J. Org. Chem. 1985, 50, 3781-3787

angles of 24 reflections in the range $41° < \theta < 44°$, measured by the computer-controlled diagonal slit method of centering. The monoclinic cell parameters and calculated volume are $a = 13.215$ (3) Å, $b = 9.548$ (2) Å, $c = 12.705$ (4) Å, $\beta = 118.50$ (2)°, and $V = 1409$ (1) A^3. For $Z = 2$ and $FW = 543.62$ the calculated density was 1.281 g/cm^3. The space group was determined to be $P2_1$.

The details of data collection, structure solution and refinement, and tables of bond distances, bond angles, tortional angles, and intensity data are provided as supplementary material. All calculations were performed on a PDP-11 computer using SDP-PLUS.[12]

(+)-Strigol (1). To a stirred solution of (+)-strigol *N*-[(*R*)-1-(1-naphthyl)ethyl]carbamate (**3**) (0.151 g, 0.349 mmol) and triethylamine (0.07 g, 0.70 mmol) in benzene (10 mL) under nitrogen was added slowly $SiHCl_3$ (1 mL of a 0.5 M solution in benzene). The mixture was stirred 16 h, after which water (10 mL) was added. The phases were separated, the organic phase was washed with saturated aqueous NaCl (10 mL), then dried over $MgSO_4$, and the solvent was evaporated to give crude material, which was purified by chromatography (silica gel, 40–50% ethyl acetate in dichloromethane) providing (+)-strigol (0.067 g, 56%); observed $[\alpha]_D$ +270° (c 0.2, $CHCl_3$) [lit.[4] $[\alpha]_D$ +293° (c 0.15, $CHCl_3$)].

(−)-Strigol. In a similar manner as above (−)-strigol *N*-[(*R*)-1-(1-naphthyl)ethyl] carbamate (**4**) was treated with triethylamine and $SiHCl_3$ to provide (−)-strigol; observed $[\alpha]_D$ −272° (c 0.18, $CHCl_3$) [lit.[4] $[\alpha]_D$ −279° (c 0.11, $CHCl_3$)].

Acknowledgment. We express application to the United States Department of Agriculture and Purdue University for financial support and to Drs. S. Vail, A. Pepperman, and O. Daily for helpful discussions concerning this project. The X-ray structural facility was supported by the Monsanto Fund and the NSF Chemical Instrumentation Program (Grant 8204994).

Supplementary Material Available: A detailed description of the X-ray crystallographic experimental procedures, tables of structural solution parameters, bond distances, bond angles, tortional angles, and intensity data, and figures of the unit cell of **3** are provided (35 pages). Ordering information is given on any current masthead page.

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(12) Frenz, B. A. In "Computing in Crystallography"; Schenk, H., Olthof-Hazelkamp, R., van Konigsveld, H., Bassi, G. C., Eds.; Delft University Press: Delft, Holland, 1978; pp 64–71.

π-Face Stereoselection Operative during [3 + 4] Cycloaddition of Oxyallyl Cations to Isodicyclopentadiene[1]

Leo A. Paquette* and Tina M. Kravetz

Evans Chemical Laboratories, The Ohio State University, Columbus, Ohio 43210

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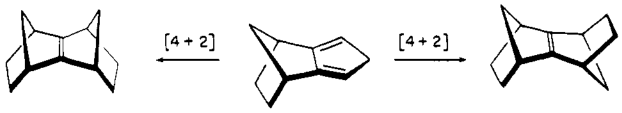
The 1,3-diphenyl-2-oxyallyl dipolar ion, generated by several different reductive methods and therefore complexed to metal ions of various type, has been added to isodicyclopentadiene. Of the six adducts possible, only five were isolated. Although the relative ratios of these ketones varied substantially with conditions, there was always encountered a strong bias for above-plane [3 + 4] cycloaddition. The structures of the adducts were elucidated by a combustion of X-ray analysis and base-catalyzed equilibration. The stereochemical course of the tetramethyl-2-oxyallyl dipolar species was also examined and shown to prefer above-plane approach. Transition-state profiles are given. The results, particularly for those processes proceeding with extended arrangements of the reaction partners, are shown to be consistent with closed-shell orbital arguments advanced earlier for anti-Alder [4 + 2] cycloadditions to isodicyclopentadiene.

Studies of the Diels–Alder chemistry of isodicyclopentadiene (1) have played a pivotal role in the development of our understanding of π-facial stereoselectivity during [4 + 2] cycloadditions.[2] Two detailed theories have been advanced to account for the customarily favored[3] below-plane selectivity leading to *syn*-sesquinorbornene products (e.g., **2**). In the Gleiter–Paquette view,[2b,4] the subjacent ψ_1 π orbital of the diene unit is characterized by disrotatory tilting of the terminal lobes toward the methano bridge as a direct consequence of strong σ/π interaction with high-lying σ levels of the neighboring norbornyl framework. As the dienophile with its filled HOMO begins to approach 1 from below in anti-Alder fashion[3] (see **4**),



2 1 3

4 5

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(1) Electronic Control of Stereoselectivity. 28. For Part 27, see: Paquette, L. A.; Green, K. E.; Gleiter, R.; Schäfer, W.; Gallucci, J. C. *J. Am. Chem. Soc.* **1984**, *106*, 8232.

(2) (a) Paquette, L. A. In "Stereochemistry and Reactivity of Pi Systems"; Watson, W. H., Ed.; Verlag Chemie International: Deerfield Beach, FL, pp 41–73. (b) Gleiter, R.; Paquette, L. A. *Acc. Chem. Res.* **1983**, *16*, 328.

(3) For key exceptions, consult: (a) Paquette, L. A.; Green, K. E.; Hsu, L.-Y. *J. Org. Chem.* **1984**, *49*, 3650. (b) Bartlett, P. D.; Wu, C. *Ibid.* **1984**, *49*, 1880. It is obviously required of a dienophile that anti-Alder approach be operative to avoid differential steric control. With highly reactive dienophiles such as the triazolinediones and tetracyanoethylene, the early timing of the transition states may depend heavily on favorable secondary orbital overlap and the Alder arrangement necessary to its realization. Under these circumstances, steric contributions from the norbornyl or norbornenyl moiety are likely to override the more subtle electronic features of the cyclopentadiene π system.

(4) (a) Gleiter, R.; Böhm, M. C. *Pure Appl. Chem.* **1983**, *55*, 237. (b) Gleiter, R.; Böhm, M. C. In "Stereochemistry and Reactivity of Pi Systems"; Watson, W. H., Ed.; Verlag Chemie International: Deerfield Beach, FL, 1983; pp 105–146.

