Cyclopentane Construction by $Rh_2(OAc)_4$-Mediated Intramolecular C-H Insertion: Steric and Electronic Effects

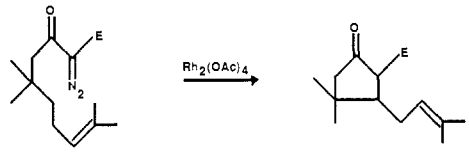
Douglass F. Taber*[1] and Robert E. Ruckle, Jr.

Contribution from the Department of Chemistry, University of Delaware, Newark, Delaware 19716. *Received March 12, 1986*

Abstract: Factors which govern the regiospecificity of cyclopentane formation by rhodium(II) acetate mediated intramolecular C-H insertion (**1** → **2**) have been studied. The order of reactivity of the target C-H site is found to be methine > methylene > methyl. Allylic and benzylic C-H are found to be *less* reactive than aliphatic C-H. These results are interpreted as being due to the availability of the electron density in the C-H bond. Steric influences on the course of the cyclization are also reported.

Traditionally, carbon-carbon bond-forming processes have required that both organic fragments be specifically activated. There are isolated reports[3] of an alternative approach, based on carbene insertion into a C-H bond. In this approach, only *one* of the two organic fragments need be activated, an inherently more efficient process. There have been two limitations to this approach: the requisite carbene precursors are expensive, and C-H insertion tends not to be highly selective for a specific site.[2] The first limitation was largely overcome by the introduction of rhodium(II) acetate catalysis[3] of diazo[4] insertion. It remained to explore the selectivity of the C-H insertion process.

We[5a] and Wenkert[5b] recently observed that rhodium(II) acetate mediate intramolecular C-H insertion (**1** → **2**) proceeds smoothly to give five-membered-ring formation. We have shown selectivity between diastereotopic methylene C-H bonds, allowing enantioselective cyclopentane construction.[6] We have also shown[7] that C-H insertion proceeds with retention of configuration. We now report a detailed study of steric and electronic factors governing the regioselectivity of this ring-forming reaction.[8]



1 2

Electronic Effects

To explore electronic effects on regioselectivity, we have prepared a series of β-keto esters **5a-18a** (**Tables** I and II) which have two competing sites for C-H insertion and studied their cyclization. The ratio of the two products, normalized for the number of equivalent C-H bonds, was taken as a ratio of reactivity. We first addressed the relative reactivities of methyl, methylene, and methine C-H bonds. We had previously observed (**1** → **2**)[2a] that methylene is more reactive than methyl. Despite a 3:1 statistical preference, none of the methyl insertion product was detected.[4a] We have now observed (entry 1, Table I) that methine insertion is preferred over methylene insertion. These results (methine > methylene > methyl) are to be contrasted with

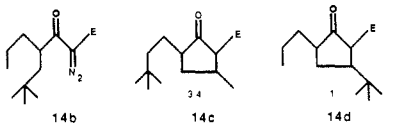
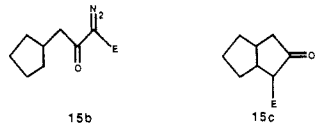
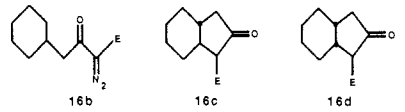
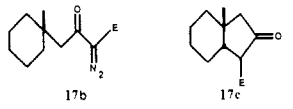
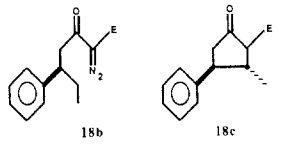
Table I

entry	compd	products	yield, %	statistically corrected preference
1	5b	5c 2 3 : 5d 1	84	4.6
2	6b	6c 2 9 : 6d 1	88	2.9
3	7b	7c 2 3 : 7d 1	75	2.3
4	8b	8c 3 5 : 8d 1	81	7.0
5	9b	9c ONLY : 9d	89	all
6	10b	10c 1 1 : 10d 1	93	1.1
7	11b	11c 0 4 : 11d 1	78	0.2
8	12b	12c	76	
9	13b	13c 1 2 : 13d 1	92	1.2

(1) Fellow of the Alfred P. Sloan Foundation, 1982-1987.
(2) Burke, S. D.; Grieco, P. A. *Org. React. (N.Y.)* **1979**, *26*, 361.
(3) (a) Anciaux, A. J.; Hubert, A. J.; Noels, A. F.; Petinot, N.; Teyssie, P. *J. Org. Chem.* **1980**, *45*, 695. (b) Demonceau, A.; Noels, A. F.; Hubert, A. J.; Teyssie, P. *J. Chem. Soc., Chem. Commun.* **1981**, 688.
(4) (a) Regitz, M.; Hocker, J.; Liedhegener, A. *Organic Synthesis*; Wiley: New York, 1973; Collect. Vol. V, p 179. (b) Hendrickson, J. B.; Wolf, W. A. *J. Org. Chem.* **1968**, *33*, 3610. (c) We have found methanesulfonyl azide to be the most satisfactory reagent for diazo transfer with β-keto esters.
(5) (a) Taber, D. F.; Petty, E. H. *J. Org. Chem.* **1982**, *47*, 4808. (b) Wenkert, E.; Davis. L. L.; Mylari, B. L.; Solomon, M. F.; daSilva, R. R.; Shulman, S.; Warnet, R. J.; Ceccherelli, P.; Curini, M.; Pellicciari, R. *J. Org. Chem.* **1982**, *47*, 3242.
(6) Taber, D. F.; Raman, K. *J. Am. Chem. Soc.* **1983**, *105*, 5935.
(7) Taber, D. F.; Petty, E. H.; Raman, K. *J. Am. Chem. Soc.* **1985**, *107*, 196.
(8) For other recent studies of selectivity in Rh-mediated intramolecular C-H insertion, see: (a) Moyer, M. P.; Feldman, P. L.; Rapoport, H. *J. Org. Chem.* **1985**, *50*, 5223. (b) Jeffford, C. W.; Zaslona, A. *Tetrahedron Lett.* **1985**, *26*, 6035.

0002-7863/86/1508-7686$01.50/0

Table II

entry	compd	products	yield, %
1		14b 14c 14d	73
2		15b 15c	45[a]
3[a]		16b 16c 16d	63[b]
4		17b 17c	93
5		18b 18c	77

[a] A 22% yield of the spiro compound resulting from methine insertion was also observed. [b] With $Rh_2(OAc)_4$, **16c**:**16d** = 3:1; with dirhodium tetraoctanoate, **16c**:**16d** = 5:1; with tetraphenylporphyrinrhodium chloride, **16c**:**16d** = 15:1.

those of Bergman,[9,10] who has observed, for rhodium-mediated C–H activation, the opposite reactivity.

The reactivity detailed above is consistent with that observed for intramolecular C–H insertion[11] via a metal-free carbenoid. In striking contrast to the metal-free carbenoid systems, however, is the observation that rhodium(II) acetate mediated insertion into allylic and benzylic methylenes is *disfavored* when compared to insertion into aliphatic methylene (entries 2 and 3, Table I). Allylic and benzylic methylenes are also less reactive than aliphatic methylene when compared to methine (entries 4 and 5, Table I).

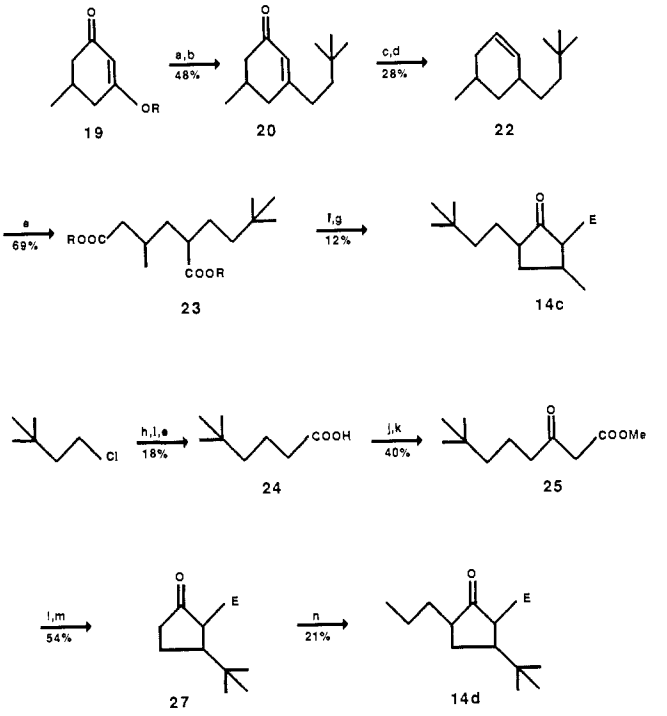
A possible rationalization for this and the methine, methylene, and methyl selectivities is that alkyl groups are inductively electron donating and so increase the electron density of the C–H bond, making it more susceptible to attack by the electrophilic rhodium–carbene species. Vinyl and phenyl are inductively electron withdrawing and so decrease the reactivity of the adjacent C–H bond. A factor in this selectivity may be an initial, rapidly reversible precomplexation of the rhodium carbenoid with the C–H bond, as observed by Jones for intermolecular rhodium-mediated C–H activation.[12] The ratios observed speak strongly against significant charge separation in the transition state.

The competition between C–H insertion and intramolecular cyclopropanation (entries 6 and 7, Table I) was also considered. When the competition is with methine, insertion is marginally selected over cyclopropanation. However, in the methylene case, cyclopropanation occurs to a greater extent than C–H insertion.[13]

Insertion into an aromatic ring also occurs efficiently (entry 8, Table I). Another competitive cyclization shows that this process is approximately equal in energy with methylene insertion (entry 9, Table I). In the intermolecular series, aryl insertion is greatly favored over aliphatic insertion.[14] This effect has been

(9) Periana, R. A.; Bergman, R. G. *Organometallics* **1984**, *3*, 508.
(10) Yang, G. K.; Bergman, R. G. *Organometallics* **1985**, *4*, 129.
(11) Gilbert, J. C.; Giamalva, D. H.; Weerasooriya, U. *J. Org. Chem.* **1983**, *48*, 5251.
(12) Jones, W. D.; Feher, F. J. *J. Am. Chem. Soc.* **1985**, *107*, 620.
(13) Cyclopropanation can also occur for compounds **6b** and **8a** to give bicyclo[4.1.0]heptanes. Such cyclopropanes, observed in only trace amounts in the $Rh_2(OAc)_4$-mediated cyclizations, are the dominant products when the starting diazo esters are exposed to copper bronze powder in refluxing toluene.
(14) Jones, W. D.; Feher, F. J. *J. Am. Chem. Soc.* **1984**, *106*, 1650.

Scheme I[a]



[a] Reagents: (a) Isobutyl alcohol, *p*-toluenesulfonic acid; (b) C_4H_9-CH_2CH_2MgCl; (c) *p*-toluenesulfonyl hydrazide; (d) catecholborane; (e) $RuO_2 \cdot xH_2O$, $NaIO_4$; (f) K_2CO_3, MeI; (g) NaH, THF; (h) Mg; (i) allyl bromide; (j) oxalyl chloride; (k) methyl lithioacetate; (l) mesyl azide; (m) $Rh_2(OAc)_4$; (n) 2.5 equiv of LDA, *n*-propyl iodide.

rationalized as being due to initial coordination of the rhodium complex with the π-system of the arene. In this intramolecular case, such precoordination is sterically precluded.

Steric Effects

In the competition between methylene and methyl,[4a] no methyl insertion product was detected. The methine to methylene reactivity ratio is much smaller than this. A rationale for this apparent anomaly could be that insertion into the sterically more hindered methine, when compared to insertion into methylene, is retarded by nonbonding interactions.

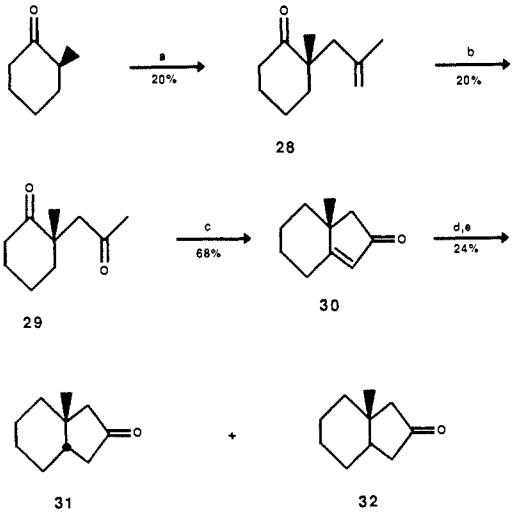
The effect of steric bulk near the site of insertion is illustrated by the results of the reaction of compound **14b** (entry 1, Table II). In this case, electronic effects are nearly equal, and the steric effect of the *tert*-butyl group predominates, causing insertion into the propyl side chain to predominate. In other words, van der Waals interactions between the *tert*-butyl group and the ligands on rhodium disfavor insertion to give **14d**.

