

of 1,3-dithietanes **8b** and **8c** from 1,2,2-trichlorovinyl and 1,2,3,4,4-pentachlorobuta-1,3-dienyl 2-nitrophenyl disulfides (**6b** and **6c**) was also observed.

N-Dodecylpyridoxal in cetyltrimethylammonium micelles, an enzyme model that mimics β -lyase activity,^{3a,11} was used to investigate potential biological thioketene formation from cysteine *S*-conjugates. With this system, *S*-conjugate **1a** gave thianorbornene **7a**, as demonstrated by GC-MS analysis. In the absence of cyclopentadiene, dithietane **8a** was formed in low yield, by could be detected by GC-MS with selected ion monitoring.

This is the first report of thioketene formation from α -chloroalkenyl thiolates. Because thioketene formation from cysteine *S*-conjugates was also detected with a biologically relevant enzyme model, these results indicate that thioketenes are potential biological reactive intermediates. α -Chloroalkenyl 2-nitrophenyl disulfides should find utility in exploring the reactions of thioketenes with cellular macromolecules, which may contribute to the observed toxicity of cysteine *S*-conjugates.

Supplementary Material Available: Physical, spectral, and analytical data for compounds **5a**, **6a-c**, **7b,c**, **8b,c**, **9**, and **10** (3 pages). Ordering information is given on any current masthead page.

(11) (a) Kondo, H.; Kikuchi, J.; Uchida, S.; Kitamikado, T.; Koyanagi, E.; Sunamoto, J. *Bull. Chem. Soc. Jpn.* **1985**, 675-681. (b) Incubation mixtures contained 10 mM phosphate buffer, pH 8.0, 0.25 mM *N*-dodecylpyridoxal bromide, 5 mM *S*-(1,2-dichloro-3,3,3-trifluoro-1-propenyl)-L-cysteine,^{11c} 3 mM cetyltrimethylammonium chloride, and 1 mM tetrasodium ethylenediaminetetraacetate in a final volume of 1.0 mL and were incubated for 30 min at 37 °C. The incubation mixtures were extracted once with 1 mL of CHCl₃, and 1 μ L of the extract was injected into the GC-MS apparatus. (c) Vamvakas, S.; Kremling, E.; Dekant, W. *Biochem. Pharmacol.* **1989**, 38, 2297-2304.

Transition Metal Template Controlled Cycloaddition Reactions. An Efficient Chromium(0)-Mediated [6 π + 2 π] Cycloaddition

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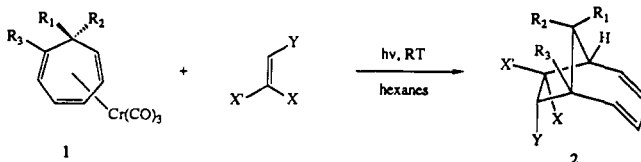
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The photochemically "allowed" interaction of a 6 π addend with a 2 π partner to produce the important bicyclo[4.2.1]nonane carbon skeleton has received relatively little attention to date due, in large measure, to expected low periselectivity levels during the cycloaddition event. In most instances, multiple, competitive pathways afford complex product mixtures in which the [6 + 2] species is only a minor component.¹ Recent variations on this theme have met with greater success. Feldman and co-workers have demonstrated that an intramolecular version of this photocycloaddition can be achieved under acidic conditions in the tropone series.²

(1) (a) Woodward, R. B.; Hoffmann, R. *The Conservation of Orbital Symmetry*; Verlag Chemie: Berlin, 1970. (b) Jenner, G.; Papadopoulos, M. *J. Org. Chem.* **1986**, 51, 585. (c) Wu, T.-C.; Houk, K. N. *J. Am. Chem. Soc.* **1985**, 107, 5308. (d) Yang, N.-C. C.; Chiang, W. L. *J. Am. Chem. Soc.* **1977**, 99, 3163. (e) Mori, A.; Takeshita, H. *Chem. Lett.* **1975**, 599. (f) Bellus, D.; Helfrich, G.; Weis, C. D. *Helv. Chim. Acta* **1971**, 54, 463. (g) Tabushi, I.; Yamada, H.; Yoshida, Z.; Kuroda, H. *Tetrahedron Lett.* **1971**, 1093. (h) Kende, A. S.; Chu, J. Y.-C. *Tetrahedron Lett.* **1970**, 4837. (i) Moriconi, E. J.; Hummel, C. F.; Kelly, J. F. *Tetrahedron Lett.* **1969**, 5325.