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Table I. Metal-Promoted [3 + 4] Cycloadditions of 8 to 1

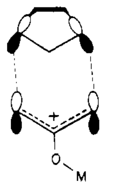
reducing agent	reactant ratio (wt of **8**, g)	reacn cond.	yield,[d] %	product distribution, %[a]					face selectivity, exo:endo
				12	**13**	**14**	**15**	**16**	
NaI/Cu	2:1:4:3[b] (0.37)	5 h, RT[c]	56	1	8		66	25	91:9
NaI/Cu	2:1:4:3[b] (1.84)	5 h, RT[c]	50	3	8		71	18	89:11
NaI/Cu	2:1:4:3[b] (1.84)	5 h, RT[c]	43	3	6		77	14	91:9
NaI/Cu	2:1:4:3[b] (2.10)	5 h, RT[c]	69	3.1	5.3	0.5	68.9	22.2	92:8
$Fe_2(CO)_9$	2:1:1.3[d] (0.37)	C_6H_6, 60 °C	18		3	34	50	13	97:3
$Fe_2(CO)_9$	2:1:1.3[d] (0.37)	C_6H_6, 60 °C	14		4	30	49	17	96:4
$Fe_2(CO)_9$	2:1:1.3[d] (0.37)	THF, 60 °C	41		6	13	56	25	94:6
NaI	2:1:excess[d]	RT[c]	23		14		57	29	86:14
Zn(Cu)	1:1:excess[d]	glyme, Δ	6		9	28	35	28	91:9

[a] These values are normalized to reflect the relative amounts of the adducts in the individual mixtures. [b] The components were 1:8:NaI:Cu. [c] Acetone–acetonitrile (1:1) was utilized as solvent. RT = room temperature. [d] The components were 1:8:$Fe_2(CO)_9$ (or alternative reducing agent). Overall yield.

a greater mismatch of antibonding four-electron orbital overlap occurs on that face relative to the above-plane option (as in **5**).[5] The more destabilizing orbital alignment in **5** acts to enhance the global transition-state energy for Diels–Alder bonding relative to that associated with pathway **4**. Steric bias on either face is considered to be too remote during anti-Alder approach to be of primary importance.[3]

Brown and Houk have proposed that torsional and steric contributions from the norbornane subunit are most influential in controlling the stereoselectivity of [4 + 2] cycloadditions to **1**.[6] In their analysis, the fact that endo bonding induces out-of-plane bending of the hydrogens attached to the terminal diene carbons and downward pyramidalization of the developing central double bond is sufficiently rewarding energetically to exert a kinetic preference. Steric effects, where operative, can be overriding in the opposite direction.

Herein we examine the stereochemical course of [4 + 3] cycloadditions of oxyallyl cations to **1**.[7] It is obviously required of these dipolar intermediates that their bonding centers be separated to a greater extent than those percent in the usual dienophiles. As a result of these altered spatial requirements, the electronic effects that we hypothesize to be operative in Diels–Alder additions to **1** (viz., **4** and **5**) should be reversed (see **6** and **7**). The situation now becomes one in which the relevant filled orbitals interact more intensely in antibonding fashion on the endo face (**6**). Indeed, this analysis anticipates that a crossover in stereoselection should be observed in [4 + 3] cycloadditions, with above-plane bonding now being kinetically preferred.



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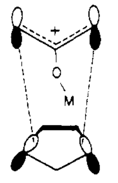

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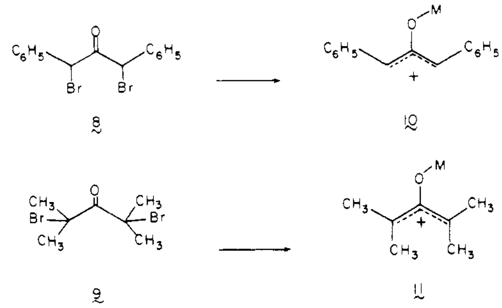
Results

Two oxyallyl cations were selected for study. The methodology employed consisted of reducing dibromo ketones **8** and **9** according to predescribed conditions.[8-10] Detailed theoretical calculations have been applied to the parent 2-oxyallyl dipolar ion and shown it to be very labile in the free form.[11,12] Under these circumstances, the tendency for cyclization to cyclopropanone and/or allene oxide appears to be very great. Stabilization can, however, be achieved by positioning electron-releasing groups at C-1 and C-3 and by increasing the covalent character of the M–O bond. The strength of the M–O bond is, in turn, greatly influenced by the nature of M and the particular reaction solvent. Recognition of these criteria has led us to apply to **8** a variety of reducing conditions involving different metal counterions. More specically, recourse was made to NaI/Cu,[13] NaI,[14] Zn(Cu),[15] and $Fe_2(CO)_9$.[16]



The cyclocondensation of **10** with **1** can afford six possible adducts. In the present study, five of the ketones (**12–16**) have been identified following their isolation in differing amounts depending upon reaction conditions (Table I). Use of sodium iodide alone or in combination with copper powder gave rise to product mixtures consisting almost entirely of the symmetrical adducts **12**, **13**, **15**, and **16**. However, when recourse was made to iron enneacarbonyl or zinc–copper couple, trans adduct **14** was obtained as the second most prevalent product and no **12** was found. Further investigation revealed that $Fe_2(CO)_9$ in tetrahydrofuran as solvent gave significantly increased yields relative to reactions performed in benzene solution.

The individual ketones were separated chromatographically. Although the several adducts were formed in differing relative proportions, their composite ratios reveal at a least 9:1 preference for above-plane face selectivity. Compounds **12**, **13**, and **15** proved to be highly crystalline

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(5) A relevant energy diagram can be found in: Böhm, M. C.; Carr, R. V. C.; Gleiter, R.; Paquette, L. A. *J. Am. Chem. Soc.* **1980**, *102*, 7218.

(6) Brown, F. K.; Houk, K. N. *J. Am. Chem. Soc.* **1985**, *107*, 1971.

(7) Preliminary communications: (a) Paquette, L. A.; Hathaway, S. J.; Kravetz, T. M.; Hsu, L.-Y. *J. Am. Chem. Soc.* **1984**, *106*, 5741. (b) Paquette, L. A.; Hsu, L.-Y.; Gallucci, J. C.; Korp, J. D.; Bernal, I.; Kravetz, T. M.; Hathaway, S. J. *Ibid.* **1984**, *106*, 5743.

(8) Hoffmann, H. M. R. *Angew. Chem., Int. Ed. Engl.* **1973**, *12*, 819; **1984**, *23*, 1.

(9) Noyori, R. *Acc. Chem. Res.* **1979**, *12*, 61.

(10) Noyori, R.; Hayakawa, Y. *Org. React.* (*N. Y.*) **1983**, *29*, 163.

(11) Hoffmann, R. *J. Am. Chem. Soc.* **1983**, *90*, 1475.

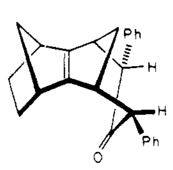
(12) Bingham, R. C.; Dewar, M. J. S.; Lo, D. H. *J. Am. Chem. Soc.* **1975**, *97*, 1302.

(13) Rawson, D. I.; Carpenter, B. K.; Hoffmann, H. M. R. *J. Am. Chem. Soc.* **1979**, *101*, 1786.

(14) Cookson, R. C.; Nye, M. J. *Proc. Chem. Soc., London* **1963**, 129.

(15) Vinter, J. G.; Hoffmann, H. M. R. *J. Am. Chem. Soc.* **1974**, *96*, 5466.

