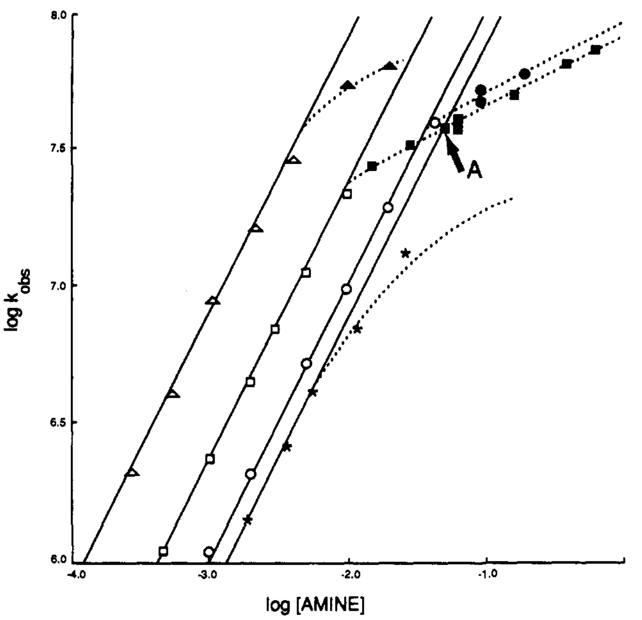


Figure 2. Plots for log k_{obs} vs log [amine]: (△) PCPD + *N*-methylaniline (monitored at λ = 310 nm); (▲) PCPD + *N*-methylaniline (λ = 400 nm); (□) PCPD + diethylamine (λ = 310 nm); (■) PCPD + diethylamine (λ = 340 nm); (○) PMPD + diethylamine (λ = 310 nm); (●) PMPD + diethylamine (λ = 340 nm); and (*) PCPD + triethylamine (λ = 310 nm).

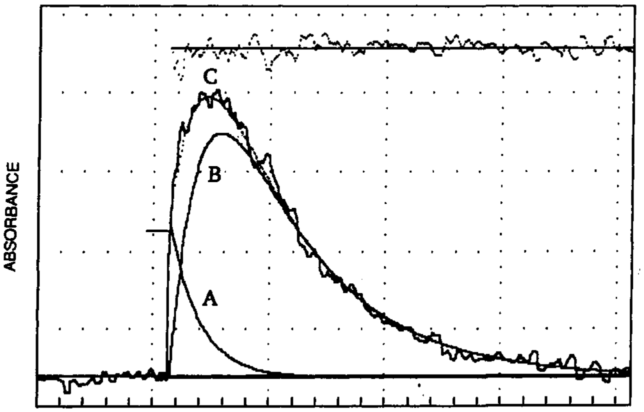
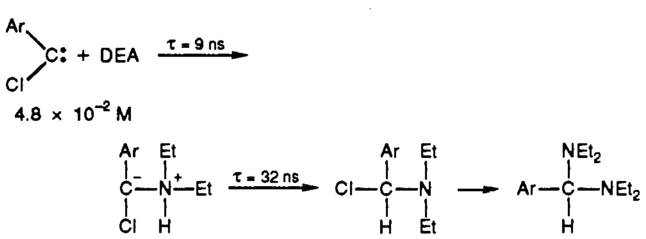


Figure 3. Analysis of the transient absorption at 340 nm for a solution of 3-chloro-3-(*p*-chlorophenyl)diazirine (0.015 M) and DEA (0.048 M) in isooctane (excitation 355 nm, 200 ps; temperature 27 °C): (A) decay of the *p*-chlorophenylchlorocarbene: 10 ns lifetime (B) growth and decay of the ylide with 10 and 32 ns growth and decay times; and (C) experimental data fitted with the sum of the theoretical curves A and B.

rapid disappearance of the ylide with $k = 3.1 \times 10^7\ s^{-1}$ (1/32 ns) is attributed to the 1,2 proton transfer in the ammonium ylide.



At high [DEA], the lifetime of the ylide measured at 340 nm (■ in Figure 2) decreases as [DEA] increases. This indicates that the proton transfer in the ylide is base catalzyed. Similarly, LFP of 3-chloro-3-(*p*-methylphenyl)diazirine (PMPD) in isooctane yielded *p*-CH_3-PhC̈Cl (**2**). The quenching of carbene **2**, monitored at 310 nm, at 27 °C yielded very similar results with $k_q(\mathbf{2}, DEA) = 1.08 \times 10^9\ M^{-1}\ s^{-1}$ for [DEA] = 1-40 mM and a minimum [DEA] around 40 mM to get a detectable ylide absorption, and a similar lifetime for the ylide i.e. similar rate constant for the 1,2 proton transfer. The spectrum of this ylide is similar to the one given in Figure 1 except that the λ_{max} is blue shifted by 10 nm.

