JOC*Article*

# Halo-Enediynes: Probing the Electronic and Stereoelectronic Contributions to the Bergman Cycloaromatization

Gary W. Plourde II, Philip M. Warner, Dennis A. Parrish, and Graham B. Jones*

*Department of Chemistry, Northeastern University, Boston, Massachusetts 02115*

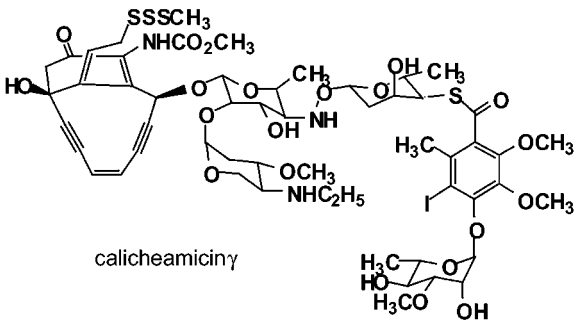
*gr.jones@neu.edu*

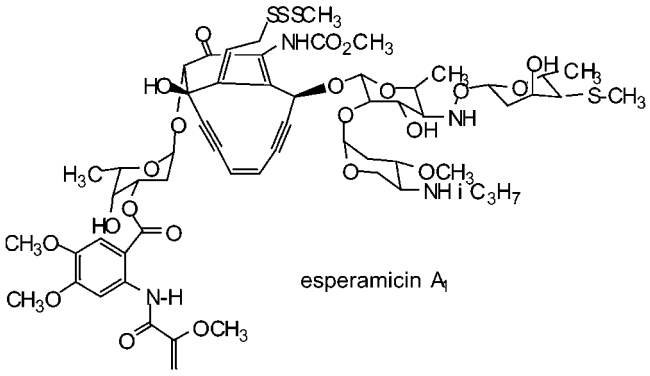
*Received March 26, 2002*

A series of halogen-substituted cyclic enediynes were prepared with use of carbenoid coupling strategy. DFT analysis, initially used to identify synthesis candidates, was also employed to rationalize the propensity for cycloaromatization of the compounds. In all cases studied the halogen atom had a strongly retardative effect on the thermal Bergman cycloaromatization reaction. The isolation of the first C-9 monochloroenediyne is noteworthy, and may find application in prodrug design.

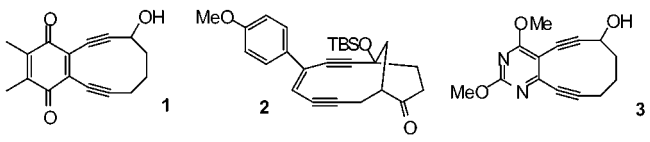
Interest in the enediyne antibiotics stems from their observed antitumoral activity, as exemplified by calicheamicin and esperamicin, both of which have entered clinical trials.[1] The enediynes are not biologically active per se, but undergo cycloaromatization of the enediyne core to yield cytotoxic diyl radicals which subsequently interact with macromolecule targets.[2] In the case of cyclic C-10 enediynes, this process is generally referred to as the Bergman cycloaromatization, following the pioneering discoveries made on related hex-3-en-1,5-diynes.[3] The naturally occurring enediynes all possess triggering functions, which become activated in vitro to promote the Bergman cycloaromatization.[2,4] This typically involves a conformational change in the architecture of the enediyne such that on relief of strain, the alkyne termini adopt a more favorable orientation for the cycloaromatization event. In this manner, a strained enediyne that is indefinitely stable at ambient temperature can be converted to a species with a half-life of seconds. Accordingly, much research has been conducted to exploit this method of activation together with investigation of alternate modes of triggering.[4]

Though strain relief plays a commanding role in the cycloaromatization profiles of many natural and synthetic enediynes,[5] a variety of other factors can influence the process, including subtle electronic effects. In the case




of synthetic C-10 enediyne cores, the electronic contribution to Bergman cyclization was first examined with quinone enediyne **1**.[6] Bioreduction of the quinone to the hydroquinone form serves to stabilize the enediyne




(1) Schor, N. F. In *Cancer Therapeutics: Experimental and Clinical Agents*; Teicher, B., Ed.; Humana Press: Totowa, NJ, 1996; pp 229−240. Schmitt, D. A.; Kisanuki, K.; Kimura, S.; Oka, K.; Pollard, R. B.; Maeda, H.; Suzuki, F. *Anticancer Res.* **1992**, *12*, 2219. Takahashi, T.; Yamaguchi, T.; Kitamura, K.; Noguchi, A.; Mitsuyo, H.; Otsuji, E. *Jpn. J. Cancer Res.* **1993**, *84*, 976. Lee, M. D.; Durr, F. E.; Hinman, L. H.; Haman, P. R.; Ellestad, G. A. In *Advances in Medicinal Chemistry*; Maryanoff, B. E., Maryanoff, C. A., Eds.; Jai Press: Greenwich, CT, 1993; Vol. 2.