Since compounds **14c** and **14d** were inseparable by column chromatography, authentic materials were synthesized (Scheme I) and compared to the mixture obtained from the reaction of **14b** after each of the three samples had been equilibrated to the thermodynamic ratio of diastereomers by treatment with *tert*-butoxide/*tert*-butyl alcohol. Integration of the ^1H NMR signals for the methines between the carbonyls allowed us to determine the ratio of products.

We next investigated diastereoselectivity in the formation of bicyclic systems. When insertion occurs into a cyclopentyl ring (entry 2, Table II),[15] only the cis product is formed. When insertion occurs into a cyclohexyl ring, (entries 3 and 4, Table II), diastereoselectivity is a function of both the catalyst used and the substitution on the cyclohexane. We interpret the dependence on the catalyst as evidence that the rhodium is bound to the central carbon, as opposed to the oxygens, of the metallocarbene in the transition state.

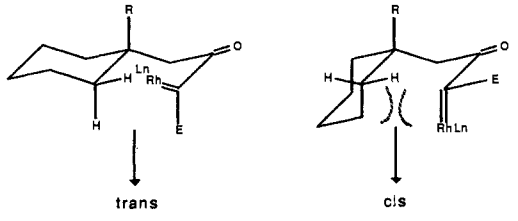
(15) Prof. Cane previously effected the cyclization of the ethyl ester of **15b** to give similar results: Cane, D. E.; Thomas, P. J. *J. Am. Chem. Soc.* **1984**, *106*, 5295. We thank him for sharing his results with us prior to publication.

Scheme II[a]



[a] Reagents: (a) potassium *tert*-butoxide, methallyl chloride, *tert*-butyl alcohol; (b) $RuO_2 \cdot xH_2O$, $NaIO_4$; (c) potassium *tert*-butoxide, *tert*-butyl alcohol; (d) Na/NH_3 (l), *tert*-butyl alcohol; (e) PCC, sodium acetate.

For 1-methylcyclohexyl (entry 4, Table II), only the cis product was formed. The angular methyl apparently blocks the approach of the rhodium–carbene moiety to that C–H bond which would lead to the trans product. Product stereochemistry was confirmed by comparing authentic cis and trans ketones **31** and **32** obtained by the dissolving metal reduction of enone **30** (Scheme II)[30] to the ketone obtained by the decarbomethoxylation of **17c**. The selectivity observed can be rationalized by assuming perpendicular approach[16] of the rhodium carbenoid to the C–H bond.



It follows from the above analysis that an isolated ternary center could induce the relative stereochemistry at the newly formed stereogenic center. Such is indeed the case (entry 5, Table II).[17] Since precursors with single acyclic ternary centers are readily available in high optical purity, this suggests a general method for the construction of 3,4-dialkylcyclopentanes.

Summary

While the mechanism of Rh-mediated C–H insertion is not yet fully established,[31] it is apparent that selectivity is governed by both steric and electronic considerations. Electronic effects and steric effects are in delicate balance, as evidenced by insertion into methine in preference to methylene (entry 1, Table I). It may be possible to tune this balance by modifying the electronic demand and steric bulk of the ligands on the rhodium.[18] Investigations in this direction are ongoing.

Experimental Section[19,20]

Methyl 6-Methyl-3-oxoheptanoate (3). NaH (31.69 g of 50% oil dispersion, 0.66 mol, 2.5 equiv) was placed in flame-dried, three-necked flask equipped with a mechanical stirrer and an N_2 inlet and rinsed with petroleum ether (3 × 75 mL). THF (350 mL), dimethyl carbonate (55.5 mL, 0.66 mol, 2.5 equiv), and methanol (1 drop) were added. 5-Methyl-2-hexanone (30 g, 0.26 mol) was added dropwise as a neat liquid at room temperature over 10 min; the mixture was allowed to stir 12 h, cooled to 0 °C, and cautiously quenched with 10% aqueous HCl. The mixture was extracted with diethyl ether (3 × 500 mL). The combined organic phases were dried over $Na_2S_2O_4$ and concentrated in vacuo. The residual oil was distilled bulb-to-bulb at 85–95 °C (0.2 mmHg) to give **3** as a colorless oil: 27.7 g (61%); R_f (10% EtOAc/hexane) 0.32; ^1H NMR δ 0.87 (d, J = 6.3 Hz, 6 H), 1.4–1.55 (m, 3 H), 2.52 (t, J = 7.5 Hz, 2 H), 3.44 (s, 2 H), 3.71 (s, 3 H); ^{13}C NMR δ 22.3 (q, 2), 27.5 (d), 32.2 (t), 41.1 (t), 49.0 (t), 52.3 (q), 167.7 (s), 203.0 (s); IR 2860, 1750, 1720, 1655, 1630, 1470, 1450, 1440, 1405, 1385, 1370, 1320, 1240, 1150 cm^{-1}; MS, m/z (relative intensity) 172 (42), 129 (100), 116 (20), 105 (12), 104 (10), 101 (10); exact mass calcd for $C_9H_{16}O_3$ 172.110, obsd 172.110.

Methyl 3-Oxoheptanoate (4). Following the procedure for **3**, 10.0 g (0.1 mol) of 2-hexanone was reacted and chromatographed on 50 g of silica gel with pure petroleum ether. The first 750 mL was discarded. The next 1500 mL was concentrated in vacuo to give **4** as a colorless oil: 6.0 g (48%); R_f (20% EtOAc/hexane) 0.42; ^1H NMR δ 0.91 (t, J = 7.3 Hz, 3 H), 1.31 (m, 2 H), 1.58 (m, 2 H), 2.55 (t, J = 7.3 Hz, 2 H), 3.47 (s, 2 H), 3.73 (s, 3 H); ^{13}C NMR δ 13.8 (q), 22.2 (t), 25.7 (t), 42.7 (t), 49.0 (t), 52.2 (q), 167.8 (s), 202.7 (s); IR 2960, 1750, 1722, 1655, 1628, 1450, 1440, 1410, 1320, 1240, 1195, 1150 cm^{-1}; MS, m/z (relative intensity) 158 (16), 129 (14), 116 (100), 101 (56); exact mass calcd for $C_8H_{14}O_3$ 158.094, obsd 158.094.

Methyl 6-Methyl-3-oxo-4-propylheptanoate (5a). Alkylation was effected by the method of Weiler.[21] Thus, diisopropylamine (3.8 mL, 27.0 mmol, 2.4 equiv) was dissolved in THF (15 mL) in a 100-mL flame-dried, three-necked flask equipped with an N_2 inlet and a low-temperature thermometer. The flask was cooled to −78 °C. *n*-BuLi (11.8 mL of 2.1 M, 24.8 mmol, 2.2 equiv) was added rapidly but slowly enough that the internal temperature was ≤−40 °C. The temperature was brought to −10 °C by immersion in an ice/salt bath for 15 min, and then the flask was recooled to −78 °C. Ketone **3** (2.0 g, 11 mmol) in THF (2 mL) was added dropwise via syringe over 5 min. The cooling bath was removed, the mixture was stirred for 30 min and then 1-iodopropane (3.3 mL, 34 mmol, 3 equiv) was added all at once. Stirring was continued for 10 min, and then the reaction was quenched with 10% aqueous HCl and extracted with ether (3 × 40 mL). The combined organic extracts were dried over $MgSO_4$ and concentrated in vacuo. The residual oil was chromatographed on 50 g of silica gel with 2% EtOAc/petroleum ether. The first 200 mL was discarded. The next 350 mL was concentrated in vacuo to give **5a** as a colorless oil: 1.91 g (79%); R_f (10% EtOAc/hexane) 0.50; ^1H NMR δ 0.78–0.86 (m, 9 H), 1.1–1.6 (m, 7 H), 2.6–2.7 (m, 1 H), 3.41 (s, 2 H), 3.65 (s, 3 H); ^{13}C NMR δ 14.1 (q), 20.5 (t), 22.4 (q), 22.9 (q), 26.0 (d), 33.9 (t), 40.4 (t), 48.0 (t), 50.4 (d), 52.3 (q), 167.7 (s), 206.4 (s); IR 2960, 1755, 1715, 1655, 1625, 1450, 1405, 1385, 1370, 1240, 1150, 1035 cm^{-1}; MS, m/z (relative intensity) 215 (3), 172 (28), 158 (19), 129 (100), 116 (11), 101 (13). Anal. Calcd for $C_{12}H_{22}O_3$: C, 67.26; H, 10.35. Found: C, 67.29; H, 10.82.

Methyl 2-Diazo-6-methyl-3-oxo-4-propylheptanoate (5b). A flame-dried, one-necked flask equipped with an N_2 inlet and a septum was charged with **5a** (1.88 g, 8.7 mmol), methanesulfonyl azide[22] (1.16 g, 9.6 mmol, 1.1 equiv), and CH_3CN (14 mL). To this solution was added triethylamine (2.4 mL, 17.4 mmol, 2 equiv). The reaction was followed by TLC. It typically took about 3 h at room temperature. The mixture was diluted with 10% aqueous NaOH and extracted with extraction solvent (3 × 20 mL). The combined organic extracts were dried over $MgSO_4$ and concentrated in vacuo. The residual oil was chromatographed on 50 g of silica gel with 2% EtOAc/petroleum ether. The first 100 mL was discarded. The next 350 mL was concentrated in vacuo to give α-diazo β-keto ester **5b** as a yellow oil: 1.63 g (78%); R_f (20% EtOAc/hexane) 0.53; ^1H NMR δ 0.87–0.91 (m, 9 H), 1.15–1.75 (m, 7 H), 3.7–3.8 (m, 1 H), 3.84 (s, 3 H); ^{13}C NMR δ 14.2 (q), 20.4 (t), 22.7 (q), 22.9 (q), 26.2 (d), 34.9 (t), 41.0 (t), 44.7 (d), 52.1 (q), 76.13 (s), 161.6 (s), 196.9 (s); IR 2960, 2140, 1730, 1660, 1560, 1440, 1310, 1200, 1020, 910 cm^{-1}; MS, m/z (relative intensity) 137 (31), 113 (110), 101 (40).

Methyl 5,5-Dimethyl-2-oxo-3-propylcyclopentanecarboxylate (5c) and Methyl 5-Methyl-3-(2-methyl-1-propyl)-2-oxocyclopentanecarboxylate (5d). A flame-dried, two-necked flask equipped with an addition funnel and an N_2 inlet was charged with a catalytic amount of $Rh_2(OAc)_4$ (20

(16) Sailard, J.-Y.; Hoffmann, R. *J. Am. Chem. Soc.* **1984**, *106*, 2006.
(17) Taber, D. F.; Ruckle, R. E., Jr. *Tetrahedron Lett.* **1985**, *26*, 3059.
(18) Le, J. C.; Chavan, M. Y.; Chau, L. K.; Bear, J. L.; Kadish, K. M. *J. Am. Chem. Soc.* **1985**, *107*, 7195.
(19) The ^{13}C multiplicites were determined with the aid of an INEPT sequence (Morris, G. A.; Freeman, R. *J. Am. Chem. Soc.* **1979**, *101*, 760).
(20) Column chromatography was carried out with TLC-mesh silica (Taber, D. F. *J. Org. Chem.* **1982**, *47*, 1351).
(21) Huckin, S. N.; Weiler, L. *J. Am. Chem. Soc.* **1974**, *96*, 1082.
(22) (a) Horner, L.; Christmann, A. *Chem. Ber.* **1963**, *96*, 388. (b) Boyer, J. H.; Mack, C. H.; Goebel, N.; Morgan, L. R., Jr. *J. Org. Chem.* **1958**, *23*, 1051.

mg). CH_2Cl_2 (6 mL) was added, and **5b** (205 mg, 0.8 mmol) in CH_2Cl_2 (6 mL) was added dropwise over 1 h. The initial slurry of $Rh_2(OAc)_4$ changed to a clear emerald green solution after addition of the first few drops of diazo solution. TLC analysis showed that the reaction was over when addition was complete. The material was directly concentrated in vacuo, and the residue was chromatographed on 10 g of silica gel with 1% EtOAc/petroleum ether. The first 170 mL was discarded. The next 80 mL was concentrated in vacuo to give **5c** as a colorless oil: 106 mg (59%); R_f (20% EtOAc/hexane) 0.51; ^{1}H NMR δ 0.91, 0.92 (t, J = 6.7 Hz, 3 H), 1.06, 1.14 (s, 3 H), 1.29 (s, 3 H), 1.2–2.1 (m, 6 H), 2.4 (m, 1 H), 2.94, 2.96 (s, 1 H), 3.68, 3.72 (s, 3 H); ^{13}C NMR δ 14.0 (q), 20.7 (t), 21.0 (t), 23.9 (q), 25.3 (q), 29.5 (q), 32.7 (t), 33.1 (t), 38.9 (s), 42.4 (t), 43.6 (t), 47.6 (d), 47.9 (d), 51.8 (q), 65.7 (d), 65.8 (d), 169.3 (s), 213.7 (s); IR 2980, 1745, 1735, 1660, 1470, 1450 cm^{-1}; MS, m/z (relative intensity) 212 (14), 197 (72), 181 (35), 171 (14), 170 (87), 169 (14), 166 (23), 165 (100), 139 (18), 138 (93), 137 (17), 115 (39), 112 (65), 111 (17), 110 (30), 109 (46), 101 (15); exact mass calcd for $C_{12}H_{20}O_3$ 212.141, obsd 212.142.

