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A Convenient Synthesis of 1,2-Disubstituted Cyclooctatetraenes

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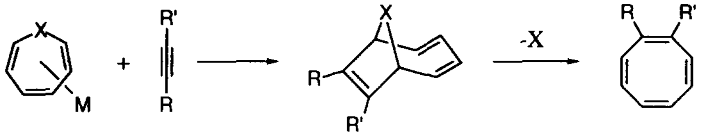
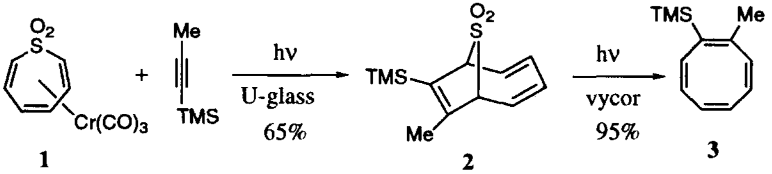
Summary: Substituted cyclooctatetraenes can be prepared in two steps employing a Cr-(0)-promoted [6π+2π] thiepin dioxide-alkyne cycloaddition followed by photoactivated sulfur dioxide extrusion.

Cyclooctatetraene and its derivatives continue to attract attention, particularly with regard to the theoretical implications of their fluxional behavior.[1] To date, preparative access to substituted members of this series of compounds has generally relied on multistep sequences.[2] An attractive alternative two-step entry into 1,2-disubstituted cyclooctatetraenes can be envisioned that would employ a metal-promoted [6π+2π] cycloaddition[3] between an appropriate heterocyclic triene-metal complex and an alkyne for construction of the eight-membered carbocycle. Extrusion of the heteroatom would follow to provide the tetraene(Scheme I). In this context, the elements of sulfur dioxide offer numerous advantages as the heteroatom component.[2j,4]

Scheme I



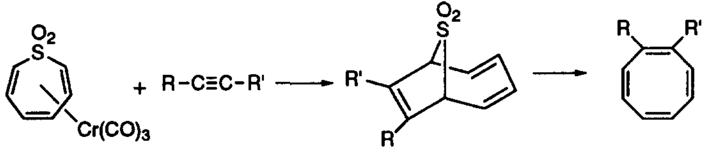
Crucial to the success of this endeavor is the ability to effect [6+2] cycloaddition between the thiepin dioxide complex (**1**)[5] and alkyne reaction partners. While other cyclic triene complexes are well-behaved participants in the [6+2] cycloaddition manifold,[6] complex **1** is not. Indeed, this material has been shown to undergo a rapid three-component cycloaddition process when reacted with terminal alkynes.[7] However, by careful control of reaction conditions internal alkynes have been found to undergo effective 1:1 [6+2] cycloaddition. Thus, irradiation of **1** in the presence of a small excess of 1-trimethylsilylpropyne delivered the desired 1:1 adduct **2**[8] in 65% yield.



1 **2** **3** (1)

With compound **2** in hand, a second irradiation (vycor filter) was performed to effect cheletropic extrusion of sulfur dioxide to afford the corresponding cyclooctatetraene **3**[8] in excellent yield. No evidence of double bond shifting was observed, and no significant quantity of the corresponding 1,8-isomer appeared to be formed during the heteroatom excision operation.[1a,2i,j,9] The relatively short reaction times (15 min) may account for the observed product homogeneity in these reactions. Several additional examples of this sequence are compiled in Table 1.

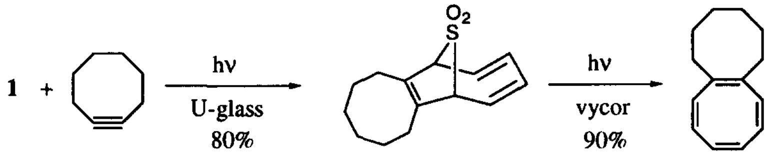
Table 1



Entry	R	R'	Yield (%)	Yield (%)
1	n-Pr	TMS	65[a]	95[a]
2	n-Bu	TMS	65[a]	95[a]
3	Ph	TMS	78[a]	92[a]
4	n-Pr	TMS	41[a,b]	90[a]
5	Ph	Et	42[a,b]	85[a]