(2) Xi, Z.; Goldberg, I. DNA damaging enediyne compounds. In *Comprehensive Natural Products Chemistry*; Barton, D. H. R., Nakanishi, K., Eds.; Pergamon: Oxford, UK, 1999; Vol. 7, p 553. Smith, A. L.; Nicolaou, K. C. *J. Med. Chem.* **1996**, *39*, 2103. Grissom, J. W.; Gunawardena, G. U.; Klingberg, D.; Huang, D. *Tetrahedron* **1996**, *52*, 6453.

(3) Bergman, R. G. *Acc. Chem. Res.* **1973**, *6*, 25.

(4) Reviews of enediyne prodrugs: Maier, M. E. *Synlett* **1995**, 13. Jones, G. B.; Fouad, F. S. *Curr. Pharm. Des.* **2002**, *8*, in press.

(5) Magnus, P.; Fortt, S.; Pitterna, T.; Snyder, J. P. *J. Am. Chem. Soc.* **1990**, *112*, 4986.

(6) Nicolaou, K. C.; Smith, A. L.; Wendeborn, S. V.; Hwang, C. K. *J. Am. Chem. Soc.* **1991**, *113*, 3106.

10.1021/jo025763e CCC: $22.00 
Published on Web 06/20/2002

**TABLE 1. Theoretically Calculated Bergman Cyclization Barriers for Substituted Enediynes 4, and 7[a]**

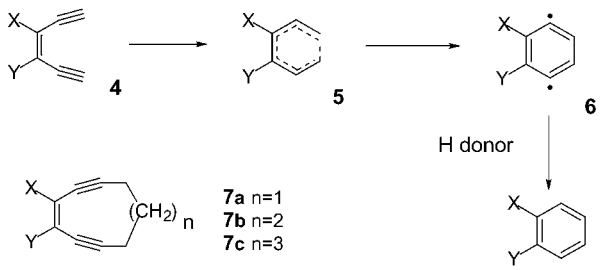
| | *d* | | | | |
|---|---|---|---|---|---|
| comnpd | enediyne[b] | transition state[b] | $\Delta H^{I}$ [c] | $\Delta\Delta H^{IThinSpace}$ [d] | refs |
| **4**, X = Y = H | 4.546 | 2.078 | 27.4 | (0.0) | 10−13 |
| **4**, X = F, Y = H | 4.544 | 2.039 | 29.1 | 1.7 | 10 |
| **4**, X = Cl, Y = H | 4.477 | 2.046 | 28.9 | 1.5 | 10 |
| **4**, X = Br, Y = H | 4.494 | 2.050 | 28.9 | 1.5 | this work |
| **4**, X = Y = F | 4.523 | 2.036 | 32.7 | 5.3 | 10 |
| **4**, X = Y = Cl | 4.325 | 2.006 | 31.5 | 4.1 | 10 |
| **4**, X = Y = Br | 4.344 | 2.013 | 30.9 | 3.5 | this work |
| **7a**, X = Y = H | 2.924 | 1.947 | 15.4 | (0.0) | 11, this work |
| **7a**, X = F, Y = H | 2.923 | 1.908 | 17.2 | 1.8 | this work |
| **7a**, X = Cl, Y = H | 2.925 | 1.914 | 17.1 | 1.7 | this work |
| **7a**, X = Br, Y = H | 2.926 | 1.918 | 16.9 | 1.5 | this work |
| **7a**, X = Y = F | 2.934 | 1.924 | 20.2 | 4.8 | this work |
| **7a**, X = Y = Cl | 2.934 | 1.879 | 20.5 | 5.1 | this work |
| **7a**, X = Y = Br | 2.935 | 1.884 | 19.9 | 4.5 | this work |
| **7b**, X = Y = H | 3.405 | 1.973 | 23.7 | (0.0) | 10, 11 |
| **7b**, X = F, Y = H | 3.403 | 1.938 | 26.2 | 2.5 | this work |
| **7b**, X = Cl, Y = H | 3.401 | 1.945 | 26.0 | 2.3 | 10 |
| **7b**, X = Br, Y = H | 3.402 | 1.949 | 25.9 | 2.2 | this work |
| **7b**, X = Y = F | 3.425 | 1.961 | 30.2 | 6.5 | this work |
| **7b**, X = Y = Cl | 3.400 | 1.908 | 30.0 | 6.3 | this work |
| **7b**, X = Y = Br | 3.400 | 1.915 | 29.3 | 5.6 | this work |
| **7b**, X = *syn*-OH, Y = H | 3.400 | 1.937 | 26.0 | 2.3 | this work |
| **7b**, X = *anti*-OH, Y = H | 3.389 | 1.954 | 24.5 | 0.8 | this work |
| **7c**, X = Y = H ($C_s$) | 4.020 | 1.988 | 28.8 | (0.0) | this work |
| **7c**, X = Y = H ($C_2$) | 3.580 | 1.966 | 30.6 | 1.8 | 11, this work |
| **7c**, X = F, Y = H ($C_s$) | 4.010 | 1.945 | 31.2 | 2.4 | this work |
| **7c**, X = Cl, Y = H ($C_s$) | 4.000 | 1.953 | 30.9 | 2.1 | this work |
| **7c**, X = Cl, Y = H ($C_2$) | 3.573 | 1.939 | 33.4 | 4.6 | this work |
| **7c**, X = Y = F ($C_s$) | 4.011 | 1.967 | 34.8 | 6.0 | this work |
| **7c**, X = Y = Cl ($C_s$) | 3.960 | 1.917 | 34.3 | 5.5 | this work |