The next 70 mL was concentrated in vacuo to give **5d** as a colorless oil: 45 mg (25%); R_f (20% EtOAc/hexane) 0.42; ^{1}H NMR δ 0.88 (d, J = 6.3 Hz, 3 H), 0.92 (d, J = 6.3 Hz, 3 H), 1.18 (d, J = 6.4 Hz, 3 H), 1.0–1.4 (m, 3 H), 2.4 (m, 2 H), 2.5 (m, 1 H), 2.77 (d, J = 11.6 Hz, 1 H), 3.76 (s, 3 H); ^{13}C NMR δ 19.3 (q), 21.5 (q), 23.4 (q), 26.2 (d), 34.3 (d), 36.9 (t), 39.1 (t), 49.1 (d), 52.4 (q), 62.8 (d), 169.8 (s), 213.3 (s); IR 2990, 1745, 1735, 1470, 1290, 1135, 1075 cm^{-1}; MS, m/z (relative intensity) 212 (2), 181 (18), 165 (18), 157 (17), 156 (100), 137 (22), 125 (16), 124 (92), 123 (11), 116 (13), 111 (15), 109 (26), 101 (61); exact mass calcd for $C_{12}H_{20}O_3$ 212.141, obsd 212.141.

Methyl 3-Oxo-4-propyloct-7-enoate (6a). Following the procedure for **5a**, 0.61 g of **4** was alkylated with 4-bromo-1-butene (3 equiv). The residual oil was chromatographed on 20 g of silica gel with 2% EtOAc/petroleum ether. The first 100 mL was discarded. The next 500 mL was concentrated in vacuo to give **6a** as a colorless oil: 618 mg (77%); R_f (20% EtOAc/hexane) 0.55; ^{1}H NMR δ 0.90 (t, J = 7.1 Hz, 3 H), 1.2–2.0 (m, 8 H), 2.6–2.7 (m, 1 H), 3.49 (s, 2 H), 3.71 (s, 3 H), 5.0 (7, 2 H), 5.7 (m, 1 H); ^{13}C NMR δ 14.2 (q), 20.4 (t), 30.2 (t), 31.4 (t), 33.5 (t), 48.4 (t), 51.5 (d), 52.3 (q), 115.3 (t), 137.8 (d), 167.7 (s), 206.2 (s); IR 2960, 1755, 1715, 1660, 1630, 1450, 1410, 1240, 1200, 1150, 1010, 915 cm^{-1}; MS, m/z (relative intensity) 212 (7), 183 (11), 158 (42), 139 (16), 130 (14), 129 (100), 124 (15), 123 (21), 116 (17), 109 (12), 101 (48); exact mass calcd for $C_{12}H_{20}O_3$ 212.141, obsd 212.140.

Methyl 2-Diazo-3-oxo-4-propyloct-7-enoate (6b). Following the procedure for **5b**, diazo transfer was performed on **6a** (446 mg, 2.1 mmol). The residual oil was chromatographed on 20 g of silica gel with 3.5% EtOAc/petroleum ether. The first 175 mL was discarded. The next 175 mL was concentrated in vacuo to give α-diazo β-keto ester **6b** as a yellow oil: 474 mg (95%); R_f (20% EtOAc/hexane) 0.6; ^{1}H NMR δ 0.89 (t, J = 7.1 Hz, 3 H), 1.2–2.1 (m, 8 H), 3.6–3.8 (m, 1 H), 3.84 (s, 3 H), 5.0 (m, 2 H), 5.7 (m, 1 H); ^{13}C NMR δ 14.2 (q), 20.4 (t), 31.1 (t), 31.6 (t), 34.3 (t), 46.4 (d), 52.1 (q), 76.5 (s), 114.7 (t), 138.4 (d), 161.6 (s), 196.4 (s); IR 2960, 2140, 1730, 1660, 1560, 1440, 1315, 1010, 920 cm^{-1}; MS, m/z (relative intensity) 168 (28), 139 (33), 136 (61), 113 (100), 109 (36), 108 (25), 107 (31), 101 (33), 100 (36); CH_4 CI exact mass calcd for $C_{12}H_{19}N_2O_3$ 239.140, obsd 239.138.

Methyl 3-(1-But-3-enyl)-5-methyl-2-oxocyclopentanecarboxylate (6c) and Methyl 5-Ethenyl-2-oxo-3-propylcyclopentanecarboxylate (6d). Following the procedure for **5c** and **5d**, cyclization was effected on **6b** (474 mg, 2.1 mmol). The material was directly concentrated in vacuo,and the residue was chromatographed on 20 g of silica gel with 2.5% EtOAc/petroleum ether. The first 175 mL was discarded. The next 100 mL was concentrated in vacuo to give **6c** as a colorless oil: 274 mg (66%); R_f (20% EtOAc/hexane) 0.49; ^{1}H NMR δ 1.18 (d, J = 6.4 Hz, 3 H), 1.1–2.5 (m, 8 H), 2.8 (d, J = 11.6 Hz, 1 H), 3.76 (s, 3 H), 5.0 (m, 2 H), 5.7 (m, 1 H); ^{13}C NMR δ 19.2 (q), 28.9 (t), 31.5 (t), 34.2 (d), 36.2 (t), 49.9 (d), 52.4 (q), 63.0 (d), 115.4 (t), 137.7 (d), 169.7 (s), 212.8 (s); IR 2990, 1760, 1735, 1660, 1645, 1440, 1340, 1295, 1210, 1140, 1065, 915 cm^{-1}; MS, m/z (relative intensity) 210 (26), 192 (17) 179 (16), 178 (11), 168 (12), 157 (13), 156 (86), 150 (13), 137 (32), 136 (11), 135 (13), 133 (11), 125 (21), 124 (100), 109 (29), 108 (12), 101 (62); exact mass calcd for $C_{12}H_{18}O_3$ 210.126, obsd 210.126.

The next 100 mL was concentrated in vacuo to give **6d** as a colorless oil: 96 mg (23%); R_f (20% EtOAc/hexane) 0.53; ^{1}H NMR δ 0.92 (t, J = 7.0 Hz, 3 H), 1.3–2.4 (m, 8 H), 3.0 (d, J = 11.8 Hz, 1 H), 3.76 (s, 3 H), 5.1 (m, 2 H), 5.7 (m, 1 H); ^{13}C NMR δ 14.0 (q), 20.6 (t), 31.8 (t), 34.0 (t), 42.8 (d), 49.7 (d), 52.5 (q), 60.8 (d), 115.9 (t), 138.3 (d), 169.3 (s), 212.0 (s); IR 2980, 1760, 1740, 1665, 1650, 1620, 1440, 1355, 1250, 990, 915 cm^{-1}; MS, m/z (relative intensity) 210 (40), 179 (25), 178 (30), 168 (91), 156 (74), 151 (44), 150 (26), 137 (25), 136 (100), 135 (23), 124 (91), 121 (19), 113 (60), 111 (25), 110 (19), 109 (47), 108 (61), 107 (28), 101 (98); exact mass calcd for $C_{12}H_{18}O_3$ 210.126, obsd 210.125.

Methyl 3-Oxo-6-phenyl-4-propylhexanoate (7a). Following the procedure for **5a**, 0.253 g of **4** was alkylated with phenethyl bromide (3 equiv). The residual oil was chromatographed on 30 g of silica gel with 2% EtOAc/petroleum ether. The first 225 mL was discarded. The next 75 mL was concentrated in vacuo to give **7a** as a colorless oil: 80 mg (19%); R_f (20% EtOAc/hexane) 0.53; ^{1}H NMR δ 0.89 (t, J = 7.0 Hz, 3 H), 1.2–2.0 (m, 6 H), 2.5–2.6 (m, 3 H), 3.46(s, 2 H), 3.73 (s, 3 H), 7.1–7.3 (m, 5 H); ^{13}C NMR δ 14.0 (q), 20.2 (t), 32.5 (t), 33.2 (t, 2), 48.0 (t), 51.6 (d), 52.2 (q), 128.0 (d, 2), 128.1 (d, 2), 125.7 (d), 141.4 (s), 167.5 (s), 205.9 (s); IR 2960, 1755, 1725, 1660, 1630, 1450, 1410, 1240, 1155, 1035 cm^{-1}; MS, m/z (relative intensity) 158 (61), 129 (100), 116 (40), 105 (11), 104 (18), 101 (31).

Methyl 2-Diazo-3-oxo-6-phenyl-4-propylhexanoate (7b). Following the procedure for **5b**, diazo transfer was performed on **7a** (410 mg, 1.6 mmol). The residual oil was chromatographed on 20 g of silica gel with 4% EtOAc/petroleum ether. The first 60 mL was discarded. The next 180 mL was concentrated in vacuo to give α-diazo β-keto ester **7b** as a yellow oil: 443 mg (98%); R_f (20% EtOAc/hexane) 0.66; ^{1}H NMR δ 0.88 (t, J = 7.2 Hz, 3 H), 1.2–2.1 (m, 6 H), 2.58 (t, J = 8.4 Hz, 2 H), 3.7 (m, 1 H), 3.81 (s, 3 H), 7.1–7.2 (m, 5 H); ^{13}C NMR δ 14.2 (q), 20.4 (t), 33.6 (t), 33.7 (t), 34.4 (t), 46.8 (d), 52.2 (q), 76.5 (s), 125.9 (d), 128.3 (d, 2), 128.4 (d, 2), 142.1 (s), 161.6 (s), 196.1 (s); IR 2960, 2140, 1730, 1660, 1560, 1440, 1315, 1200, 1130, 1010, 910, 700 cm^{-1}; MS, m/z (relative intensity) 186 (29), 185 (36), 184 (100), 131 (36), 129 (29), 127 (33), 117 (51), 115 (22), 113 (53), 105 (29), 104 (49), 103 (22), 101 (27), 100 (82); CH_4 CI exact mass calcd for $C_{16}H_{21}N_2O_3$ 289.155, obsd 289.155.

Methyl 5-Methyl-2-oxo-3-(2-phenyl-1-ethyl)cyclopentanecarboxylate (7c) and Methyl 2-Oxo-5-phenyl-3-propylcyclopentanecarboxylate (7d). Following the procedure for **5c** and **5d**, cyclization was effected on **7b** (443 mg, 1.5 mmol). The material was directly concentrated in vacuo, and the residue was chromatographed on 20 g of silica gel with 2% EtOAc/petroleum ether. The first 700 mL was discarded. The next 200 mL was concentrated in vacuo to give **7d** as a colorless oil: 90 mg (22%); R_f (20% EtOAc/hexane) 0.49; ^{1}H NMR δ 0.94 (t, J = 7.1 Hz, 3 H), 1.2–1.7 (m, 6 H), 2.5–2.6 (m, 2 H), 3.33 (d, J = 12 Hz, 1 H), 3.72 (s, 3 H), 7.2–7.4 (m, 5 H); ^{13}C NMR δ 14.0 (q), 20.6 (t), 31.7 (t), 35.7 (t), 44.0 (d), 50.2 (d), 52.5 (q), 62.3 nd), 126.9 (d, 2), 127.2 (d), 128.8 (d, 2), 141.1 (s), 169.3 (s), 211.7 (s); IR 2960, 2860, 1760, 1730, 1440, 1340, 1280, 1170, 1130, 700 cm^{-1}; MS, m/z (relative intensity) 260 (13), 229 (13), 202 (25), 201 (100), 186 (29), 160 (23), 159 (18), 158 (62), 132 (11), 131 (82), 129 (18), 128 (12), 118 (12), 117 (33), 115 (25), 105 (14), 104 (32), 103 (39), 102 (14); exact mass calcd for $C_{16}H_{20}O_3$ 260.141, obsd 260.141.

