield can be explained by both the higher solubility of the starting terminal alkyne and the decreased reactivity of the bis-substituted fullerene group.

To complete our study, a second series of click reactions have been attempted from fullerene derivatives functionalized with azide groups. In a first attempt, methanofullerene derivatives substituted with one or two azide groups were synthesized. In all cases, the desired compounds could be detected by TLC and characterized by ^1H NMR. However, these compounds were found to be unstable in the solid

state as well as in solution. Indeed, untractable materials were always obtained, most probably as a result of cycloaddition reactions between the C_{60} and the azide groups leading to polymers. We have however been capable of preparing a fullerene derivative bearing two azide groups that was stable enough to be used in click reactions. Rather than using mono-substituted fullerene building blocks, we have used a disubstituted one. Compound **17** (Scheme 3) was still quite unstable in the solid state but reasonably stable in solution. The latter observation clearly shows the decreased reactivity of the fullerene moiety by increasing the number of substituents on the carbon cage. The preparation of compound **17** is depicted in Scheme 3.

Reaction of bis-malonic acid **10** with alcohol **14** under esterification conditions (DCC, DMAP, HOBt) yielded bis-malonate **15**. Subsequent treatment with sodium azide in DMF at room temperature gave **16** in 76% yield. Bis-adduct **17** was then obtained in 16% yield by the reaction of **16** with C_{60}, I_2, and DBU in toluene at room temperature. Upon purification, the best is to use diazide **17** for the click reactions within the next 4 h to obtain good yields. Reaction of **17** with phenylacetylene under the conditions optimized for the preparation of compound **9** afforded bis-1,2,3-triazole **18** in 78% yield.[14] The structure of compound **18** was confirmed by its ^1H and ^{13}C NMR spectra as well as by mass spectrometry. Inspection of the ^1H NMR spectra clearly indicates the disappearance of the CH_2-azide signal at δ 3.41 ppm. Importantly, the ^1H NMR spectrum of **18** shows the typical singlet of the 1,2,3-triazole unit at δ 7.75 ppm as well as the signal corresponding to the CH_2-triazole protons at δ 4.42 ppm. Finally, the click reaction conditions were used to produce derivative **19** from terminal alkyne **8** and bis-azide **17**.[15] As seen for compound **18**, the ^1H NMR spectrum of **19** is characterized by the typical singlet of the 1,2,3-triazole unit at δ 7.33 ppm as well as by the signal corresponding to the CH_2-triazole protons at δ 4.30 ppm. The structure of **19** has also been confirmed by FAB mass spectrometry showing the expected molecular ion peak at m/z 3889 (MH^+, calcd for $C_{278}H_{145}N_6O_{20}$: 3889.24).



Scheme 3. Reagents and conditions: (i) **10**, DCC, DMAP, HOBt, CH_2Cl_2, 0 °C to rt (46%); (ii) NaN_3, DMF, rt (76%); (iii) C_{60}, DBU, I_2, PhMe, rt (16%); (iv) phenylacetylene, $CuSO_4{\cdot}5H_2O$, sodium ascorbate, CH_2Cl_2/H_2O, rt (78%); (v) **8**, $CuSO_4{\cdot}5H_2O$, sodium ascorbate, CH_2Cl_2/H_2O, rt (50%).

In conclusion, we have shown that the copper-mediated Huisgen 1,3-dipolar cycloaddition of azides and alkynes is an interesting tool for the functionalization of fullerene derivatives. The reactivity of C_{60} towards azides is not significantly competing with the cycloaddition leading to the desired 1,2,3-triazole derivatives and good yields can be obtained when fullerene derivatives with reasonable solubility are used as starting materials.

Acknowledgements

This work was supported by the CNRS (UMR 7509) and the Conselho Nacional de Desenvolvimento Científico e Tecnológico (Brazil).

