

high-field ^1H , ^{13}C , ^{19}F NMR) of the products, and tables of positional and thermal X-ray parameters for (\pm)-**8**, **11**, and the (*S*)-1-phenethylamide of **5** (34 pages).³⁰ Ordering information is given on any current masthead page.

(30) X-ray crystal data were collected on a Nicolet R3m/ μ diffractometer: $\lambda = 1.5418 \text{ \AA}$, $T = 298 \text{ K}$, θ - 2θ scan mode, $5^\circ \leq 2\theta \leq 100^\circ$. For (\pm)-**8** (from hexanes): $\text{C}_{18}\text{H}_{30}\text{NOF}_2$, $0.19 \times 0.20 \times 0.23 \text{ mm}$, $P1$, $Z = 2$, $a = 9.516 (3) \text{ \AA}$, $b = 10.425 (4) \text{ \AA}$, $c = 12.063 (6) \text{ \AA}$, $\alpha = 108.09 (3)^\circ$, $\beta = 98.03 (4)^\circ$, $\gamma = 112.89 (3)^\circ$, $V = 1000.5 (7) \text{ \AA}^3$, $D_{\text{calc}} = 1.46 \text{ g/cm}^3$. A total of 2011 unique reflections were measured; 1811 were considered observed [$I > 3.0\sigma(I)$] and were used in subsequent structure analysis, yielding $R = 0.066$, $R_w = 0.067$, and $\text{GOF} = 1.79$. For **11** (from hexanes): $\text{C}_{28}\text{H}_{39}\text{NO}_3\text{F}_2$, $0.18 \times 0.36 \times 0.52 \text{ mm}$, $P2_1/n$, $Z = 4$, $a = 15.912 (3) \text{ \AA}$, $b = 9.710 (3) \text{ \AA}$, $c = 18.298 (6) \text{ \AA}$, $\beta = 105.94 (2)^\circ$, $V = 2718 (1) \text{ \AA}^3$, $D_{\text{calc}} = 1.18 \text{ g/cm}^3$. A total of 2777 unique reflections were measured; 2300 were considered observed [$I > 3.0\sigma(I)$] and were used in the subsequent structure analysis, yielding $R = 0.059$, $R_w = 0.067$, and $\text{GOF} = 1.62$. A difference map revealed that the ester ethyl group was disordered; this disorder was fit by using two positions for the ethyl group (3:1 population). The hydrogens for this disordered group were not located. For the (*S*)-1-phenethylamide of **5** (from methanol): $\text{C}_{24}\text{H}_{29}\text{NOF}_2$, $0.13 \times 0.21 \times 0.34 \text{ mm}$, $P2_1$, $Z = 4$, $a = 9.737 (2) \text{ \AA}$, $b = 10.540 (3) \text{ \AA}$, $c = 23.068 (7) \text{ \AA}$, $\beta = 90.49 (2)^\circ$, $V = 2367 (1) \text{ \AA}^3$, $D_{\text{calc}} = 1.10 \text{ g/cm}^3$. A total of 2599 unique reflections were measured; 2168 were considered observed [$I > 3.0\sigma(I)$] and were used in the subsequent structure analysis, yielding $R = 0.061$, $R_w = 0.063$, and $\text{GOF} = 1.01$.

Synthetic Studies on Transition-Metal-Mediated Higher Order Cycloaddition Reactions: Highly Stereoselective Construction of Substituted Bicyclo[4.4.1]undecane Systems

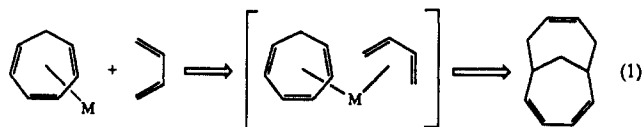
James H. Rigby* and Humy S. Ateeq

Department of Chemistry, Wayne State University
Detroit, Michigan 48202

Received February 22, 1990

Revised Manuscript Received June 25, 1990

So called higher order cycloaddition reactions ($6\pi + 4\pi$, $4\pi + 4\pi$, $6\pi + 2\pi$) are typically characterized by a high level of stereoselectivity and relatively low chemical efficiency. Tropone, for example, participates in a thermally allowed $[6 + 4]$ cycloaddition with a limited range of dienes to provide adducts in modest yields with extremely high stereoselectivity.¹ Cycloheptatriene on the other hand, displays little periselectivity in thermal reactions with dienes, giving a myriad of products of which the $[6 + 4]$ adduct is only a minor component.² The notion of employing a transition-metal template to enhance the efficiency of the higher order process by rendering the reaction temporarily intramolecular is quite appealing. Surprisingly, this strategy has received relatively little attention in the realm of higher order cycloaddition chemistry.³ In the present case, it was envisioned that an appropriate metal could serve to precomplex both the 6π and 4π addends, thus providing an opportunity for promoting the desired pathway as depicted in eq 1.