The next 300 mL was concentrated in vacuo to give **7c** as a colorless oil: 211 mg (45%); R_f (20% EtOAc/hexane) 0.45; ^{1}H NMR δ 1.18 (d, J = 6.4 Hz, 3 H), 1.6–1.7 (m, 2 H), 2.3–2.8 (m, 7 H), 3.75 (s, 3 H), 7.2–7.3 (m, 5 H); ^{13}C NMR δ 19.2 (q), 31.5 (t), 33.5 (t), 34.2 (d), 36.4 (t), 49.8 (d), 52.3 (q), 63.0 (d), 126.1 (d), 128.4 (d, 2), 128.5 (d, 2), 141.3 (s), 169.6 (s), 212.4 (s); IR 2960, 1755, 1735, 1460, 1440, 1335, 1295, 1136, 700 cm^{-1}; MS, m/z (relative intensity) 260 (6), 157 (10), 156 (100), 124 (62), 104 (12); exact mass calcd for $C_{16}H_{20}O_3$ 260.141, obsd 260.141.

Methyl 4-(2-Methyl-1-propyl)-3-oxooct-7-enoate (8a). Following the procedure for **5a**, 1.9 g of **3** was alkylated with 4-bromo-1-butene (2.5 equiv). The residual oil was chromatographed on 50 g of silica gel with 1% EtOAc/petroleum ether. The first 300 mL was discarded. The next 450 mL was concentrated in vacuo to give **8a** as a colorless oil: 314 mg (12%); R_f (20% EtOAc/hexane) 0.56; ^{1}H NMR δ 0.90 (d, J = 6.2 Hz, 3 H), 0.91 (d, J = 6.2 Hz, 3 H), 1.2–2.0 (m, 7 H), 2.7 (m, 1 H), 3.50 (s, 2 H), 3.75 (s, 3 H), 5.0 (m, 2 H), 5.8 (m, 1 H); ^{13}C NMR δ 22.5 (q), 22.8 (1), 26.0 (d), 30.6 (t), 31.3 (t), 40.4 (t), 48.1 (t), 49.7 (d), 52.3 (q), 115.4 (t), 137.7 (d), 167.6 (s), 206.1 (s); IR 2960, 1755, 1715, 1655, 1625, 1445, 1405, 1385, 1370, 1240, 1150, 915, 665 cm^{-1}; MS, m/z (relative intensity) 226 (4), 183 (17), 172 (15), 170 (10), 129 (100), 101 (15); exact mass calcd for $C_{13}H_{22}O_3$ 226.157, obsd 226.157.

Methyl 2-Diazo-4-(2-methyl-1-propyl)-3-oxooct-7-enoate (8b). Following the procedure for **5b**, diazo transfer was performed on **8a** (365 mg, 1.6 mmol). The residual oil was chromatographed on 20 g of silica gel with 2% EtOAc/petroleum ether. The first 125 mL was discarded. The next 125 mL was concentrated in vacuo to give α-diazo β-keto ester **8b** as a yellow oil: 361 mg (89%); R_f (20% EtOAc/hexane) 0.63; ^{1}H NMR δ 0.88 (d, J = 6.4 Hz, 3 H), 0.89 (d, J = 6.4 Hz, 3 H), 1.2–2.0 (m, 7 H), 3.6 (m, 1 H), 3.84 (s, 3 H), 5.0 (m, 2 H), 5.8 (m, 1 H); ^{13}C NMR δ 22.7 (q), 22.8 (q), 26.2 (d), 31.5 (t), 31.8 (t), 41.1 (t), 44.6 (d), 52.1 (q), 76.2 (s), 114.8 (t), 138.3 (d), 161.5 (s), 196.4 (s); IR 2960, 2140, 1730, 1660, 1560, 1440, 1310, 1200, 1130, 1010, 915 cm^{-1}; MS, m/z (relative intensity) 198 (18), 168 (38), 155 (33), 149 (27), 137 (28),

136 (100), 135 (22), 127 (25), 123 (22), 121 (25), 113 (63), 109 (45), 108 (75), 107 (25), 101 (45), 100 (32).

Methyl 3-(1-But-3-enyl)-5,5-dimethyl-2-oxocyclopentanecarboxylate (8c) and Methyl 5-Ethenyl-3-(2-methyl-1-propyl)-2-oxocyclopentanecarboxylate (8d). Following the procedure for **5c** and **5d**, cyclization was effected on **8b** (361 mg, 1.4 mmol). The material was directly concentrated in vacuo, and the residue was chromatographed on 20 g of silica gel with 2% EtOAc/petroleum ether. The first 150 mL was discarded. The next 100 mL was concentrated in vacuo to give **8c** as a colorless oil: 202 mg (63%); R_f (20% EtOAc/hexane) 0.56; ^{1}H NMR δ 1.06, 1.13 (s, 3 H), 1.29 (s, 3 H), 1.2–2.5 (m, 7 H), 2.96 (s), 1 H), 3.68, 3.77 (s, 3 H), 5.0 (m, 2 H), 5.8 (m, 1 H); ^{13}C NMR δ 23.9 (q), 26.8 (t), 29.5 (q), 33.6 (t), 38.7 (s), 43.6 (t), 47.6 (d), 51.8 (q), 65.6 (d), 114.8 (d), 138.3 (t), 169.2 (s), 213.3 (s); IR 2990, 1740, 1660, 1450, 915 cm^{-1}; MS, m/z (relative intensity) 238 (19), 223 (94), 207 (20), 191 (100), 183 (31), 170 (91), 163 (33), 151 (54), 138 (94), 135 (26), 123 (30), 122 (22), 121 (31), 115 (31), 111 (30), 110 (24), 109 (37), 107 (28), 101 (9).

The next 100 mL was concentrated in vacuo to give **8d** as a colorless oil: 59 mg (18%); R_f (20% EtOAc/hexane) 0.53; ^{1}H NMR δ 0.89 (d, J = 8.7 Hz, 3 H), 0.92 (d, J = 8.8 Hz, 3 H), 1.1–1.8 (m, 5 H), 2.3–2.5 (m, 2 H), 3.1–3.3 (m, 1 H), 3.76 (s, 3 H), 5.1 (m, 2 H), 5.8 (m, 1 H); ^{13}C NMR δ 21.4 (q), 23.4 (q), 26.1 (d), 34.3 (t), 38.8 (d), 39.0 (t), 48.6 (d), 52.4 (q), 60.9 (d), 117.2 (t), 135.0 (d), 169.8 (s), 212.8 (s); IR 2990, 1740, 1450, 1290, 1170, 920 cm^{-1}; MS, m/z (relative intensity) 238 (4), 197 (25), 191 (22), 182 (73), 170 (20), 165 (47), 163 (22), 153 (73), 151 (24), 150 (86), 140 (65), 138 (25), 137 (29), 135 (33), 127 (25), 123 (33), 122 (67), 121 (27), 112 (27), 111 (24), 110 (20), 109 (100), 108 (71), 107 (35).

Methyl 4-(2-Methyl-1-propyl)-3-oxo-6-phenylhexanoate (9a). Following the procedure for **5a**, 1.2 g of **3** was alkylated with phenethyl bromide (3 equiv). The residual oil was chromatographed on 50 g of silica gel with 2% EtOAc/petroleum ether. The first 250 mL was discarded. The next 500 mL was concentrated in vacuo to give **9a** as a colorless oil: 981 mg (51%); R_f (20% EtOAc/hexane) 0.48; ^{1}H NMR δ 0.87 (t, J = 6.1 Hz, 6 H), 1.3–1.9 (m, 5 H), 2.5–2.7 (m, 3 H), 3.4 (s, 2 H), 3.72 (s, 3 H), 7.1–7.3 (m, 5 H); ^{13}C NMR δ 22.3 (q), 22.5 (q), 25.9 (d), 32.9 (t), 33.2 (t), 40.2 (t), 47.7 (t), 49.8 (d), 51.9 (q), 125.9 d), 128.2 (d, 2), 128.3 (d, 2), 141.3 (s), 167.3 (s), 205.5 (s); IR 2950, 1750, 1715, 1655, 1625, 1495, 1450, 1405, 1385, 1370, 1235, 1145, 695 cm^{-1}; MS, m/z (relative intensity) 277 (63), 172 (60), 130 (10), 129 (100), 114 (13), 105 (13), 104 (11); CH_4 CI exact mass calcd for $C_{17}H_{25}O_3$ 277.180, obsd 277.181.

Methyl 2-Diazo-4-(2-methyl-1-propyl)-3-oxo-6-phenylhexanoate (9b). Following the procedure for **5b**, diazo transfer was performed on **9a** (355 mg, 1.3 mmol). The residual oil was chromatographed on 20 g of silica gel with 2% EtOAc/petroleum ether. The first 125 mL was discarded. The next 125 mL was concentrated in vacuo to give α-diazo β-keto ester **9b** as a yellow oil: 310 mg (79%); R_f (20% EtOAc/hexane) 0.49; ^{1}H NMR δ 0.88 (d, J = 6.4 Hz, 6 H), 1.3–2.0 (m, 5 H), 2.6 (t, J = 8.2 Hz, 2 H), 3.8 (m, 1 H), 3.81 (s, 3 H), 7.1–7.3 (m, 5 H); ^{13}C NMR δ 22.8 (q, 2), 26.1 (d), 33.6 (t), 34.2 (t), 41.1 (t), 44.9 (d), 52.2 (q), 125.9 (d), 128.3 (d, 2), 128.4 (d, 2), 142.0 (s), 161.5 (s), 196.4 (s); IR 2960, 2140, 1730, 1660, 1560, 1440, 1310, 1010, 700 cm^{-1}; MS, m/z (relative intensity) 217 (34), 198 (100), 186 (29), 155 (59), 131 (33), 127 (40), 117 (41), 113 (36), 105 (34), 104 (45), 101 (29), 100 (55); CH_4 CI exact mass calcd for $C_{17}H_{23}N_2O_3$ 303.171, obsd 303.169.

Methyl 5,5-Dimethyl-2-oxo-3-(2-phenyl-1-ethyl)cyclopentanecarboxylate (9c). Following the procedure for **5c** and **5d**, cyclization was effected on **9b** (310 mg, 1.3 mmol). The material was directly concentrated in vacuo, and the residue was chromatographed on 20 g of silica gel with 2% EtOAc/petroleum ether. The first 125 mL was discarded. The next 125 mL was concentrated in vacuo to give **9c** as a colorless oil: 245 mg (89%); R_f (20% EtOAc/hexane) 0.53; ^{1}H NMR δ 1.02, 1.08 (s, 3 H), 1.13, 1.27 (s, 3 H), 1.4–2.4 (m, 5 H), 2.8 (m, 2 H), 2.94, 2.96 (s, 3 H), 3.65, 3.69 (s, 3 H), 7.1–7.4 (m, 5 H); ^{13}C NMR δ 23.9 (q), 25.2 (q), 29.5 (q), 29.6 (q), 32.3 (t), 32.6 (t), 33.6 (t), 33.8 (t), 38.6 (s), 42.4 (t), 43.6 (t), 47.1 (d), 47.2 (d), 51.7 (q), 65.7 (d), 65.8 (d), 125.9 (d), 126.0 (d, 2), 128.4 (d, 2), 141.4 (s), 141.6 (s), 169.1 (s), 213.1 (s); IR 2960, 1760, 1630, 1460, 1440, 1375, 1270, 1240, 1175, 1095, 1050, 1030, 700 cm^{-1}; MS, m/z (relative intensity) 274 (13), 259 (46), 243 (29), 227 (51), 218 (17), 215 (24), 171 (22), 170 (100), 138 (84), 131 (33), 117 (17), 115 (30), 112 (46), 110 (37), 105 (29), 104 (24); exact mass calcd for $C_{17}H_{22}O_3$ 274.157, obsd 274.157.

Methyl 4-(2-Methyl-1-propyl)-3-oxohept-6-enoate (10a). Following the procedure for **5a**, 0.75 g of **3** was alkylated with allyl bromide (3 equiv). The residual oil was chromatographed on 50 g of silica gel with 1% EtOAc/petroleum ether. The first 600 mL was discarded. The next 500 mL was concentrated in vacuo to give **10a** as a colorless oil: 720 mg (77%); R_f (20% EtOAc/hexane) 0.43; ^{1}H NMR δ 0.90 (m, 6 H), 1.1–2.8 (m, 6 H), 3.48 (s, 2 H), 3.73 (s, 3 H), 5.0 (m, 2 H), 5.7 (m, 1 H); ^{13}C NMR δ 22.4 (q), 22.8 (q), 25.9 (d), 36.0 (t), 40.0 (t), 48.5 (t), 50.1 (d), 52.2 (q), 117.3 (t), 135.0 (d), 167.5 (s), 205.6 (s); IR 2960, 1755, 1720, 1655, 1625, 1470, 1450, 1405, 1340, 1320, 1240, 1150, 1038, 918 cm^{-1}; MS, m/z (relative intensity) 212 (7), 169 (70), 156 (100), 155 (41), 139 (44), 138 (32), 137 (32), 124 (51), 111 (32), 110 (27), 109 (42); exact mass calcd for $C_{12}H_{20}O_3$ 212.141, obsd 212.142.