(2) (a) Feldman, K. S.; Come, J. H.; Freyer, A. J.; Kosmider, B. J.; Smith, C. M. *J. Am. Chem. Soc.* **1986**, 108, 1327. (b) Feldman, K. S.; Come, J. H.; Fegley, G. J.; Smith, B. D.; Parvez, M. *Tetrahedron Lett.* **1987**, 28, 607. (c) Feldman, K. S.; Come, J. H.; Kosmider, B. J.; Smith, P. M.; Rotella, D. P.; Wu, M.-J. *J. Org. Chem.* **1989**, 54, 592. (d) Feldman, K. S.; Wu, M.-J.; Rotella, D. P. *J. Am. Chem. Soc.* **1990**, 112, 8490.

Table I. Metal-Mediated [6 π + 2 π] Cycloaddition Reactions

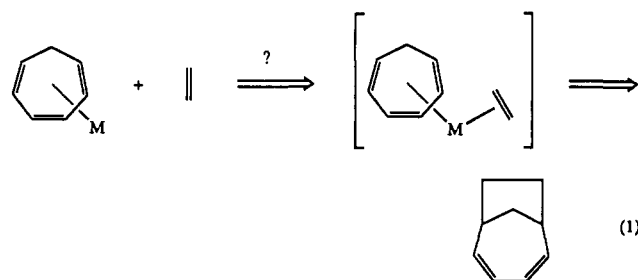


entry	triene complex	alkene	time, ^a min	yield, ^b %
1	R ₁ , R ₂ , R ₃ = H	Y = CO ₂ Et; X, X' = H	15	92
2	R ₁ , R ₂ , R ₃ = H	Y = COMe; X', X = H	15	97
3	R ₁ , R ₂ , R ₃ = H	Y, X = CO ₂ Et; X' = H	17	80
4	R ₁ , R ₂ , R ₃ = H	Y = CO ₂ Me; X' = H; X =	30	91 ^c
5	R ₁ , R ₂ , R ₃ = H	Y = CO ₂ Me; X = H; X' =	20	93 ^d
6	R ₁ , R ₃ = H; R ₂ = OMe	Y = CO ₂ Et; X, X' = H	10	68
7	R ₁ = Me; R ₂ , R ₃ = H	Y = CO ₂ Et; X, X' = H	12	83
8	R ₁ , R ₂ = H; R ₃ = OMe	Y = CO ₂ Et; X, X' = H	90 ^e	81
9	R ₁ , R ₂ , R ₃ = H	Y = CO ₂ Et; X' = Me, X = H	90 ^e	58
10	R ₁ , R ₂ , R ₃ = H	Y = CN; X, X' = H	90 ^e	36
11	R ₁ , R ₂ , R ₃ = H	Y = OBu; X, X' = H	90	0
12	R ₁ , R ₂ , R ₃ = H	maleic anhydride	90 ^e	0

^aAll reactions performed by using a Pyrex filter unless otherwise indicated. ^bAll products described in the table are purified and exhibit spectral (¹H NMR, ¹³C NMR, IR) and analytical (HRMS or combustion analysis) data consistent with the assigned structures. ^cA 91% de was obtained based on ¹H NMR integration. ^dA 90% de was obtained based on ¹H NMR integration. ^eIrradiated through a quartz filter.

Sporadic reports of metal-facilitated [6 + 2] reactions have also appeared; however, these have generally been of limited scope.³

We have previously reported that transition-metal centers can serve as powerful templates capable of transforming normally inefficient higher order cycloaddition reactions into high-yielding, synthetically useful processes (eq 1).⁴ We now disclose that



chromium(0) complexes of cycloheptatriene undergo an unprecedented photoinduced [6 π + 2 π] cycloaddition with electron deficient alkene partners. These results serve to further illustrate the potentially general nature of transition metal template control in cycloaddition chemistry.