(16) Takaya, H.; Makino, S.; Hayakawa, Y.; Noyori, R. *J. Am. Chem. Soc.* **1978**, *100*, 1765.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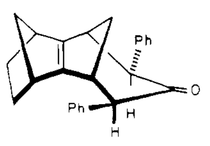
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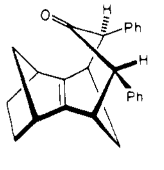
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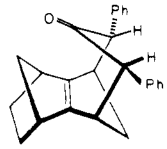
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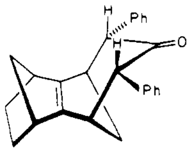
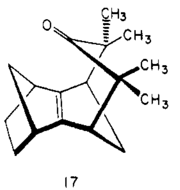

16

solids, and their three-dimensional structural features were therefore deduced by X-ray analysis (Figures 1–6). The substantial propensity of the phenyl rings to be positioned equatorially is manifested in all three molecules. In fact, **13** adopts a somewhat deformed cyclohexanone conformation to accommodate these substituents (Figure 4). The relevant interplanar angle about the central double bond in these adducts (170.7°, 168.2°, and 168.8°, respectively) reveal a common molecular distortion. The closely comparable deviation from planarity in this triad eliminates the particular cyclohexanone conformation as contributory to the phenomenon. When the structural features of the tropone–isodicyclopentadiene [6 + 4] adducts[7] are also considered, it becomes clear that the axial or equatorial status of the α and α' substituents has equally little effect. In actuality, all other intramolecular influences also appear to be discountable as causative factors. These findings demonstrate, therefore, that syn fusion of two norbornene units[17] is not required to attain high levels of rigid pyramidal constraint.[18,19]

The identification of **14** was achieved by subjecting **15** to the action of hot sodium methoxide in methanol for 2 days. These conditions promoted partial isomerization to the unsymmetrical **14**, thus requiring that this pair of molecules be stereochemically related. Confirmation that **16** was the planar-symmetric structure shown was achieved by subjecting this ketone to comparable alkaline equilibration. In this instance, both **14** and **15** resulted.

Cycloaddition of the tetramethyloxyallyl cation **11** to **1** was successful only when generated with Fe$_2$(CO)$_9$ (Table II). Some variance in product distribution was noted as the relative proportions of the reactants were altered. However, the principal adduct invariably proved to be **17**. Its identification as the product of above-plane cycloaddition was accomplished by X-ray analysis (Figure 7). Isomer **18** was difficult to purify since the contaminating self-coupling product of **9** coeluted under a variety of chromatographhic conditions. Multiple-elution preparative TLC and the implementation of band-shaving techniques eventually gave material of respectable purity.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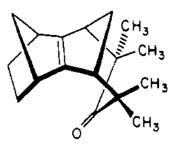
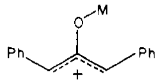
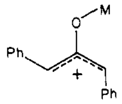
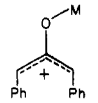

18

Discussion

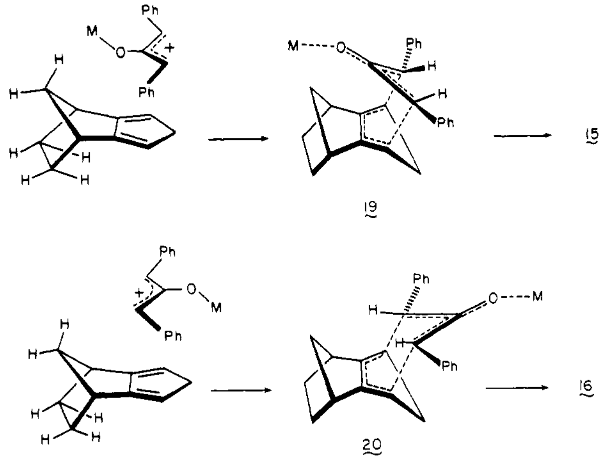
Oxyallyl cation **10** can in principle exist in the three conformations **10a–c**. Much as with the intensively investigated 1,3-diphenylallyl anions[20,21] and the dibenzylideneethylene dianion,[22] **10** can be expected to adopt that exo,exo arrangement when M is a loosely held or effectively very small metal ion. However, as the size of M increases or the degree of covalency in the M–O bond is enhanced, the conformational equilibrium should shift in favor of exo,endo isomer **10b**. At the extreme, large metals might force the dipolar species into the endo,endo geometry **10c**.[21]


10a


10b


10c

The structures of adducts **12–16** provide considerable insight into the conformational nature of the 3π donor as it undergoes reaction and reveal the particular surface of the diene that is experiencing bonding. Thus, it is readily determined that the principal adducts **15** and **16** arise from the capture of **10a** on the exo surface of **1**. As illustrated below, the distinction between these pathways resides in the geometry of approach of the oxyallyl species. Since the quantities of **15** isolated are seen to exceed those of **16** by 2–3-fold depending upon conditions, the more compact arrangement given by **19** is clearly somewhat preferred over that found in **20**.



Exo,exo conformer **10a** is also the reactive species involved in the formation of minor adducts **12** and **13**. Our data denote that when below-plane cycloaddition does operate, the extended "O-outside" global arrangement represented by **22** is more amenable to bond formation. In fact, the experiments involving Fe$_2$(CO)$_9$ and Zn(Cu)

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(17) (a) Watson, W. H.; Galloy, J.; Bartlett, P. D.; Roof, A. A. M. *J. Am. Chem. Soc.* **1981**, *103*, 2022. (b) Hagenbuch, J.-P.; Vogel, P.; Pinkerton, A. A.; Schwarzenbach, D. *Helv. Chim. Acta* **1981**, *64*, 1818. (c) Paquette, L. A.; Charumilind, P.; Böhm, M. C.; Gleiter, R.; Bass, L. S.; Clardy, J. *J. Am. Chem. Soc.* **1983**, *105*, 3136. (d) Paquette, L. A.; Hayes, P. C.; Charumilind, P.; Böhm, M. C.; Gleiter, R.; Blount, J. F. *Ibid.* **1983**, *105*, 3148.

(18) Structurally simpler norbornenes also exhibit this outward orbital distortion, although to a lesser extent: (a) Pinkerton, A. A.; Schwarzenbach, D.; Stibbard, J. H.; Carrupt, P.-A.; Vogel, P. *J. Am. Chem. Soc.* **1981**, *103*, 2095. (b) Paquette, L. A.; Schaefer, A. G.; Blount, J. F. *Ibid.* **1983**, *105*, 3642. (c) Mackenzie, K.; Miller, A. S.; Muir, K. W.; Manojlović-Muir, Lj. *Tetrahedron Lett.* **1983**, 4747.

(19) Most,[17a,c,d] though not all anti-sesquinorbornenes[3a] [Ermer, O.; Bodecker, C. D. *Helv. Chim. Acta* **1983**, *66*, 943], possess an essentially flat bond.

(20) Childs, R. F.; Lund, E. F.; Marshall, A. G.; Morrisey, W. J.; Rogerson, C. V. *J. Am. Chem. Soc.* **1976**, *98*, 5924 and relevant references cited therein.

(21) Boche, G.; Buckl, K.; Martens, D.; Schneider, D. R. *Liebigs Ann. Chem.* **1980**, 1135 and relevant references cited therein.

(22) Wilhelm, D.; Clark, T.; Schleyer, P. v. R. *Tetrahedron Lett.* **1983**, 3985.