Methyl 2-Diazo-4-(2-methyl-1-propyl)-3-oxohept-6-enoate (10b). Following the procedure for **5b**, diazo transfer was performed on **10a** (505 mg, 2.4 mmol). The residual oil was chromatographed on 20 g of silica gel with 2% EtOAc/petroleum ether. The first 100 mL was discarded. The next 75 mL was concentrated in vacuo to give α-diazo β-keto ester **10b** as a yellow oil: 544 mg (95%); R_f (20% EtOAc/hexane) 0.56; ^{1}H NMR δ 0.87 (d, J = 6.4 Hz, 3 H), 0.88 (d, J = 6.4 Hz, 3 H), 1.2–2.4 (m, 5 H), 3.7 (m, 1 H), 3.84 (s, 3 H), 5.0 (m, 2 H), 5.8 (m, 1 H); ^{13}C NMR δ 22.6 (q), 22.8 (q), 26.0 (d), 36.7 (t), 40.3 (t), 44.5 (d), 52.1 (q), 76.18 (s), 116.7 (t), 135.6 (d), 161.5 (s), 196.0 (s); IR 2960, 2140, 1730, 1660, 1560, 1440, 1310, 1210, 1120, 910 cm^{-1}; MS, m/z (relative intensity) 182 (14), 169 (14), 154 (11), 153 (16), 137 (52), 135 (17), 127 (19), 122 (61), 121 (16), 113 (100), 109 (19), 107 (11); CH_4 CI exact mass calcd for $C_{12}H_{19}N_2O_3$ 239.140, obsd 239.138.

Methyl 5,5-Dimethyl-2-oxo-3-(1-prop-2-enyl)cyclopentanecarboxylate (10c) and Methyl 3-(2-Methyl-1-propyl)-2-oxobicyclo[3.1.0]hexane-1-carboxylate (10d). Following the procedure for **5c** and **5d**, cyclization was effected on **10b** (544 mg, 2.3 mmol). The material was directly concentrated in vacuo, and the residue was chromatographed on 30 g of silica gel with 2% EtOAc/petroleum ether. The first 300 mL was discarded. The next 150 mL was concentrated in vacuo to give **10c** as a colorless oil: 238 mg (50%); R_f (20% EtOAc/hexane) 0.53; ^{1}H NMR δ 1.06, 1.13 (s, 3 H), 1.29 (s, 3 H), 1.2–2.5 (m, 5 H), 2.93 (s, 1 H), 3.69, 3.72 (s, 3 H), 5.0 (m, 2 H), 5.8 (m, 1 H); ^{13}C NMR δ 23.9 (q), 29.4 (q), 34.4 (t), 38.7 (s), 42.8 (t), 47.3 (d), 51.8 (q), 65.8 (d), 116.9 (t), 135.3 (d), 169.1 (s), 212.6 (s); IR 2990, 1740, 1660, 1620, 1450, 920 cm^{-1}; MS, m/z (relative intensity) 210 (25), 195 (88), 179 (29), 178 (29), 163 (100), 150 (19), 137 (37), 135 (54), 133 (23), 122 (21), 121 (96), 115 (35), 109 (44), 108 (23), 107 (33); exact mass calcd for $C_{12}H_{18}O_3$ 210.126, obsd 210.126.

The polarity was increased to 6%, and the next 750 mL was discarded. The following 300 mL was concentrated in vacuo to give **10d** as a white solid: 208 mg (43%); R_f (20% EtOAc/hexane) 0.37; mp 54–55 °C; ^{1}H NMR δ 0.84 (d, J = 6.3 Hz, 3 H), 0.91 (d, J = 6.3 Hz, 3 H), 1.0–2.5 (m, 9 H), 3.76 (s, 3 H); ^{13}C NMR δ 21.3 (q), 23.2 (t), 23.4 (q), 25.8 (d), 29.0 (t), 31.4 (d), 27.7 (s), 39.3 (t), 41.2 (d), 52.3 (q), 169.1 (s), 208.4 (s); IR 1745, 1445, 1380, 1330 cm^{-1}; MS, m/z (relative intensity) 179 (13), 154 (75), 153 (35), 141 (12), 123 (13), 122 (100), 113 (29), 108 (10), 102 (19), 95 (19). Anal. Calcd for $C_{12}H_{18}O_3$: C, 68.55; H, 8.63. Found: C, 68.17; H, 8.81.

Methyl 3-Oxo-4-propylhept-6-enoate (11a). Following the procedure for **5a**, 0.405 g of **4** was alkylated with allyl bromide (3 equiv). The residual oil was chromatographed on 50 g of silica gel with 3% EtOAc/petroleum ether. The first 300 mL was discarded. The next 200 mL was concentrated in vacuo to give **11a** as a colorless oil: 358 mg (69%); R_f (20% EtOAc/hexane) 0.50; ^{1}H NMR δ 0.89 (t, J = 7.1 Hz, 3 H), 1.2–1.8 (m, 4 H), 2.2–2.4 (m, 2 H), 2.6–2.8 (m, 1 H), 3.48 (s, 2 H), 3.71 (s, 3 H), 5.0 (m, 2 H), 5.7 (m, 1 H); ^{13}C NMR δ 14.1 (q), 20.3 (t), 33.0 (t), 35.4 (t), 48.7 (t), 51.9 (d), 52.3 (q), 117.2 (t), 135.1 (d), 167.5 (s), 205.6 (s); IR 2960, 1755, 1720, 1655, 1625, 1450, 1405, 1355, 1310, 1240, 1150, 1035, 918 cm^{-1}; MS, m/z (relative intensity) 198 (11), 156 (54), 155 (34), 125 (43), 124 (51), 101 (100); exact mass calcd for $C_{11}H_{18}O_3$ 198.126, obsd 198.125.

Methyl 2-Diazo-3-oxo-4-propylhept-6-enoate (11b). Following the procedure for **5b**, diazo transfer was performed on **11a** (57 mg, 0.3 mmol). The residual oil was chromatographed on 2.5 g of silica gel with 1.5% EtOAc/petroleum ether. The first 10 mL was discarded. The next 15 mL was concentrated in vacuo to give α-diazo β-keto ester **11b** as a yellow oil: 47 mg (72%); R_f (20% EtOAc/hexane) 0.51; ^{1}H NMR δ 0.88 (t, J = 7.3 Hz, 3 H), 1.2–2.5 (m, 6 H), 3.7–3.8 (m, 1 H), 3.84 (s, 3 H), 5.0 (m, 2 H), 5.8 (m, 1 H); ^{13}C NMR δ 14.2 (q), 20.4 (t), 33.6 (t), 36.0 (t), 46.5 (d), 52.1 (q), 116.6 (t), 135.7 (d), 161.6 (s), 195.8 (s); IR 2960, 2140, 1730, 1660, 1560, 1440, 1390, 1315, 1130, 920 cm^{-1}; MS, m/z (relative intensity) 158 (58), 133 (34), 129 (29), 122 (82), 121 (45), 119 (53), 118 (42), 115 (29) 113 (100), 100 (34); CH_4 CI exact mass calcd for $C_{11}H_{17}N_2O_3$ 225.124, obsd 225.122.

Methyl 5-Methyl-2-oxo-3-(1-prop-2-enyl)cyclopentanecarboxylate (11c) and Methyl 2-Oxo-3-propylbicyclo[3.1.0]hexane-1-carboxylate (11d). Following the procedure for **5c** and **5d**, cyclization was effected on **11b** (193 mg, 0.9 mmol), the material was directly concentrated in vacuo, and the residue was chromatographed on 10 g of silica gel with 5% EtOAc/petroleum ether. The first 90 mL was discarded. The next 30 mL was concentrated in vacuo to give **11c** as a colorless oil: 37 mg (22%); R_f (20% EtOAc/hexane) 0.42; ^{1}H NMR δ 1.18 (d, J = 6.3 Hz,

3 H), 2.1–2.6 (m, 6 H), 2.67 (d, J = 11.6 Hz, 1 H), 3.76 (s, 3 H), 5.0 (m, 2 H), 5.7 (m, 1 H); ^{13}C NMR δ 19.2 (q), 33.8 (t), 34.2 (t), 35.8 (d), 50.2 (d), 52.2 (q), 63.1 (d), 116.9 (t), 135.3 (d), 169.6 (s), 211.6 (s); IR 2970, 1755, 1735, 1440, 1335, 1295, 1135, 918 cm^{-1}; MS, m/z (relative intensity) 196 (37), 178 (31), 168 (40), 165 (51), 164 (51), 149 (34), 137 (40), 136 (86), 123 (51), 121 (60), 119 (57), 101 (60), 108 (40), 101 (100); exact mass calcd for $C_{11}H_{16}O_3$ 196.110, obsd 196.109.

The next 200 mL was discarded. The following 140 mL was concentrated in vacuo to give **11d** as a colorless oil: 94 mg (56%); R_f (20% EtOAc/hexane) 0.23; ^{1}H NMR δ 0.90 (t, J = 7.1 Hz, 3 H), 1.1–1.4 (m, 4 H), 1.45 (t, J = 5.2 Hz, 2 H), 1.7–2.6 (m, 4 H), 3.75 (s, 3 H); ^{13}C NMR δ 13.5 (q) 19.9 (t), 22.6 (t), 28.1 (t), 31.0 (d), 31.7 (t), 37.3 (s), 42.3 (d), 51.7 (q), 168.5 (s), 207.6 (s); IR 2960, 1765, 1740, 1441, 1380, 1325, 1270, 1200, 1175 cm^{-1}; MS, m/z (relative intensity) 196 (5), 165 (22), 154 (90), 153 (41), 123 (14), 122 (100), 121 (13), 113 (43), 108 (13); exact mass calcd for $C_{11}H_{16}O_3$ 196.110, obsd 196.111.

Methyl 3-Oxo-4-phenylbutanoate (12a). Following the procedure for **15a**, phenylacetyl chloride (1.98 mL, 15 mmol) was homologated. The residue was chromatographed on 60 g of silica gel with 2% EtOAc/petroleum ether. The first 1000 mL was discarded. The next 2000 mL was concentrated in vacuo to give **12a** as a colorless oil: 2.46 g (85%); R_f (20% EtOAc/hexane) 0.34; ^{1}H NMR δ 3.4 (s, 2 H), 3.6 (s, 3 H), 3.8 (s, 2 H), 7.1–7.3 (m, 5 H); ^{13}C NMR δ 47.6 (t), 49.4 (t), 51.7 (q), 126.9 (d), 128.4 (d, 2), 129.2 (d, 2), 133.1 (s), 167.1 (s), 199.8 (s); IR 1750, 1720, 1460, 1440, 1420, 1325, 1290, 1240, 1200, 1160, 1029, 700 cm^{-1}; MS, m/z (relative intensity) 192 (81), 122 (60), 119 (26), 118 (88), 107 (17), 105 (97), 101 (100); exact mass calcd for $C_{11}H_{12}O_3$ 192.079, obsd 192.078.

Methyl 2-Diazo-3-oxo-4-phenylbutanoate (12b). Following the procedure for **5b**, diazo transfer was performed on **12a** (750 mg, 3.8 mmol). The residue was chromatographed on 20 g of silica gel with 3% EtOAc/petroleum ether. The first 40 mL was discarded. The next 100 mL was concentrated in vacuo to give α-diazo β-keto ester **12b** as a colorless oil: 722 mg (85%); R_f (20% EtOAc/hexane) 0.40; ^{1}H NMR δ 3.83 (s, 3 H), 4.2 (s, 2 H), 7.3 (s, 5 H); ^{13}C NMR δ 45.8 (t), 52.2 (q) 76.0 (s), 127.1 (d), 128.5 (d, 2), 129.7 (d, 2), 134.0 (s), 161.6 (s), 190.1 (s); IR 2960, 2140, 1730, 1660, 1560, 1440, 1260, 1130, 1010 cm^{-1}; MS, m/z (relative intensity) 218 (56), 159 (26), 158 (26), 131 (56), 130 (100), 103 (56), 102 (58); exact mass calcd for $C_{11}H_{10}N_2O_3$ 218.069, obsd 218.069.