[a] Calculations are at the BLYP/6-311+G**//BLYP/6-31G* level, with rovibrational corrections from the BLYP/6-31G* frequency results. [b] *d* is the distance, in Å, between the terminal acetylenic carbons of the enediyne unit ("c−d" distance[2]) and the same distance in the cyclization transition state. [c] $\Delta H^{I}$ is the enthalpy difference between the enediyne and its associated cyclization transition state. [d] $\Delta\Delta H^{I}$ is the difference between $\Delta H^{I}$ for a substituted case and its cognizant unsubstituted parent.

toward cycloaromatization, constituting a form of redox-activation. Another interesting example is the bicyclo-[7.3.1] system **2**. Though this enediyne is essentially stable, the parent structure (devoid of the alkoxyaryl group on the vinyl position) cyclizes readily, pointing to a potent electronic contribution.[7] Electronic contributions also play a role in the photo-Bergman cycloaromatization of heterocycle **3**,[8] and it is conceivable that various aryl substituents would have a marked impact on the process.[9] Intrigued by these observations, we undertook a series of DFT studies to try to identify specific vinyl substituents that would have a marked impact on the Bergman process, and that might be amenable to chemical synthesis with methods developed in this and other laboratories.

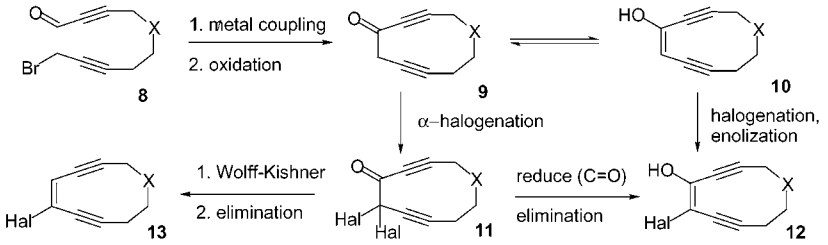
## Theoretical Studies

We have previously conducted a theoretical analysis of the effects of halogens and chalcogens on the cyclization barriers of linear enediynes (e.g. **4** → **5** → **6**, X = F, Cl, OH; Y = H, F, Cl).[10] Since cyclic enediynes represent realistic drug candidates, we undertook a study of several cyclic analogues **7**, including examples with 9, 10-, and 11-membered rings. The data are summarized in Table 1. It is seen that the apparent enediyne-stabilizing effect of halogen is greater for the cyclodecenediyne than for the other cases. As discussed in detail in our earlier paper,[10] the stabilizing effect of halogen can be attributed to a