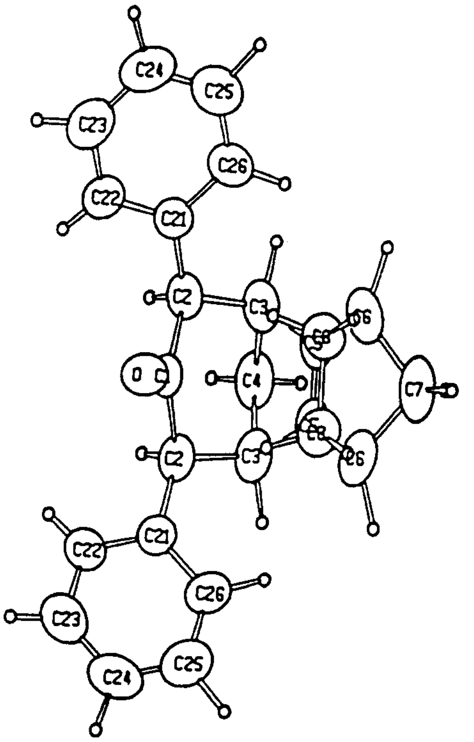


Figure 1. ORTEP drawing of 12. Non-hydrogen atoms are drawn with 50% probability ellipsoids. Hydrogen atoms have been drawn artificially small.

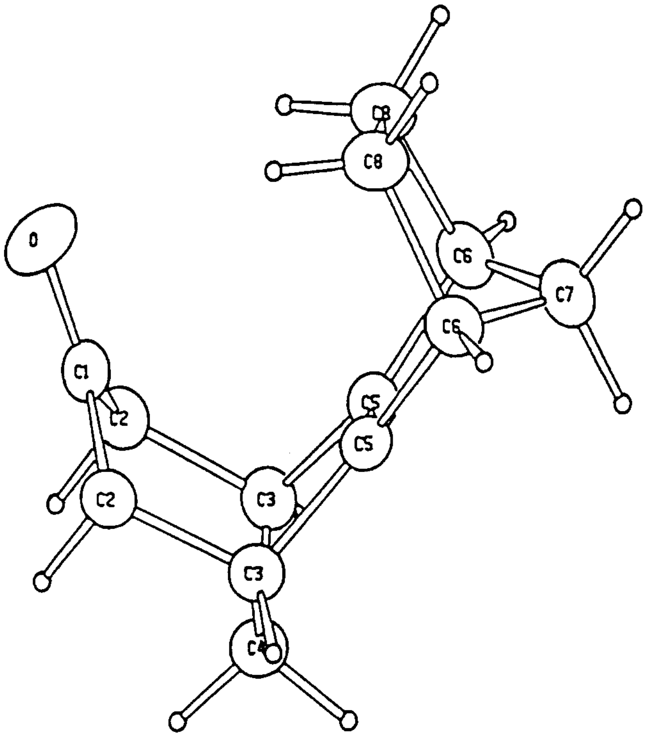


Figure 2. ORTEP drawing of 12 from which the phenyl substituents have been deleted to permit a clearer view of the framework conformation.

gave no adduct 12. We believe that coordination of metal ions of this size to oxygen in **10a** may complicate approach as in **21** for steric reasons.

Adduct **14** can arise via four mechanistically distinctive pathways. Should oxyallyl cation **10a** be involved in its formation, allowance must be made for the obvious loss of configuration. The operation of a stepwise process involving an intermediate sufficiently long-lived to experience rotation about at least one of the newly formed bonds

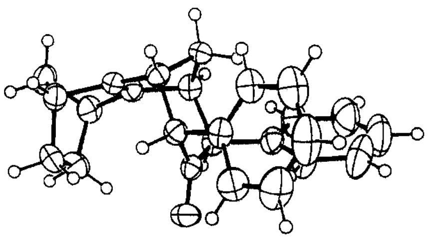


Figure 3. ORTEP drawing of 13. Non-hydrogen atoms are drawn with 50% probability ellipsoids. Hydrogen atoms have been drawn artificially small.

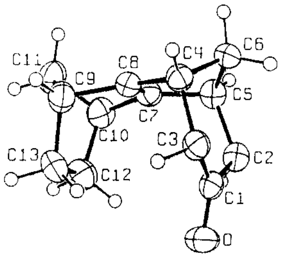


Figure 4. ORTEP drawing of 13 from which the phenyl substituents have been deleted to permit a clearer view of the framework conformation.

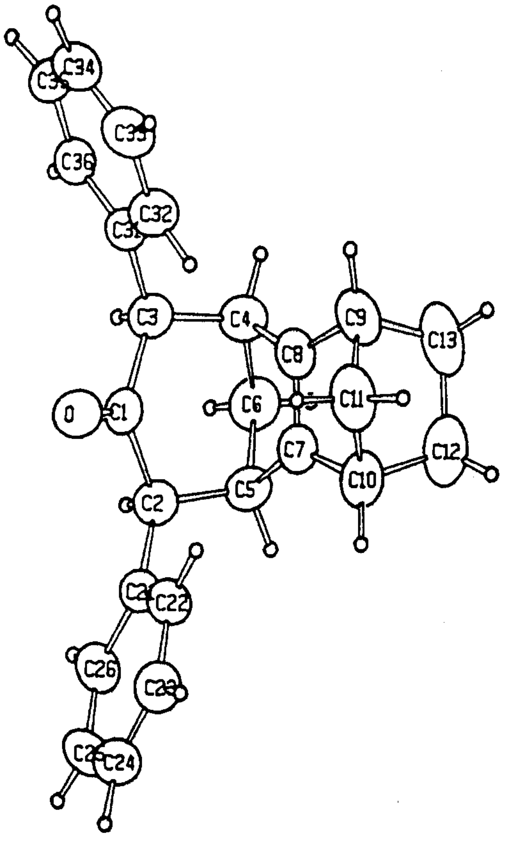
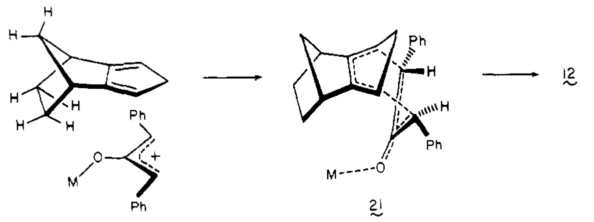


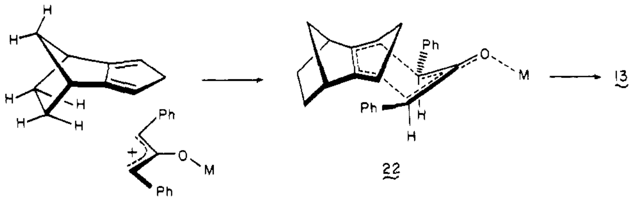
Figure 5. ORTEP drawing of 15. Non-hydrogen atoms are drawn with 50% probability ellipsoids. Hydrogen atoms have been drawn artificially small.

