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# Synthesis and Characterization of Cyclic Alkyl Tetraynes

**Andreea Spantulescu,[†] Thanh Luu,[†] Yuming Zhao,[‡] Robert McDonald,[†] and Rik R. Tykwinski*,[†]**

*Department of Chemistry, University of Alberta, Edmonton AB T6G 2G2, Canada, and Department of Chemistry, Memorial University of Newfoundland, St. John's, NL A1B 3X7, Canada*

*rik.tykwinski@ualberta.ca*

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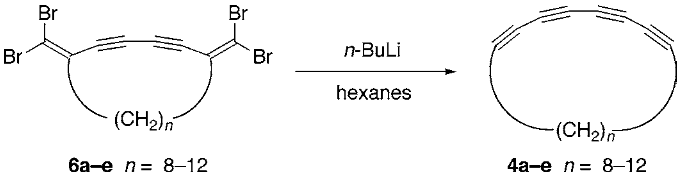
## ABSTRACT



**Cyclic (4a–e) and linear (10) tetraynes have been studied. Macrocycles 4a–e are unstable to isolation as neat compounds, but 4b–e have been characterized in solution. $^{13}$C NMR spectroscopy shows a consistent downfield shift of the acetylenic resonances of 4c–e as ring strain increases. UV–vis spectroscopy demonstrates that ring strain has little effect on the HOMO–LUMO gap. X-ray crystallography of tetrabromoolefin 6b confirms the monomeric constitution of the precursors.**

The discovery of $C_{60}$ as a stable carbon allotrope proved to be an invigorating step in acetylene chemistry when cyclic polyynes were invoked as possible intermediates in the formation of fullerenes.[1] The rational synthesis of cyclo[*n*]carbons (**1**, Figure 1) has been targeted by several groups in ongoing efforts to decipher the enigma of fullerene formation. These elusive carbon-rich molecules are also predicted to have interesting electronic properties as a result of their conjugated framework.[2] To date, synthetic efforts have succeeded in the gas-phase formation of a number of derivatives, and species as small as cyclo-$C_{12}$ and as large as cyclo-$C_{36}$ have been generated from the appropriate precursors.[3,4] A natural question that arises when considering cyclic polyynes such as cyclo[*n*]carbons is, simply, will they be stable? Numerous studies have shown that 1,3-butadiynyl segments can be "bent" to an amazing extent, while still providing stable or reasonably stable products.[5,6] Less is known about cyclic triynes,[7] although recent studies by the groups of Tobe[5,8a,b] and Haley[8c,d] are shedding light on this question. Finally, a few cyclic tetraynes have been reported,[7b,9]

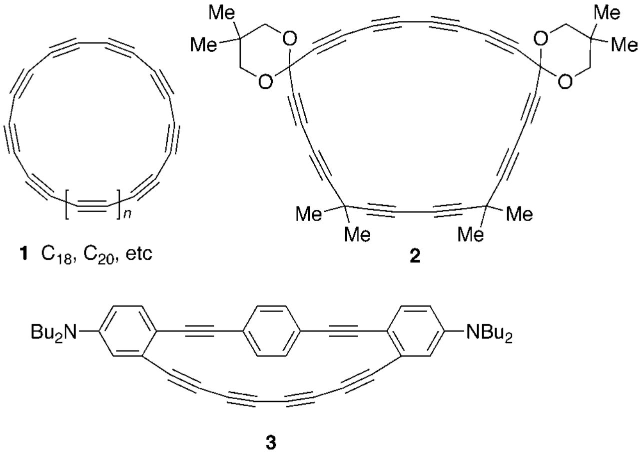


**Figure 1.** Cyclo[*n*]carbons **1** and examples of strained tetraynes **2** and **3**.

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[†] University of Alberta.

[‡] Memorial University of Newfoundland.

(1) (a) Goroff, N. S. *Acc. Chem. Res.* **1996**, *29*, 77−83. (b) Faust, R. *Angew. Chem., Int. Ed.* **1998**, *37*, 2825−2828.

(2) Diederich, F.; Rubin, Y. *Angew. Chem., Int. Ed. Engl.* **1992**, *31*, 1101−1123.

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including several with some measure of strain in their structure, most notably **2**[10] and **3**.[11]

Our interest in polyynes led us to consider whether simple, cyclic alka-1,3,5,7-tetraynes could be synthesized and studied as model systems for larger unsaturated molecules such as the cyclo[*n*]carbons. With the ultimate goal of exploring kinetic stability and spectroscopic characteristics of such molecules as a function of ring strain, we report herein our preliminary efforts in the study of cyclic alkyl tetraynes.