destabilizing interaction between an in-plane halogen lone pair and an in-plane acetylenic filled orbital. This interaction grows as the acetylenes bend inward toward the cyclization transition state. Since the nine-membered ring is already considerably bent, the increase in the destabilizing interaction as the transition state is approached may be muted relative to that of the 10-membered ring interactions. It is also seen that the various halogens have quite similar effects, which probably represents a balance between orbital size matching (between F and C) and atomic size. For synthetic purposes, Br and/or Cl would appear the best choices. The fact that a second halogen has a more than additive inhibitory effect on cyclization may be due to halogen−

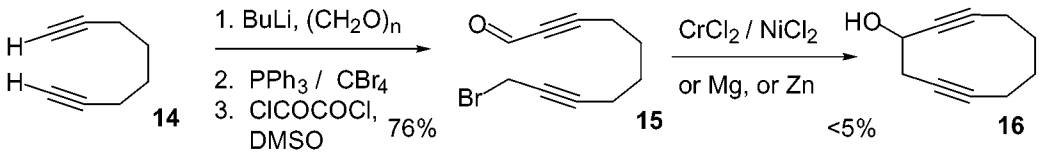



(7) Maier, M. E.; Greiner, B. *Liebigs Ann. Chem.* **1992**, 855.
(8) Choy, N.; Blanco, B.; Wen, J.; Krishan, A.; Russell, K. C. *Org. Lett.* **2000**, *2*, 3761.
(9) Alabugin, I. V.; Manoharan, M.; Kovalenko, S. V. *Org. Lett.* **2002**, *4*, 1119.
(10) Jones, G. B.; Warner, P. M. *J. Am. Chem. Soc.* **2001**, *123*, 2134.

**SCHEME 1. Projected Keto-Diyne Route to Halo and Oxo Enediynes**




**SCHEME 2. Synthesis and Attempted Closure on Bromoaldehyde 15**



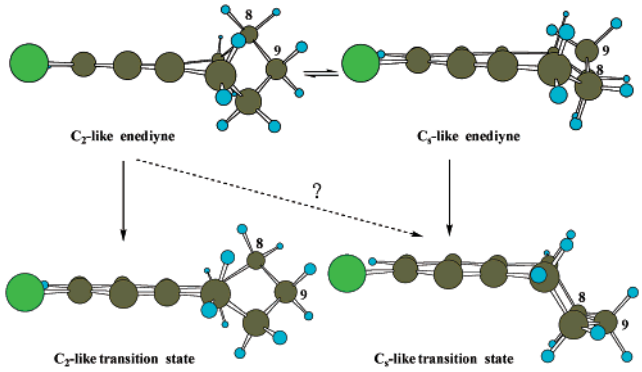
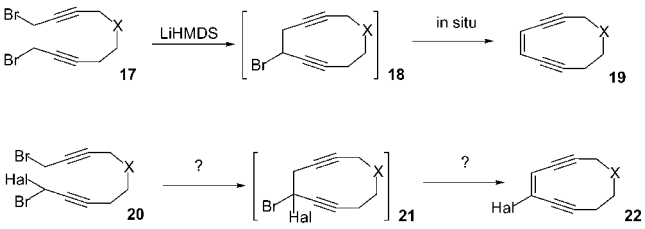




**FIGURE 1.** 3-Chlorocycloundec-3-ene-1,5-diyne and related cyclization transition state conformations.

**SCHEME 3. Intramolecular Carbenoid Route to Unsubstituted Enediynes**




halogen repulsion, which moves them relatively closer to the in-plane acetylenic position.

Hydroxyl substitution leads to two rotational isomers: the ca. 1 kcal/mol more stable anti isomer ($\angle C_4C_3OH = 180°$) has similar reactivity to the parent case, while the syn isomer ($\angle C_4C_3OH = 0°$) has the same inhibitory effect as a halogen. It thus appears that cyclic 3,4-dioxy substitution has the potential to mimic 3,4-dihalo substitution, an interesting possibility for theoretical and experimental pursuit.