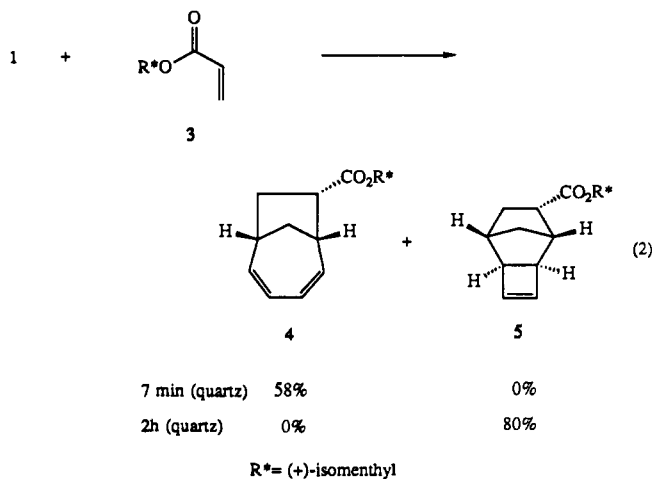
(3) (a) Ward, J. S.; Pettit, R. *J. Am. Chem. Soc.* **1971**, 93, 262. (b) Davis, R. E.; Dodds, T. A.; Hseu, T.-H.; Wagnon, J. C.; Devon, T.; Tancredi, J.; McKennis, J. S.; Pettit, R. *J. Am. Chem. Soc.* **1974**, 96, 7562. (c) Kreiter, C. G.; Micheis, E.; Kurz, H. *J. Organomet. Chem.* **1982**, 232, 249. (d) Mack, K.; Antropiusova, H.; Sedmera, P.; Hanus, V.; Turecek, F. *J. Chem. Soc., Chem. Commun.* **1983**, 805. (e) Bourner, D. G.; Brammer, L.; Green, M.; Moran, G.; Orpen, A. G.; Reeve, C.; Schaverien, C. J. *J. Chem. Soc., Chem. Commun.* **1985**, 1409.

(4) Rigby, J. H.; Ateeq, H. S. *J. Am. Chem. Soc.* **1990**, 112, 6442 and references cited therein.

Irradiation (450-W Canrad-Hanovia medium pressure Hg vapor lamp, Pyrex filter) of a mixture of tricarbonyl(η -1,3,5-cycloheptatriene)chromium (1) (1 equiv) and the alkene (1.5 equiv) in hydrocarbon solvent at room temperature for periods ranging from 10 to 90 min produced the *metal-free* bicyclo[4.2.1]nonadiene adducts 2 in excellent yields. In each case studied to date, a single diastereomer resulting from an endo approach of the trienophile is isolated.^{5,6}

Examination of Table I reveals a number of noteworthy features of this reaction. Of particular note is the observation that diethyl maleate produced a cycloadduct exhibiting no loss of stereochemical integrity (entry 3).⁷ Opportunities for achieving significant levels of asymmetric induction in select situations are also available as evidenced by the results in entries 4 and 5. Complexes with either an endo or exo substituent affixed to the C₇ position of the triene ligand undergo smooth cycloaddition to provide highly substituted adducts (entries 6 and 7).⁸ Substituents residing at the bond-forming centers in the 6 π partner normally preclude cycloaddition in related systems;⁹ however, the metal-mediated [6 + 2] process occurs efficiently and with complete regioselectivity with 1-substituted cycloheptatriene complexes (entry 8). Efforts to induce cycloaddition with electron-rich and cyclic alkene systems have not been successful (entries 11 and 12). It is noteworthy that the efficiency of the previously described metal-mediated [6 π + 4 π] reaction was found to be virtually independent of the electronic nature of the participants.⁴

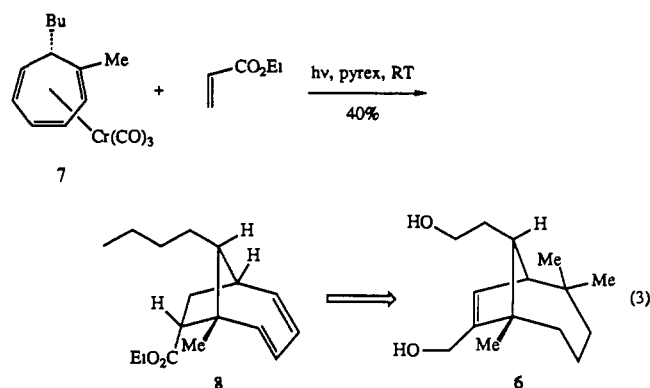
Another facet of this reaction was revealed during the attempted cycloaddition of (+)-isomenthyl acrylate (3) with chromium(0) complex 1 (eq 2). Extended reaction times resulted in the pro-



duction of the stereochemically rich tricycle 5 as a mixture of diastereomers (80% yield, 0% de).^{10,11} This phenomenon is general for the majority of [6 + 2] reactions described in this study. Shorter reaction times or irradiation through a Pyrex filter sup-

presses the electrocyclic ring closure so that efficient access to either series can be conveniently controlled by simply selecting reaction conditions. This anomalous behavior presumably stems from the metal-free nature of the initial adduct produced during the cycloaddition which may then undergo further photochemical transformations.¹²