References and notes

1. Hirsch, A.; Brettreich, M. *Fullerenes—Chemistry and Reactions*; Wiley-VCH: Weinheim, 2005.
2. (a) Segura, J. L.; Martín, N.; Guldi, D. M. *Chem. Soc. Rev.* **2005**, *34*, 31–37; (b) Nierengarten, J.-F. *New J. Chem.* **2004**, *28*, 1177–1191; (c) Figueira-Duarte, T. M.; Gégout, A.; Nierengarten, J.-F. *Chem. Commun.* **2007**, 109–119.
3. Kolb, H. C.; Finn, M. G.; Sharpless, K. B. *Angew. Chem., Int. Ed.* **2001**, *40*, 2004–2021.
4. (a) Huisgen, R. *Pure Appl. Chem.* **1989**, *61*, 613–628; (b) Huisgen, G.; Szeimies, W.; Moebius, L. *Chem. Ber.* **1967**, *100*, 2494–2507; (c) Rostovtsev, V. V.; Green, L. G.; Fokin, V. V.; Sharpless, K. B. *Angew. Chem., Int. Ed.* **2002**, *41*, 2596–2599.
5. For selected examples, see: (a) Ornelas, C.; Aranzaes, J. L.; Cloutet, E.; Alves, S.; Astruc, D. *Angew. Chem., Int. Ed.* **2007**, *46*, 872–877; (b) Helms, B.; Mynar, J. L.; Hawker, C. J.; Fréchet, J. M. J. *J. Am. Chem. Soc.* **2004**, *126*, 15020–15021; (c) Wilkinson, B. L.; Bornaghi, L. F.; Poulsen, S.-A.; Houston, T. A. *Tetrahedron* **2006**, *62*, 8115–8125; (d) Lee, B.-Y.; Park, S. R.; Jeon, H. B.; Kim, K. S. *Tetrahedron Lett.* **2006**, *47*, 5105–5109; (e) Wu, P.; Feldman, A. K.; Nugent, A. K.; Hawker, C. J.; Scheel, A.; Voit, B.; Pyun, J.; Fréchet, J. M. J.; Sharpless, K. B.; Fokin, V. V. *Angew. Chem., Int. Ed.* **2004**, *116*, 4018–4022.
6. For selected examples, see: (a) Prato, M.; Li, Q. C.; Wudl, F.; Lucchini, V. *J. Am. Chem. Soc.* **1993**, *115*, 1148–1150; (b) Yamakoshi, Y. N.; Yagami, T.; Sueyoshi, S.; Miyata, N. *J. Org. Chem.* **1996**, *61*, 7236–7237; (c) Hawker, C. J.; Saville, P. M.; White, J. M. *J. Org.*

Chem. **1994**, *59*, 3503–3505; (d) Yashiro, A.; Nishida, Y.; Ohno, M.; Eguchi, S.; Kobayashi, K. *Tetrahedron Lett.* **1998**, *39*, 9031–9034.