An unexpected observation when analyzing the 11-membered-ring cases was the emergence of unusual conformational effects. Prior work elucidated the cyclization of the parent $C_2$ conformer.[11] We also located a 2.6 kcal/mol more stable $C_s$ conformer that has a ca. 0.5 Å longer distance (*d*) between the acetylene termini. Surprisingly, this isomer is associated with a $C_s$ cyclization transition state that lies 4.4 kcal/mol below the $C_2$ transition state; both transition states have a similar *d* value (see Table 1). A similar situation applies to the 3-chlorocycloundec-3-ene-1,5-diyne case, where the $C_s$-like conformer is 2.3 kcal/mol more stable than the $C_2$-like one, and the $C_s$-like transition state is 4.8 kcal/mol below the $C_2$-like one. Figure 1 depicts the structures viewed from the side. The $C_s$-type transition state has a conformation in which C-9 is flipped down relative to the $C_s$-type enediyne conformation. This is made possible by the smaller *d* in the transition state; attempts to find the transition state $C_s$ conformation for the enediyne structure and the enediyne $C_s$ conformation for the transition state structure returned only the conformations shown. It is intriguing that the higher energy $C_2$-type conformer might also cyclize via the $C_s$-type transition state by flipping C-8 downward, but this would not be kinetically distinguishable from $C_s$-type cyclization in these simple systems. A recent X-ray analysis of a tribenzo 11-membered-ring enediyne revealed a $C_s$ structure (although a $C_2$ structure is probably prohibited by the benzo fusions).[14]

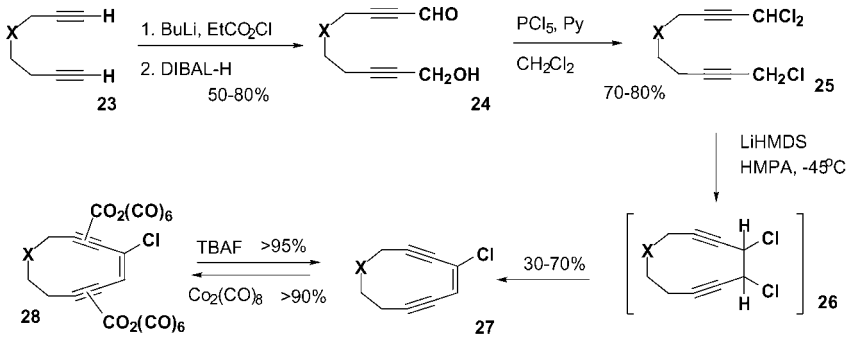
Taken in entirety, the DFT results (Table 1) confirmed that both halo and oxo substituents would be attractive targets for synthesis, with marked changes in properties (relative to parent structure) expected.[15] Moreover, in addition to allowing inductive effects to be gauged, these functional groups might also serve as sites for subsequent introduction of other functional groups to produce libraries of analogues.

**Initial Synthetic Route.** Our original route to the desired oxo and haloenediynes was to involve cyclic ketodiyne **9**, which might be accessed via Ni/Cr coupling of bromoaldehyde **8** and subsequent oxidation.[16] Keto−enol tautomerization in combination with α-halogenation would then give access to a range of substituted enediynes,[17] including **10**−**13** (Scheme 1). Accordingly, a

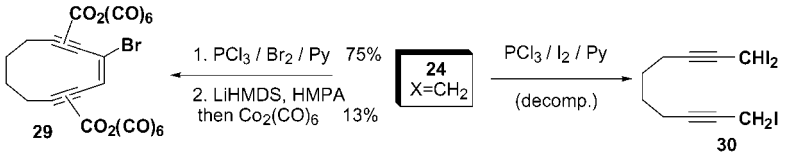
(11) Schreiner, P. R. *J. Am. Chem. Soc.* **1998**, *120*, 4184.

(12) Cramer, C. J. *J. Am. Chem. Soc.* **1998**, *120*, 6261.
(13) Grafenstein, J.; Hjerpe, A. M.; Kraka, E.; Cremer, D. *J. Phys. Chem.* **2000**, *104*, 1748.
(14) Wandel, H.; Wiest, O. *J. Org. Chem.* **2002**, *67*, 388.
(15) Jones, G. B.; Plourde, G. W. *Org. Lett.* **2000,** 2, 1757.
(16) Place, P.; Verniere, C.; Gore, J. *Tetrahedron* **1981**, *37*, 1359.
(17) Majetich, G.; Zhang, Y.; Dreyer, G. *Tetrahedron Lett.* **1993**, *34*, 449.

