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Reactions of Terminal Polyynes with Benzyl Azide

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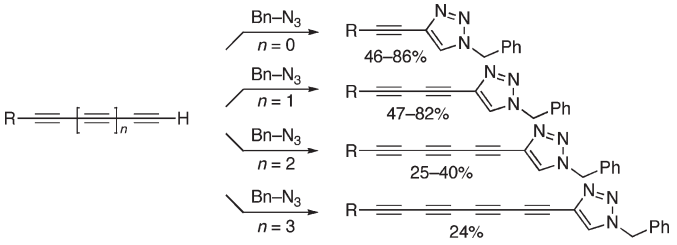
Received September 22, 2010



Terminal di-, tri-, tetra-, and pentaynes substituted with a variety of functional groups react with benzyl azide in the presence of $CuSO_4 \cdot 5H_2O$ and ascorbic acid to give derivatives of 4-ethynyl-, 4-butadiynyl-, 4-hexatriynyl-, and 4-octatetraynyl-1,2,3-triazoles in moderate to good yields. These reactions appear to proceed regioselectively, and functionalization occurs exclusively at the terminal alkyne moiety. As well, no evidence of multiple azide additions to the polyyne framework is observed. X-ray crystallographic analysis of nine derivatives is used to document the regioselectivity of the reaction as well as outline structural characteristics of the 1,2,3-triazole products.

Introduction

Molecules constructed of conjugated triple bonds (i.e., polyynes)[1] are useful building blocks for advanced materials,[2] molecular wires,[3] and supramolecular assemblies,[4] just to name a few.[5] Polyyne natural products are also an important class of molecules and have been isolated from a variety of species of fungi, bacteria, plants, and sponges.[6] Whether as materials or natural products, however, it is recognized that terminal polyynes are often unstable in their neat form. In some cases, this potential reactivity can be selectively harnessed, such as demonstrated by Fowler and Lauher toward the topochemical polymerization of terminal diyne derivatives.[7] Bryce and co-workers, on the other hand, have shown that under controlled

(1) Chalifoux, W. A.; Tykwinski, R. R. *C. R. Chim.* **2009**, *12*, 341–358.
(2) (a) Witulski, B.; Schweikert, T.; Schollmeyer, D.; Nemkovich, N. A. *Chem. Commun.* **2010**, *46*, 2953–2955. (b) Kivala, M.; Diederich, F. *Acc. Chem. Res.* **2009**, *42*, 235–248. (c) Samoc, M.; Dalton, G. T.; Gladysz, J. A.; Zheng, Q.; Velkov, Y.; Agren, H.; Norman, P.; Humphrey, M. G. *Inorg. Chem.* **2008**, *47*, 9946–9957. (d) Spitler, E. L.; Haley, M. M. *Org. Biomol. Chem.* **2008**, *6*, 1569–1576. (e) Zheng, Q.; Bohling, J. C.; Peters, T. B.; Frisch, A. C.; Hampel, F.; Gladysz, J. A. *Chem.—Eur. J.* **2006**, *12*, 6486–6505. (f) Eisler, S.; Slepkov, A. D.; Elliott, E.; Luu, T.; McDonald, R.; Hegmann, F. A.; Tykwinski, R. R. *J. Am. Chem. Soc.* **2005**, *127*, 2666–2676. (g) Slepkov, A. D.; Hegmann, F. A.; Eisler, S.; Elliott, E.; Tykwinski, R. R. *J. Chem. Phys.* **2004**, *120*, 6807–6810.
(3) (a) Ballmann, S.; Hieringer, W.; Secker, D.; Zheng, Q.; Gladysz, J. A.; Görling, A.; Weber, H. B. *ChemPhysChem* **2010**, *11*, 2256–2260. (b) Wang, C.; Batsanov, A. S.; Bryce, M. R.; Martin, S.; Nichols, R. J.; Higgins, S. J.; Garcia-Suárez, V. M.; Lambert, C. J. *J. Am. Chem. Soc.* **2009**, *131*, 15647–15654. (c) Long, N. J.; Williams, C. K. *Angew. Chem., Int. Ed.* **2003**, *42*, 2586–2617.
(4) (a) Hisaki, I.; Shigemitsu, H.; Sakamoto, Y.; Hasegawa, Y.; Okajima, Y.; Nakano, K.; Tohnai, N.; Miyata, M. *Angew. Chem., Int. Ed.* **2009**, *48*, 5465–5469. (b) Tahara, K.; Lei, S.; Mamdouh, W.; Yamaguchi, Y.; Ichikawa, T.; Uji-i, H.; Sonoda, M.; Hirose, K.; De Schryver, F. C.; De Feyter, S.; Tobe, Y. *J. Am. Chem. Soc.* **2008**, *130*, 6666–6667. (c) Campbell, K.; Kuehl, C. J.; Ferguson, M. J.; Stang, P. J.; Tykwinski, R. R. *J. Am. Chem. Soc.* **2002**, *124*, 7266–7267. (d) Nishinaga, T.; Nodera, N.; Miyata, Y.; Komatsu, K. *J. Org. Chem.* **2002**, *67*, 6091–6096.
(5) (a) *Carbon-Rich Compounds: Molecules to Materials*; Haley, M. M., Tykwinski, R. R., Eds.; Wiley-VCH: Weinheim, Germany, 2006. (b) *Acetylene Chemistry: Chemistry, Biology, and Material Science*; Diederich, F., Stang, P. J., Tykwinski, R. R., Eds.; Wiley-VCH: Weinheim, Germany, 2005. (c) Szafert, S.; Gladysz, J. A. *Chem. Rev.* **2006**, *106*, PR1–PR33. Szafert, S.; Gladysz, J. A. *Chem. Rev.* **2003**, *103*, 4175–4205.
(6) (a) Pan, Y.; Lowary, T. L.; Tykwinski, R. R. *Can. J. Chem.* **2009**, *87*, 1565–1582. (b) Shi Shun, A. L. K.; Tykwinski, R. R. *Angew. Chem., Int. Ed.* **2006**, *45*, 1034–1057. (c) Bohlmann, F.; Burkhardt, H.; Zdero, C. *Naturally Occurring Acetylenes*; Academic Press: New York, 1973.
(7) (a) Li, Z.; Fowler, F. W.; Lauher, J. W. *J. Am. Chem. Soc.* **2009**, *131*, 634–643. (b) Xi, O.; Fowler, F. W.; Lauher, J. W. *J. Am. Chem. Soc.* **2003**, *125*, 12400–12401.

Published on Web 11/11/2010 DOI: 10.1021/jo101870y

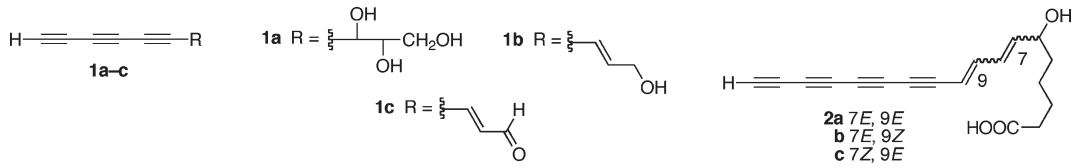


FIGURE 1. Examples of naturally occurring tri- and tetraynes.

circumstances, quite a number of diynes, triynes, and even a tetrayne can be isolated as stable solids, and numerous substrates have been characterized by X-ray crystallography.[8] Meanwhile, terminal di-, tri-, and tetraynes have been obtained from different natural sources, and some of these compounds have exhibited interesting biological activity. For example, triynes **1a**−**c** have been found in the culture medium of *Coprinus quadrifidus* by Jones and Stephenson,[9] while tetraynes **2a**−**c** (caryoynencins A, B, and C) have been isolated from the liquid cultures of the plant pathogen *Pseudomonas caryophylli* and showed remarkable antibiotic activity (Figure 1).[10] In addition to those natural products already discovered, it seems quite likely that some terminal polyynes have not been or cannot be obtained and fully characterized due to kinetic instability that would cause them to decompose during the isolation process.[11] In view of this premise, a potential solution to this challenge has been explored, in which terminal polyynes with many different pendent functional groups can be trapped in solution as a stable substrate that can be more easily characterized.

An obvious possibility would be to exploit the potential of a terminal alkyne to undergo a 1,3-dipolar cycloaddition with an azide[12] in the presence of a Cu(I) or Cu(II) catalyst, as has been reported independently by Meldal[13] and Sharpless.[14] This type of reaction has been widely applied to alkynes of nearly every flavor, and much of this work has been reviewed.[15] Even in light of the widespread application of this reaction, several questions remained in terms of its application to terminal polyynes:[16,17] (a) Would the general reaction, as reported, be suitable for trapping of the more reactive di-, tri-, tetra-, and pentaynes? (b) Would the regioselectivity of the reaction remain consistent and produce only 1,4-adducts? (c) Would multiple additions occur from the reaction of terminal polyynes with benzyl azide? Answers to these questions and others are provided by this report.[18]

Results and Discussion

Synthesis. Initial efforts targeted formation of 4-ethynyl-1,2,3-triazole derivatives **3a**−**r** (Table 1) from the terminal diynes derived from **4a**−**r**. In many cases, the kinetic stability of the terminal diyne was either insufficient for isolation or unknown. Thus, a two-step process of desilylation followed by trapping of the terminal polyyne intermediate with benzyl azide was employed. The Me_3Si- or *i*-Pr_3Si-protecting group was first removed by subjecting the diyne to either K_2CO_3/THF/MeOH or TBAF/THF, respectively, at room temperature. Following an aqueous workup, DMF (ca. 2 mL) was added to the resulting organic solution, which was then concentrated under vacuum to approximately 2 mL[19] and subsequently diluted with additional DMF (10 mL). The resulting diyne was then used for a Cu-catalyzed Huisgen reaction with benzyl azide (ca. 0.66−1.0 equiv[20] based on **4**), in the presence of $CuSO_4 \cdot 5H_2O$, ascorbic acid, and water. Reactions were typically complete within several hours, and the products could be isolated by either column chromatography or recrystallization. This general protocol gave 1,2,3-triazole adducts **3a**−**r** in 46−86% yields (with the exception of **3o**).