The difference in the reactivities of carbenes **1** and **2** is clearly due to the electronic effect of the para substituent. Since, in the ylide, the carbene is the electron-accepting species, any substituent which increases the electron density on the carbene center will decrease the reactivity.

Behavior of carbene **1** with tertiary (triethylamine, TEA) and aromatic (*N*-methylaniline, MAN) amines was examined. The quenching of carbene **1** by these amines at low concentrations gave the following rate constants: $k_q(\mathbf{1}, TEA) = 7.2 \times 10^8\ M^{-1}\ s^{-1}$ and $k_q(\mathbf{1}, MAN) = 8.0 \times 10^9\ M^{-1}\ s^{-1}$.

In the case of TEA, the ylide lifetime is an order of magnitude longer than for DEA, but the lack of a clear absorption spectrum makes an exact determination difficult. Further experiment will examine the reaction of arylchlorocarbenes with other amines.

Acknowledgment. M. T. H. Liu thanks NSERC of Canada for an International Collaborative Research Grant.

Tandem Diels-Alder/Double Intramolecular Two-Alkyne Annulations of Fischer Carbene Complexes: A One-Pot Construction of All Four Rings of the Steroid Ring System

Jianming Bao, Vera Dragisich, Steve Wenglowsky, and William D. Wulff*

Department of Chemistry, Searle Chemistry Laboratory
The University of Chicago, Chicago, Illinois 60637

Received September 6, 1991

All of the reported syntheses that have employed annulations of Fischer carbene complexes[1] produce benzene rings in a process that incorporates the carbene carbon and 1 equiv of the alkyne.[2,3] Analogous annulations that incorporate the carbene ligand and 2 equiv of the alkyne have not been employed in synthesis.[4-7] We report here the first examples of double intramolecular two-alkyne

---

(1) For reviews, see: (a) Dötz, K. H. In *Organometallics in Organic Synthesis: Aspects of a Modern Interdisciplinary Field*; tom Dieck, H., de Meijere, A., Eds.; Springer: Berlin, 1988. (b) *Advances in Metal Carbene Chemistry*; Schubert, U., Ed.; Kluwer Academic Publishers: Boston, MA, 1989. (c) Wulff, W. D. In *Advances in Metal-Organic Chemistry*; Liebeskind, L. S., Ed.; JAI Press Inc.: Greenwich, CT, 1989; Vol. 1. (d) Wulff, W. D. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon Press: New York, 1991; Vol. 5.

(2) For a list of citations to syntheses, see ref 1d and footnote 6 in the following: Wulff, W. D.; Bauta, W. E.; Kaesler, R. W.; Lankford, P. J.; Miller, R. A.; Murray, C. K.; Yang, D. C. *J. Am. Chem. Soc.* **1990**, *112*, 3642.

(3) For recent syntheses not cited in references 1d or 2, see: (a) Yamashita, A.; Toy, A.; Scahill, T. A. *J. Org. Chem.* **1989**, *54*, 3625. (b) Yamashita, A.; Toy, A.; Ghazal, N. B.; Muchmore, C. R. *J. Org. Chem.* **1989**, *54*, 4581. (c) Parker, K. A.; Coburn, C. A. *J. Org. Chem.* **1991**, *56*, 1666. (d) King, J.; Quayle, P.; Malone, J. F. *Tetrahedron Lett.* **1990**, *31*, 5221. (e) Boger, D. L.; Jacobson, I. C. *J. Org. Chem.* **1991**, *56*, 2115. (f) Boger, D. L.; Jacobson, I. C., *Tetrahedron Lett.* **1989**, *30*, 2037. (g) Boger, D. L.; Jacobson, I. C. *J. Org. Chem.* **1990**, *55*, 1919.

(4) Tang, P. C.; Wulff, W. D. *J. Am. Chem. Soc.* **1984**, *106*, 1132.