Table II. Fe$_2$(CO)$_9$-Promoted [3 + 4] Cycloadditions of 9 to 1[a]

reactant ratio[b]	yield,[c] %	Ratio 17:18[d]
2:1:2	40	3.5:1
1:2:2	78	1.7:1
1:1:1	24	2:1
1:2:1	57	1:1

[a] Benzene solution, 60 °C, 36 h. [b] Diene 1:dibromo ketone 9:Fe$_2$(CO)$_9$. [c] Combined adduct yield. [d] Difficultly separable impurities accompanied 18 (see text).

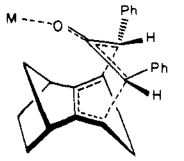




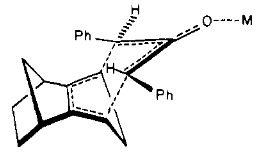
22

would be consistent with the overall stereochemical result.[13]

Alternatively, the nature of M in those reactions that produce this adduct may well be adequately large to foster population of conformer **10b**. Therefore, transition states represented by **23** and **24** could be involved. Since both



23



24

formalisms give rise to the same product (after thermodynamically driven ring flipping to arrive at the more stable conformer), no distinction can be made between them. This dilemma is also present when dealing with tetramethyloxyallyl cation **11**.

The fourth possibility, isomerization of **15** or **16** to **14** under the conditions of cycloaddition, has been ruled out by suitable control experiments (see Experimental Section).

In this connection, it must be recognized that the interpretation offered is based upon the relative distribution of two products (**13** and **16**). For this reason, their ratios must be shown not to be distorted by side reactions. In suitable control experiments, neither was found to be selectively destroyed nor isomerized under the original conditions of cycloaddition. Another possible caveat must also be dismissed. In all but one case (that involving the use of sodium iodide alone), it remains conceivable that the metallic species present not only engages in oxyallyl ion generation but in the complexation of the isodicyclopentadiene as well. As a consequence, it becomes necessary to show that the **13**:**16** ratio is not distorted by the selective blocking of one side of the diene by the metal.

Noyori and co-workers have previously reported on their inability to isolate stable diene–Fe(II) complexes from this type of reaction.[15] Our experience with **1** was no different. It becomes important to recognize, however, that when a diene–Fe(0) complex reacts with a dibromo ketone, the central metal becomes Fe(II) and, consequently, the diene can no longer remain as a persistent ligand on the Fe atom. A delicate balance in timing could therefore materialize between the liberation of the diene ligand from the Fe(II) atom and its capture by the oxyallyl species. In an independent study,[23] we have shown that **1** reacts with a wide

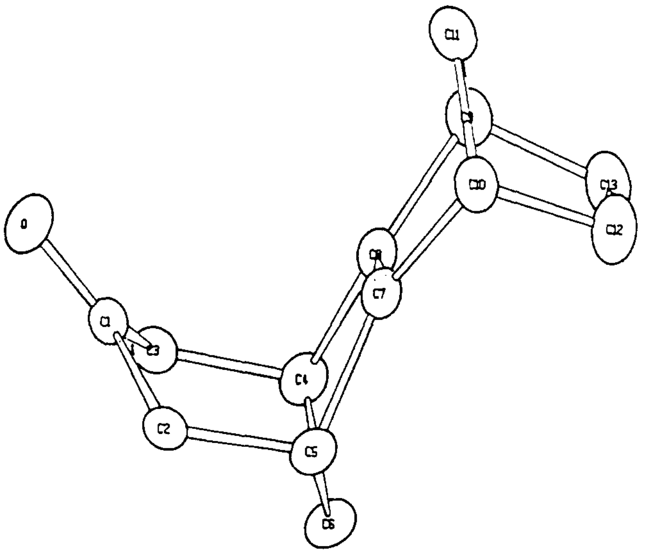


Figure 6. ORTEP drawing of **15** from which the phenyl substituents have been deleted to permit a clearer view of the framework conformation.

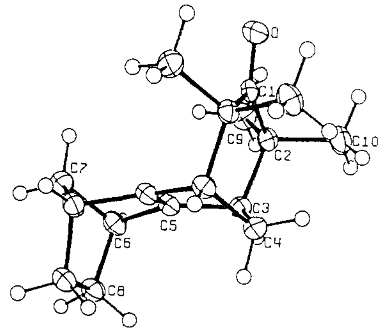


Figure 7. ORTEP drawing of **17**. Non-hydrogen atoms are drawn with 50% probability ellipsoids. Hydrogen atoms have been drawn artificially small.

variety of metals to form complexes in which the metal is coordinated predominantly, if not exclusively, on its exo surface. Since exo face selectivity dominates heavily in the distribution of ketones **12**–**16** (Table I), complete dissociation would have to occur if complexation materialized at all. Attempted coupling of **8** to [(isodicyclopentadiene)FeCO)$_2$]$_2$, prepared from **1** and Fe$_2$(CO)$_9$ at more elevated temperatures, led only to (isodicyclopentadiene)Fe(CO)Br$_2$.[24] This observation parallels the unreactivity of cyclobutadieneiron tricarbonyl to **9**.[15]

Presumably, secondary orbital interactions contribute favorably to the evolution of more compact transition states such as found in **19**.[25] To the extent that this particular form of electronic stabilization gains importance, isodicyclopentadiene (**1**) will respond more favorably to bond formation as in **19** relative to that in **21**. This is because above-plane approach is linked to downward folding of the developing central π bond (see X-ray structures). Less steric congestion develops as a consequence, with nonbonded interactions contributing less to the overall enthalpy of this cycloaddition reaction course.[26] Since the factors just discussed do not bear on the original

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[23] (a) Hsu, L.-Y. Hathaway, S. J.; Paquette, L. A. *Tetrahedron Lett.* **1984**, 259. (b) Paquette, L. A.; Schirch, P. F. T.; Hathaway, S. J.; Hsu, L.-Y.; Gallucci, J. C. *J. Organomet. Chem.*, in press. (c) Paquette, L. A.; Hathaway, S. J.; Schirch, P. F. T.; Gallucci, J. C. *Ibid.*, in press.

[24] For a leading reference, consult: Diel, B. N. *J. Organomet. Chem.* **1985**, *284*, 257.

[25] Hoffmann, H. M. R.; Joy, D. R. *J. Chem. Soc. B.* **1968**, 1182.

[26] Alder-type [4 + 2] cycloadditions to **1** are known to occur only above-plane, presumably because of comparable interplay of nonbonded steric interactions. See ref 17a,c,d and: Paquette, L. A.; Kravetz, T. M.; Hsu, L.-Y., to be submitted for publication.

purpose of this investigation, the relative proportions of **12** and **15** should be regarded as nonrelevant to our considerations of ground-state orbital tilting in **1**.

As regards transition states **20** and **22**, however, one might argue that a great deal less prima facie evidence for steric control is apparent in either case. The expectation follows that existing imbalances in electronic inducement for bonding to one or the other face should now become apparent. Table I reveals that the preference for transition-state **20** falls into the range 2.1–4.3 for all the experiments performed. The role of product stability on the observed stereoselection remains unclear but is probably not significant. For example, ketones **12**, **13**, and **15** possess comparably pyramidalized central double bond geometry.