Several of these reactions deserve specific comment. The Me_3Si-protecting groups of **4a**,**b** were selectively removed with K_2CO_3 in THF/MeOH, and the reaction of the resulting

(8) (a) Wang, C.; Batsanov, A. S.; West, K.; Bryce, M. R. *Org. Lett.* **2008**, *10*, 3069–3072. (b) West, K.; Wang, C.; Batsanov, A. S.; Bryce, M. R. *Org. Biomol. Chem.* **2008**, *6*, 1934–1937. (c) West, K.; Hayward, L. N.; Batsanov, A. S.; Bryce, M. R. *Eur. J. Org. Chem.* **2008**, 5093–5098. (d) West, K.; Wang, C.; Batsanov, A. S.; Bryce, M. R. *J. Org. Chem.* **2006**, *71*, 8541–8544.

(9) Jones, E. R. H.; Stephenson, J. S. *J. Chem. Soc.* **1959**, 2197–2203.

(10) For isolation, see: (a) Kusumi, T.; Ohtani, I.; Nishiyama, K.; Kakisawa, H. *Tetrahedron Lett.* **1987**, *28*, 3981–3984. For the synthesis of **2a**, see: (b) Yamaguchi, M.; Park, H. J.; Hirama, M.; Torisu, K.; Nakamura, S.; Minami, T.; Nishihara, H.; Hiraoka, T. *Bull. Chem. Soc. Jpn.* **1994**, *67*, 1717–1725.

(11) Luu, T.; Tykwinski, R. R. *J. Org. Chem.* **2006**, *71*, 8982–8985.

(12) Huisgen, R. In *1,3-Dipolar Cycloaddition Chemistry*; Padwa, A., Ed.; Wiley: New York, 1984; pp 1−176.

(13) (a) Tornøe, C. W.; Meldal, M. *Peptides 2001, Proceedings of the American Peptide Symposium*; Lebl, M., Houghten, R. A., Eds.; American Peptide Society and Kluwer Academic Publishers: San Diego, CA, 2001; pp 263−264. (b) Tornøe, C. W.; Christensen, C.; Meldal, M. *J. Org. Chem.* **2002**, *67*, 3057–3064.

(14) Rostovtsev, V. V.; Green, L. G.; Fokin, V. V.; Sharpless, K. B. *Angew. Chem., Int. Ed.* **2002**, *41*, 2596–2599.

(15) For selected reviews, see: (a) Hein, J. E.; Fokin, V. V. *Chem. Soc. Rev.* **2010**, *39*, 1302–1315. (b) Amblard, F.; Cho, J. H.; Schinazi, R. F. *Chem. Rev.* **2009**, *109*, 4207–4220. (c) Meldal, M.; Tornøe, C. W. *Chem. Rev.* **2008**, *108*, 2952–3015. (d) Meldal, M. *Macromol. Rapid Commun.* **2008**, *29*, 1016–1051. (e) Johnson, J. A.; Finn, M. G.; Koberstein, J. T.; Turro, N. J. *Macromol. Rapid Commun.* **2008**, *29*, 1052–1072. (f) Tron, G. C.; Pirali, T.; Billington, R. A.; Canonico, P. L.; Sorba, G.; Genazzani, A. A. *Med. Res. Rev.* **2008**, *28*, 278–308. (g) Lutz, J.-F. *Angew. Chem., Int. Ed.* **2007**, *46*, 1018–1025. (h) Moses, J. E.; Moorhouse, A. D. *Chem. Soc. Rev.* **2007**, *36*, 1249–1262. (i) Bock, V. D.; Hiemstra, H.; van Maarseveen, J. H. *Eur. J. Org. Chem.* **2006**, 51–68.

(16) Parts of this work have been communicated, see: Luu, T.; McDonald, R.; Tykwinski, R. R. *Org. Lett.* **2006**, *8*, 6035–6038.

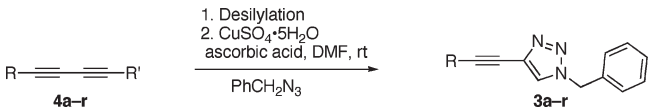
(17) At the start of our work in this area (see ref 16), the reaction of terminal tri-, tetra-, or pentaynes with organic azides under Cu(I)/Cu(I) catalysis had not been explored, whereas one example existed for the reaction with a terminal diyne, see: Reck, F.; Zhou, F.; Girardot, M.; Kern, G.; Eyermann, C. J.; Hales, N. J.; Ramsay, R. R.; Gravestock, M. B. *J. Med. Chem.* **2005**, *48*, 499–506. Since this time, several reports have appeared, see: (a) Aizpurua, J. M.; Azcune, I.; Fratila, R. M.; Balentova, E.; Sagartzazu-Aizpurua, M.; Miranda, J. I. *Org. Lett.* **2010**, *12*, 1584–1587. (b) Fiandanese, V.; Bottalico, D.; Marchese, G.; Punzi, A.; Quarta, M. R.; Fittipaldi, M. *Synthesis* (*Stuttgart*) **2009**, 3853–3859. (c) Gauthier, S.; Weisbach, N.; Bhuvanesh, N.; Gladysz, J. A. *Organometallics* **2009**, *28*, 5597–5599. (d) Fiandanese, V.; Bottalico, D.; Marchese, G.; Punzi, A.; Capuzzolo, F. *Tetrahedron* **2009**, *65*, 10573–10580. (e) Reference 8c. (f) Monkowius, U.; Ritter, S.; König, B.; Zabel, M.; Yersin, H. *Eur. J. Inorg. Chem.* **2007**, 4597–4606.

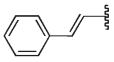
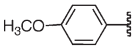
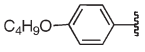
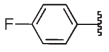
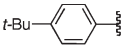
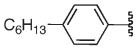
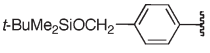
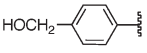
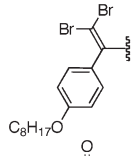
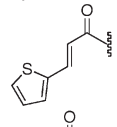
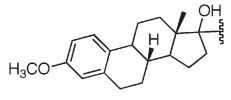
(18) The thermal reaction of azides with di- and triynes has been reported, see: (a) Domnin, I. N.; Remizova, L. A.; Starova, G. L.; Rominger, F. *Russ. J. Org. Chem.* **2009**, *45*, 1678–1682. (b) Bettison, R. M.; Hitchcock, P. B.; Walton, D. R. M. *J. Organomet. Chem.* **1988**, *341*, 247–254. (c) Tikhonova, L. G.; Serebryakova, E. S.; Proidakov, A. G.; Sokolov, I. E.; Vereshchagin, L. I. *J. Org. Chem. USSR* **1981**, *17*, 645–648. (d) Sokolyanskaya, L. V.; Volkov, A. N.; Trofimov, B. A. *Khim. Geterotsikl. Soedin.* **1979**, 849−849; *Chem. Heterocycl. Compd.* **1979**, *15*, 689−689. (e) Dornow, A.; Rombush, R. *Chem. Ber.* **1958**, *91*, 1841–1851.

(19) It is important to note that during the concentration process, heat should not be applied and the solution should not be reduced to dryness since this could result in decomposition of the terminal alkyne.

(20) The amount of benzyl azide was roughly based on the apparent success of the desilylation reaction, and varied from 0.66 to 1.0 equiv. Isolated yields are reported based on the amount of benzyl azide used; see the Experimental Section for details.

TABLE 1. Synthesis of Triazoles 3a–r from Diynes 4a–r



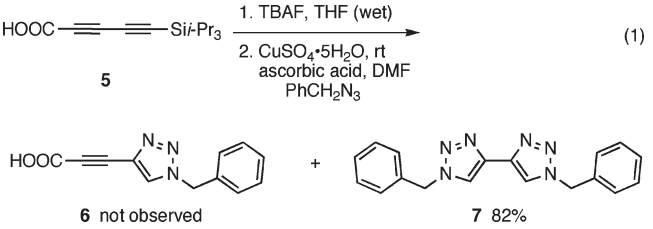
	R	R'	desilylation conditions	yield (%)
a	*t*-BuMe$_2$Si	Me$_3$Si	K_2CO_3/MeOH	75
b	*i*-Pr$_3$Si	Me$_3$Si	K_2CO_3/MeOH	67
c	Ph	Me$_3$Si	K_2CO_3/MeOH	73
d	2-pyrenyl	Me$_3$Si	K_2CO_3/MeOH	62
e	2-thienyl	Me$_3$Si	K_2CO_3/MeOH	71
f		Me$_3$Si	K_2CO_3/MeOH	69
g		Me$_3$Si	K_2CO_3/MeOH	83
h		Me$_3$Si	K_2CO_3/MeOH	82
i		*i*-Pr$_3$Si	TBAF/THF	72
j		Me$_3$Si	K_2CO_3/MeOH	74
k		Me$_3$Si	K_2CO_3/MeOH	73
l		Me$_3$Si	K_2CO_3/MeOH	71[a]
m[b]		Me$_3$Si	TBAF/THF	86[c]
n		Me$_3$Si	K_2CO_3/MeOH	65
o		Me$_3$Si	K_2CO_3/MeOH[d]	5
p		Me$_3$Si	K_2CO_3/MeOH	68
q		*i*-Pr$_3$Si	TBAF/THF	46
r		*i*-Pr$_3$Si	TBAF/THF	75

[a]The *t*-BuMe$_2$Si group is not removed during desilylation of the alkyne. [b]Starting material is **4l**, product is **3m**. [c]The *t*-BuMe$_2$Si group is removed during desilylation of the alkyne. [d]Desilylation in situ, see text.

terminal diyne with benzyl azide afforded **3a**,**b** in good yield, with a *t*-BuMe$_2$Si- or *i*-Pr$_3$Si-group in place for further elaboration. Aryl and vinyl terminated diynes **4c**–**n** gave triazoles **3c**–**n** with no particular trend observed in yield with respect to the electronic nature of the substituents. For diyne **4l**, desilylation with K_2CO_3 in THF/MeOH and trapping with benzyl azide produced **3l** in 71% yield with *t*-BuMe$_2$Si-protected benzyl alcohol still intact. Conversely, subjecting **4l** to TBAF in the alkyne deprotection step resulted in removal of both the *t*-BuMe$_2$Si- and Me$_3$Si-protecting groups, ultimately generating triazole **3m** with a benzyl alcohol moiety. Trapping the terminal diyne derived from dibromoolefinic diyne **4n** with a benzyl azide gave **3n** in 65% yield with no evidence of reaction between the dibromoolefin moiety and the Cu-catalyst (i.e., the Castro–Stephens reaction[21]). The formation of ynone **3o**, however, was not particularly successful, seemingly due to rapid decomposition of the terminal alkyne during desilylation (observed as the formation of a black precipitate). An attempt was made to effect formation of **3o** through a one-pot desilylation/trapping reaction with **4o** via the addition of K_2CO_3 and MeOH to a DMF solution of **4o** containing benzyl azide, $CuSO_4 \cdot 5H_2O$, ascorbic acid, and water. While this procedure did allow for isolation of the desired product, the yield remained abysmal (5%). Finally, the estrone 3-methyl ether end-capped diyne **4r** was also successfully deprotected with TBAF and the resulting terminal diyne was reacted under the general conditions to give compound **3r** in good yield.