7. Bingel, C. *Chem. Ber.* **1993**, *126*, 1957–1959.
8. To a mixture of **4** (92 mg, 0.096 mmol) and benzyl azide (39 mg, 0.293 mmol) in CH_2Cl_2 (2 mL) and H_2O (2 mL) were added $CuSO_4{\cdot}5H_2O$ (2 mg, 0.012 mmol) and sodium ascorbate (6 mg, 0.030 mmol). The reaction mixture was stirred for 96 h under N_2. The organic layer was diluted with CH_2Cl_2, washed with water, dried over $MgSO_4$, and concentrated. Column chromatography (SiO_2, toluene/AcOEt 7/3) gave **5** (75 mg, 48%) as a dark red glassy product. IR (neat): 1738 (C=O); ^{1}H NMR ($CDCl_3$, 300 MHz): 2.22 (m, 4H), 2.85 (t, $J = 7$ Hz, 4H), 4.52 (t, J= 6 Hz, 4H), 5.48 (s, 4H), 7.29 (m, 12H); ^{13}C NMR ($CDCl_3$, 75 MHz) 22.1, 28.1, 50.9, 54.0, 66.5, 67.2, 71.5, 121.0, 128.0, 128.7, 129.1, 134.8, 138.9, 140.9, 141.8, 142.2, 142.9, 143.0, 143.1, 143.9, 144.5, 144.6, 144.7, 144.9, 145.1, 145.2, 145.2, 145.3, 146.8, 163.5; Anal. Calcd for $C_{87}H_{28}N_6O_4{\cdot}4H_2O$: C, 80.80; H, 2.81; N, 6.50. Found: C, 81.04; H, 2.94; N, 6.50; FAB-MS: 1221 (M^+, calcd for $C_{87}H_{28}N_6O_4$, 1221.22).
9. As described for **5** in Ref. 8 from **8** (114 mg, 0.084 mmol), benzyl azide (22 mg, 0.165 mmol), $CuSO_4{\cdot}5H_2O$ (1 mg, 0.006 mmol), and sodium ascorbate (4 mg, 0.02 mmol) in CH_2Cl_2 (2 mL) and H_2O (2 mL) for 4 h, column chromatography (SiO_2, hexane/CH_2Cl_2/MeOH 49/49/2) gave **9** (99 mg, 80%) as a dark red glassy product. IR (neat): 1735 (C=O); ^{1}H NMR ($CDCl_3$, 250 MHz): 0.88 (t, $J = 7$ Hz, 6H), 1.22–1.45 (m, 36H), 1.73 (m, 4H), 2.20 (m, 2H), 2.84 (t, $J = 7$ Hz, 2H), 3.87 (t, $J = 7$ Hz, 4H), 4.50 (t, $J = 6$ Hz, 2H), 5.42 (s, 2H), 5.49 (s, 2H), 6.38 (t, $J = 2$ Hz, 1H), 6.58 (d, $J = 2$ Hz, 2H), 7.37 (m, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz): 14.1, 22.1, 22.7, 26.1, 29.3, 29.4, 29.5, 29.6, 29.7, 29.7, 31.9, 51.9, 66.5, 68.2, 68.9, 71.4, 101.6, 107.2, 121.0, 128.0, 128.7, 129.1, 136.8, 138.7, 139.2, 140.8, 141.8, 142.2, 143.0, 143.8, 144.4, 144.5, 144.6, 144.8, 145.0, 145.1, 145.2, 45.3, 160,5, 163.3, 163.3; Anal. Calcd for $C_{106}H_{69}N_3O_6{\cdot}1.3\ CH_2Cl_2$: C, 81.05; H, 4.64; N, 2.74. Found: C, 80.82; H, 4.88; N, 3.00; FAB-MS: 1481 (M^+, calcd for $C_{106}H_{69}N_3O_6$, 1480.73).
10. Cardullo, F.; Seiler, P.; Isaacs, L.; Nierengarten, J.-F.; Haldimann, R. F.; Diederich, F.; Mordasini-Denti, T.; Thiel, W.; Boudon, C.; Gisselbrecht, J.-P.; Gross, M. *Helv. Chim. Acta* **1997**, *80*, 343–371.
11. (a) Nierengarten, J.-F.; Gramlich, V.; Cardullo, F.; Diederich, F. *Angew. Chem., Int. Ed.* **1996**, *35*, 2101–2103; (b) Nierengarten, J.-F.; Herrmann, A.; Tykwinski, R. R.; Rüttimann, M.; Diederich, F.; Boudon, C.; Gisselbrecht, J.-P.; Gross, M. *Helv. Chim. Acta* **1997**, *80*, 293–316; (c) Nierengarten, J.-F.; Habicher, T.; Kessinger, R.; Cardullo, F.; Diederich, F.; Gramlich, V.; Gisselbrecht, J.-P.; Boudon, C.; Gross, M. *Helv. Chim. Acta* **1997**, *80*, 2238–2276.
12. Zhang, S.; Rio, Y.; Cardinali, F.; Bourgogne, C.; Gallani, J.-L.; Nierengarten, J.-F. *J. Org. Chem.* **2003**, *68*, 9787–9797. and references therein.