(5) (a) Wulff, W. E.; Kaesler, R. W.; Peterson, G. A.; Tang, P. C. *J. Am. Chem. Soc.* **1985**, *107*, 1060. (b) Semmelhack, M. F.; Park, J. *Organometallics* **1986**, *5*, 2550. (c) Hoye, T. R.; Rehberg, G. M. *Organometallics* **1989**, *8*, 2070. (d) Parlier, A.; Rudler, H.; Platzer, H.; Fontanille, M.; Soum, A. *J. Chem. Soc., Dalton Trans.* **1987**, 1041.

(6) (a) Reference 5a. (b) Reference 1c. (d) Sivavec, T. M.; Katz, T. J. *Tetrahedron Lett.* **1985**, *26*, 2159. (d) Xu, Y. C.; Wulff, W. D. *J. Org. Chem.* **1987**, *52*, 3263.

(7) (a) Wulff, W. D.; Xu, Y. C. *Tetrahedron Lett.* **1988**, *29*, 415. (b) Xu, Y. C.; Challener, C. A.; Dragisich, V.; Brandvold, T. A.; Peterson, G. A.; Wulff, W. D.; Williard, P. G. *J. Am. Chem. Soc.* **1989**, *111*, 7269. (c) Anderson, B. A.; Wulff, W. D.; Rheingold, A. L. *J. Am. Chem. Soc.* **1990**, *112*, 8615.

0002-7863/91/1513-9873$02.50/0

Scheme I

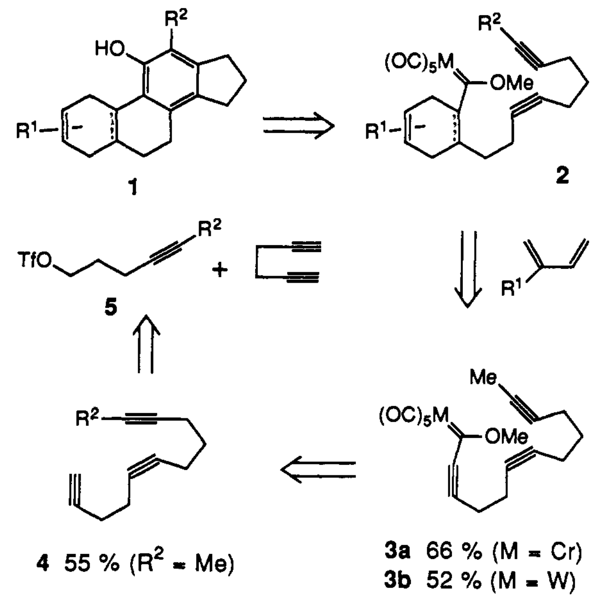
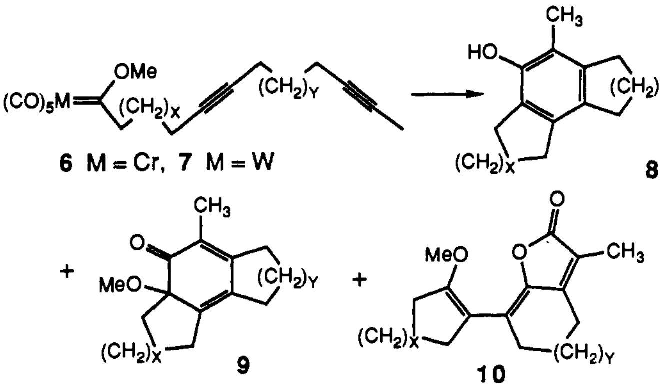


Table I. Double Intramolecular Two-Alkyne Annulations[a]