Two potential routes toward the desired tetraynes **4** were envisioned (Figure 2). Route A would rely on the initial synthesis of precursor terminal diynes **5**, which could then be subjected to an oxidative acetylenic homocoupling reaction. Two issues caused concern. First, it was anticipated that the formation and manipulation of the precursors **5** would be challenging, given the fact that terminal diynes are often unstable.[12] Second, the ring strain encountered in the ring-forming step from **5** to **4** might hinder product formation. Thus, the alternative, route B, was employed, using a 2-fold Fritsch−Buttenberg−Wiechell (FBW) rearrangement to assemble the tetrayne framework of **4** from dibromoolefinic precursors **6**.[13]

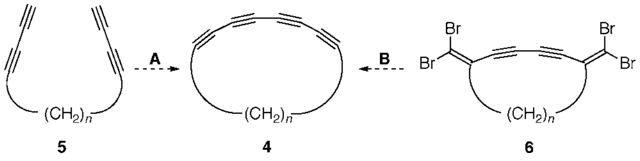
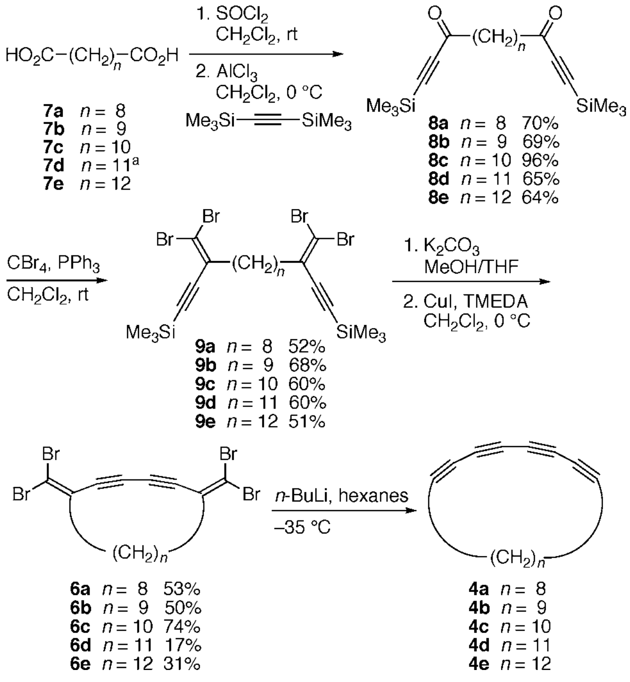


**Figure 2.** Potential synthesis of tetraynes **4**. Route A would use an oxidative homocoupling reaction, while Route B would use the Fritsch−Buttenberg−Wiechell rearrangement.

Cyclic tetraynes **4** (Scheme 1) were formed from dicarboxylic acids **7**, beginning with acyl chloride formation followed by a Friedel−Crafts acylation reaction[14] with bis(trimethylsilyl)acetylene (BTMSA) in the presence of $AlCl_3$. The resulting diketones **8a**−**e** were obtained in satisfactory yields, and a subsequent Corey−Fuchs reaction[15] yielded tetrabromoolefins **9a**−**e**, also in reasonable yields. Removal of the two trimethylsilyl groups ($K_2CO_3$, MeOH) from **9a**−**e** afforded enynes that showed only limited stability in their neat form. Thus, following workup, these products were taken on to the macrocyclization step without further purification.

**Scheme 1**



[a] $PCl_3$ was used instead of $SOCl_2$ to form the acyl chloride.

The formation of cycles **6a**−**e** under Hay conditions[16] was more difficult than anticipated due to competition from intermolecular cyclization and from byproducts that appeared

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(3) (a) Diederich, F.; Gobbi, L. *Top. Curr. Chem.* **1999**, *201*, 43−79. (b) Tobe, Y.; Wakabayashi, T. In *Polyynes: Synthesis, Properties and Applications*; Cataldo, F., Ed.; CRC Press: Taylor & Francis: 2006; p 99. (c) Tobe, Y.; Wakabayashi, T. In *Acetylene Chemistry: Chemistry, Biology and Material Science*; Diederich, F., Stang, P. J., Tykwinski, R. R., Eds.; Wiley-VCH: Weinheim, 2005; p 387. (d) Tobe, Y.; Matsumoto, H.; Naemura, K.; Achiba, Y.; Wakabayashi, T. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 1800−1802.