Sesquiterpenes such as secolongifolenediol (6)¹³ that possess the bicyclo[4.2.1]nonane substructure represent particularly appealing targets for displaying the attributes of the metal-mediated [6 π + 2 π] cycloaddition protocol. The viability of this strategy was established by performing a photocycloaddition between the readily available substituted cycloheptatriene complex 7¹⁴ and ethyl acrylate under standard conditions (eq 3). This provided a single



product in 40% yield (not optimized). Structure 8 was assigned to this material on the basis of extensive ¹H NMR decoupling experiments. Modification of this basic sequence for the ultimate assembly of secolongifolenediol itself is currently underway in our laboratory.¹⁵

The successful execution of a transition metal mediated [6 π + 2 π] cycloaddition represents a significant advance in the exploitation of the unique features of the metal-template effect for promoting cycloaddition reactions. The dramatic influence of Cr(0) in achieving a cycloaddition that normally fails under thermal or photochemical conditions attests to the usefulness of this metal-mediated reaction.

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Supplementary Material Available: Typical experimental procedures and full characterizations (¹H and ¹³C NMR, IR, MS, HRMS, and elemental analysis) of all new compounds (8 pages). Ordering information is given on any current masthead page.

(5) The ¹H NMR spectra of many of these compounds display a diagnostic doublet centered around 2 ppm ($J = 12$ Hz) for the proton on the one-carbon bridge anti to the two-carbon bridge; see ref 1e and: Antkowiak, T. A.; Sanders, D. C.; Trimitsis, G. B.; Press, J. B.; Shechter, H. *J. Am. Chem. Soc.* **1972**, *94*, 5366.

(6) The endo nature of the cycloaddition was established by comparison with known adducts prepared by another route (ref 1f), as well as by NOE experiments performed on the cycloadduct from entry 6 in Table I.

(7) No evidence for the production of [6 + 2] adducts could be detected when a mixture of cycloheptatriene and diethyl maleate was irradiated under standard conditions in the absence of a metal center.

(8) For the general preparation of substituted cycloheptatriene metal complexes, see: Pauson, P. L.; Todd, K. H. *J. Chem. Soc. C* **1970**, 2315 and references cited therein.

(9) (a) Rigby, J. H.; Moore, T. L.; Rege, S. *J. Org. Chem.* **1986**, *51*, 2398. (b) Garst, M. E.; Roberts, V. A.; Prussin, C. *Tetrahedron* **1983**, *39*, 581.

(10) Electrocyclic reactions of this type are well-known in cycloheptadienes: Schuster, D. I.; Skolnick, B. R.; Lee, F.-T. H. *J. Am. Chem. Soc.* **1968**, *90*, 1300.

(11) The relative stereochemistry of the cyclobutene ring in the resultant tricyclo[4.2.1.0^{2,3}]nonane series was established by examining the ¹H NMR coupling constants between the two sets of bridgehead protons in the adduct derived from the photocycloaddition—electrocyclic closure of (7-*exo*-methoxycycloheptatriene)tricarbonylchromium and ethyl acrylate. The assignment was supported by comparing dihedral angles for the exo and endo isomers obtained from MM2 calculations and examining Dreiding molecular models.

(12) Several adduct dienes were irradiated under standard conditions (quartz filter) in the absence of a metal center, and each provided the corresponding cyclobutene isomer.

(13) (a) Yadav, J. S.; Chawla, H. P. S.; Dev, S. *Indian J. Chem.* **1983**, *22B*, 212. (b) Dorn, F.; Arigoni, D. *Experientia* **1974**, *30*, 851.

(14) The requisite hydrocarbon was prepared by 1,8-addition of *n*-BuLi to tropone, followed by 1,2-addition of MeCeCl₂ and regioselective dehydration. Treatment of the resultant disubstituted cycloheptatriene with (MeCN)₃Cr(CO)₃ gave 7. The spectral data displayed by complex 7 is consistent with that expected for the endo-C₇ isomer; see ref 4 and: Pauson, P. L.; Smith, G. H.; Valentine, J. H. *J. Chem. Soc. C* **1967**, 1061.

(15) For an alternative entry into the bicyclo[4.2.1]nonane sesquiterpenes, see: Jung, M. E.; Kaas, S. M. *Tetrahedron Lett.* **1989**, *30*, 641 and references cited therein.