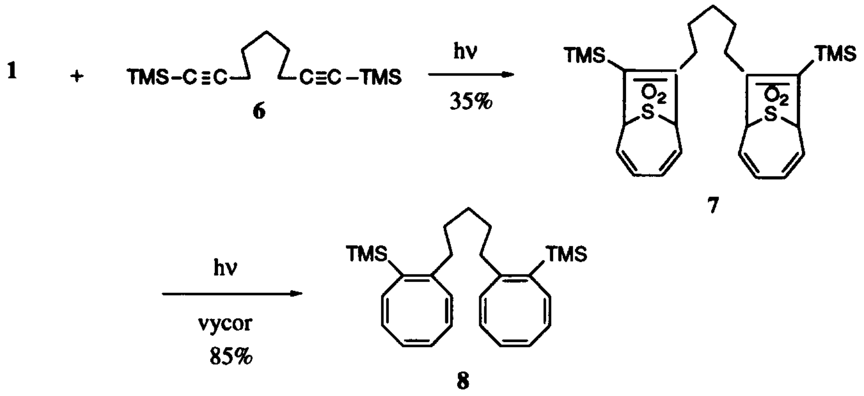
[a] Reference 8. [b] Accompanied by 20% of the 2:1 alkyne/triene adduct.

Other types of alkyne reaction partners can participate in the sequence as well. For example, readily available cyclooctyne[10] undergoes smooth cycloaddition with complex **1** to deliver tricycle **4**[8] in 80% yield, and photoinduced SO_2 extrusion affords the known fused bicyclic tetraene **5**.[11] It is noteworthy, however, that larger cycloalkynes provided primarily 2:1 alkyne/triene cycloadducts in these reactions.



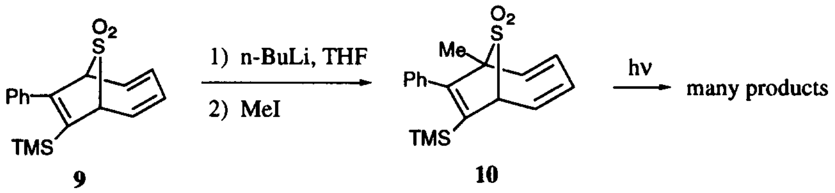
4 **5** (2)

Compounds possessing multiple cyclooctatetraene substructures tethered by acyclic carbon chains have gained importance recently due to their novel optical and electrical properties when the connecting tethers permit π-conjugation.[12] In light of these developments, a model study was performed in which a bis-alkyne was examined as a cycloaddition reaction partner for the introduction of multiple cyclooctatetraene moieties in one operation. In the event, treatment of diyne **6** with excess complex **1** under standard photocycloaddition conditions afforded the bis-cycloadduct **7**[8] in 35% yield. Subsequent SO_2 extrusion yielded the biscyclooctatetraene **8**[8] in 85% yield.



(3)

Finally, the well-known ability to deprotonate at the bridgehead position in the 9-thiabicyclo[4.2.1]nona-triene-9,9-dioxide cycloadducts[2i,j] was examined as a means for producing more highly substituted cyclooctatetraenes. Thus treatment of adduct **9** (entry 3, Table I) with excess *n*-BuLi followed by quenching with MeI afforded the monoalkylated bicycle **10**.[8] It is noteworthy that metalation occurred only at the position adjacent to the phenyl ring in this substrate, while related compounds without phenyl substituents gave dialkylated products under these conditions. Neighboring phenyl rings are known to direct the regiochemical course of metalation in other systems.[13]



(4)

Unfortunately, attempted cheletropic extrusion of SO_2 in this case produced many products in low yield. The positioning of three contiguous substituents in the resultant tetraene system may promote rapid bond shifts [2i,9] and other isomerization pathways that are not readily available to the less substituted systems.

In summary, the sequential [6+2] cycloaddition of alkynes and thiepin dioxide promoted by Cr(0) followed by photoextrusion of sulfur dioxide provides an efficient entry into 1,2-disubstituted cyclooctatetraenes.