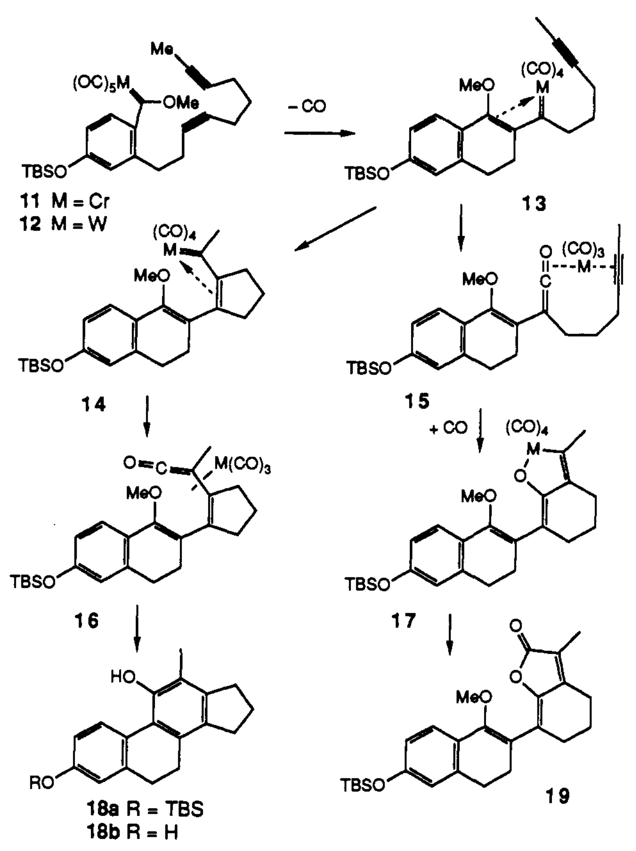
series	M	*X*	*Y*	solvent	8	9	10
a	Cr	1	1	benzene	58		
				THF	61	7	
				CH_3CN	31	41	
				DMF	10	16	
a	W	1	1	CH_3CN/CO[b]	61		
b	Cr	1	0	benzene			41
b	W	1	0	benzene	30		
				CH_3CN/CO[b]	48		
c	Cr	2	1	benzene	24		19[c]
c	W	2	1	CH_3CN/CO[b]	36		

[a] All reactions were carried out at 0.005 M in carbene complex and required 16–24 h. Reactions of **6** were at 70 °C, and those of **7** were at 110 °C. [b] Reaction mixtures were sealed in a reaction flask[14] at 25 °C under 1 atm of CO and heated to 110 °C. [c] Isolated as ketone **10d** resulting from hydrolysis of methyl enol ether **10c**.

annulations and a new approach to the tetracyclic carbon nucleus of the steroid skeleton via the tandem Diels–Alder/double intramolecular two-alkyne annulation of Fischer carbene complexes, where all four rings are constructed in a single pot according to the general approach indicated in Scheme I.[8]

There have been no reports of double intramolecular two-alkyne annulations, and therefore, an analysis of the scope of this reaction was undertaken (Table I). The efficiency of the reaction for the production of phenol products is highly dependent on the sizes of the rings in the tricyclic product. The chromium complex **6a**[9] gives a total of 72% yield of the bis-fused cyclopentanoid products as a mixture of the phenol **8a** and the nonreduced cyclohexadienone **9a**.[5a,6d,7b] In contrast, the lower homologous chromium complex **6b** gives none of the expected benzocyclobutene **8b** but rather the unprecedented lactone **10b**, which has incorporated both of the alkyne functions as well as two of the carbon monoxide ligands of the carbene complex.[7b,c]

Scheme II



M	Solvent [a]	Yield **18a**	Yield **19**
Cr	benzene	30	29
W	benzene	51	
	THF	53	
	CH_3CN	63	
	CH_3CN / CO [b]	78 [c]	

[a] Reaction conditions in Table I. [b] See footnote *b* in Table I. [c] Total yield; **18a**:**18b** = 1.5.

The thermolysis of the chromium complex **6c** is the model system for the proposed synthetic approach to the steroid tetracyclic carbon skeleton that is outlined in Scheme I, and thus it was disappointing that this reaction gave only a 24% yield of the tricyclic phenol **8c**. However, it was anticipated that a complex of the type **2** may provide for more efficient two-alkyne annulations due to the presence of the six-membered ring, which should serve to restrict the conformations of the diyne side chain with respect to the carbene-complexed metal unit. The chromium complex **11** was the target for this test and was prepared from complex **3a** in a Diels–Alder reaction (0.1 M in benzene, 25 °C, 12 h) with Danishefsky's diene (1.5 equiv) in 87% yield (82% for **12**).[2,11] A

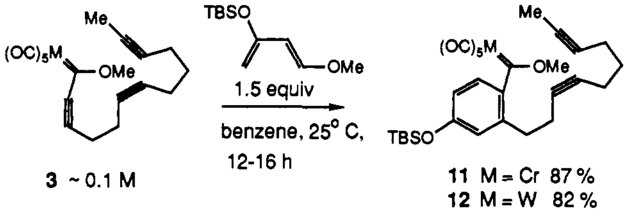
---

(8) This work was presented in preliminary form at the 201st National Meeting of the American Chemical Society, Atlanta, GA, April 14–19, 1991; Abstract 196.