Consequently, our findings are consistent with the conclusion that orbital tilting within **1** does play a stereochemically determinative role as this diene enters into [3 + 4] cycloaddition. Preferred above-plane bonding contrasts strikingly with the course of anti-Alder [4 + 2] cycloadditions. This reversal in π-facial stereoselectivity is construed as reflective of the closed-shell repulsion arguments presented in pictorial form in **4**–**7**. We note that a possible relationship between internuclear distance separating bonding centers and cycloaddition stereochemistry has not previously been entertained or recognized. Bartlett and co-workers have previously recognized a dependence of 1,2- vs. 1,4-cycloaddition ratios on diene terminus distance within the "1122" diene.[27] The present findings and the comparably stereoselective course of [6 + 4] tropone–isodicyclopentadiene cycloadditions[7,28] point up the possibility that suitable mismatching of orbital alignments may have impact in a continuum of reaction types. The stereochemical response of neutral isodicyclopentadienes and their anions to metal complexation,[23] to be reported separately, is another instructive example.

Experimental Section

All reactions were performed under a nitrogen atmosphere. Infrared spectra were recorded on a Perkin-Elmer Model 467 spectrophotometer. Proton NMR spectra were obtained with Bruker WP-200 and WM-300 spectrometers. Carbon NMR spectra were determined on a Bruker WP-80 spectrometer. Mass spectra were recorded on a Kratos MS-30 instrument. Melting points are uncorrected. Elemental analyses were performed by the Scandinavian Microanalytical Laboratory, Herlev, Denmark.

Cycloaddition of 1,3-Dibromo-1,3-diphenylpropan-2-one to Isodicyclopentadiene. Method A (Copper–Sodium Iodide). A solution of **8** (2.09 g, 5.7 mmol) in acetone–acetonitrile (1:1, 10 mL) was added at room temperature to a well stirred mixture of **1** (1.5 g, 11.4 mmol), sodium iodide (3.14 g, 21 mmol), and copper powder (1.08 g, 17 mmol) in the same solvent system (25 mL). After 5 h of continued stirring, the reaction mixture was poured into a separatory funnel containing concentrated ammonium hydroxide (15 mL), water (15 mL), and ether (75 mL). This mixture was shaken, and the deep blue aqueous layer was separated. The organic phase was washed with dilute ammonium hydroxide (3 × 20 mL) and water (until neutral), dried, filtered, and evaporated. The residual pale orange oil was separated into its components by sequential MPLC (elution with 4% ethyl acetate in petroleum ether) and preparative TLC on silica gel (elution with 5% ethyl acetate in petroleum ether). The following five products were isolated in a combined yield of 69%.

For **13**: colorless prisms, mp 150–151 °C (from hexanes); 55 mg (2.8%); IR (KBr) 3070, 2985, 2910, 2890, 1705, 1610, 1505, 1460, 1305, 1090, 750, 743, 707, 550 cm^{-1}; ^{1}H NMR (300 MHz, CDCl$_3$) δ 7.20–7.06 (m, 10 H), 3.78 (s, 2 H), 3.27 (d, J = 4.6 Hz, 2 H), 3.07 (s, 2 H), 2.45 (d, J = 11.4 Hz, 1 H), 2.15–2.10 (m, 1 H), 1.80 (d, J = 7.5 Hz, 2 H), 1.59 (d, J = 8.1 Hz, 1 H), 1.27 (d, J = 8.1 Hz, 1 H), 1.10 (dd, J = 7.5 and 2.3 Hz, 2 H); ^{13}C NMR (CDCl$_3$) 211.76 (s), 154.53 (s), 138.67 (s), 128.37 (d), 128.09 (d), 126.50 (d), 57.48 (d), 51.90 (t), 42.86 (d), 42.22 (d), 39.20 (t), 26.99 (m) ppm; mass spectrum calcd (M$^+$) m/z 340.1827, obsd m/z 340.1834.

Anal. Calcd for $C_{25}H_{24}O$: C, 88.20; H, 7.11. Found: C, 88.04; H, 7.17.

For **16**: colorless plates, mp 78–79 °C (from hexanes); 229 mg (11.8%); IR (CHCl$_3$) 3070, 3040, 2980, 2950, 1700, 1605, 1500, 1455, 1120, 1085, 1070 cm^{-1}; ^{1}H NMR (300 MHz, CDCl$_3$) δ 7.21–7.09 (m, 10 H), 3.93 (s, 2 H), 3.09 (d, J = 4.0 Hz, 2 H), 2.97 (s, 2 H), 2.57 (d, J = 11.2 Hz, 1 H), 2.06–2.01 (m, 1 H), 1.84 (d, J = 7.2 Hz, 2 H), 1.70 (d, J = 8.0 Hz, 1 H), 1.45 (d, J = 7.8 Hz, 1 H), 1.20 (dd, J = 7.2 and 2.1 Hz, 2 H); ^{13}C NMR (CDCl$_3$) 212.40 (s), 156.57 (s), 139.00 (s), 128.40 (d), 128.08 (d), 126.48 (d), 59.98 (d), 54.55 (t), 41.07 (d), 40.95 (d), 39.16 (t), 26.51 (m) ppm; mass spectrum, calcd (M$^+$) m/z 340.1827, obsd m/z 340.1818.

For **14**: colorless crystals, mp 130–131° (from hexanes); 5 mg (0.3%); IR (KBr) 3040, 2980, 2950, 1710, 1615, 1505, 1460, 1300, 1095, 755, 705 cm^{-1}; ^{1}H NMR (300 MHz, CDCl$_3$) δ 7.35–7.10 (m, 10 H), 3.95 (s, 1 H), 3.87 (d, J = 2.9 Hz, 1 H), 3.17 (m, 1 H), 3.00 (m, 1 H), 2.80 (m, 1 H), 2.73 (m, 1 H), 2.45 (d, J = 10.9 Hz, 1 H), 2.14–2.10 (m, 1 H), 1.89–1.60 (m, 3 H), 1.36 (d, J = 7.4 Hz, 1 H), 1.02–0.96 (m, 2 H); ^{13}C NMR (CDCl$_3$) 216.17, 155.55, 155.42, 139.83, 139.45, 129.23, 128.72, 128.21, 127.82, 126.80, 126.67, 63.31, 58.58, 52.13, 46.76, 45.48, 43.06, 41.84, 41.20, 26.45, 26.19 ppm; mass spectrum, calcd (M$^+$) m/z 340.1827, obsd m/z 340.1816.

For **12**: colorless prisms, mp 238–239 °C (from hexanes); 32 mg (1.6%); IR (KBr) 3070, 3040, 2960, 2940, 2890, 1710, 1610, 1500, 1450, 1300, 1050, 730, 695 cm^{-1}; ^{1}H NMR (300 MHz, CDCl$_3$) δ 7.35–7.20 (m, 10 H), 4.12 (s, 2 H), 3.63 (d, J = 3.8 Hz, 2 H), 3.09 (s, 2 H), 2.70 (dt, J = 10.5 and 5.3 Hz, 1 H), 2.35 (d J = 10.5 Hz, 1 H), 1.61 (d, J = 7.8 Hz, 1 H), 1.34 (d, J = 7.4 Hz, 2 H), 1.22 (d, J = 7.8 Hz, 1 H), 0.31 (dd, J = 7.4 and 2.3 Hz, 2 H); ^{13}C NMR (CDCl$_3$) 240.11, 153.70, 137.18, 129.06, 127.69, 126.59, 60.92, 52.40, 50.77, 44.14, 43.49, 25.61 ppm; mass spectrum, calcd (M$^+$) m/z 340.1827, obsd m/z 340.1824.