Methyl 2-Oxo-2,3-dihydro-1*H*-indene-1-carboxylate (12c). Following the procedure for **5c** and **5d**, cyclization was effected on **12b** (260 mg, 1.2 mmol). The residue was chromatographed on 20 g of silica gel with 4% acetone/petroleum ether. The first 150 mL was discarded. The next 175 mL was concentrated in vacuo to give **12c** as a colorless oil: 173 mg (76%); R_f (20% EtOAc/hexane) 0.36; ^{1}H NMR δ 3.5 (s, 2 H), 3.7 (s, 1 H), 3.9 (s, 3 H), 7.1 (d, J = 7.8 Hz, 1 H), 7.2–7.4 (m, 2 H), 7.6 (d, J = 7.6 Hz, 1 H); ^{13}C NMR δ 37.7 (t), 51.5 (q), 105.1 (s), 120.2 (d), 123.6 (d), 123.7 (d), 127.1 (d), 133.1 (s), 139.5 (s), 169.3 (s), 180.9 (s); IR 1660, 1595, 1480, 1445, 1365, 1345, 1235, 1200, 1055 cm^{-1}; MS, m/z (relative intensity) 190 (53), 159 (20), 158 (100), 131 (30), 130 (59), 119 (11), 118 (10), 104 (13), 103 (30), 102 (93); exact mass calcd for $C_{11}H_{10}O_3$ 190.063, obsd 190.064.

Methyl 3-Oxo-4-phenylheptanoate (13a). Following the procedure for **5a**, **12a** (601 mg, 3.1 mmol) was alkylated with propyl iodide. The residue was chromatographed on 20 g of silica gel with 2% EtOAc/petroleum ether. The first 250 mL was discarded. The next 250 mL was concentrated in vacuo to give **13a** as a colorless oil: 589 mg (81%); R_f (20% EtOAc/hexane) 0.46; ^{1}H NMR δ 0.88 (t, J = 7.2 Hz, 3 H), 1.2–1.3 (m, 2 H), 1.7 (m, 1 H), 2.0 (m, 1 H), 3.4 (q, J = 15.5 Hz, 2 H), 3.65 (s, 3 H), 3.77 (t, J = 7.3 Hz, 1 H), 7.2–7.4 (m, 5 H); ^{13}C NMR δ 13.9 (q), 20.4 (t), 33.9 (t), 47.8 (t), 52.2 (q), 58.9 (d), 127.6 (d), 128.5 (d, 2), 129.0 (d, 2), 138.0 (s), 167.6 (s), 202.3 (s); IR 2960, 1755, 1722, 1655, 1625, 1460, 1440, 1410, 1320, 1290, 1160, 700 cm^{-1}; MS, m/z (relative intensity) 234 (74), 160 (26), 134 (38), 133 (100), 115 (24), 105 (24), 104 (29), 103 (26), 101 (57); exact mass calcd for $C_{14}H_{18}O_3$ 234.126, obsd 234.125.

Methyl 2-Diazo-3-oxo-4-phenylheptanoate (13b). Following the procedure for **5b**, diazo transfer was performed on **13a** (589 mg, 2.5 mmol). The residue was chromatographed on 20 g of silica gel with 3% EtOAc/petroleum ether. The first 100 mL was discarded. The next 100 mL was concentrated in vacuo to give α-diazo β-keto ester **13b** as a colorless oil: 590 mg (91%); R_f (20% EtOAc/hexane) 0.53; ^{1}H NMR δ 0.89 (t, J = 7.3 Hz, 3 H), 1.2–1.3 (m, 2 H), 1.8 (m, 1 H), 2.0 (m, 1 H), 3.80 (s, 3 H), 4.8 (t, J = 7.3 Hz, 1 H), 7.2–7.4 (m, 5 H); ^{13}C NMR δ 13.9 (q), 20.7 (t), 35.6 (t), 52.1 (q), 52.7 (d), 127.1 (d), 128.5 (d, 2), 128.7 (d, 2), 138.9 (s), 161.4 (s), 193.0 (s); IR 2960, 2140, 1730, 1660, 1445, 1315, 700 cm^{-1}; MS, m/z (relative intensity) 260 (14), 200 (40), 189 (33), 171 (31), 158 (100), 144 (26), 133 (62), 129 (31), 121 (57), 117 (29), 115 (50), 104 (31), 103 (33), 102 (29); exact mass calcd for $C_{14}H_{16}N_2O_3$ 260.1168 obsd 260.117.

Methyl 3-Propyl-2-oxo-2,3-dihydro-1*H*-indene-1-carboxylate (13c) and Methyl 5-Methyl-2-oxo-3-phenylcyclopentanecarboxylate (13d). Following the procedure for **5c** and **5d**, cyclization was effected on **13b** (590 mg, 2.3 mmol). The residue was chromatographed on 20 g of silica gel with 3% EtOAc/petroleum ether. The first 200 mL was discarded. The next 125 mL was concentrated in vacuo to give **13c** as a colorless oil: 224 mg (42%); R_f (20% EtOAc/hexane) 0.40; ^{1}H NMR δ 0.90 (t, J = 7.3 Hz, 3 H), 1.2–1.4 (m, 2 H), 1.9 (m, 2 H), 3.57 (t, J = 5.9 Hz, 1 H), 3.94 (s, 3 H), 7.1–7.6 (m, 4 H), 11.1 (br s, 1 H); ^{13}C NMR δ 14.2 (q), 18.7 (t), 32.2 (t), 47.9 (d), 51.5 (q), 104.1 s), 120.1 (d), 122.9 (d), 123.7 (d), 127.1 (d), 138.2 (s), 138.7 (s), 169.5 (s), 184.1 (s); IR 2960, 2880, 1745, 1660, 1470, 1450, 1340, 1220, 910, 670 cm^{-1}; MS, m/z (relative intensity) 232 (21), 200 (42), 159 (20), 158 (100), 157 (17), 132 (12), 131 (22), 130 (10), 129 (48), 128 (17), 116 (10), 115 (43), 102 (19), 101 (17); exact mass calcd for $C_{11}H_{16}O_3$ 232.110, obsd 232.109.

The next 150 mL was concentrated in vacuo to give **13d** as a colorless oil: 261 mg (50%); R_f (20% EtOAc/hexane) 0.36; ^{1}H NMR δ 1.73 (q, J = 12.8 Hz, 1 H), 1.26 (d, J = 6.1 Hz, 3 H), 2.5–2.8 (m, 2 H), 2.9 (d, J = 11.3 Hz, 1 H), 3.6 (dd, J = 11, 7 Hz, 1 H), 3.78 (s, 3 H), 7.2–7.4 (m, 5 H); ^{13}C NMR δ 19.1 (q), 33.9 (d), 37.9 (t), 52.5 (q) 56.3 (d), 63.2 (d), 127.2 (d), 128.1 (d, 2), 128.7 (d, 2), 137.3 (s), 169.5 (s), 209.6 (s); IR 2960, 1755, 1740, 1600, 1450, 1440, 1005, 690 cm^{-1}; MS, m/z (relative intensity) 232 (44), 200 (12), 190 (11), 175 (11), 173 (13), 172 (45), 149 (23), 145 (13), 144 (20), 133 (16), 132 (11), 131 (23), 129 (19), 128 (20), 122 (15), 120 (23), 118 (13), 117 (23), 115 (23), 106 (15), 105 (100), 104 (99), 103 (29); exact mass calcd for $C_{14}H_{16}O_3$ 232.110, obsd 232.110.

Methyl 6,6-Dimethyl-3-oxo-4-propylheptanoate (14a). Following the procedure for **5a**, 0.160 g of **25** was alkylated with propyl iodide (3 equiv). The residual oil was chromatographed on 10 g of silica gel with 1% EtOAc/petroleum ether. The first 60 mL was discarded. The next 60 mL was concentrated in vacuo to give **14a** as a colorless oil: 68 mg (49% based on 45 mg of recovered **25**); R_f (20% EtOAc/hexane) 0.60; ^{1}H NMR δ 0.86 (s, 9 H), 0.90 (t, J = 7.1 Hz, 3 H), 1.0–1.7 (m, 8 H), 2.5 (m, 1 H), 3.47 (s, 2 H), 3.74 (s, 3 H); ^{13}C NMR δ 14.2 (q), 20.5 (t), 26.3 (t), 29.2 (q, 3), 30.3 (s), 33.5 (t), 41.4 (t), 48.2 (t), 52.3 (q), 53.0 (d), 167.7 (s), 206.4 (s); IR 2960, 1755, 1718, 1655, 1628, 1450, 1410, 1370, 1320, 1255, 1240, 1198, 1150, 1100, 1035 cm^{-1}; MS, m/z (relative intensity) 200 (12), 195 (13), 171 (16), 169 (11), 159 (12), 158 (77), 157 (24), 130 (12), 129 (100), 126 (13), 125 (14), 116 (35), 101 (48). Anal. Calcd for $C_{14}H_{24}O_3$: C, 69.38; H, 10.81. Found: C, 69.21; H, 11.35.

Methyl 2-Diazo-6,6-dimethyl-3-oxo-4-propylheptanoate (14b). Following the procedure for **5b**, diazo transfer was performed on **14a** (96 mg, 0.4 mmol). The residual oil was chromatographed on 10 g of silica gel with 1.5% EtOAc/petroleum ether. The first 50 mL was discarded. The next 50 mL was concentrated in vacuo to give α-diazo β-keto ester **14b** as a yellow oil: 94 mg (88%); R_f (20% EtOAc/hexane) 0.58; ^{1}H NMR δ 0.85 (s, 9 H), 0.90–2.1 (m, 11 H), 2.5 (m, 1 H), 3.84 (s, 3 H); ^{13}C NMR δ 14.3 (q), 20.5 (t), 27.0 (t), 29.3 (q, 3), 30.3 (s), 34.8 (t), 41.4 (t), 47.5 (d), 52.1 (q), 161.7 (s), 196.8 (s); IR 2960, 2140, 1730, 1660, 1560, 1440, 1315, 1130, 910 cm^{-1}; MS, m/z (relative intensity) 165 (19), 156 (25), 155 (81), 151 (20), 141 (33), 137 (45), 127 (21), 124 (16), 123 (53), 113 (100), 111 (14), 110 (15), 109 (55), 101 (33), 100 (25).

Methyl 3-(3,3-Dimethyl-1-butyl)-5-methyl-2-oxocyclopentanecarboxylate (14c) and Methyl 5-(1,1-Dimethyl-1-ethyl)-2-oxo-3-propylcyclopentanecarboxylate (14d). Following the procedure for **5c** and **5d**, cyclization was effected on **14b** (94 mg, 0.135 mmol). The material was directly concentrated in vacuo, and the residue was chromatographed on 10 g of silica gel with 1% EtOAc/petroleum ether. The first 190 mL was discarded. The next 100 mL was concentrated in vacuo to give **14c** and **14d** as a colorless oil: 61 mg (73%); R_f (20% EtOAc/hexane) 0.47. Spectra are consistent with a 3.4:1 ratio of authentic **14d** and **14c** made via alternative pathways.

Methyl 4-(1-Cyclopentyl)-3-oxobutanoate (15a). A flame-dried, one-necked flask equipped with an N_2 inlet and a septum was charged with cyclopentylacetic acid (3.07 g, 24 mmol), DMF (3 drops, catalytic), and CH_2Cl_2 (25 mL). The flask was cooled to 0 °C, and oxalyl chloride[23] (3.5 mL, 41 mmol, 1.7 equiv) was cautiously added via syringe. The flask was allowed to warm to room temperature over 1 h and then the mixture stirred at room temperature for 3 h. The material was concentrated by rotary evaporation, without further evacuation at the pump.

A flame-dried, three-necked flask equipped with an N_2 inlet, a low-temperature thermometer, and a septum was charged with diisopropylamine (10 mL, 72 mmol, 3 equiv) and 80 mL of THF. The flask was cooled to −78 °C, and *n*-BuLi (27.2 mL of 2.55 M, 69 mmol, 2.9 equiv) was added at a rate that allowed the internal temperature to remain at

(23) Burgstahler, A. W.; Weigel, L. O.; Shaefer, C. G. *Synthesis* **1976**, 767.

or below -40 °C. The flask was warmed to -10 °C in an ice/salt bath for 20 min and then recooled to -78 °C. Methyl acetate (5.7 mL, 72 mmol, 3 equiv) was added at a rate that allowed the temperature to remain at or below -65 °C. This mixture was stirred at -78 °C for 5 min, then the crude acid chloride from above was added all at once as a solution in THF, and the reaction mixture was allowed to warm to room temperature. The mixture was diluted with 10% aqueous HCl and extracted with extraction solvent (3 × 100 mL). The combined organic extracts were dried over $MgSO_4$ and concentrated in vacuo. The residue was chromatographed on 50 g of silica gel with 1% EtOAc/petroleum ether. The first 1000 mL was discarded. The next 500 mL was concentrated in vacuo to give **15a** as a colorless oil: 4.1 g (93%); R_f (20% EtOAc/hexane) 0.45; ^{1}H NMR δ 1.0–2.3 (m, 9 H), 2.57 (d, J = 7.1 Hz, 2 H), 3.46 (s, 2 H), 3.73 (s, 3 H); ^{13}C NMR δ 25.0 (t, 2), 32.6 (t, 2), 35.3 (d), 49.2 (t), 49.3 (t), 52.2 (q), 167.7 (s), 202.5 (s); IR 2960, 1750, 1721, 1655, 1625, 1450, 1440, 1410, 1320, 1240, 1195, 1038 cm^{-1}; MS, m/z (relative intensity) 184 (12), 129 (9), 117 (85), 116 (100), 111 (67), 110 (19), 101 (48); exact mass calcd for $C_{10}H_{16}O_3$ 184.110, obsd 184.109.