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References and Notes

1. (a) Paquette, L. A. *Acc. Chem. Res.* **1993**, *26*, 57. (b) Anderson, J. E.; Kirsch, P. A. *J. Chem. Soc. Perkin Trans II* **1992**, 1951. (c) Pirrung, M. C.; Krishnamurthy, N.; Nunn, D. S.; McPhail, A. T. *J. Am. Chem. Soc.* **1991**, *113*, 4910. (d) Paquette, L. A.; Trova, M. P.; Luo, J.; Clough, A. E.; Anderson, L. B. *Ibid* **1990**, *112*, 228. (e) Paquette, L. A.; Wang, T.-Z.; Luo, J.; Cottrell, C. E.; Clough, A. E.; Anderson, L. B. *Ibid* **1990**, *112*, 239 (f) Paquette, L. A.; Trova, M. P. *Tetrahedron Lett.* **1986**, *27*, 1895. (g) Paquette, L. A. *Tetrahedron* **1975**, *31*, 2855.
2. Selected methods for cyclooctatetraene synthesis: From cyclooctanes: (a) Lyttle, M. H.; Streitwieser, A. ; Miller, M. J. *J. Org. Chem.* **1989**, *54*, 2331. (b) Miller, M. J.; Lyttle, M. H.; Streitwieser, Jr., A. *Ibid* **1981**, *46*, 1977. via rearrangement: (c) Paquette, L. A.; Photis, J. M. *Tetrahedron Lett.* **1975**, 1145. (d) Paquette, L. A.; Photis, J. M.; Gifkins, K. B.; Clardy, J. *J. Am. Chem. Soc.* **1975**, *97*, 3536. (e) Paquette, L. A.; Russell, R. K.; Wingard, R. E. *Tetrahedron Lett.* **1973**, 1713. via cycloaddition: (f) Fray, G. I.; Geen, G. R.; Whiteside, N. A. *Synthesis* **1982**, 956. (g) Tinnemans, A.H.A.; Neckers, D. C. *J. Am. Chem. Soc.* **1977**, *99*, 6459. via cyclotetramerization of alkynes. (h) Leto, J. R.; Leto, M. F. *J. Am. Chem. Soc.* **1961**, *83*, 2944. via heteroatom extrusion: (i) Gottesfeld, M. R.; Masoudi, F. A.; Hansen, D. E.; *Tetrahedron Lett.*, **1992**, *33*, 447. (j) Paquette, L. A.; Ley, S. V.; Meisinger, R. H.; Russell, R. K.; Oku, M. *J. Am. Chem. Soc.* **1974**, *96*, 5806.
3. For an overview of metal-promoted higher-order cycloaddition, see: Rigby, J. H. in "Advances in Metal-Organic Chemistry," Liebeskind, L. S., Ed.; JAI Press, Greenwich: 1995, Vol. 4, pp. 89-127.
4. Mock, W. L. *J. Am. Chem. Soc.* **1975**, *97*, 3673.
5. Rigby, J. H.; Ateeq, H. S.; Krueger, A. C. *Tetrahedron Lett.* **1992**, *33*, 5873.
6. (a) Chaffee, K.; Kuo, P.; Sheridan, J. B.; Barbieri, A.; Aistars, A.; Lalancette, R. A.; Ostrander, R. L.; Rheingold, A. L. *J. Am. Chem. Soc.* **1995**, *117*, 1900. (b) Rigby, J. H.; Ateeq, H. S.; Charles, N. R.; Henshilwood, J. A.; Short, K. M.; Sugathapala, P. M. *Tetrahedron* **1993**, *49*, 5495. (c) Fischler, I.; Grevels, F.-W.; Leitich, J.; Özkar, S. *Chem. Ber.* **1991**, *124*, 2857.
7. Rigby, J. H.; Warshakoon, N. C.; Heeg, M. J. *J. Am. Chem. Soc.* **1996**, *118*, 6044.
8. This compound exhibited spectral (^{1}H NMR, ^{13}C NMR, IR) and analytical (combustion analysis and/or HRMS) data consistant with the assigned structure.
9. (a) Paquette, L. A.; Hanzawa, Y.; Hefferon, G. J.; Blount, J. F. *J. Org. Chem.* **1982**, *47*,. 265. (b) Hanzawa, Y.; Paquette, L. A. *J. Am. Chem. Soc.* **1981**, *103*, 2269.
10. Brandsma, L.; Verkruijsse, H. D. *Synthesis* **1978**, 290.
11. Miller, R. D.; Abraitys, V. Y. *Tetrahedron Lett.* **1971**, 891.
12. (a) Scherf, U.; Müllen, K. *Synthesis* **1992**, 23. (b) Auchter-Krummel, P.; Müllen, K. *Angew Chem. Intl. Ed. Engl.* **1991**, *30*, 1003.
13. Posner, G. H.; Lentz, C. M. *J. Am. Chem. Soc.* **1979**, *101*, 934.

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