In the formative stages of this study, we were intrigued by reports from the Kreiter laboratory of a photochemical ligand exchange involving several cyclic triene-chromium complexes that

Table I. $[6 + 4]$ Cycloaddition of Tricarbonyl- η -1,3,5-cycloheptatriene Chromium

entry	triene 1	diene 2	yield, ^{a,b} %
1	$R_1, R_2 = \text{H}$	$X, Y = \text{H}; Z = \text{OMe}$	64
2	$R_1, R_2 = \text{H}$	$X, Y = \text{H}; Z = \text{OTMS}$	56
3	$R_1, R_2 = \text{H}$	$X, Y = \text{H}; Z = \text{OAc}$	67
4	$R_1, R_2 = \text{H}$	$X = \text{H}; Y, Z = \text{OAc}$	65
5	$R_1, R_2 = \text{H}$	$X = \text{H}; Y, Z = \text{CO}_2\text{Me}$	59
6	$R_1 = \text{H}; R_2 = \text{OMe}$	$Y, Z = \text{H}; X = \text{Me}$	66
7	$R_1 = \text{OMe}; R_2 = \text{H}$	$Y, Z = \text{H}; X = \text{Me}$	60
8	$R_1 = \text{OMe}; R_2 = \text{H}$	$X, Y = \text{H}; Z = \text{OAc}$	60
9	$R_1 = \text{Me}; R_2 = \text{H}$	$X, Y = \text{H}; Z = \text{OMe}$	47
10	$R_1 = \text{Me}; R_2 = \text{H}$	$X = \text{H}; Y, Z = \text{CO}_2\text{Me}; Z = \text{Me}$	59
11	$R_1, R_2 = \text{H}$	$Y, Z = \text{H}; X = \text{OTMS}$	82 ^{c,d}
12	$R_1, R_2 = \text{OMe}$	$Y, Z = \text{H}; X = \text{Me}$	67 ^e

^a All products described in this table are purified and exhibit spectral (^1H NMR, ^{13}C NMR, IR) and analytical (HRMS and combustion analysis) data consistent with the assigned structures. ^b Yields are reported for isolated and purified adducts after metal decomplexation. ^c Yield is for combined TMS enol ether and ketone products. ^d Intermediate observed in this entry was not isolated. ^e This compound was correlated with the corresponding cycloadduct derived from tropone.

produced the desired bicycle stereoselectively in simple cases.⁴ In light of the significant potential for rapid assembly of highly substituted systems exhibiting substantial stereochemical information, we elected to explore the photochemical behavior of variously 7-substituted tricarbonyl- η -1,3,5-cycloheptatriene-chromium complexes with representative dienes. We report that transition-metal-mediated cycloadditions can effectively produce highly functionalized bicycles stereoselectively with none of the limitations that often plague the thermal versions. The results of this work are compiled in Table I. Typically, the reactions in this study were performed by irradiating a solution of the triene chromium tricarbonyl complex and diene partner at 280 nm at 0–5 °C for several hours, followed by decomplexation with trimethyl phosphite to give the organic product.

Examination of Table I reveals a number of noteworthy features of this reaction. Of particular importance is the observation that the efficiency of the transformation appears to be independent of the electronic nature of the diene. Thus, both electron-rich partners (entries 1–4, 8, 9, and 11) and electron-deficient dienes (entries 5 and 10) participate smoothly. The comparable yields obtained for the reactions of 1,4-diacetoxybutadiene (entry 4) and dimethyl muconate (entry 5) are particularly dramatic illustrations of this point. The ability to effect this cycloaddition with either exo or endo 7-substituted cycloheptatriene complexes,⁵ both of which are readily available with numerous substituents, makes this a powerful method for producing adducts possessing considerable stereochemical information. Indeed, as many as five contiguous stereogenic centers can be created in one step, using this protocol (entries 8–10). Exploitation of the well-known facial bias that prevails in the resultant bicyclic systems to install additional substituents in a stereocontrolled fashion around the periphery of the ring is an additional advantage of this methodology.^{1d} A remarkable result was obtained when 2-[(trimethylsilyloxy]butadiene was employed as the diene addend (entry 11). In this case, the expected bicyclo[4.4.1]undecane complex was not produced during the photochemical step. Instead, an unstable and structurally ill-defined intermediate was obtained, which could be induced to collapse efficiently to the desired complex by stirring

(1) (a) Cookson, R. C.; Drake, B. V.; Hudec, J.; Morrison, A. J. *J. Chem. Soc., Chem. Commun.* **1966**, 15. (b) Ito, S.; Fujise, Y.; Okuda, T.; Inoue, Y. *Bull. Chem. Soc. Jpn.* **1966**, 39, 1351. (c) Garst, M. E.; Roberts, V. A.; Prussin, C. *Tetrahedron* **1983**, 39, 581. (d) Rigby, J. H.; Moore, T. L.; Rege, S. J. *Org. Chem.* **1986**, 51, 2398. (e) Paquette, L. A.; Hathaway, S. J.; Schirch, P. F. T. *J. Org. Chem.* **1985**, 50, 4199.