This protocol was also employed to trap two diynes that have been previously isolated and identified from natural sources. The terminal ynone derived from desilylation of **4p** has been isolated from the crown daisy (*Chrysanthemum coronarium*) by Bohlmann and co-workers,[22] and could be trapped with benzyl azide under the described conditions to produce **3p** in 68% yield. The diyne derived from desilylation of **4q** has been obtained from the Laughing Jim mushroom (*Gymnopilus spectabilis*) by Jones and co-workers,[23] and the reaction with benzyl azide produced triazole **3q** in 46% yield.

The *i*-Pr$_3$Si-protected diyne acid **5** was reacted with TBAF in THF, and the resulting product was subjected to benzyl azide under typical reaction conditions toward the formation of compound **6** (eq 1). This sequence did not give the expected triazole, but rather the bis-triazole **7** in 82% yield.[24,25] While the mechanism of this reaction has not been explored, presumably decarboxylation occurred under the reaction conditions to liberate the second terminal alkyne moiety, which then underwent a reaction with benzyl azide. The solubility of compound **7** was quite low under conditions of the reaction, and it thus precipitated out of solution and was easily isolated by filtration; no trace of the expected alkynyl triazole **6** was observed.



Finally, this methodology was extended to the formation of bis-triazole **8** from precursor **9**,[26] which proceeded in good yield. Purification of the product was problematic due to its

(21) Stephens, R. D.; Castro, C. E. *J. Org. Chem.* **1963**, *28*, 3313–3315.
(22) Bohlmann, F.; Arndt, C.; Bornowski, H.; Kleine, K.-M.; Herbst, P. *Chem. Ber.* **1964**, *97*, 1179–1192. Bohlmann, F.; Herbst., P.; Dohrmann, I. *Chem. Ber.* **1963**, *96*, 226–236.
(23) Hearn, M. T. W.; Jones, E. R. H.; Pellatt, M. G.; Thaller, V.; Turner, J. L. *J. Chem. Soc., Perkin Trans. 1* **1973**, 2785–2788.
(24) Compound **7** has been previously prepared by another method, see ref 17f.
(25) The successful thermal reaction of azides with propriolic acid has been reported: Alonso, G.; Garcia-Lopez, M. T.; Garcia-Munoz, G.; Madronero, R.; Rico, M. *J. Heterocycl. Chem.* **1970**, *7*, 1269–1272.
(26) Shi Shun, A. L. K.; Chernick, E. T.; Eisler, S.; Tykwinski, R. R. *J. Org. Chem.* **2003**, *68*, 1339–1347.

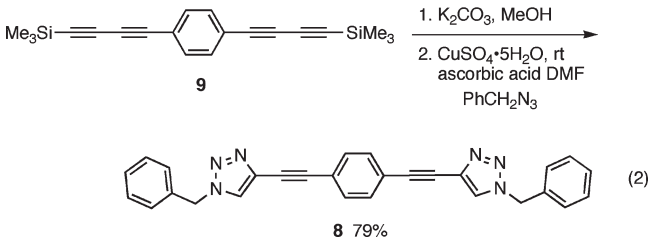
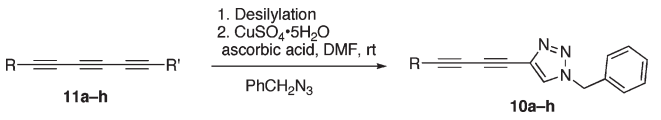
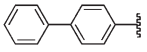


TABLE 2. Synthesis of Butadiynyl Triazoles 10a−h from Triynes 11a−h



	R	R'	desilylation conditons	yield (%)
a	Bu	*i*-Pr_3Si	TBAF/THF	71
b	Hex	Me_3Si	K_2CO_3/MeOH	47
c	*t*-$BuMe_2SiO$	*i*-Pr_3Si	TBAF/THF	47[a]
d	Ph	Me_3Si	K_2CO_3/MeOH	68
e		*i*-Pr_3Si	TBAF/THF	63
f	H_3CO 	*i*-Pr_3Si	TBAF/THF	82
g	*t*-Bu 	Me_3Si	K_2CO_3/MeOH	73
h	*i*-Pr_3Si	Me_3Si	K_2CO_3/MeOH	56

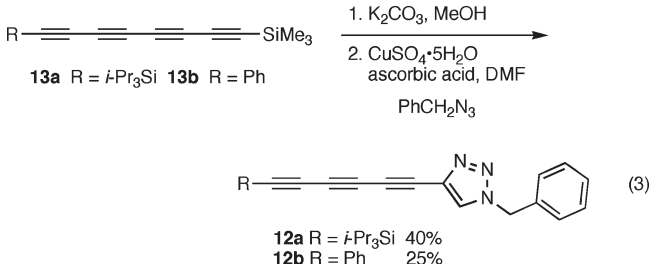
[a]The *t*-$BuMe_2Si$ group also removed during desilylation of alkyne.

minimal solubility in common solvents, but the pure yellow product could be isolated by recrystallization and characterized by ^{1}H NMR spectroscopy and mass spectrometry.

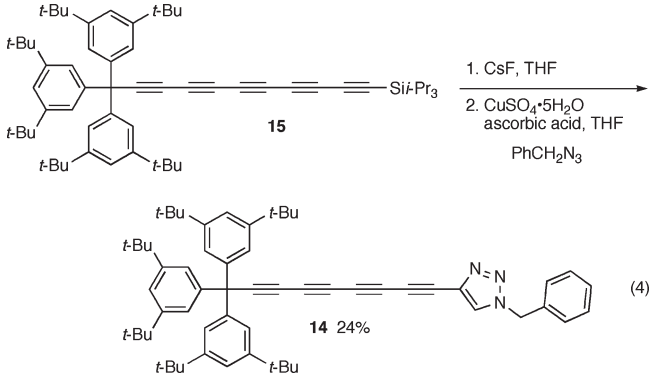
With a successful protocol in hand, attention was then turned to the trapping of terminal triynes with benzyl azide. In general, the same procedure used for the formation of **3a**−**r** was followed for **10a**−**h** (Table 2). It should be noted here that extreme care must be taken to ensure that, following removal of the Me_3Si- or *i*-Pr_3Si-group of **11a**−**h**, the solution containing the terminal triyne was neither heated nor concentrated to dryness due to the known and potentially dangerous instability of these compounds.[27] These reactions produced alkyl-, aryl-, and silyl-terminated butadiynyl-1,2,3-triazole derivatives **10a**−**h** in yields ranging from 47% to 82% starting with triynes **11a**−**h** (Table 2). Isolated yields were, more or less, independent of both the nature of the terminal group of the triyne precursor and whether an *i*-Pr_3Si- or Me_3Si-group was removed prior to trapping.

Noteworthy is the terminal triynol resulting from the exhaustive desilylation of **11c**, which has been proposed as a product from the hydrolysis of the antibiotic fungal natural product marasin, isolated in 1959 by Bendz from *Marasmius ramealis*[28] and more recently by Jones and co-workers from *Aleurodiscus roseus*[29] and *Cortinellus berkeleyanus*.[30] Trapping of the terminal triyne with benzyl azide gave triazole **10c** in a reasonable yield of 47%.

The prospect of forming triazoles via the trapping of terminal tetraynes was then explored toward producing **12a** and **12b** (eq 3). Great care must be taken during the desilylation of both **13a** and **13b** to guarantee that they remain solvated at all times in order to prevent decomposition of these highly unstable terminal alkyne products prior to reaction with benzyl azide. Following desilylation, conversion of the resulting alkyne to the desired triazole proceeded reasonably well under normal conditions to give **12a** and **12b** in 40% and 25% yield, respectively. An attempt to circumvent the isolation/concentration step following desilylation was also made. The one-pot reaction was attempted with **13a** toward the in situ formation and trapping of the terminal tetrayne. As described above for the formation of **3o**, to the precursor **13a** were added DMF, K_2CO_3, MeOH, $CuSO_4 \cdot 5H_2O$, ascorbic acid, and benzyl azide, and the reaction was stirred at room temperature. Standard aqueous workup and column chromatography gave **12b** in a similar yield (21%) to the two-step route.



The formation of terminal pentaynes can be plagued by their instability, but formation and trapping of one example (as well as an analogous hexayne) with benzyl azide has been recently reported by Gladysz and co-workers.[17c] In this case, the penta- and hexaynes were end-capped with a platinum acetylide moiety. Using the conditions described above, one purely organic pentayne[31] has been successfully trapped, giving the triazole product **14** in 24% yield over two steps from pentayne **15** (eq 4).



Purification and Characterization. In general, the triazole products described above could be obtained through a

(27) **Caution:** It should be noted that Armitage has reported that the terminal triyne derived from **11d** "exploded at 0 °C in the absence of air", see: Armitage, J. B.; Entwistle, N.; Jones, E. R. H.; Whiting, M. C. *J. Chem. Soc.* **1954**, 147–154. One should, therefore, not attempt to isolate this terminal triyne neat. Although we have not experienced any problems, the terminal polyynes reported herein should all be treated as potentially explosive and handled with care.

(28) Bendz, G. *Ark. Kemi* **1959**, *14*, 305–321.

(29) Cambie, R. C.; Hirschberg, A.; Jones, E. R. H.; Lowe, G. *J. Chem. Soc.* **1963**, 4120–4130.