For **15**: colorless prisms, mp 158–159 °C (from hexanes); 710 mg (53%); IR (KBr) 3080, 3040, 2990, 2945, 2880, 1725, 1615, 1505, 1460, 1305, 1055, 760, 715, 705 cm^{-1}; ^{1}H NMR (300 MHz, CDCl$_3$) δ 7.35–7.16 (m, 10 H), 3.94 (d, J = 3.0 Hz, 2 H), 2.92 (m, 2 H), 2.78 (s, 2 H), 2.52 (d, J = 10.6 Hz, 1 H), 2.41 (dt, J = 10.5 and 5.2 Hz, 1 H), 1.79 (d, J = 8.3 Hz, 1 H), 1.66 (d, J = 7.2 Hz, 2 H), 1.38 (d, J = 7.6 Hz, 1 H), 0.96 (dd, J = 7.4 and 2.3 Hz, 2 H); ^{13}C NMR (CDCl$_3$) 208.31 (s), 154.65 (s), 140.09 (s), 129.29 (d), 128.14 (d), 126.67 (d), 62.09 (d), 53.53 (t), 50.78 (t), 45.48 (d), 43.12 (d), 26.25 (m) ppm; mass spectrum, calcd (M$^+$) m/z 340.1827, obsd m/z 340.1821.

Anal. Calcd for $C_{25}H_{24}O$: C, 88.20; H, 7.11. Found: C, 88.20; H, 7.14.

Method B (Sodium Iodide). A solution of **1** (264 mg, 2.0 mmol) and **8** (368 mg, 1 mmol) in acetone–acetonitrile (1:1, 10 mL) containing sodium iodide (1.84 g, 12.2 mmol) was heated at the reflux temperature for 1 h. The reaction mixture was diluted with chloroform, washed with sodium thiosulfate solution and water, dried, filtered, and freed of solvent. The light brown oil was subjected to MPLC on silica gel (elution with 4% ethyl acetate in petroleum ether). The following three products were isolated in a combined yield of 21%: **13** (10 mg, 3%), **16** (20 mg, 6%), and 15 (40 mg, 18%).

Method C (Zinc–Copper Couple). A solution of **1** (250 mg, 1.89 mmol) in anhydrous glyme (2 mL) containing zinc–copper couple (25 mg) was treated with a solution of **8** (463 mg, 1.70 mmol) at room temperature. Three additional 25-mg portions of the couple were introduced at 30-min intervals, and the reaction mixture was heated overnight at the reflux temperature with stirring. After filtration through Celite, the filtrate was diluted with dichloromethane, washed with water (2 × 3 mL), filtered again through Celite, and dried. The dark orange oil was separated into its components as described above to give **13** (3 mg, 0.5%), **16** (9 mg, 1.7%), **14** (9 mg, 1.7%), and **15** (11 mg, 2.1%).

Method D (Diiron Enneacarbonyl). A mixture of **1** (264 mg, 2 mmol), **8** (368 mg, 1 mmol), and diiron enneacarbonyl (490 mg, 1.3 mmol) in anhydrous tetrahydrofuran (3 mL) was stirred at room temperature for 6 h. Benzene (10 mL) was added, and the mixture was washed with water. The organic phase was dried, filtered, and evaporated to afford a light orange oil, chromato-

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[27] Bartlett, P. D.; Wingrove, A. S.; Owyang, *J. Am. Chem. Soc.* **1968**, *90*, 6067.

[28] Paquette, L. A.; Hathaway, S. J. *J. Org. Chem.*, in press.

graphic purification of which was carried out in the predescribed manner. The following four products were isolated in a combined yield of 41%: **13** (9 mg, 2.5%), **16** (35 mg, 10.3%), **14** (18 mg, 5.3%), and **15** (77 mg, 22.6%).

When benzene was utilized as solvent, the combined yield fell to 18%, and the product distribution was as follows: **13** (2 mg, 0.5%), **16** (8 mg, 2.3%), **14** (20 mg, 6%), **15** (30 mg, 9%).

Cycloaddition of 2,4-Dibromo-2,4-dimethylpentan-3-one to Isodicyclopentadiene. Method D. A solution of **1** (264 mg, 2 mmol) and **9** (272 mg, 1 mmol) in anhydrous benzene (5 mL) was treated with diiron enneacarbonyl (800 mg, 2.2 mmol) and heated at 60 °C for 36 h. The cool dark reaction mixture was diluted with ethyl acetate (5 mL) and water (5 mL) and filtered through Celite. The organic phase was washed with water, dried, filtered, and evaporated. The oily residue was filtered through a short column of silica gel and subjected to MPLC on the same adsorbent (elution with 2% ethyl acetate in petroleum ether) to give two fractions, one of which was pure isomer **17**. The other fraction consisted of a mixture of **18** plus impurities and was subjected to multiple-elution preparative thin-layer chromatography on silica gel (elution with 3% ethyl acetate in petroleum ether) to separate one impurity. The other impurity could not be removed, and spectral data were therefore recorded on this mixture. Capillary gas chromatographic analysis was used to determine the percent yield and isomer ratio.

For **17**: colorless crystals, mp 66–67 °C (from hexanes); 70 mg (29%); IR ($CHCl_3$) 2980, 2880, 1700, 1470, 1380, 1295, 1030 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 2.82 (t, J = 1.7 Hz, 2 H), 2.50 (d, J = 11.2 Hz, 1 H), 2.24 (d, J = 4.9 Hz, 2 H), 1.91 (dt, J = 11.2 and 5.0 Hz, 1 H), 1.73–1.68 (m, 2 H), 1.55–1.47 (m, 1 H), 1.32 (d, J = 8.0 Hz, 1 H), 1.21 (s, 6 H), 1.05 (s, 8 H); ^{13}C NMR ($CDCl_3$) 222.56 (s), 155.42 (s), 52.06 (t), 51.04 (s), 48.17 (d), 42.74 (d), 41.84 (t), 28.24 (q), 26.25 (q), 25.90 (t) ppm; mass spectrum, calcd (M^+) m/z 244.1827, obsd m/z 244.1809.

Anal. Calcd for $C_{17}H_{24}O$: C, 83.55; H, 9.90. Found: C, 83.56; H, 9.95.

For **18**: colorless oil; 17 mg (7%); ^1H NMR (300 MHz, $CDCl_3$) δ 3.10 (m, 1 H), 3.00–2.90 (m, 3 H), 1.85 (m, 2 H), 1.61 (m, 2 H), 1.34 (s, 6 H), 1.33 (s, 6 H), 1.26–1.01 (series of m, 4 H); ^{13}C NMR ($CDCl_3$) 216.43 (s), 152.16 (s), 50.53 (s), 46.76 (t), 45.55 (t), 38.78 (d), 34.88 (d), 28.11 (m), 24.85 (q), 24.40 (q) ppm; mass spectrum, calcd (M^+-CH_3) *m/z* 229.1593, obsd *m/z* 229.1598.