(2) Houk, K. N.; Woodward, R. B. *J. Am. Chem. Soc.* **1970**, 92, 4143.

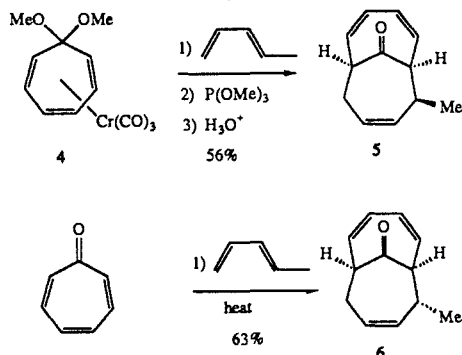
(3) A notable exception is the nickel-mediated $4\pi + 4\pi$ "cycloaddition" process: (a) Wender, P. A.; Ihle, N. C. *J. Am. Chem. Soc.* **1986**, 108, 4678. (b) Wender, P. A.; Ihle, N. C. *Tetrahedron Lett.* **1987**, 28, 2451.

(4) (a) Oezkar, S.; Kurz, H.; Neugebauer, D.; Kreiter, C. G. *J. Organomet. Chem.* **1978**, 160, 115. (b) Kreiter, C. G.; Kurz, H. *Ibid.* **1981**, 214, 339. (c) Michels, E.; Kreiter, C. G. *Ibid.* **1983**, 252, C1.

(5) (a) Munro, J. D.; Pauson, P. L. *J. Chem. Soc.* **1961**, 3475. (b) Pauson, P. L.; Smith, G. H.; Valentine, J. H. *J. Chem. Soc. C* **1967**, 1057, 1061. (c) Pauson, P. L.; Todd, K. H. *J. Chem. Soc. C* **1970**, 2315.

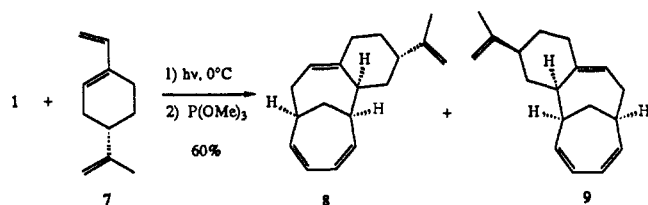
under an atmosphere of carbon monoxide. This observation may have important mechanistic implications for this class of reactions and is suggestive of a stepwise pathway.

A consistently high level of diastereoselection appears to be another characteristic of this cycloaddition process.^{4a} The relative stereochemistry of the photoproducts has been established as being endo in nature by comparison with the appropriate exo tropone cycloadduct. In practice, this was accomplished by reacting the readily available 7,7-dimethoxycycloheptatriene complex **4**⁶ with

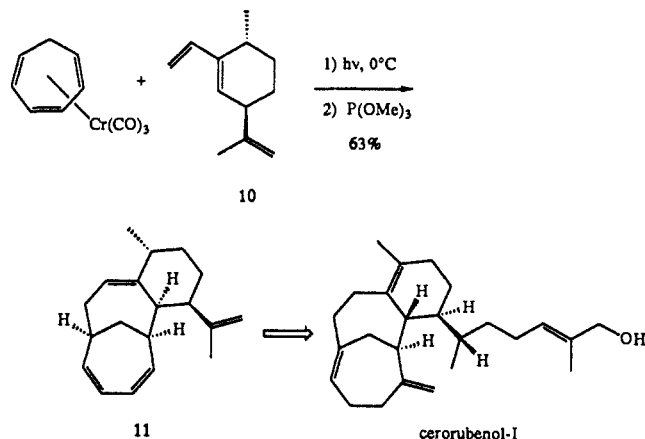


a given diene under standard conditions. This gave a single adduct which was shown not to be identical with the corresponding tropone adduct.⁷ An important consequence of this feature of the metal-mediated sequence is that it provides, for the first time, a convenient method for constructing bicyclo[4.4.1]undecanone systems displaying stereogenicity complementary to that obtained in the tropone series.