(4) (a) Tobe, Y.; Umeda, R.; Iwasa, N.; Sonoda, M. *Chem. Eur. J.* **2003**, *9*, 5549−5559. (b) Diederich, F.; Rubin, Y.; Chapman, O. L.; Goroff, N. S. *Helv. Chim. Acta* **1994**, *77*, 1441−1457.

(5) For an excellent review of strained dehydrobenzannulenes, see: Hisaki, I.; Sonoda, M.; Tobe, Y. *Eur. J. Org. Chem.* **2006**, 833−847.

(6) See, for example: Eisler, S.; McDonald, R.; Loppnow, G. R.; Tykwinski, R. R. *J. Am. Chem. Soc.* **2000**, *122*, 6917−6928 and references therein.

(7) To our knowledge, only two reports of cyclic alkyl triynes have appeared; see: (a) Dale, J.; Hubert, A. J.; King, G. S. D. *J. Chem. Soc.* **1963**, 73−86. (b) Bergel'son, L. D.; Molotkovskii, Y. G. *Bull. Acad. Sci. USSR. Div. Chem. Sci. (Engl. Transl.)* **1963**, 94−98.

(8) (a) Hisaki, I.; Eda, T.; Sonoda, M.; Niino, H.; Sato, T.; Wakabayashi, T.; Tobe, Y. *J. Org. Chem.* **2005**, *70*, 1853−1864. (b) Tobe, Y.; Ohki, I.; Sonoda, M.; Niino, H.; Sato, T.; Wakabayashi, T. *J. Am. Chem. Soc.* **2003**, *125*, 5614−5615. (c) Bell, M. L.; Chiechi, R. C.; Johnson, C. A.; Kimball, D. B.; Matzger, A. J.; Wan, W. B.; Weakley, T. J. R.; Haley, M. M. *Tetrahedron* **2001**, *57*, 3507−3520. (d) Wan, W. B.; Chiechi, R. C.; Weakley, T. J. R.; Haley, M. M. *Eur. J. Org. Chem.* **2001**, 3485−3490.

(9) See, for example: (a) Kivala, M.; Mitzel, F.; Boudon, C.; Gisselbrecht, J.-P.; Seiler, P.; Gross, M.; Diederich, F. *Chem. Asian J.* **2006**, *1*, 479−489. (b) Heuft, M. A.; Collins, S. K.; Fallis, A. G. *Org. Lett.* **2003**, *5*, 1911−1914. (c) Haley, M. M.; Bell, M. L.; Brand, S. C.; Kimball, D. B.; Pak, J. J.; Wan, W. B. *Tetrahedron Lett.* **1997**, *38*, 7483−7486.

(10) Leibrock, B.; Vostrowsky, O.; Hirsch, A. *Eur. J. Org. Chem.* **2001**, 4401−4409.

(11) Heuft, M. A.; Collins, S. K.; Yap, G. P. A.; Fallis, A. G. *Org. Lett.* **2001**, *3*, 2883−2886.

(12) Terminal diynes can, however, be stable; see: West, K.; Wang, C.; Batsanov, A. S.; Bryce, M. R. *J. Org. Chem.* **2006**, *71*, 8541−8544.

(13) For recent examples of polyyne formation using the FBW rearrangement, see: (a) Chalifoux, W. A.; Tykwinski, R. R. *Chem. Rec.* **2006**, *6*, 169−182. (b) Luu, T.; Elliott, E.; Slepkov, A. D.; Eisler, S.; McDonald, R.; Hegmann, F. A.; Tykwinski, R. R. *Org. Lett.* **2005**, *7*, 51−54. (c) Eisler, S.; Slepkov, A. D.; Elliott, E.; Luu, T.; McDonald, R.; Hegmann, F. A.; Tywkinski, R. R. *J. Am. Chem. Soc.* **2005**, *127*, 2666−2676. (d) Tobe, Y.; Umeda, R.; Iwasa, N.; Sonoda, M. *Chem. Eur. J.* **2003**, *9*, 5549−5559.

(14) Walton, D. R. M.; Waugh, F. *J. Organomet. Chem.* **1972**, *37*, 45−56.