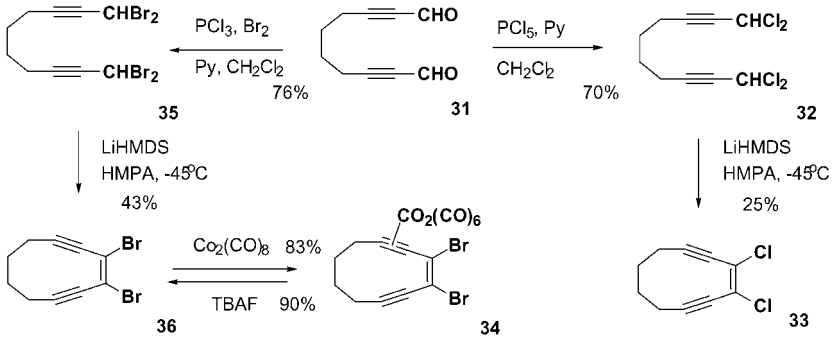
**SCHEME 4. Synthesis of Monochloroenediynes**




**SCHEME 5. Modified Routes to Bromo- and Iodoenediynes**



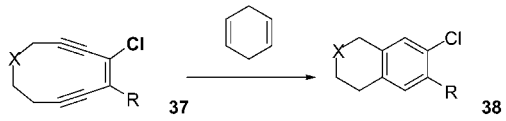

**SCHEME 6. Synthesis of Dihalocyclodecenediynes**




model substrate **15** was prepared from commercially available diyne **14** via hydroxymethylation, monobromination, and oxidation (Scheme 2). Unfortunately, even under a wide range of prescribed conditions, efficient closure to alcohol **16** could not be effected; rather, product decomposition or polymerization occurred. In light of this problem we focused our efforts on modification of a related closure developed in this laboratory for the synthesis of unsubstituted cyclic enediynes.[18] Specifically, intramolecular coupling of propargylic bromides **17** proceeds via intermediate bromodiyne **18** to give enediynes **19** directly.

The process is amenable to synthesis of (9−11)-membered systems,[18] and also oxygenated heterocycles (Scheme 3).[19] Accordingly, we entertained the possibility of modifying this route to incorporate halogen functionality. Since no obvious method for conversion of **17** to **20** is available,[20] we opted to modify the synthesis. Thus, dialkynes **23** (X = −, $CH_2$, or $CH_2CH_2$) were converted to hydroxyaldehydes **24** and then subjected to trichlorination to give **25** (Scheme 4). Intramolecular carbenoid coupling gave enediynes **27** in moderate to good yield, via the presumed intermediates **26**. Though the chloroenediynes proved more thermally stable than their unsubstituted analogues, they were routinely stored as the corresponding cobalt carbonyl complexes **28**, and readily converted back to the desired enediyne on demand with TBAF.[21] Particularly encouraging was isolation of the C-9 chloroenediyne **27**, X = −, the unsubstituted parent of which has never been isolated. Spurred by these findings, we also investigated bromo and iodoenediyne preparation. Tribromination of **24**, X = $CH_2$ was followed by direct conversion to the bromoenediyne. However, this product proved extremely difficult to handle, and instead was isolated as the cobalt complex **29** (Scheme 5). Similar efforts for the iodo enediyne were unsuccessful, since required triiodide **30** decomposed rapidly on forming, precluding purification.