(30) Bew, R. E.; Chapman, J. R.; Jones, E. R. H.; Lowe, B. E.; Lowe, G. *J. Chem. Soc. C* **1966**, 129–135.

(31) Chalifoux, W. A.; Tykwinski, R. R. *Nat. Chem.* **2010**, *2*, 967−971.

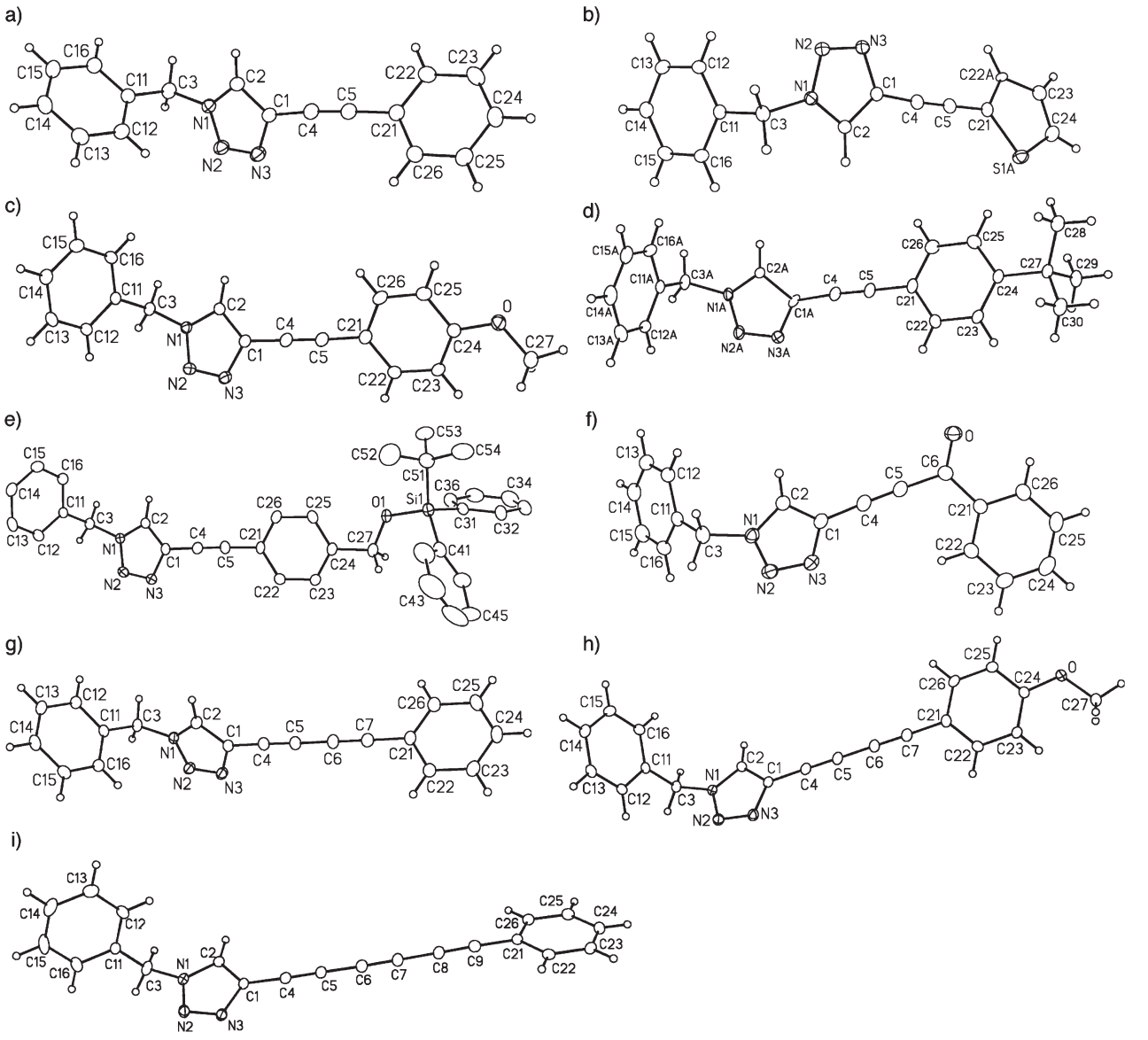


FIGURE 2. ORTEP drawings (20% probability level) for (a) **3c**, (b) **3e**, (c) **3g**, (d) **3j**, (e) **3l**, (f) **3p**, (g) **10d**, (h) **10f**, and (i) **12b**.

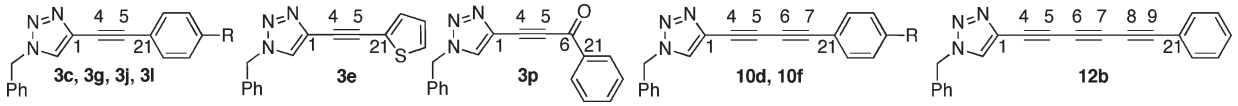
simple process of aqueous workup and concentration of the resulting solution to give a solid (except for compounds **3a**,**o**, **10a**,**h**, and **12a** which are oils). The solid was then washed with a minimal amount of hexanes (ca. 10−20 mL) at 0 °C to remove any remaining DMF as well as soluble byproducts. The compounds at this point were often sufficiently pure for spectroscopic characterization. Alternatively, column chromatography or crystallization was used in cases where additional purification was required.

EI mass spectral analysis of the 1,2,3-triazole derivatives shows a common fragmentation pattern. Most derivatives readily lose the N_2 fragment to generate $[M - 28]^+$, while the base peak typically arises from the benzyl group to give tropylium at m/z 91.

All products, with the exception of bis(triazoles) **7** and **8**, are sufficiently soluble for NMR spectroscopic analysis.[32] In no case did the ^{1}H or ^{13}C NMR spectra of the isolated products show evidence of multiple azide additions to the polyyne skeleton, although the occurrence of multiple additions cannot be rigorously excluded given that these productions would likely show only limited solubility. ^{1}H NMR spectroscopy could also, in principle, be used to distinguish between regioisomers resulting from 1,4- or 1,5-addition, based on the studies of Tikhonova and co-workers, who report that the proton of the triazole ring for 1,4-isomers typically resonates between 8.06 and 7.42 ppm versus those of the 1,5-isomers that are found slightly upfield at 7.59−7.42 ppm.[18c] Unfortunately, there is no clear-cut point from this trend to rule out 1,5-addition. The triazole protons of ethynyl compounds **3a**−**r** have chemical shifts ranging from 7.81−7.41 ppm, with the most downfield shifts observed for compounds **3o** and **3p** (7.77 and 7.81 ppm, respectively) resulting from the electronic withdrawing carbonyl group. Symmetrical disubstituted triazole **7** shows the proton at 7.98 ppm. This may result from the effect of the adjacent triazole ring, which is also electron deficient. Thus, the

(32) See the Supporting Information for spectra of new compounds.

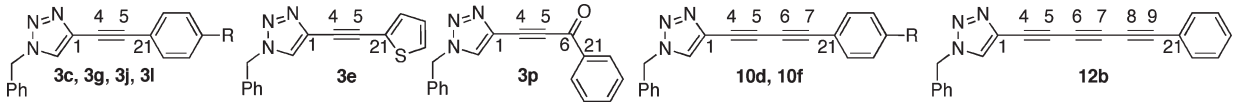
TABLE 3. Selected Bond Lengths of Compounds 3c,e,g,j,*l*,p, 10d,f, and 12b



	selected bond lengths (Å)									
compd	C1−C4	C4−C5	C5−C6	C6−C7	C7−C8	C8−C9	C5−C21	C6−C21	C7−C21	C9−C21
3c	1.4301(18)	1.1948(18)					1.4378(18)			
3e	1.432(3)	1.193(3)					1.419(3)			
3g	1.4284(19)	1.200(2)					1.4395(19)			
3j[a]	1.409(17)[b]	1.192(2)[d]					1.435(2)[d]			
	1.443(16)[c]	1.192(2)[d]					1.435(2)[d]			
3*l*[e]	1.421(6)[f]	1.202(6)[f]					1.453(6)[f]			
	1.418(6)[g]	1.180(6)[g]					1.442(6)[g]			
3p	1.419(3)	1.194(3)	1.452(3)					1.476(3)		
10d	1.426(2)	1.196(2)	1.372(2)	1.200(2)					1.435(2)	
10f	1.4262(18)	1.199(2)	1.376(2)	1.201(2)					1.4347(19)	
12b	1.425(3)	1.203(3)	1.368(3)	1.205(3)	1.371(3)	1.199(3)				1.430(3)

[a]Two equally-abundant orientations (A and B) of the disordered benzyltriazine unit. [b]Orientation A. [c]Orientation B. [d]Common to both orientations. [e]Two crystallographically independent molecules found in the unit cell, molecules A and B. [f]Molecule A. [g]Molecule B.

TABLE 4. Selected Bond Angles of Compounds 3c,e,g,j,*l*,p, 10d,f, and 12b



	selected bond angles (deg)								
compd	C1−C4−C5	C4−C5−C6	C5−C6−C7	C6−C7−C8	C7−C8−C9	C4−C5−C21	C5−C6−C21	C6−C7−C21	C8−C9−C21
3c	174.45(14)					176.95(14)			
3e	176.3(2)					178.8(2)			
3g	179.25(17)					177.01(16)			
3j[a]	173.9(8)[b]					178.9(3)[d]			
	173.3(9)[c]					178.9(3)[d]			
3*l*[e]	179.5(6)[f]					175.3(5)[f]			
	178.7(5)[g]					174.4(5)[g]			
3p	177.7(2)	173.9(2)					117.18(16)		
10d	176.85(18)	178.12(18)	177.64(19)					178.33(18)	
10f	177.69(16)	179.06(16)	178.27(17)					177.14(17)	
12b	178.4(2)	179.5(3)	178.9(3)	177.8(3)	177.5(3)				176.2(3)

[a]Two equally-abundant orientations (A and B) of the disordered benzyltriazine unit. [b]Orientation A. [c]Orientation B. [d]Common to both orientations. [e]Two crystallographically independent molecules found in the unit cell, molecules A and B. [f]Molecule A. [g]Molecule B.

observed chemical shifts for the triazole proton are more consistent with the expected 1,4-addition, but not definitive. It is interesting to note that within the homologous series of phenyl-terminated derivatives, there is essentially no variance in the chemical shift of the triazole proton at δ 7.61 (**3c**), 7.60 (**10d**), and 7.62 (**12b**). Likewise, there is little change in the chemical shift of the benzylic protons within the same series, found at δ 5.55 (**3c**), 5.52 (**10d**), and 5.52 (**12b**). Overall, the resonances observed for the benzylic protons span from 5.44 (**3g**) to 5.60 ppm (**3d**), and the relative values reflect, more or less, the electronic rich/poor nature of the polyyne substituent pendent to the triazole.