(15) (a) Ramirez, F.; Desai, N. B.; McKelvie, N. *J. Am. Chem. Soc.* **1962**, *84*, 1745−1747. (b) Corey, E. J.; Fuchs, P. L. *Tetrahedron Lett.* **1972**, 3769−3772.

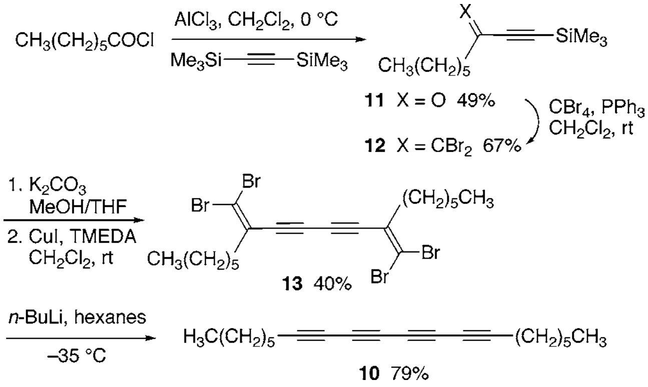
(16) Hay, A. S. *J. Org. Chem.* **1962**, *27*, 3320−3321.

to result from Castro−Stephens chemistry at the dibromoolefin moiety.[17] After significant experimentation with concentration and temperature for this reaction, macrocycles **6a**−**e** could be produced in useful quantities, albeit yields over the two steps remained variable.[18]

With the tetrabromoolefins **6a**−**e** in hand, conversion into the desired cyclic tetraynes **4a**−**e** was explored using the FBW rearrangement. The dibromoolefin was dissolved in dried hexanes, cooled to −35 °C, and *n*-BuLi slowly added. After the reaction mixture was warmed to ca. −5 °C, it was quenched. For macrocycles **4b**−**e**, the crude reaction mixture was concentrated, passed through a plug of silica gel to remove baseline material, concentrated again, and finally subjected to column chromatography (silica gel, hexanes) to provide pure samples for analysis. Samples with 10−12 methylene linkers (**4c**−**e**) were sufficiently stable to allow for $^{1}$H and $^{13}$C NMR, IR, and UV−vis spectroscopic characterization. The next smallest macrocycle, **4b**, could not be analyzed by NMR spectroscopy due to decomposition, although UV−vis spectroscopy was successful. All attempts to form and characterize macrocycle **4a** from **6a** were unsuccessful due to the instability of the product. None of the products **4b**−**e** was sufficiently stable to isolate as a neat sample,[19] and yields of the rearrangement step could not be determined.

Acyclic tetrayne **10**[11] was formed in the same fashion and served as an unstrained model compound (Scheme 2).[20,21]

**Scheme 2**



Heptanoyl chloride was subjected to Friedel−Crafts acylation with BTMSA to give ketone **11**, which was easily converted to **12**. Desilylation to generate a terminal alkyne and homocoupling gave tetrabromide **13** in 40% yield. The acyclic tetrayne **10** was then obtained via rearrangement and is a stable oil that can be handled neat for short periods of time under ambient conditions and stored under refrigeration without appreciable decomposition.

Single crystals of tetrabromoolefin **6b** suitable for X-ray crystallographic analysis were grown by slow evaporation of a CDCl$_3$ solution at 4 °C (Figure 3).[22] First and foremost, this structure provides confirmation of intramolecular ring closure to a “monomeric” structure during the conversion of **9b** → **6b**. In the solid state, several interesting features are observed. The structure of compound **6b** is quite unsymmetrical. The two alkylidene bond angles C(1)−C(2)−C(4) and C(7)−C(8)−C(10) differ substantially, at 113.9(5)° and 118.3(5)°, respectively, and convey some evidence of ring strain present in the molecule. Each acetylene unit of the diyne framework is distorted from linearity, with C≡C−C bond angles that range from 168.6(6)° to 175.4(6)°, with an average of 173.0°.

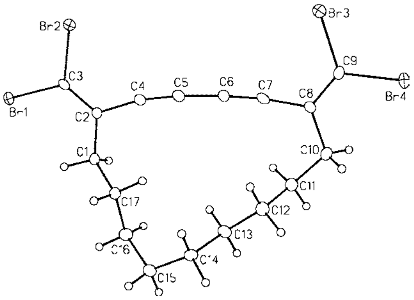


**Figure 3.** ORTEP drawing of compound **6b** (20% probability level). Selected bond angles (deg): C(2)−C(4)−C(5) 168.6(6), C(4)−C(5)−C(6) 174.1(6), C(5)−C(6)−C(7) 175.4(6), C(6)−C(7)−C(8) 174.1(6).