13. As described for **5** in Ref. 8 from **12** (75 mg, 0.06 mmol), benzyl azide (26 mg, 0.19 mmol) $CuSO^4{\cdot}5H_2O$ (1 mg, 0.006 mmol), and sodium ascorbate (4 mg, 0.02 mmol) in CH_2Cl_2 (2 mL) and H_2O (2 mL) for 60 h, column chromatography (SiO_2, toluene/AcOEt 7/3) gave **13** (64 mg, 70%) as a dark-red glassy product. ^{1}H NMR ($CDCl_3$, 300 MHz): 2.10 (m, 4H), 2.80 (t, $J = 7$ Hz, 4H), 4.38 (m, 4H), 5.20 (d, $J = 12$ Hz, 2H), 5,47 (s, 4H), 5.80 (d, $J = 12$ Hz, 2H), 7.15 (m, 15H), 7.30 (s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): 21.9, 28.1, 49.3, 54.0, 66.2, 67.0, 67.5, 70.7, 120.9, 123.9, 126.8, 128.0, 128.7, 129.1, 130.0, 134.8, 135.8, 136.2, 136.6, 140.0, 140.9, 141.3, 142.3, 143.0, 143.3, 143.6, 143.8, 144.0, 144.2, 144.3, 144.4, 144.7, 145.0, 145.2, 145.3, 145.4, 145.7, 145.8, 145.8, 146.1, 146.8, 147.4, 147.6, 148.6, 162.8, 162.9; Anal. Calcd for $C_{98}H_{36}N_6\ O_8{\cdot}4.8CH_2Cl_2$: C, 67.36; H, 2.51; N 4.50. Found: C, 67.43; H, 2.93; N, 4.52; MALDI-TOF: 1426 (MH^+, calcd for $C_{98}H_{37}N_6O_8$, 1426.41).
14. As described for **5** in Ref. 8 from **17** (84 mg, 0.07 mmol), phenylacetylene (15.8 mg, 0.15 mmol), $CuSO_4{\cdot}5H_2O$ (1 mg, 0.006 mmol), and sodium ascorbate (4 mg, 0.02 mmol) in CH_2Cl_2 (3 mL) and H_2O (3 mL) for 24 h, columnchromatography (SiO_2, CH_2Cl_2/methanol 99.5/0.5) gave **18** (78%) as a dark orange glassy product. IR (neat): 1742 (C=O);^{1}H NMR ($CDCl_3$, 300 MHz): 2.41 (m, 4H), 4.42 (m, 4H), 4.50 (t, $J = 7$ Hz, 4H), 5.30 (d, $J = 13$ Hz, 2H), 5.87 (d, $J = 13$ Hz, 2H), 7.30–7.44 (m, 9H), 7.55 (s, 1H), 7.75 (s, 2H), 7.77–7.84 (m, 4H); ^{13}C NMR ($CDCl_3$, 75 MHz): 29.3, 29.6, 30.9, 46.7, 63.4, 67.7, 119.9, 124.5, 125.7, 127.2, 128.2, 128.8, 130.4, 135.6, 135.8, 136.5, 138.1, 140.1, 141.0, 141.4, 142.3, 142.8, 143.4, 143.6, 143.9, 144.1, 144.2, 144.4, 144.7, 144.9, 145.0, 145.1, 145.3, 145.4, 145.5, 145.7, 145.8, 146.0, 146.1, 146.2, 147.6, 147.9, 148.4, 162.7, 163.0; Anal. Calcd for $C_{96}H_{32}O_8N_6{\cdot}CHCl_3$: C, 76.88; H, 2.20; N, 5.55. Found: C, 76.31; H, 2.19; N, 5.20; FAB-MS: 1397 (M^+, calcd for $C_{96}H_{32}N_6O_8$: 1397.35).
15. As described for **5** in Ref. 8 from **17** (50 mg, 0.031 mmol), **8** (209.4 mg, 0.15 mmol), $CuSO_4{\cdot}5H_2O$ (0.5 mg, 0.003 mmol), and sodium ascorbate (2 mg, 0.009 mmol) in CH_2Cl_2 (1 mL) and H_2O (1 mL) for 1 h, column chromatography (SiO_2, CH_2Cl_2/methanol 99.5/0.5) gave **19** (50%) as a dark red glassy product. IR (neat): 1743 (C=O); ^{1}H NMR ($CDCl_3$, 300 MHz): 0.87 (t, $J = 7$ Hz, 12H), 1.24 (m, 72H), 1.56 (m, 8H), 1.72 (m, 8H), 2.20 (m, 4H), 2.35 (m, 4H), 2.86 (t, $J = 7$ Hz, 4H), 3.87 (t, $J = 6$ Hz, 8H), 4.38 (m, 4H), 4.42 (t, $J = 7$ Hz, 4H), 4.50 (t, $J = 6$ Hz, 4H), 5.27 (d, $J = 13$ Hz, 2H), 5.43 (s, 4H), 5.88 (d, $J = 13$ Hz, 2H), 6.38 (t, $J = 2$ Hz, 2H), 6.58 (d, $J = 2$ Hz, 4H), 7.30–7.44 (m, 5H), 7.50 (s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz, δ): 14.1, 21.9, 22.6, 26.1, 28.0, 29.2, 29.3, 29.4, 29.6, 29.7, 31.9, 46.5, 49.1, 51.9, 63.4, 66.4, 66.8, 67.7, 68.1, 68.9, 70.5, 71.4, 101.7, 107.2, 121.4, 124.2, 127.1, 128.8, 134.3, 135.7, 136.0, 136.5, 138.0, 138.6, 139.2, 140.1, 140.8, 140.9, 141.0, 141.4, 141.7, 141.8, 142.1, 142.3, 142.8, 142.9, 142.95, 142.97, 142.99, 143.05, 143.3, 143.6, 145.7, 143.8, 143.9, 144.1, 144.2, 144.4, 144.45, 144.5, 144.55, 144.6, 144.62, 144.65, 144.7, 144.8, 144.9, 144.96, 144.97, 145.1, 145.14, 145.19, 145.23, 145.29, 145.5, 145.6, 145.7, 145.9, 146.1, 146.5, 147.3, 147.5, 147.6, 148.4, 160.4, 162.6, 162.9, 163.4; Anal. Calcd for $C_{278}H_{144}N_6O_{20}{\cdot}2CHCl_3$: C, 81.54; H, 3.57; N, 2.04. Found: C, 81.60; H, 3.15; N, 2.22; FAB-MS: 3889 (MH^+, calcd for $C_{278}H_{145}N_6O_{20}$: 3889.24).