X-ray crystallography has been used to confirm the regioselectivity of the products isolated from the trapping reactions and to explore the structure of ethynyl-, butadiynyl-, and hexatriynyl-1,2,3-triazole derivatives.[33] Crystals of **3c**, **3e**, **3g**, **3j**, **3*l***, **3p**, **10d**, **10f**, and **12b** have been analyzed.[34] Structures are shown in Figure 2, while selected bond lengths and angles are tabulated in Tables 3 and 4, respectively. These data show that the C1−C4 bond that links the alkyne chain to the triazole moiety is consistently shorter than that to the pendent aryl- or keto-group (i.e., C5−C21, C7−C21, or C9−C21). The only exception to this trend is thienyl derivative **3e**, where C5−C21 at 1.419(3) Å is shortened versus C1−C4 at 1.432(3) Å, likely due to the mesomeric effect from the thienyl to the electron-poor ethynyl triazole moiety. As is typical for alkynes and polyynes,[5c] bending of the C≡C—C bonds is also observed for several of the triazole derivatives examined in this study, including C1−C4−C5 for **3c** (174.45(14)°) and **3j** (173.3(8)° and 173.9(8)°), as well as C4−C5−C6 for **3p** (173.9(2)°).

Conclusions

It has been successfully demonstrated that the terminal di-, tri-, tetra-, and pentaynes can be trapped with benzyl azide using the Huisgen reaction in the presence of $CuSO_4$ and ascorbic acid. In general, the procedure generates useful yields

(33) For the crystallographic characterization of other ethynyl-1,2,3-triazole derivatives, see refs 17c 18a 18b, and the following: Adamson, G. A.; Rees, C. W. *J. Chem. Soc., Perkin Trans. 1* **1996**, 1535–1543.

(34) The structures of **3c**, **3g**, and **10d** have been communicated, see ref 16.

of 4-ethynyl-, 4-butadiynyl-, 4-hexatriynyl-, and 4-octatetraynyl-substituted 1,2,3-triazole derivatives. This approach has also been used to trap three natural products or their analogues, suggesting that it should be useful toward the identification of naturally occurring terminal polyynes that might not otherwise be found due to instability. Finally, the reactions described above appear to be quite selective: only 1,4-adducts are isolated from these transformations, as demonstrated by X-ray crystallography of nine derivatives, and no evidence of multiple addition(s) to the polyyne skeleton is observed.

Experimental Section

X-ray Crystallographic Details. Single crystals for X-ray crystallography were obtained by (a) diffusion of hexanes into a solution of in CH_2Cl_2 at rt (**3c**, **3g**, **10d**), (b) diffusion of hexanes into a solution of in hexanes/CH_2Cl_2 at rt (**3p**), (c) slow evaporation of a solution of $CHCl_3$ (**3j**, **3l**) or $CDCl_3$ (**10f**) at 4 °C, or (d) slow evaporation of a CH_2Cl_2 solution at rt (**3e**) or 0 °C (**12b**). The crystallographic coordinates have been deposited with the Cambridge Crystallographic Data Centre. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre, 12 Union Rd., Cambridge CB2 1EZ, UK or via www.ccdc.cam.ac.uk/conts/retrieving.html.

Crystal data for 3c: $C_{17}H_{13}N_3$, MW = 259.30; crystal dimensions 0.68 × 0.29 × 0.28 mm^3; monoclinic space group $P2_1/n$ (an alternate setting of $P2_1/c$ [No. 14]); a = 5.7277(8) Å, b = 14.2042(18) Å, c = 16.811(2) Å; β = 93.6141(18)°; V = 1365.0(3) Å^3; Z = 4; ρ_{calc} = 1.262 g cm^{-3}; μ = 0.077 mm^{-1}; λ = 0.71073 Å; T = −80 °C; $2\theta_{max}$ = 52.80°, total data collected = 7513; $R_1(F)$ = 0.0409 (2030 observations [$F_o^2 \geq 2\sigma(F_o^2)$]); $wR_2(F^2)$ = 0.1147 for 181 variables and all 2800 unique data; residual electron density = 0.134 and −0.184 e Å^{-3}. CCDC deposition no. 623595.

Crystal data for 3e: $C_{15}H_{11}N_3S$, MW = 265.33; crystal dimensions 0.78 × 0.65 × 0.20 mm^3; monoclinic space group $P2_1/n$ (an alternate setting of $P2_1/c$ [No. 14]); a = 9.9330(10) Å, b = 5.7873(6) Å, c = 23.287(2) Å; β = 101.4178(14)°; V = 1312.2(2) Å^3; Z = 4; ρ_{calc} = 1.343 g cm^{-3}; μ = 0.235 mm^{-1}; λ = 0.71073 Å; T = −80 °C; $2\theta_{max}$ = 52.74°; total data collected = 6037; $R_1(F)$ = 0.0456 (2254 observations [$F_o^2 \geq 2\sigma(F_o^2)$]); $wR_2(F^2)$ = 0.1209 for 179 variables, 4 restraints, and all 2672 unique data; residual electron density = 0.341 and −0.652 e Å^{-3}. The following restraints were applied to distances involving the minority-conformer (10%) atoms of the disordered thienyl group: d(S1B−C21) = 1.70(1) Å; d(S1B−C23) = 1.68(1) Å; d(C21−C22B) = 1.41(1) Å; d(C22B−C24) = 1.44(1) Å. CCDC deposition no. 770998.

Crystal data for 3g: $C_{18}H_{15}N_3O$, MW = 289.33; crystal dimensions 0.72 × 0.21 × 0.19 mm^3; monoclinic space group $P2_1$ (No. 4); a = 9.1938(9) Å, b = 5.6198(6) Å, c = 14.7114(14) Å; β = 102.6687(14)°, V = 741.59(13) Å^3; Z = 2; ρ_{calc} = 1.296 g cm^{-3}; μ = 0.083 mm^{-1}; λ = 0.71073 Å; T = −80 °C; $2\theta_{max}$ = 52.82°; total data collected = 5655; $R_1(F)$ = 0.0303 (2779 observations [$F_o^2 \geq 2\sigma(F_o^2)$]); $wR_2(F^2)$ = 0.0792 for 199 variables and all 3025 unique data; residual electron density = 0.105 and −0.141 e Å^{-3}. CCDC deposition no. 623596.

Crystal data for 3j: $C_{21}H_{21}N_3$, MW = 315.41; crystal dimensions 0.38 × 0.35 × 0.23 mm^3; monoclinic space group $P2_1$ (No. 4); a = 5.7566(11) Å, b = 7.9092(15) Å, c = 18.846(4) Å; β = 90.312(3) Å^3; V = 858.1(3) Å^3; Z = 2; ρ_{calc} = 1.221 g cm^{-3}; μ = 0.073 mm^{-1}; λ = 0.71073 Å; T = −80 °C; $2\theta_{max}$ = 52.68°; total data collected = 6808; $R_1(F)$ = 0.0532 (2805 observations [$F_o^2 \geq 2\sigma(F_o^2)$]); $wR_2(F^2)$ = 0.1431 for 325 variables and all 3498 unique data; residual electron density = 0.198 and −0.218 e Å^{-3}. CCDC deposition no. 770999.

Crystal data for 3l: $C_{34}H_{33}N_3OSi$, MW = 527.72; crystal dimensions 0.58 × 0.57 × 0.08 mm^3; monoclinic space group Cc (No. 9); a = 45.300(8) Å, b = 10.1710(17) Å, c = 13.213(2) Å; β = 99.865(5); V = 5998.0(17); Z = 8; ρ_{calc} = 1.169 g cm^{-3}; μ = 0.108 mm^{-1}; λ = 0.71073 Å; T = −80 °C; $2\theta_{max}$ = 50.00°; total data collected = 8809; $R_1(F)$ = 0.0436 (5665 observations [$F_o^2 \geq 2\sigma(F_o^2)$]); $wR_2(F^2)$ = 0.0956 for 704 variables and all 8809 unique data; residual electron density = 0.309 and −0.152 e Å^{-3}. CCDC deposition no. 771000.

Crystal data for 3p: $C_{18}H_{13}N_3O$, MW = 287.31; crystal dimensions 0.38 × 0.16 × 0.10 mm^3; triclinic space group $P\bar{1}$ (No. 2); a = 7.8486(8) Å, b = 8.8827(9) Å, c = 12.1321(13) Å; α = 70.6508(19)°, β = 79.5467(19)°, γ = 68.0695(19)°; V = 738.68(13) Å^3; Z = 2; ρ_{calc} = 1.292 g cm^{-3}; μ = 0.083 mm^{-1}; λ = 0.71073 Å; T = −80 °C; $2\theta_{max}$ = 50.00°; total data collected = 5108; $R_1(F)$ = 0.0428 (1724 observations [$F_o^2 \geq 2\sigma(F_o^2)$]); $wR_2(F^2)$ = 0.1208 for 199 variables and all 2608 unique data; residual electron density = 0.130 and −0.181 e Å^{-3}. CCDC deposition no. 771001.

Crystal data for 10d: $C_{19}H_{13}N_3$, MW = 283.32; crystal dimensions 0.60 × 0.19 × 0.16 mm^3; triclinic space group $P\bar{1}$ (No. 2); a = 6.3632(8) Å, b = 7.9519(9) Å, c = 15.1874(18) Å; α = 102.3564(18)°, β = 95.3363(18)°, γ = 91.0645(18)°; V = 746.84(15) Å^3; Z = 2; ρ_{calc} = 1.260 g cm^{-3}; μ = 0.076 mm^{-1}; λ = 0.71073 Å; T = −80 °C; $2\theta_{max}$ = 52.78°; total data collected = 5468; $R_1(F)$ = 0.0436 (2130 observations [$F_o^2 \geq 2\sigma(F_o^2)$]); $wR_2(F^2)$ = 0.1274 for 199 variables and all 3013 unique data; residual electron density = 0.178 and −0.179 e Å^{-3}. CCDC deposition no. 623597.