It was not possible to obtain single crystals of the cyclic tetraynes **4a**−**e** for crystallographic analysis due to their kinetic instability. Thus, bond angles were estimated using semiempirical calculations at the AM1 level.[23] While compounds **4b** and **4e** are approximately $C_2$ symmetric, the optimized structures of the other three cycles are unsymmetrical, as observed for the precursor **6b**. Thus, rather than concentrating on individual angles, the average alkyne bond angle across tetrayne framework for **4a**−**e** has been used as an approximation of the overall strain across the acetylenic skeleton (Table 1).[18] It is clear that even with only moderate ring strain, the tetraynes **4a**−**e** show drastically reduced kinetic stability in comparison to, for example, diynes. This is highlighted by the fact that there are numerous examples of strained diynes with alkynyl angles of <160° that show

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(17) Stephens, R. D.; Castro, C. E. *J. Org. Chem.* **1963**, *28*, 3313−3315.

(18) See the Supporting Information for details.

(19) Decomposition of **4a**−**e** upon concentration typically gives rise to a reddening of the solution followed by the formation of an intractable black solid. While the mechanism is not understood, these observations are consistent with an intermolecular cross-linking that gives rise to a material with extended conjugation, as reported for the solid-state behavior of tetraynes; see, for example: Sarkar, A.; Okada, S.; Matsuzawa, H.; Matsuda, H.; Nakanishi, H. *J. Mat. Chem.* **2000**, *10*, 819−828.

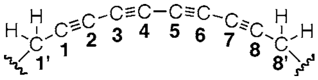
(20) Based on a previously reported protocol, see: Eisler, S. Ph.D. Thesis, University of Alberta 2003.

(21) For examples of other alkyl tetraynes, see: (a) Balova, I. A.; Remizova, L. A. *J. Org. Chem. USSR* **1994**, *30*, 213−215. (b) Armitage, J. B.; Jones, E. R. H.; Whiting, M. C. *J. Chem. Soc.* **1952**, 2014−2018.

(22) Crystal data for **6b**: $C_{17}H_{18}Br_4$, $M = 541.95$; orthorhombic space group *Pbca* (No. 61); $P_c = 2.007$ g cm$^{-3}$; $a = 6.3174(7)$ Å, $b = 23.129(3)$ Å, $c = 24.546(3)$ Å; $V = 3586.5(7)$ Å$^3$; $Z = 8$; $\mu = 8.968$ mm$^{-1}$. Final $R(F) = 0.0393$ (2187 observations with $[F_o^2 \geq 2\sigma(F_o^2)]$); $wR_2(F^2) = 0.0856$ for 190 variables and 3161 data with $F_o^3 \geq -3\sigma(F_o^2)$; CCDC 667863.

(23) Geometry minimization, HyperChem Pro. 5.11.

**Table 1.** Calculated Average Bond Angles and $^{13}$C NMR and UV Spectroscopic Data for Compounds **4a**−**e** and **10**



| compd | bond angle[a] (deg) | $\delta_C$ for C(**1**,**8**)[b] (ppm) | $\delta_C$ for C(**4**,**5**)[b] (ppm) | $\lambda_{max}$ values region 1 (nm) | $\lambda_{max}$ values region 2[c] (nm) |
|---|---|---|---|---|---|
| **4a** | 163.1 | N/A | N/A | N/A | N/A |
| **4b** | 166.3 | N/A | N/A | 224, 234, 246 | 298, 317, 339 |
| **4c** | 166.5 | 102.5 | 68.0 | 222, 233, 244 | 297, 315, 339, 365 |
| **4d** | 168.2 | 96.6 | 66.0 | 221, 232, 244 | 294, 314, 338, 364 |
| **4e** | 170.0 | 91.8 | 64.2 | 220, 231, 243 | 293, 312, 335, 360 |
| **10** | 180.0 | 80.5 | 60.7 | 217, 228, 240 | |

[a] Averaged alkyne bond angle (C1′ to C8′), based on AM1 calculations. [b] Measured in CDCl$_3$. [c] Given the extremely low intensity of these signals, there is larger error in these values than would be expected, ca. ±2 nm.

sufficient kinetic stability to be handled without special precautions.[6]