The course of the photocycloaddition of more elaborate dienes has also been examined in detail. Diene **7**⁷ [from (*S*)-(-)-



perillaldehyde] provided a 1:3 mixture of tricyclic adducts **8**⁷ and **9**⁷ in 60% overall yield.⁸ A more significant level of diastereoselection was observed in the cycloaddition of optically pure diene **10**⁷ [derived from *R,R*-(+)-dihydrocarvone],⁹ which gave adduct



11¹⁰ in 63% yield.¹¹ The adduct produced in this example can

(6) Pauson, P. L.; Todd, K. H. *J. Chem. Soc. C* **1970**, 2638.

(7) This compound exhibited spectral (¹H NMR, ¹³C NMR, IR) and analytical (HRMS and/or combustion analysis) data consistent with the assigned structure.

(8) Available data do not permit unambiguous structural assignments to be made for the two diastereomeric products in this instance.

(9) This diene was prepared in 75% overall yield by a Pd(0)-mediated coupling of vinyltri-*n*-butylstannane with the vinyl triflate derived from the kinetic enolate of *R,R*-(+)-dihydrocarvone: (a) McMurry, J. E.; Scott, W. J. *Tetrahedron Lett.* **1983**, *24*, 979. (b) Scott, W. J.; Crisp, G. T.; Stille, J. K. *J. Am. Chem. Soc.* **1984**, *106*, 4630.

be viewed as a convenient model for the convergent synthesis of the unusual sesterterpene cerorubenol I.^{12,13} A significant feature of this result is the production of an adduct displaying the natural absolute configuration at the C-ring side chain.

These last two examples point to an important fundamental distinction between the transition-metal-mediated reaction described herein and the corresponding thermal [6 + 4] process in the tropone series. It is well established that a rather limited repertoire of diene partners will successfully engage the latter in a higher order cycloaddition reaction. Indeed, neither diene **7** nor **10** provided identifiable products when exposed to tropone under standard thermal conditions, whereas we have yet to encounter a class of dienes that does not provide good yields of cycloadducts in the photochemical version of this reaction. Further work on elucidating the mechanism of this process is currently underway as is a study on general synthetic applications.

Acknowledgment. We thank the National Institutes of Health (CA-36543) and the National Science Foundation (CHE-8719185) for financial support of this research.

Supplementary Material Available: Typical experimental procedures and full characterizations (boiling points, ¹H and ¹³C NMR, IR, MS, and HRMS) of all new compounds (11 pages). Ordering information is given on any current masthead page.

(10) Support for the structure assigned to **11** was obtained by an NOE difference experiment in which irradiation of the B-ring vinyl proton multiplet at δ 5.45 caused enhancement of the C-ring methyl group signal at δ 1.05. This result is most consistent with the assigned structure.

(11) Less than 5% of the alternative diastereomer could be detected.

(12) Tempesta, M. S.; Iwashita, T.; Miyamoto, F.; Yoshihara, K.; Naya, Y. *J. Chem. Soc., Chem. Commun.* **1983**, 1182.

(13) For an alternative entry into a cerorubenate sesterterpene, see: Paquette, L. A.; Poupart, M.-A. *Tetrahedron Lett.* **1988**, *29*, 273.

ROH₂⁺ Formation from Ionized *n*-Hexyl Ethers: An Unequivocal Dissociation through an Ion-Neutral Complex in the Gas Phase

Mohammed S. Ahmed,[†] Charles E. Hudson,^{†,‡}
John C. Traeger,[§] C. S. Giam,[‡] and David J. McAdoo^{*,†}

Marine Biomedical Institute
University of Texas Medical Branch
Galveston, Texas 77550
Department of Marine Sciences
Texas A&M University at Galveston
Galveston, Texas 77553
Department of Chemistry, LaTrobe University
Bundoora, Victoria, Australia

Received April 9, 1990
Revised Manuscript Received July 6, 1990

The idea that many unimolecular decompositions of ions in the gas phase occur through partially dissociated partners held together by ion-dipole and/or ion-induced dipole attractions, i.e., by a gas-phase analogue of cage effects in solution, has been widely applied.¹ Evidence for intermediate complexes consists of reactions between groups at opposite ends of rigid steroid nuclei,² isomerizations expected of the suspected ionic partner in the complex,³ hydrogen exchange between the putative partners,⁴ ab

[†] University of Texas Medical Branch.

[‡] Texas A&M University at Galveston.

[§] LaTrobe University.

(1) (a) Morton, T. M. *Tetrahedron* **1982**, *38*, 3195-3243. (b) McAdoo, D. J. *Mass Spectrom. Rev.* **1988**, *7*, 363-393.

(2) Longevialle, P.; Botter, R. *J. Chem. Soc., Chem. Commun.* **1980**, 823-825.