Crystal data for 10f: $C_{20}H_{15}N_3O$, MW = 313.35; crystal dimensions 0.56 × 0.31 × 0.12 mm^3; monoclinic space group $P2_1$ (No. 4); a = 10.7789(10) Å, b = 5.6104(5) Å, c = 14.1828(13) Å; β = 108.6532(13)°; V = 812.64(13); Z = 2; ρ_{calc} = 1.281 g cm^{-3}; μ = 0.081 mm^{-1}; λ = 0.71073 Å; T = −80 °C; $2\theta_{max}$ = 52.78°; total data collected = 6447; $R_1(F)$ = 0.0306 (3069 observations [$F_o^2 \geq 2\sigma(F_o^2)$]); $wR_2(F^2)$ = 0.0817 for 218 variables and all 3302 unique data; residual electron density = 0.143 and −0.167 e Å^{-3}. CCDC deposition no. 771002.

Crystal data for 12b: $C_{21}H_{13}N_3$, MW = 307.34; crystal dimensions 0.55 × 0.25 × 0.07 mm^3; orthorhombic space group $Pca2_1$ (No. 29); a = 10.8926(10) Å, b = 20.0670(19) Å, c = 7.3933(7) Å; V = 1616.0(3) Å^3, Z = 4; ρ_{calc} = 1.263 g cm^{-3}; μ = 0.076 mm^{-1}; λ = 0.71073 Å; T = −80 °C; $2\theta_{max}$ = 52.76°; total data collected = 11984; $R_1(F)$ = 0.0332 (1621 observations [$F_o^2 \geq 2\sigma(F_o^2)$]); $wR_2(F^2)$ = 0.1070 for 217 variables and all 1796 unique data; residual electron density = 0.169 and −0.148 e Å^{-3}. CCDC deposition no. 771003.

General Procedure: The Reaction of Di-, Tri-, and Tetraynes with Benzyl Azide Unless otherwise stated, a mixture of the appropriate trimethylsilyl- or triisopropylsilyl-protected polyyne (0.3−0.9 mmol) and K_2CO_3 (ca. 0.05 g) or TBAF (2.0 equiv) in wet THF/MeOH (1:1 v/v, 5 mL) or THF (10 mL), respectively, were combined and stirred at rt until TLC analysis showed complete conversion to the terminal alkyne. Et_2O and saturated aq NH_4Cl were added, then the organic phase was separated, washed with saturated aq NH_4Cl (2 × 10 mL) and saturated aq NaCl (10 mL), dried over $MgSO_4$, and filtered. DMF (2 mL) was then added and the solution concentrated to 1−2 mL via rotary evaporation to remove Et_2O, THF, or MeOH. To the resulting mixture was added DMF (10 mL), followed by benzyl azide (0.66−1.0 equiv based on the starting silylated polyyne),[20] $CuSO_4 \cdot 5H_2O$ (0.1 g), ascorbic acid (0.1 g), and H_2O (2 mL). This mixture was then stirred at rt until TLC analysis showed that either the terminal polyyne or benzyl azide had been consumed. Saturated aq NH_4Cl (10 mL) and Et_2O (10 mL) were added, then the organic phase was separated, washed with saturated aq NaCl (2 × 10 mL), dried over $MgSO_4$, and filtered. Concentration of the resulting solution gave a solid (except for compounds **3a,o**, **10a**,**h**, and **12a** which are oils) that was washed with a minimal amount of hexanes (ca. 10−20 mL) at 0 °C to remove any remaining DMF as well as soluble

byproducts. When necessary, additional purification via column chromatography (silica gel) or recrystallization gave analytically pure material. The synthesis and spectral characterization of the following compounds and their precursors are described in ref 16: **3a**−**c**,**g**,**i**,**j**,***l***,**p**,**q**, **10a**,**c**−**g**, and **12a**,**b**.

Compound 3d: Diyne **4d**[26] (159 mg, 0.490 mmol) and benzyl azide (58.6 mg, 0.440 mmol) were used as per the general procedure and yielded **3d** (105 mg, 62%) as a yellow powder. Mp 168−171 °C. R_f = 0.2 (CH_2Cl_2). IR (CH_2Cl_2, cast) 3139 (w), 3041 (w), 2216 (w), 1456 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.61 (d, J = 9.1 Hz, 1H), 8.20−8.12 (m, 4H), 8.10−8.07 (m, 2H), 8.02 (d, J = 9.0 Hz, 1H), 8.01 (t, J = 7.6 Hz, 1H), 7.73 (s, 1H), 7.43−7.38 (m, 3H), 7.33−7.31 (m, 2H), 5.60 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 134.2, 132.0, 131.8, 131.6, 131.2, 131.0, 129.6, 129.3, 129.0, 128.5, 128.4, 128.2, 127.2, 126.3, 125.9, 125.8, 125.7, 125.5, 124.5, 124.4, 124.2, 116.7, 91.9, 83.9, 54.5. EIMS m/z 383.1 (M^+, 53); HRMS m/z calcd for $C_{27}H_{17}N_3$ (M^+) 383.1422, found 383.1417. Anal. Calcd for $C_{27}H_{17}N_3$: C, 84.57; H, 4.47; N, 10.96. Found: C, 84.18; H, 4.56; N, 10.81.

Compound 3e: Diyne **4e**[26] (182 mg, 0.893 mmol) and benzyl azide (107 mg, 0.800 mmol) were used as per the general procedure and yielded **3e** (150 mg, 71%) as a white crystalline solid. Mp 86−88 °C. R_f = 0.35 (CH_2Cl_2). IR (CH_2Cl_2, cast) 3129, 3105, 3090, 3066, 3053, 2953, 2220 (vw), 1457 (w) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.60 (s, 1H), 7.39−7.36 (m, 3H), 7.31−7.26 (m, 4H), 6.99 (dd, J = 3.7, 5.1 Hz, 1H), 5.54 (s, 2H); ^{13}C NMR (125 MHz, APT, $CDCl_3$) δ 134.0, 132.7, 131.2, 129.2, 129.0, 128.2, 128.0, 127.1, 125.9, 122.2, 86.0, 82.1, 54.4. EIMS m/z 265.1 (M^+, 14), 237.1 ([M − N_2]$^+$, 14), 91 ([C_7H_7]$^+$, 100); HRMS m/z calcd for $C_{15}H_{11}N_3S$ (M^+) 265.0674, found 265.0675. Anal. Calcd for $C_{15}H_{11}N_3S$: C, 67.90; H, 4.18; N, 15.84. Found: C, 67.64; H, 4.25; N, 15.37.

Compound 3f: Diyne **4f**[26] (107 mg, 0.476 mmol) and benzyl azide (56.5 mg, 0.424 mmol) were used as per the general procedure and yielded **3f** (83 mg, 69%) as a yellow solid. Mp 113−115 °C. R_f = 0.3 (CH_2Cl_2). IR (CH_2Cl_2, cast) 3126, 3054, 3028, 3006, 1454 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.53 (s, 1H), 7.40−7.25 (m, 10H), 7.03 (d, J = 16.3 Hz, 1H), 6.30 (d, J = 16.3 Hz, 1H), 5.52 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 142.3, 136.0, 134.1, 131.6, 129.2, 129.0, 128.9, 128.7, 128.1, 126.4, 125.6, 107.1, 92.1, 80.5, 54.4. EIMS m/z 285.1 (M^+, 15), 257.1 ([M − N_2]$^+$, 28), 91 ([C_7H_7]$^+$, 100); HRMS m/z calcd for $C_{19}H_{15}N_3$ (M^+) 285.1266, found 285.1266. Anal. Calcd for $C_{19}H_{15}N_3$: C, 79.98; H, 5.30; N, 14.73. Found: C, 79.55; H, 5.32; N, 14.52.

Compound 3h: Diyne **4h**[26] (69 mg, 0.27 mmol) and benzyl azide (30 mg, 0.224 mmol) were used as per the general procedure and yielded **3h** (61 mg, 82%) as a white crystalline solid. Mp 117−119 °C. R_f = 0.3 (CH_2Cl_2). IR ($CHCl_3$, cast) 3099, 3067, 3037, 2958, 2229 (w), 1608 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.55 (s, 1H), 7.41 (d, J = 8.9 Hz, 2H), 7.39−7.34 (m, 3H), 7.27−7.25 (m, 2H), 6.82 (d, J = 8.9 Hz, 2H), 5.52 (s, 2H), 3.94 (t, J = 6.6 Hz, 2H), 1.74 (quint, J = 7.0 Hz, 2H), 1.47 (sex, J = 7.4 Hz, 2H), 0.95 (t, J = 7.4 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.6, 134.2, 133.1, 131.8, 129.2, 128.9, 128.1, 125.4, 114.6, 114.1, 92.7, 67.8, 54.3, 31.2, 19.2, 13.8 (one signal coincident or not observed). EIMS m/z 331.2 (M^+, 41), 246.1 ([M − N_2 − C_4H_9]$^+$, 94); HRMS m/z calcd for $C_{21}H_{21}ON_3$ (M^+) 331.1685, found 331.1686. Anal. Calcd for $C_{21}H_{21}ON_3$: C, 76.11; H, 6.39; N, 12.68. Found: C, 75.89; H, 6.44; N, 12.55.