**SCHEME 7. Controlled Cycloaromatization of Chloroenediynes**



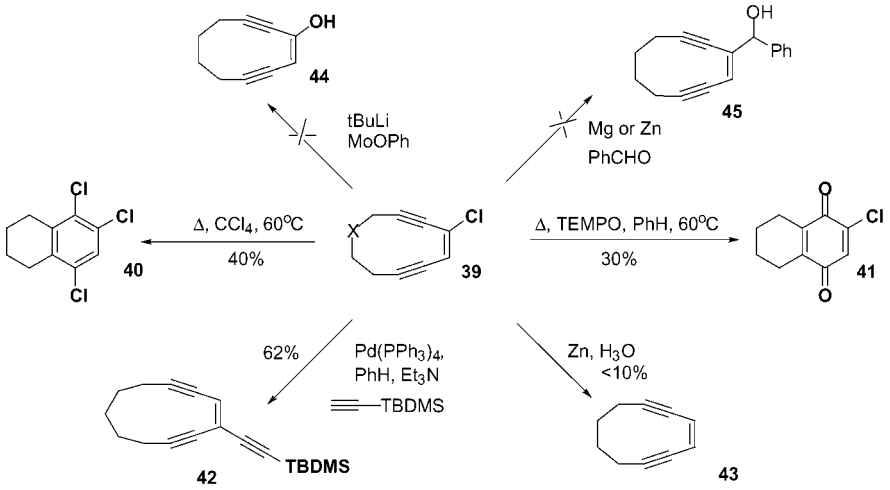

(18) Jones, G. B.; Wright, J. M.; Plourde, G. W., II; Hynd, G.; Huber, R. S.; Mathews, J. E. *J. Am. Chem. Soc.* **2000**, *122*, 1937.

(19) Jones, G. B.; Kilgore, M. W.; Pollenz, R. S.; Li, A.; Mathews, J. E.; Wright, J. M.; Huber, R. S.; Tate, P. L.; Price, T. L.; Sticca, R. P. *Bioorg. Med. Chem. Lett.* **1996**, *6*, 1971.

(20) Jones, G. B.; Mathews, J. E. Synthesis of Carbon Atoms Bearing Halogens and Heteroatoms. In *Organic Functional Group Transformations*; Pergamon: Oxford, UK, 1995; p 35.

(21) Jones, G. B.; Wright, J. M.; Rush, T. M.; Plourde, G. W., II; Kelton, T. F.; Mathews, J. E.; Huber, R. S.; Davidson, J. P. *J. Org. Chem.* **1997**, *62*, 9379.

**SCHEME 8. Synthetic Manipulation of Monochloroenediynes**




In the case of dihaloenediyne synthesis, conditions were again modified: dialdehyde **31**, which was available via hydroxymethylation of **14** followed by oxidation, was initially tetrachlorinated to give **32** (Scheme 6). Carbenoid coupling gave dichloroenediyne **33** directly, its remarkable thermal stability removing the need for cobalt protection. Similarly, tetrabromination of **31** gave **35**, which could be converted, in moderate yield, to dibromoenediyne **36**. Interestingly, all attempts to complex this enediyne resulted in formation of the red monocomplex **34**.

**Determination of half-lives.** With a variety of substrates in hand, and intrigued by the predicted effect of the halogen on cycloaromatization based on calculations, controlled Bergman rearrangements were conducted. Conversion of mono- and dihaloenediynes **37** to the corresponding cycloaromatized arenes **38** (Scheme 7) at various temperatures was assessed by using neat 1,4-cyclohexadiene as hydrogen donor, since it has been reported that the availability of trapping agent has a profound impact on the cycloaromatization profile at low concentration (Table 2).[22] Though labile, the controlled cycloaromatization of the nine-membered enediyne **27**, X = −, is noteworthy, as its parent is unisolable. A clear correlation of half-life with temperature emerged for C-10 monochloroenediyne, whereas in the case of the C-11 monochloroenediyne and C-10 dichloroenediyne, the enhanced stability of the substrates was marked, and high-temperature decomposition prevented us from obtaining even approximate activation parameters. The observed activation enthalpies are in good agreement with calculations (Table 2), and in the case of the C-11 monochloroenediyne, the conformational effects may relate to the finding on half-life (Figure 1). Unfortunately, repeated attempts to subject bromoenediyne **36** and that derived from **29** to controlled cycloaromatization resulted in decomposition, preventing accurate determination of half-lives. Clearly, the impact of the halogen atom on cycloaromatization is pronounced, and the results also serve to underscore the predictive role of DFT analysis. Indeed, based on these findings, it is likely that halogen-stabilized analogues of various naturally occurring enediynes could be designed. In the case of the enediyne chromoproteins C-1027 and kedarcidin, stabilizing interactions between the chromophore (enediyne) and apoprotein have been suggested, yet in-depth spectroscopic analysis is hindered due to the lability of the chromophore.[2] It is thus conceivable that halo-substituted analogues might find application as tools for structure−activity correlation.