Methyl 4-(1-Cyclopentyl)-2-diazo-3-oxobutanoate (15b). Following the procedure for **5b**, diazo transfer was performed on **15a** (552 mg, 3.0 mmol). The residue was chromatographed on 20 g of silica gel with 3% EtOAc/petroleum ether. The first 75 mL was discarded. The next 150 mL was concentrated in vacuo to give α-diazo β-keto ester **15b** as a yellow oil: 584 mg (93%); R_f (20% EtOAc/hexane) 0.49; ^{1}H NMR δ 1.2–2.3 (m, 9 H), 2.88 (d, J = 7.1 Hz, 2 H), 3.84 (s, 3 H); ^{13}C NMR δ 24.9 (t, 2), 32.5 (t, 2), 36.0 (d), 46.0 (t), 52.1 (q), 75.81 (s), 161.8 (s), 192.6 (s); IR 2960, 2140, 1730, 1615, 1440, 1315, 1210 cm^{-1}; MS, m/z (relative intensity) 142 (100), 111 (29), 101 (48); exact mass calcd for $C_{10}H_{14}N_2O_3$ 210.100, obsd 210.099.

Methyl 2-Oxo-1,2,3,3aα,4,5,6,6aα-octahydropentalene-1-carboxylate (15c). Following the procedure for **5c** and **5d**, cyclization was effected on **15b** (779 mg, 3.7 mmol). The residue was chromatographed on 20 g of silica gel with 4% EtOAc/petroleum ether. The first 60 mL was discarded. The next 60 mL was concentrated in vacuo to give **15c** as a colorless oil: 301 mg (45%); R_f (20% EtOAc/hexane) 0.47; ^{1}H NMR δ 1.2–2.3 (m, 8 H), 2.6–2.9 (m, 2 H), 3.1 (m, 1 H), 3.74, 3.76 (s, 3 H); ^{13}C NMR δ 25.2 (t), 25.4 (t), 32.5 (t), 32.9 (t), 33.3 (t), 35.1 (t), 36.3 (d), 38.2 (d), 39.9 (t), 44.5 (t), 44.6 (d), 45.1 (d), 51.0 (q), 52.4 (q), 60.9 (d), 103.8 (s), 170.0 (s), 175.3 (s), 212.8 (s); IR 2990, 1740, 1670, 1455, 1280, 1200 cm^{-1}; MS, m/z (relative intensity) 182 (33), 154 (40), 151 (43), 150 (100), 140 (14), 122 (53), 121 (84), 113 (14), 111 (32), 110 (13), 109 (18), 108 (64), 107 (19); exact mass calcd for $C_{10}H_{14}O_3$ 182.094, obsd 182.095.

Methyl 4-(1-Cyclohexyl)-3-oxobutanoate (16a). Following the procedure for **15a**, cyclohexylacetic acid (3.04 g) was homologated. The residue was chromatographed on 50 g of silica gel with 2.5% EtOAc/petroleum ether. The first 500 mL was discarded. The next 400 mL was concentrated in vacuo to give **16a** as a colorless oil: 3.72 g (88%); R_f (20% EtOAc/hexane) 0.45; ^{1}H NMR δ 0.90–2.0 (m, 11 H), 2.41 (d, J = 6.9 Hz, 1 H), 3.44 (s, 2 H), 3.72 (s, 3 H); ^{13}C NMR δ 26.1 (t, 2), 26.2 (t), 33.1 (t, 2), 33.6 (d), 49.6 (t), 50.6 (t), 52.3 (q), 167.7 (s), 202.4 (s); IR 2940, 1755, 1722, 1655, 1630, 1450, 1440, 1410, 1320, 1240, 1150, 908 cm^{-1}; MS, m/z (relative intensity) 198 (8), 125 (39), 117 (76), 116 (100), 101 (35); exact mass calcd for $C_{11}H_{18}O_3$ 198.126, obsd 198.125.

Methyl 4-(1-Cyclohexyl)-2-diazo-3-oxobutanoate (16b). Following the procedure for **5b**, diazo transfer was performed on **16a** (523 mg, 2.6 mmol). The residue was chromatographed on 20 g of silica gel with 2.5% EtOAc/petroleum ether. The first 100 mL was discarded. The next 250 mL was concentrated in vacuo to give α-diazo β-keto ester **16b** as a yellow oil: 549 mg (94%); R_f (20% EtOAc/hexane) 0.54; ^{1}H NMR δ 0.9–1.9 (m, 11 H), 2.74 (d, J = 6.8 Hz, 2 H), 3.84 (s, 3 H); ^{13}C NMR δ 26.1 (t, 2), 26.2 (t), 33.1 (t, 2), 34.6 (d), 47.3 (t), 52.1 (a), 76.05 (s), 161.8 (s), 192.4 (s); IR 2930, 2850, 2140, 1730, 1660, 1560, 1455, 1440, 1315, 1200, 1020, 910 cm^{-1}; MS, m/z (relative intensity) 143 (23), 142 (100), 125 (11), 101 (21); exact mass calcd for $C_{10}H_{16}N_2O_3$ 224.116, obsd 224.116.

Methyl 2-Oxo-2,3,3aα,4,5,6,7,7aβ-octahydro-1*H*-indene-1-carboxylate (16c) and Methyl 2-Oxo-2,3,3aα,4,5,6,7,7aα-octahydro-1*H*-indene-1-carboxylate (16d). Following the procedure for **5c** and **5d**, cyclization was effected on **16b** (367 mg, 1.6 mmol). The residue was chromatographed on 30 g of silica gel with 3% EtOAc/petroleum ether. The first 700 mL was discarded. The next 400 mL was concentrated in vacuo to give **16c** and **16d** as a colorless oil: 225 mg (63%); R_f (20% EtOAc/hexane) 0.42; ^{1}H NMR δ 1.2–2.0 (m, 10 H), 2.45 (dd, J = 18, 6.7 Hz, 1 H), 2.86 (d, J = 12.4 Hz, 1 H), 3.7 (d, J = 6.1 Hz, 1 H), 3.75, 3.76 (s, 3 H); ^{13}C NMR δ 25.9 (t), 26.1 (t), 30.4 (t), 31.2 (t), 41.2 (d), 45.0 (t), 47.4 (d), 52.2 (q), 61.8 (d), 169.6 (s), 209.9 (s); IR 2940, 1755, 1735, 1450, 1435, 1335, 1305, 1285, 1245, 1145, 1075, 1045 cm^{-1}; MS, m/z (relative intensity) 196 (44), 169 (12), 168 (98), 165 (50), 164 (33), 137 (34), 136 (86), 135 (16), 125 (11), 123 (28), 122 (92), 121 (24), 119 (19), 118 (11), 113 (24), 111 (26), 109 (30), 108 (100), 107 (39), 101 (37), 100 (16); exact mass calcd for $C_{11}H_{16}O_3$ 196.110, obsd 196.110.

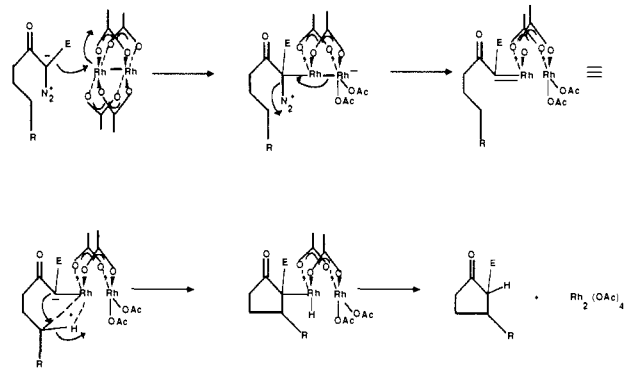
Methyl 4-(1-Methyl-1-cyclohexyl)-3-oxobutanoate (17a). Following the procedure for **15a**, (methylcyclohexyl)acetic acid[24] (1.08 g) was homologated. The residue was chromatographed on 20 g of silica gel with 3% EtOAc/petroleum either. The first 150 mL was discarded. The next 200 mL was concentrated in vacuo to give **17a** as a colorless oil: 1.255 g (86%); R_f (20% EtOAc/hexane) 0.48; ^{1}H NMR δ 1.03 (s, 3 H), 1.3–1.5 (m, 10 H), 2.46 (s, 2 H), 3.45 (s, 2 H), 3.73 (s, 3 H); ^{13}C NMR δ 21.9 (t, 2), 25.0 (q), 26.1 (t), 34.0 (s), 37.8 (t, 2), 51.4 (t), 52.3 (q), 53.3 (t), 167.7 (s), 202.6 (s); IR 2970, 1755, 1720, 1655, 1630, 1450, 1405, 1240, 1155, 1040 cm^{-1}; MS, m/z (relative intensity) 212 (3), 139 (32), 118 (11), 117 (100), 116 (82), 101 (40); exact mass calcd for $C_{12}H_{20}O_3$ 212.141, obsd 212.141.

Methyl 2-Diazo-4-(1-methyl-1-cyclohexyl)-3-oxobutanoate (17b). Following the procedure for **5b**, diazo transfer was performed on **17a** (500 mg, 2.4 mmol). The residue was chromatographed on 10 g of silica gel with 4% EtOAc/petroleum ether. The first 30 mL was discarded. The next 90 mL was concentrated in vacuo to give α-diazo β-keto ester **17b** as a yellow oil: 483 mg (83%); R_f (20% EtOAc/hexane) 0.56; ^{1}H NMR δ 1.03 (s, 3 H), 1.2–1.5 (m, 10 H), 2.86 (s, 2 H), 3.83 (s, 3 H); ^{13}C NMR δ 22.0 (t, 2), 24.7 (q), 26.2 (t), 35.0 (t), 38.0 (t, 2), 49.0 (s), 52.1 (q), 161.9 (s), 192.3 (s); IR 2940, 2140, 1730, 1660, 1560, 1440, 1310 cm^{-1}; MS, m/z (relative intensity) 143 (38), 142 (100), 114 (13); CH_4 CI exact mass calcd for $C_{12}H_{19}N_2O_3$ 239.140, obsd 239.138.

Methyl 3aα-Methyl-2-oxo-2,3,3aα,4,5,6,7,7aα-octahydro-1*H*-indene-1-carboxylate (17c). Following the procedure for **5c** and **5d**, cyclization was effected on **17b** (215 mg, 0.9 mmol). The residue was chromatographed on 10 g of silica gel with 3% EtOAc/petroleum ether. The first 80 mL was discarded. The next 100 mL was concentrated in vacuo to give **17c** as a colorless oil: 176 mg (93%); R_f (20% EtOAc/hexane) 0.40; ^{1}H NMR δ 1.23 (s, 3 H), 1.1–2.5 (m, 11 H), 3.37 (d, J = 12.1 Hz, 1 H), 3.77 (s, 3 H); ^{13}C NMR δ 19.7 (t), 21.5 (t), 22.6 (t), 24.0 (q), 33.8 (t), 35.9 (s), 45.2 (d), 52.5 (q), 55.2 (t), 56.5 (d), 169.9 (s), 211.2 (s); IR 2920, 2860, 1760, 1730, 1560, 1440, 1410, 1250, 1200, 1160, 1120, 1030, 980 cm^{-1}; MS, m/z (relative intensity) 210 (24), 195 (19), 182 (42), 179 (28), 167 (16), 163 (19), 154 (15), 151 (36), 150 (30), 136 (25), 135 (30), 133 (11), 128 (12), 123 (13), 122 (30), 121 (24), 113 (18), 111 (11), 109 (47), 108 (100), 107 (28), 100 (19); exact mass calcd for $C_{12}H_{18}O_3$ 210.126, obsd 210.126.