Compound 3k: Diyne **4k**[26] (126 mg, 0.445 mmol) and benzyl azide (53.3 mg, 0.400 mmol) were used as per the general procedure and yielded **3k** (99.7 mg, 73%) as a white solid. Mp 84−86 °C. R_f = 0.4 (CH_2Cl_2). IR ($CHCl_3$, cast) 3099, 3075, 3040, 2923, 1453 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.56 (s, 1H), 7.40 (d, J = 8.1 Hz, 2H), 7.36 (m, 3H), 7.28−7.26 (m, 2H), 7.12 (d, J = 8.1 Hz, 2H), 5.53 (s, 2H), 2.58 (t, J = 7.7 Hz, 2H), 1.60−1.58 (m, 2H), 1.28 (m, 6H), 0.86 (t, J = 6.6 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 144.0, 134.1, 131.7, 131.5, 129.2, 129.0, 128.5, 128.2, 125.6, 119.4, 92.9, 77.8, 54.4, 35.9, 31.7, 31.1, 28.9, 22.6, 14.1. ESI HRMS m/z calcd for $C_{23}H_{26}N_3$ ([M + H]$^+$) 344.2121, found 344.2122. Anal. Calcd for $C_{23}H_{25}N_3$: C, 80.43; H, 7.34; N, 12.23. Found: C, 80.23; H, 7.39; N, 12.07.

Compound 3m: Diyne ***4l***[16] (129 mg, 0.276 mmol) and benzyl azide (36.2 mg, 0.272 mmol) were used as per the general procedure using TBAF desilylation, and yielded **3m** (69 mg, 86%) as a white crystalline solid. Mp 125−127 °C. R_f = 0.4 (CH_2Cl_2). IR ($CHCl_3$, cast) 3191 (br), 3121, 3087, 2203 (w), 1452 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.58 (s, 1H), 7.48 (d, J = 8.2 Hz, 2H), 7.40−7.25 (m, 7H), 5.53 (s, 2H), 4.69 (s, 2H), 1.80 (br s, 1H); ^{13}C NMR (100 MHz, CDCl3) δ 141.5, 134.0, 131.7, 129.1, 128.9, 128.1, 126.7, 125.7, 121.4, 92.3, 78.4, 64.8, 54.3. ESI HRMS m/z calcd for $C_{18}H_{16}ON_3$ ([M + H]$^+$) 290.1288, found 290.1288.

Compound 3n: Diyne **4n** (257 mg, 0.504 mmol) and benzyl azide (59.7 mg, 0.448 mmol) were used as per the general procedure and yielded **3n** (167 mg, 65%) as a yellow solid. Mp 42−44 °C. R_f = 0.4 (CH_2Cl_2). IR ($CHCl_3$, cast) 3035, 2927, 2855, 2219 (w), 1246 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.56 (s, 1H), 7.39−7.33 (m, 5H), 7.25−7.22 (m, 2H), 6.85 (d, J = 8.8 Hz, 2H), 5.49 (s, 2H), 3.93 (t, J = 6.6 Hz, 2H), 1.76 (quint, J = 7.0 Hz, 2H), 1.46−1.43 (m, 2H), 1.32−1.27 (m, 8H), 0.87 (t, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.3, 133.9, 130.8, 129.92, 129.89, 129.3, 129.1, 128.9, 128.1, 126.1, 114.2, 99.1, 91.8, 86.1, 68.0, 54.3, 31.7, 29.2, 29.13, 29.10, 25.9, 22.6, 14.0. EIMS m/z 571.1 (M^+, 15), 57.0 ([C_4H_7]$^+$, 100); HRMS m/z calcd for $C_{27}H_{29}ON_3{}^{79}Br^{81}Br$ (M^+) 571.0657, found 571.0660. Anal. Calcd for $C_{27}H_{29}ON_3Br_2$: C, 56.76; H, 5.12; N, 7.35. Found: C, 56.83; H, 5.38; N, 7.08.

Compound 3o: Diyne **4o**[26] (120 mg, 0.464 mmol) was dissolved in DMF (10 mL) and benzyl azide (53.3 mg, 0.400 mmol), $CuSO_4 \cdot 5H_2O$ (0.1 g), ascorbic acid (0.1 g), and H_2O (2 mL) were added. To this mixture was then added K_2CO_3 (0.05 g) and MeOH (0.25 mL), and the resulting solution was stirred at rt. Saturated aq NH_4Cl (10 mL) and Et_2O (10 mL) were added, then the organic phase was separated, washed with saturated aq NaCl (2 × 10 mL), dried over $MgSO_4$, and filtered. Solvent removal and purification via column chromatography (silica gel, CH_2Cl_2/EtOAc 9:1) gave **3o** (6.6 mg, 5%) as a brown oil. R_f = 0.6 (CH_2Cl_2/EtOAc 9:1). IR ($CHCl_3$, cast) 3136 (w), 2916 (w), 2219, 1613 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.03 (d, J = 15.8 Hz, 1H), 7.77 (s, 1H), 7.47 (d, J = 5.1 Hz, 1H), 7.41−7.36 (m, 3H), 7.29−7.26 (m, 3H), 7.09 (dd, J = 5.0, 3.7 Hz, 1H), 6.63 (d, J = 15.8 Hz, 1H), 5.56 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 176.8, 141.2, 139.3, 133.6, 132.9, 130.5, 129.4, 129.2, 129.0, 128.8, 128.6, 128.2, 126.9, 89.9, 80.3, 54.6. ESI HRMS m/z calcd for $C_{18}H_{13}OSN_3Na$ ([M + Na]$^+$) 342.0672, found 342.0674.

Compound 3r: Diyne **4r** (127 mg, 0.258 mmol) and benzyl azide (30.9 mg, 0.232 mmol) were used as per the general procedure and yielded **3r** (81.6 mg, 75%) as a white solid. Mp 173−175 °C. R_f = 0.6 (CH_2Cl_2/EtOAc 3:1). IR ($CHCl_3$, μscope) 3378 (br), 3138, 2933, 1609, 1498 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.53 (s, 1H), 7.36−7.33 (m, 3H), 7.26−7.33 (m, 2H), 7.17 (d, J = 8.6 Hz, 1H), 6.69 (dd, J = 2.7, 8.6 Hz, 1H), 6.61 (d, 2.7 Hz, 1H), 2.88−2.78 (m, 2H), 2.48 (br s, 1H), 2.42−2.37 (m, 1H), 2.35−2.30 (m, 1H), 2.20 (dt, J = 4.0, 11.5 Hz, 1H), 2.10−2.04 (m, 1H), 1.92 (dt, J = 4.1, 12.9 Hz, 1H), 1.88−1.82 (m, 1H), 1.79−1.75 (m, 2H), 1.74−1.70 (m, 1H), 1.53−1.29 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.3, 137.9, 134.0, 132.5, 131.0, 129.1, 128.9, 128.1, 126.3, 125.8, 113.7, 111.4, 96.4, 80.3, 75.3, 55.1, 54.2, 49.6, 47.5, 43.3, 39.4, 38.8, 33.0, 29.8, 27.1, 26.4, 22.9, 12.8. EIMS m/z 467.3 (M^+, 10), 284.2 ([M − $C_{11}H_9N_2$]$^+$, 100); HRMS m/z calcd for $C_{30}H_{33}O_2N_3$ (M^+) 467.2573, found 467.2578. Anal. Calcd for $C_{30}H_{33}O_2N_3$: C, 77.06; H, 7.11; N, 8.99. Found: C, 76.90; H, 7.19; N, 8.78.

Compound 4n: To 4-*n*-octyloxybenzoic acid[35] (2.70 g, 10.8 mmol) in a flame-dried flask fitted with a drying tube was added $SOCl_2$ (2.58 g, 21.6 mmol). The mixture was allowed to stir at rt for 24 h. Excess $SOCl_2$ was removed in vacuo with a water aspirator and the resulting acid chloride was diluted with dry CH_2Cl_2 (20 mL). Bis(trimethylsilyl)butadiyne (2.51 g, 12.9 mmol) was added and the mixture cooled to −20 °C. $AlCl_3$ (2.16 g, 16.2 mmol) was added and the mixture allowed to warm to rt. The reaction was poured into HCl and ice (10% v:v) and the organic layer was washed with NH_4Cl (2 × 20 mL) and NaCl (2 × 20 mL), dried over $MgSO_4$, and filtered. Solvent was removed in vacuo and the crude ketone was carried to the next reaction without further characterization.

To this ketone were added PPh_3 (8.36 g, 31.9 mmol) and CBr_4 (5.00 g, 15.6 mmol) in CH_2Cl_2 (40 mL) at 0 °C. The reaction was slowly warmed to rt until the ketone was no longer observed by TLC analysis (about 3 h). The reaction was diluted with hexanes (40 mL) and filtered through a short plug of silica with hexanes to give pure **4n** (1.12 g, 20%) as a white crystalline solid. Mp 50−52 °C. R_f = 0.6 (hexanes/CH_2Cl_2 3:1). IR ($CHCl_3$, cast) 2926, 2093 (w), 1506 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.31 (d, J = 8.8 Hz, 2H), 6.85 (d, J = 8.8 Hz, 2H), 3.94 (t, J = 6.6 Hz, 2H), 1.76 (quint, J = 7.0 Hz, 2H), 1.45−1.39 (m, 2H), 1.38−1.27 (m, 8H), 0.87 (t, J = 6.4 Hz, 3H), 0.20 (s, 9); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.5, 129.9, 129.6, 129.1, 114.3, 101.6, 95.1, 87.4, 81.8, 75.2, 68.1, 31.8, 29.3, 29.23, 29.19, 26.0, 22.7, 14.1, −0.53. EI HRMS m/z calcd for $C_{23}H_{30}OSi^{79}Br^{81}Br$ 510.0412, found 510.0410. Anal. Calcd for $C_{23}H_{30}OSiBrBr$: C, 54.13; H, 5.92. Found: C, 54.08; H, 5.62.