**TABLE 2. Kinetic Data for Bergman Cyclization of Halo-Substituted Cyclic Enediynes 37 and Comparison to Theoretical Predictions**[a]

| X | R | $t_{1/2}$ (h) | temp (K) | $\Delta H^{\#}$ (kcal/mol) | $\Delta S^{\#}$ (eu) | $\Delta H^{\#}$(calcd) |
|---|---|---|---|---|---|---|
| − | H | 8.0 | 273 | 17.7 | −15 | 17.1 |
| | | 0.1 | 313 | | | |
| $CH_2$ | H | 60 | 313 | | | |
| | | 28 | 318 | 24.0 | −7 | 26.0 |
| | | 18 | 323 | | | |
| | | 5.0 | 333 | | | |
| $CH_2CH_2$ | H | 45 | 373 | *b* | *b* | 30.9 |
| | | 2 | 443 | | | |
| $CH_2$ | Cl | 60 | 373 | *c* | *c* | 30.0 |
| | | 24 | 443 | | | |

[a] See Table 1. [b] Activation parameters were not calculated because the reaction at 443 K is dominated by decomposition, in addition to cyclization. The $\Delta G^{\#}$ = 31.4 kcal/mol value at 373 K compares with $\Delta G^{\#}$(calcd) = 30.9 kcal/mol at 298 K. [c] Activation parameters were not calculated because the reaction at 443 K is dominated by decomposition, in addition to cyclization. The $\Delta G^{\#}$ = 31.6 kcal/mol value at 373 K compares with $\Delta G^{\#}$(calcd) = 32.5 kcal/mol at 298 K.

**Derivitization of Core Template.** Due to the stability of the halo enediynes, it became feasible to conduct chemistry on the *free* enediynes, and in the case of **39**, X = $CH_2$, in addition to trapping the thermally generated diradical with hydrogen donors, we were also able to isolate the products from chlorine capture (**40**) and oxidation (**41**) (Scheme 8).[23] Alternatively, ambient alkynylation gave an enediyne product that decomposed rapidly. However, the C-11 chloroenediyne **39**, X = $CH_2$-$CH_2$, was coupled under identical conditions to give **42**, which was stable at room temperature. The ability to use the carbon−halogen bond to vary the vinyl substituent

(22) Semmelhack, M. F.; Neu, T.; Foubelo, F. *J. Org. Chem.* **1994**, *59*, 5038.

(23) Grissom, J. W.; Gunawardena, G. U. *Tetrahedron Lett.* **1995**, *36*, 4951.

of C-9/C-10 enediynes has potential ramifications in the design of bioactivated enediyne *prodrugs*. From the ab initio studies, we were able to identify specific prodrug candidates for synthesis from **39** which are predicted to be more stable than either the chloro enediyne or parent.[10] Accordingly, metal halogen exchange routes were briefly investigated in the case of **39**, X = $CH_2$. Though trace quantities of **43** could be detected following quench of the alkynyl zinc intermediate, metalation and quench en route to formation of **44**−**45** failed to give any of the desired products, resulting in rapid decomposition. Clearly, to capitalize on these enediynes as synthetic building blocks, milder coupling and derivitization methods will need to be identified. Nonetheless, the ready availability of enediynes **39** via the expeditious route outlined will help facilitate this quest, which will be aided in turn by the inherent thermal stability of this class.

In summary, new classes of vinyl-substituted enediynes, calculated to have vastly different chemical stability than the parent system have been prepared and the electronic contribution to Bergman cyclization quantitiated.[24] Additionally, these unprecedented species are amenable to substitution and manipulation and can now be regarded as building blocks for materials chemistry[25] and antitumor agent design. [26]

**Acknowledgment.** We wish to acknowledge financial support from the NIH (5RO1GM57123), NSF (MCB98661), PRF (33920AC1), American Cancer Society, Elsa U. Pardee Foundation, Massachusetts Department of Health, and the GHS-CU Biomedical Cooperative research program.

**Supporting Information Available:** Synthetic procedures and spectroscopic data for the preparation of all compounds and calculation coordinates for compounds **4** and **7**. This material is available free of charge via the Internet at http://pubs.acs.org.

JO025763E

(24) Clark, A. E.; Davidson, E. R.; Zaleski, J. M. *J. Am. Chem. Soc.* **2001**, *123*, 2650.
(25) Diederich, F.; Gobbi, L. *Top. Curr. Chem.* **1999**, *201*, 43.
(26) Nicolaou, K. C.; Smith, A. L. In *Modern Acetylene Chemistry*; Stang, P. J., Diederich, F., Eds.; VCH: Weinheim, Germany, 1995; pp 203−284.