$^{13}$C NMR spectra of cyclic compounds **4c**−**e** and acyclic compound **10** were obtained and analyzed. Unlike the calculated structures for **4c**,**d**, which lacked $C_2$ symmetry, the $^{13}$C spectrum of each macrocycle confirmed $C_2$ symmetry in solution, showing four acetylenic resonances and five (for **4c**) or six (for **4d**,**e**) methylene resonances in the alkyl region. The C1 resonance (Table 1) could be confirmed through analysis of HMBC spectra and showed correlations to both the propargylic and homopropargylic protons. The C4 acetylenic carbon could also be tentatively assigned on the basis that it showed the weakest or no correlations in the HMBC spectra. Unfortunately, C2 and C3 showed similar long-range coupling in the HMBC spectra and, therefore, could not be assigned. Both the C1 and C4 resonances show a monotonic downfield shift as ring strain is increased, and this effect is much more substantial for C1 than for C4. Such trends have been previously established for the $^{13}$C resonances of diynes as a function of ring strain.[6,24] Furthermore, both theoretical calculations and experimental studies have outlined this effect recently for the $^{13}$C chemical shifts of diphenyl triynes.[5]

The UV−vis spectra of **4b**−**e** and **10** (Figure 4, Table 1) show a series of strong absorptions with accompanying vibronic structure in the range 210−250 nm (region 1). Most significantly, these data show that the $\lambda_{max}$ values do not differ appreciably as a function of strain. Cyclic derivatives **4b**−**e** also show a series of very weak absorptions at longer wavelength between 265−365 nm (region 2; these signals are vanishingly present for **10**), which has been previously observed for some acyclic alkyl tetraynes[21b] and triynes.[25] Molar absorptivities for **4b**−**e** were not, unfortunately, obtainable due to the instability of the cyclic samples.

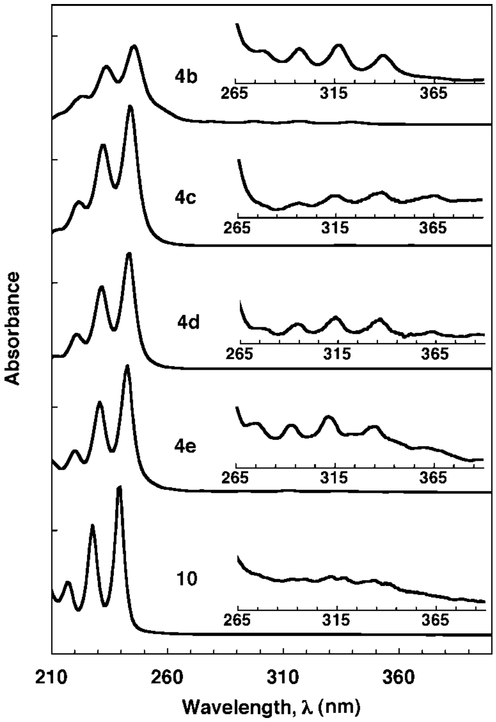


**Figure 4.** UV−vis absorption spectra for **4b**−**e** and **10** (in hexanes). The inset shows a series of low energy absorption with drastically reduced molar absorptivity from 265 to 365 nm.

In conclusion, we have demonstrated the synthesis of cyclic tetraynes using an FBW rearrangement as a key step. Evidence of strain in the tetrayne segment of **4c**−**e**, in comparison to acyclic **10**, is manifested in $^{13}$C chemical shifts of the alkynyl sp-hybridized carbons, which move to lower field as strain is increased. Surprisingly, UV−vis absorption spectroscopy shows only subtle changes in $\lambda_{max}$ values for **4b**−**e** as a function of strain. Perhaps most significant is the dramatic kinetic instability observed for these compounds. Even the least strained molecule **4e**, with an average alkyne bond angle of 170°, is unstable to isolation as a neat compound.

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**Supporting Information Available:** Experimental procedures, synthetic and spectroscopic data for new compounds, and CIF file (**6b**). This material is available free of charge via the Internet at http://pubs.acs.org.

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(24) Gleiter, R.; Kratz, D.; Schäfer, W.; Schehlmann, V. *J. Am. Chem. Soc.* **1991**, *113*, 9258−9264.

(25) Armitage, J. B.; Jones, E. R. H.; Cook, C. L.; Whiting, M. C. *J. Chem. Soc.* **1952**, 2010−2014.