Base-Catalyzed Equilibration of 15. A solution of **15** (50 mg, 0.147 mmol) in anhydrous methanol (50 mL) containing sodium methoxide (0.54 mg, 0.01 mmol—added as an aliquot from a larger volume of solution) was heated at the reflux temperature for 4 days. After cooling to 20 °C, the mixture was diluted with ether (50 mL) and washed with water (2 × 20 mL). The organic phase was dried, filtered, and evaporated to leave a mixture of ketones, the separation of which was achieved by preparative TLC on silica gel (elution with 4% ethyl acetate in petroleum ether). There were isolated 10 mg (20%) of **14** and 40 mg (80% recovery) of unchanged **15**.

Base-Catalyzed Equilibration of 16. A solution of **16** (75 mg, 0.22 mmol) was heated for 2 days with methanolic sodium methoxide as described above. Comparable workup afforded 30 mg (40%) of recovered **16**, 33 mg (44%) of **14**, and 12 mg (16%) of **15**.

Control Experiment for Base-Catalyzed Equilibration of 19. A solution of **19** (50 mg, 0.147 mmol) in anhydrous methanol (50 mL) was heated at the reflux temperature for 4 days. After cooling to 20 °C, the mixture was diluted with ether (50 mL) and washed with water (2 × 20 mL) prior to drying and evaporation. Preparative thin-layer silica gel chromatography of the resulting oil (elution with 4% ethyl acetate in petroleum ether) provided 45 mg (90%) of unchanged **19**. Minor amounts (<3 mg) of unidentifiable (decomposition?) components were detected.

Establishment of Product Stability under the Original Reaction Conditions. A. A mixture of **13** and **16** (1:2 ratio, 20 mg, 0.059 mmol), **8** (22 mg, 0.059 mmol), and diiron enneacarbonyl (28 mg, 0.076 mmol) in anhydrous tetrahydrofuran (2 mL) was stirred at 20 °C for 5 h. The mixture was diluted with benzene (10 mL) and washed with water prior to drying and evaporation. Filtration of the resulting pale orange oil through silica gel (elution with 5% ethyl acetate in petroleum ether) provided 19 mg (95%) of a colorless oil that was identical by analytical TLC and ^1H NMR with the original mixture of **13** and **16**.

B. A mixture of **15** (20 mg, 0.059 mmol), **8** (22 mg, 0.059 mmol), and diiron enneacarbonyl (28 mg, 0.076 mmol) in anhydrous tetrahydrofuran (2 mL) was stirred at 20 °C for 5 h. The mixture was diluted with benzene (10 mL) and washed with water prior to drying and evaporation. Filtration of the resulting pale orange oil through silica gel (elution with 5% ethyl acetate in petroleum ether) afforded a quantitative recovery of **15** as a colorless solid. Analytical TLC and ^1H NMR analysis proved the substance to be identical with starting material.

C. Dibromide **8** was added to a well-stirred mixture of **13** and **16** (1:2 ratio, 18 mg, 0.053 mmol), sodium iodide (35 mg, 0.24 mmol), and copper powder (11 mg, 0.18 mmol). After being stirred for 5 h at 20 °C, the reaction mixture was poured into a separatory funnel containing concentrated ammonium hydroxide (2 mL), water (2 mL), and ether (5 mL) and shaken. The deep blue aqueous layer was separated, and the organic solution was washed with dilute ammonium hydroxide (2 × 5 mL) and water (until neutral), dried, filtered, and evaporated to afford 17 mg (94%) of a light yellow oil that was identical by analytical TLC and ^1H NMR with the original mixture of **13** and **16**.

D. Dibromide 8 was added to a well-stirred mixture of **15** (20 mg, 0.053 mmol), sodium iodide (35 mg, 0.24 mmol), and copper powder (11 mg, 0.18 mmol). After 5 h of continued stirring at 20 °C, the reaction mixture was poured into a separatory funnel containing concentrated ammonium hydroxide (2 mL), water (2 mL), and ether (5 mL) and was shaken. The deep blue aqueous layer was separated, and the organic solution was washed with dilute ammonium hydroxide (2 × 5 mL) and water (until neutral), dried, filtered, and evaporated to afford a quantitative recovery of unchanged **15** as a pale yellow solid. The recovered material exhibited analytical TLC and ^1H NMR spectral properties identical with those of the starting material.

Attempted [3 + 4] Cycloadditions of 8 to [(Isodicyclopentadiene)Fe(CO)$_2$]$_2$. A. A mixture of [(isodicyclopentadiene)Fe(CO)$_2$]$_2$[29] (20 mg) and **8** (27 mg) in anhydrous, deoxygenated tetrahydrofuran (2 mL) was stirred at 20 °C for 5 h. The mixture was diluted with benzene (10 mL) and washed with water prior to drying and evaporation. Preparative thin-layer silica gel chromatography of the residue (elution with 10% ethyl acetate in petroleum ether) provided 13 mg of (isodicyclopentadiene)Fe(CO)Br$_2$ as an orange oily solid: IR (KBr) 3120, 3015, 2990, 2895, 2035, 1990, 1450, 1432, 1390, 1383, 1290, 950, 820, 577, 548 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.08 (t, J = 2.3 Hz, 1 H), 4.55 (d, J = 2.4 HZ, 2 H), 3.05 (m, 2 H), 1.93 (dt, J = 7.7 and 1.7 Hz, 2 H), 1.85 (d, J = 9.0 Hz, 1 H), 1.48 (d, J = 9.0 Hz, 1 H), 1.23 (m, 2 H).

Analytical TLC of the reaction mixture prior to workup showed the presence of unreacted [(isodicyclopentadiene)Fe(CO)$_2$]$_2$ and **8**, neither of which were isolated.

B. A mixture of [(isodicyclopentadiene)Fe(CO)$_2$]$_2$ (20 mg), **8** (27 mg, 0.074 mmol), and diiron enneacarbonyl) (26 mg, 0.074 mmol) in anhydrous, deoxygenated tetrahydrofuran (2 mL) was stirred at 20 °C for 5 h. The mixture was diluted with benzene (10 mL) and washed with water prior to drying and evaporation. Preparative thin-layer silica gel chromatography of the residue (elution with 10% ethyl acetate in petroleum ether) gave 9 mg of (isodicyclopentadiene)Fe(CO)Br$_2$ as an orange oily solid. Analytical data are identical with those reported above. Analytical TLC of the reaction mixture prior to workup indicated the presence of unreacted complex as the only other admixed substance.

Acknowledgment. We thank the National Institutes of Health for support of this research program through Grant CA-12115.

Registry No. **1**, 75725-33-6; **8**, 958-79-2; **9**, 17346-16-6; **12**, 91817-56-0; **13**, 91877-83-7; **14**, 97806-22-9; **15**, 91877-84-8; **16**, 97858-61-2; **17**, 91817-57-1; **18**, 91926-24-8; [(isocyclopentadienyl)Fe(CO)$_2$]$_2$, 97752-17-5; (isocyclopentadienyl)Fe(CO)Br$_2$, 97752-18-6.

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(29) McKinney, J.; Schirch, P. F. T., unpublished results.