Methyl 3-Oxo-5-phenylheptanoate (18a). Following the procedure for **5a**, methyl acetoacetate (2.0 mL, 18.5 mmol) was alkylated with 1-bromo-1-phenylpropane.[25] The residual oil was chromatographed on 50 g of silica gel with petroleum ether. The first 750 mL was discarded. The next 600 mL was concentrated in vacuo to give **18a** as a colorless oil: 1.24 g (29%); R_f (20% EtOAc/hexane) 0.35; ^{1}H NMR 0.76 (t, J = 7.4 Hz, 3 H), 1.5–1.9 (m, 3 H), 2.32 (d, J = 7.1 Hz, 2 H), 3.28 (s, 2 H), 3.63 (s, 3 H), 7.1–7.3 (m, 5 H); ^{13}C NMR 11.9 (q), 29.2 (t), 42.7

(24) Amsterdamsky, C.; Malissard, M.; Welvart, Z. *Bull. Soc. Chim. Fr.* **1975**, 635.
(25) Levene, P. A.; Rothen, A.; Kuna, M. *J. Biol. Chem.* **1937**, *120*, 777.
(26) Groot, Ae. de.; Jansen, B. J. M. *Tetrahedron Lett.* **1976**, *31*, 2709.
(27) Hutchins, R. O.; Kacher, M.; Rua, L. *J. Org. Chem.* **1975**, *40*, 923.
(28) Kabalka, G. W.; Yang, D. T. C.; Baker, J. D., Jr. *J. Org. Chem.* **1976**, *41*, 574.
(29) Carlsen, H. J.; Katsuki, T.; Martin, V. S.; Sharpless, K. B. *J. Org. Chem.* **1981**, *46*, 3936.
(30) Ireland, R. E.; Aristoff, P. A.; Hoyng, C. F. *J. Org. Chem.* **1979**, *44*, 4318.
(31) At the request of a reviewer, we outline below our current working hypothesis of the mechanism. Alternative suggestions from interested readers are encouraged.



(d), 49.5 (t), 49.7 (t), 52.1 (q), 126.5 (d), 127.6 (d, 2), 128.5 (d, 2), 144.0 (s), 167.4 (s), 201.5 (s); IR 2960, 1755, 1720, 1655, 1625, 1450, 1440, 1410, 1320, 1240, 1195, 700 cm^{-1}; MS, *m/z* (relative intensity) 234 (5), 216 (89), 205 (26), 161 (26), 157 (23), 156 (93), 142 (20), 132 (41), 131 (92), 119 (100), 118 (59), 117 (41), 115 (23), 107 (18), 105 (18), 104 (34), 103 (34), 101 (85); exact mass calcd for $C_{14}H_{18}O_3$ 234.126, obsd 234.126.

Methyl 2-Diazo-3-oxo-5-phenylheptanoate (18b). Following the procedure for **5b**, diazo transfer was performed on **18a** (178 mg, 0.76 mmol). The residual oil was chromatographed on 10 g of silica gel with 5% EtOAc/petroleum ether. The first 40 mL was discarded. The next 30 mL was concentrated in vacuo to give α-diazo β-keto ester **18b** as a yellow oil: 170 mg (86%); R_f (20% EtOAc/hexane) 0.44; ^1H NMR δ 0.78 (t, *J* = 6.5 Hz, 3 H), 1.5-1.8 (m, 3 H), 3.1-3.3 (m, 2 H), 3.78 (s, 3 H), 7.1-7.3 (m, 5 H); ^{13}C NMR δ 12.0 (q), 29.3 (t), 43.2 (d), 46.4 (t), 52.1 (q), 126.0 (d), 126.3 (d, 2), 127.8 (d, 2), 144.3 (s), 161.8 (s), 191.5 (s); IR 2960, 2140, 1730, 1655, 1550, 1450, 1310, 1210, 700 cm^{-1}; MS, *m/z* (relative intensity) 203 (15), 200 (51), 176 (18), 173 (47), 172 (23), 171 (100), 132 (18), 129 (30), 119 (46), 118 (22), 117 (49), 116 (18), 115 (47), 105 (18), 104 (34), 101 (24); CH_4 CI exact mass calcd for $C_{14}H_{17}N_2O_3$ 261.124, obsd 261.123.

Methyl (4*R,5*S**)-5-Methyl-2-oxo-3-phenylcyclopentanecarboxylate (18c).** Following the procedure for **5c** and **5d**, cyclization was effected on **18b** (206 mg, 0.8 mmol). The residual oil was chromatographed on 20 g of silica gel with 4.5% EtOAc/petroleum ether. The first 300 mL was discarded. The next 400mL was concentrated in vacuo to give **18c** as a colorless oil: 141 mg (77%); R_f (20% EtOAc/hexane) 0.33; ^1H NMR δ 1.07 (d, *J* = 6.2 Hz, 3 H), 3.03 (d, *J* = 11.7 Hz, 1 H), 2.5-3.0 (m, 4 H), 3.80 (s, 3 H), 7.2-7.4 (m, 5 H); ^{13}C NMR 16.9 (q), 43.3 (d), 47.3 (t), 48.5 (d), 52.5 (q), 127.3 (d), 127.5 (d, 2), 128.9 (d, 2), 140.4 (s), 169.3 (s), 208.9 (s); IR 2965, 1740, 1730, 1500, 1460, 1440, 1330, 1295, 1205, 1145, 1040, 695 cm^{-1}; MS, *m/z* (relative intensity) 232 (43), 214 (17), 201 (11), 200 (13), 173 (11), 172 (19), 132 (15), 131 (17), 105 (14), 104 (100), 101 (28); exact mass calcd for $C_{14}H_{16}O_3$ 232.110, obsd 232.110.

Acknowledgment. We thank the National Science Foundation (CHE 8306692) for support of this work and the organometallic group at Du Pont Central Research for helpful discussions. D.F.T. thanks ICI Americas for an unrestricted research grant. We thank Dr. Roger Crecely for acquisition of many NMR spectra.

Registry No. 3, 104214-14-4; **4**, 39815-78-6; **5a**, 104620-07-7; **5b**, 104620-08-8; **5c**, 104620-09-9; **5d**, 104620-10-2; **6a**, 104620-11-3; **6b**, 104620-12-4; **6c**, 104620-13-5; **6d**, 104620-14-6; **7a**, 104620-15-7; **7b**, 104620-16-8; **7c**, 104620-17-9; **7d**, 104620-18-0; **8a**, 104620-19-1; **8b**, 104620-20-4; **8c**, 104641-97-6; **8d**, 104620-21-5; **9a**, 104620-22-6; **9b**, 104620-23-7; **9c**, 104620-24-8; **10a**, 104620-25-9; **10b**, 104620-29-3; **10c**, 104620-26-0; **10d**, 104620-27-1; **11a**, 104620-28-2; **11b**, 104620-30-6; **11c**, 104620-31-7; **11d**, 104620-32-8; **12a**, 37779-49-0; **12b**, 104620-33-9; **12c**, 104620-34-0; **13a**, 104620-35-1; **13b**, 104620-36-2; **13c**, 104620-37-3; **13d**, 104620-38-4; **14a**, 104620-40-8; **14b**, 104620-41-9; **14c**, 104620-42-0; **14d**, 104620-43-1; **15a**, 104620-44-2; **15a** (acid chloride), 104620-45-3; **15b**, 104620-46-4; **15c**, 104620-47-5; **16a**, 51414-42-7; **16b**, 104156-32-3; *trans*-**16c**, 104620-48-6; *cis*-**16c**, 104712-98-3; **17a**, 104620-49-7; **17a** (acetic acid), 14352-58-0; **17b**, 104620-50-0; **17c**, 104712-99-4; **18a**, 102836-26-0; **18b**, 104620-51-1; **18c**, 102836-27-1; **19** (R = $CH_2CH(CH_3)_2$), 61692-48-6; **20**, 104620-52-2; **22**, 104620-53-3; **23** (R = CH_3), 104641-98-7; **24**, 24499-80-7; **25**, 104620-39-5; *cis*-**16c**, 104712-98-3; **27**, 104620-54-4; **28**, 65898-71-7; **29**, 27943-50-6; **30**, 16508-51-3; **31**, 13351-29-6; **32**, 20379-99-1; $Me_2CH(CH_2)_2COMe$, 110-12-3; $Me(CH_2)_3COMe$, 591-78-6; $H_2C{=}CHCH_2CH_2Br$, 5162-44-7; $C_6H_5(CH_2)_2Br$, 103-63-9; $H_2C{=}CHCH_2Br$, 106-95-6; $C_6H_5CH_2COCl$, 103-80-0; $C_5H_9CH_2CO_2H$, 1123-00-8; $C_6H_{11}CH_2CO_2H$, 5292-21-7; $MeCOCH_2CO_2Me$, 105-45-3; $C_6H_5CHBrCH_2Me$, 2114-36-5; $Me_3C(CH_2)_2Cl$, 2855-08-5; 2-methylcyclohexan-2-one, 583-60-8.

Supplementary Material Available: Complete experimental details for the preparation of **19-32** (11 pages). Ordering information is given on any current masthead page.

3*H*-Cyclonona[*def*]biphenylene: An Example of Neutral Homoantiaromaticity

Charles F. Wilcox, Jr.,*[1a] David A. Blain,[1a,d] Jon Clardy,[1a] Gregory Van Duyne,[1a] Rolf Gleiter,*[1b] and Mirjana Eckert-Maksić[1b,c]

Contribution from the Department of Chemistry, Cornell University, Ithaca, New York 14853, and the Institut für Organische Chemie der Universität Heidelberg, Heidelberg, West Germany.
Received May 14, 1986

Abstract: 3*H*-Cyclonona[*def*]biphenylene (**6**), a potentially homoantiaromatic neutral hydrocarbon, was synthesized by a bis-Wittig reaction between 1,8-biphenylenedicarboxaldehyde and the bis-ylide made from 1,3-bis(triphenylphosphino)propane dibromide. An X-ray structure of **6** revealed a bent structure for which C-2 and C-4 of the double bonds are close enough to have a theoretical β_{2-4} of about $0.24\beta_0$ (benzene). The photoelectron spectrum indicated some homoconjugation, which on detailed analysis could be accounted for by assuming a β_{2-4} value of $0.33\beta_0$. The UV/visible spectrum of **6** was red-shifted by 4 nm relative to 1,8-divinylbiphenylene (**8**), which PPP-model calculations indicated was composed of a 5-nm *hyper*conjugative *blue* shift and a 9-nm *homo*conjugative *red* shift when $\beta_{24} = 0.3\beta_0$. The ^1H NMR spectrum of **6** was complex but could be analyzed fully. The endo H at C-3 was found to resonate 2.2 ppm downfield of the exo H, which would be qualitatively consistent with a homoantiaromatic ring. However, reduction of one of the double bonds to give **7** caused this shift difference to decrease only to 0.7 ppm, indicating that another factor must be contributing as well. The pattern and magnitudes of the shifts were quantitatively consistent with a combination of local anisotropy effects and a homoantiaromatic ring current. A least-squares fit of the observed shifts to a dual model yielded a β_{2-4} of $0.39\beta_0$ with about an equal contribution from each source. These three lines of evidence all point to significant neutral homoantiaromaticity in **6**.

Since the early proposal of Winstein[2] for homoconjugative stabilization of cations, there has been considerable effort to uncover examples of neutral homoaromaticity.[3] However, an uncontested compound of this type has yet to be made. Calculations by Houk and Paquette[4] seem to indicate that neutral

(1) (a) Cornell. (b) Heidelberg. (c) Permanent address: Department of Organic Chemistry, The Rudjer Boščovič Institute, 41001 Zagreb, Yugoslavia. (d) This work is based in part on the Ph.D. dissertation of D.A.B., submitted to the Cornell Graduate School, June 1986.

(2) See: Winstein, S. *Q. Rev. Chem. Soc.* **1969**, *23*, 141-176, and references therein.

(3) (a) Warner, P. M. *Topics in Nonbenzenoid Aromatic Chemistry*; 1977; Hirokawa Publishing Co.: Tokyo, 1977; Vol. II, pp 283-352. (b) Chistoph, G. C.; Muthard, J. L.; Houk, K. N.; Gandour, R. W.; Strozier, R. W.; Paquette, L. A. *J. Am. Chem. Soc.* **1978**, *100*, 7782-7784. (c) Paquette, L. A. *Angew. Chem., Int. Ed. Engl.* **1978**, *17*, 106-117. (d) McMurry, J. E.; Haley, G. J.; Matz, J. R.; Clardy, J. C.; Van Duyne, G.; Gleiter, R.; Schäfer, W.; White, D. H. *J. Am. Chem. Soc.* **1984**, *106*, 5018-5019.

0002-7863/86/1508-7693$01.50/0