Compound 4r: Dibromoolefin 1,1-dibromo-4-triisopropylsilylbut-3-ene-4-yne[2f] (523 mg, 1.43 mmol) in Et_2O (10 mL) was cooled to −78 °C. LDA [reaction between BuLi (2.5 M in hexanes, 1.70 mL, 4.25 mmol) and *i*-Pr_2NH (0.60 mL, 0.466 g, 4.28 mmol) in Et_2O (10 mL) at −78 °C; stirred for 30 min] was added over a period of ca. 1 min and the resulting solution stirred for 1 h. Estrone 3-methyl ether (0.365 g, 1.28 mmol) was then added by syringe and the reaction allowed to warm to rt and stirred overnight. The reaction was quenched through the addition of saturated aq NH_4Cl (10 mL) and Et_2O (10 mL). The organic layer was separated, washed with saturated aq NaCl (10 mL), dried over $MgSO_4$, and filtered, and the solvent was removed. Column chromatography (silica gel, hexanes) provided **4r** (584 mg, 93%) as a white crystalline solid. Mp 155−158 °C. R_f = 0.5 (CH_2Cl_2). IR (μscope) 3402, 2943, 2866, 2216 (w), 2096, 1257 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.20 (d, J = 8.3 Hz, 1H), 6.70 (dd, J = 2.8, 8.5 Hz, 1H), 6.61 (d, J = 2.8 Hz, 1H), 3.76 (s, 3H), 2.84 (m, 2H), 2.36 (m, 2H), 2.25 (dt, J = 4.0, 11.0 Hz, 1H, ddd, J = 13.8, 12.0, 3.9 Hz, 1H), 1.94 (t, J = 3.0 Hz, 1H), 1.89−1.65 (m, 5H), 1.55−1.34 (m, 4H), 1.08 (s, 21H), 0.86 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.5, 137.9, 132.5, 126.4, 113.8, 111.5, 89.1, 85.0, 80.6, 79.8, 71.5, 55.2, 49.8, 48.0, 43.4, 39.5, 39.0, 33.1, 29.8, 27.2, 26.4, 23.0, 18.6, 12.8, 11.3. EIMS m/z 490.3 (M^+, 10), 447.3 ([M − *i*-Pr]$^+$, 41); HRMS m/z calcd for $C_{32}H_{46}O_2Si$ (M^+) 490.3267, found 490.3260.

Compound 5: A solution of compound 1,1-dibromo-4-triisopropylsilylbut-3-ene-4-yne[2f] (369 mg, 1.01 mmol) in hexanes (5 mL) was cooled to −78 °C and BuLi (2.5 M in hexanes, 0.85 mL, 2.13 mmol) was added; the mixture was stirred for 1 h. Carbon dioxide generated from dry ice and passed through a drying tube (Drierite) was bubbled into the reaction overnight. The reaction was then quenched via the addition of water (10 mL) and Et_2O (10 mL). The aqueous phase was separated and neutralized with HCl (10%) and Et_2O (10 mL) was added. The organic layer was separated, washed with saturated aq NaCl (10 mL), dried over $MgSO_4$, and filtered. Solvent removal afforded **5** (170 mg, 67%) as a light yellow oil. IR (film) 3400−2500 (br), 2946, 2868, 2246 (w), 2204, 2105, 1687 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.08 (s), COOH signal not observed; ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.2, 94.1, 87.1, 73.6, 64.8, 18.4, 11.1. EIMS m/z 250.1 (M^+, 7), 207.1 ([M − *i*-Pr]$^+$, 100); HRMS m/z calcd for $C_{14}H_{22}O_2Si$ (M^+) 250.1389, found 250.1393. ^1H and ^{13}C NMR, IR, and mass spectral data are consistent with that previously reported for the synthesis of **5** by an alternative method, see ref 36.

Compound 7: Diyne **5** (169 mg, 0.675 mmol) and benzyl azide (89.5 mg, 0.672 mmol) were used as per the general procedure and yielded **7** (86 mg, 82%) as a white powder. Mp 224−227 °C (lit.[17f] mp 228 °C). IR ($CHCl_3$, cast) 3131, 3075, 1458 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.98 (s, 2H), 7.38−7.33 (m, 6H), 7.29−7.26 (m, 4H), 5.54 (s, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 134.3, 129.2, 128.9, 128.2, 54.5 (two quaternary carbons not observed because of limited solubility). ESI HRMS m/z calcd for $C_{18}H_{17}N_6$ ([M + H]$^+$) 317.1509, found 317.1509.

Compound 8: Compound **9**[37] (188 mg, 0.591 mmol) and benzyl azide (170 mg, 1.13 mmol) were used as per the general procedure and yielded **8** (206 mg, 79%) as an orange powder. Mp > 200 °C. IR ($CHCl_3$, cast) 3119, 3072, 3036, 2924, 2853, 1479 cm^{-1}; ^1H NMR (500 MHz, CD_2Cl_2) δ 7.69 (s, 2H), 7.51 (s, 4H), 7.41−7.37 (m, 6H), 7.30 (d, J = 7.5 Hz, 4H), 5.55 (s, 4H); a useful ^{13}C NMR spectrum could not be obtained due to its low solubility. EIMS m/z 440.2 (M^+, 7), 384.2 ([M − N_4]$^+$, 7); HRMS m/z calcd for $C_{28}H_{20}N_6$ (M^+) 440.1750, found 440.1743.

Compound 10b: Triyne **11b**[37] (0.116 g, 0.502 mmol) and benzyl azide (0.061 g, 0.46 mmol) were used as per the general procedure and yielded **3h** (0.062 g, 47%) as a white crystalline solid. Mp 58−60 °C. R_f = 0.27 (hexanes/ethyl acetate 9:1). IR (microscope) 3096 (s), 3054 (s), 2952 (s), 2935 (s), 2850 (s), 2250 (w), 2162 (w), 1604 (s), 1496 (s) cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.55 (s, 1H), 7.40−7.36 (m, 3H), 7.29−7.26 (m, 2H), 5.52 (s, 2H), 2.34 (t, J = 7.0 Hz, 2H), 1.56 (quint, J = 7.6 Hz, 2H), 1.44−1.36 (m, 2H), 1.34−1.26 (m, 4H), 0.89 (t, J = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 134.0, 130.7, 129.2, 129.0, 128.1, 127.0, 86.0, 78.0, 64.6, 63.5, 54.4, 31.2, 28.5, 28.0, 22.5, 19.5, 14.0. EIMS m/z 291.2 (M^+, 1), 234.1 ([M − N_2 − C_2H_5]$^+$, 18), 91.1 ([C_7H_7]$^+$, 100). HRMS calcd m/z for $C_{19}H_{21}N_3$(M^+) 291.1735, found 291.1730.

Compound 10h: Compound **11h**[37] (40 mg, 0.132 mmol) and benzyl azide (17 mg, 0.128 mmol) were used as per the general procedure to yield **10h** (26 mg, 56%) as a yellow oil. R_f = 0.8 (hexanes/EtOAc, 1:1). IR (cast film, CH_2Cl_2) 3138 (w), 3091 (w), 3067 (w), 3034 (w), 2945 (s), 2891 (s), 2866 (s), 2219 (m), 2105 (m), 1461 (s); ^1H NMR (400 MHz, $CDCl_3$) δ 7.59 (s, 1H), 7.42−7.36 (m, 3H), 7.2 −7.24 (m, 2H), 5.53 (s, 2H), 1.09 (s, 21H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 134.0, 130.4, 129.4, 129.2, 128.3, 127.6, 89.8, 88.9, 78.3, 64.6, 54.6, 18.7, 11.4. EIMS m/z 363.2 (M^+, 1), 335.2 ([M − N_2]$^+$, 100). EI HRMS calcd for $C_{22}H_{29}N_3Si$ 363.2131, found 363.2132.

Compound 15: To a solution of **15**[31] (20 mg, 0.023 mmol) in THF (8 mL) at rt was added CsF (4 mg, 0.03 mmol) and the mixture was stirred at rt until TLC analysis showed complete desilylation, ca. 20 min. CH_2Cl_2 (15 mL) and saturated aq NH_4Cl (10 mL) were added, the organic layer was separated, washed with saturated aq NH_4Cl (10 mL), dried over ($MgSO_4$), and filtered, and the solvent was reduced in vacuo. The resulting product was plugged through silica (hexanes/CH_2Cl_2 10:1), and the solvent was removed. To this crude product was added THF (1 mL), H_2O (3 drops), benzyl azide (3 mg, 0.02 mmol),

(35) Liesbet Jongen, L.; Goderis, B.; Dolbnya, I.; Binnemans, K. *Chem. Mater.* **2003**, *15*, 212–217.

(36) Kendall, J.; McDonald, R.; Ferguson, M. J.; Tykwinski, R. R. *Org. Lett.* **2008**, *10*, 2163–2166.

(37) Eisler, S.; Chahal, N.; McDonald, R.; Tykwinski, R. R. *Chem.—Eur. J.* **2003**, *9*, 2542–2550.

$CuSO_4 \cdot 5H_2O$ (10 mg, 0.040 mmol), ascorbic acid (10 mg, 0.057 mmol), and NEt_3 (1 drop); the reaction was stirred at rt until TLC analysis confirmed the absence of starting material. CH_2Cl_2 (15 mL) and H_2O (15 mL) were added, the organic layer was separated, washed with H_2O (10 mL), dried over $MgSO_4$, and filtered, and the solvent was reduced in vacuo. The crude product was purified by column chromatography (silica gel, hexanes/CH_2Cl_2 1:2) to afford **14** (4 mg, 24%) as a yellow solid. $R_f = 0.50$ (1:2 hexanes/CH_2Cl_2). IR (microscope) 3067 (w), 2963 (s), 2905 (w), 2868 (w), 2214 (w), 2146 (w), 1591 (w) cm^{-1}; ^1H NMR (500 MHz, CD_2Cl_2) δ 7.73 (s, 1H), 7.41−7.38 (m, 3H), 7.32 (t, $J = 1.8$ Hz, 3H), 7.29−7.27 (m, 2H), 6.95 (d, $J = 1.8$ Hz, 6H), 5.53 (s, 2H), 1.21 (s, 54H); ^{13}C NMR (125 MHz, CD_2Cl_2) δ 150.4, 143.3, 134.4, 129.2, 129.05, 128.95, 128.9, 128.2, 123.5, 121.6, 87.0, 77.4, 68.8, 68.4, 65.7, 65.0, 62.0, 60.4, 57.3, 54.4, 34.7, 31.0. ESI HRMS calcd m/z for $C_{60}H_{72}N_3$ ($[M + H]^+$) 834.5726, found 834.5708.

Acknowledgment. This work has been generously supported by the University of Alberta and the Natural Sciences and Engineering Research Council of Canada (NSERC) through the Discovery and Nano Innovation Platform (NanoIP) grant programs. T.L. thanks the University of Alberta for a Dissertation Fellowship and Edward Ha for help in the reaction to form compound **10c**.

Supporting Information Available: General experimental details and copies of ^1H and ^{13}C NMR spectra for new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.