(9) The chromium complex **6c** was prepared in 51% yield by alkylation of (methylmethoxymethylene)pentacarbonylchromium(0) with 1-undeca-4,9-diynyl triflate according to procedures for related complexes.[6d] Complexes **6a** and **6b** were prepared in a related manner in 72 and 38% yields, respectively. The tungsten complex **7a** was prepared in 57% yield by the standard Fischer procedure[1] from tungsten hexacarbonyl and 1-lithioundeca-4,9-diyne, which in turn was generated from the corresponding iodide.[10] The complexes **7b** and **7c** were prepared in a similar manner in 44 and 28% yield, respectively.

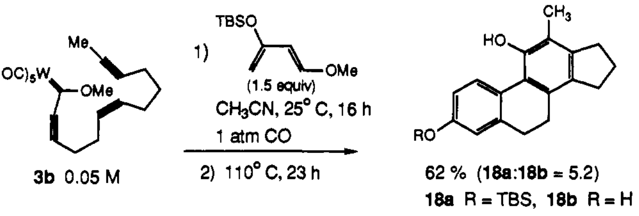
(10) (a) Bailey, W. F.; Punzalan, E. R. *J. Org. Chem.* **1990**, *55*, 5404. (b) Negishi, I.; Swanson, D. R.; Rousset, C. J. *J. Org. Chem.* **1990**, *55*, 5406.

rapidly decomposing intermediate complex could be observed by TLC, which was presumably the nonaromatized Diels–Alder adduct; however, these complexes did not survive when **11** and **12** were purified on silica gel.



Although the thermolysis of **11** at 75 °C did produce a better mass balance than did **6c**, the reaction still gives an equal distribution between phenol and lactone products, as indicated in Scheme II. According to the mechanism shown in Scheme II, the branch point between the lactone and phenol products is the vinyl carbene intermediate **13**, which undergoes either insertion of the second equivalent of alkyne to give **14** or CO insertion to give the ketene complex **15**. If this is correct, then a solution to the poor chemoselectivity would be to employ tungsten carbene complexes since it has been observed that tungsten carbene complexes give CO-inserted products less readily than chromium.[12] In fact, the thermolysis of the tungsten complex **12** at 110 °C gives exclusively the two-alkyne phenol **18** in 78% yield in acetonitrile solution under CO atmosphere. Likewise, lactone products were never observed from the thermolysis of the tungsten complexes **7a–c** indicated in Table I.

Finally, it was found that all four rings of the tetracyclic phenol **18** could be constructed in one pot in 62% yield from the triyne carbene complex **3b**.[13] This carbene complex could be readily obtained in two steps from the triflate **5** and the commercially available 1,5-hexadiyne as indicated in Scheme I.[15] This strategy for the synthesis of steroids is in the class 0 → ABCD and has been reported previously in a cobalt-mediated process.[17] The results described herein reveal that the two-alkyne annulations and Diels–Alder reactions of Fischer carbene complexes applied in tandem provide for a very straightforward approach to the steroid ring system. The strategy would be amenable to nonaromatic A-ring systems upon generation of **2** from the Diels–Alder reactions of α,β-vinylic carbene complexes.



Acknowledgment. This work was supported by a grant from the National Science Foundation (CHE-8821326). Some of the mass spectral data were obtained at the Midwest Center for Mass Spectrometry, an NSF Regional Instrument Facility (CHE-8211164). The NMR instruments used were funded in part by the NSF Chemical Instrumentation Program. We thank Dr. Mary Ellen Bos for contributions to the conceptual development of this work.

Supplementary Material Available: Spectral data for all new compounds (6 pages). Ordering information is given on any current masthead page.

---

(11) (a) Wulff, W. D.; Yang, D. C. *J. Am. Chem. Soc.* **1983**, *105*, 6726. (b) Wulff, W. D.; Yang, D. C. *J. Am. Chem. Soc.* **1984**, *106*, 7656. (c) Dötz, K. H.; Kuhn, W. *J. Organomet. Chem.* **1985**, *286*, C23.

(12) Foley, H. C.; Strubinger, L. M.; Targos, T. S.; Geoffroy, G. L. *J. Am. Chem. Soc.* **1983**, *105*, 3064.

(13) Upon completion of the Diels–Alder reaction (16 h), the solution was diluted 10-fold with acetonitrile, then sealed in a reaction flask with a threaded stopcock[14] at 25 °C under 1 atm of CO, and heated to 110 °C for 23 h.

(14) Chan, K. S.; Peterson, G. A.; Brandvold, T. A.; Faron, K. L.; Challener, C. A.; Hyldahl, C.; Wulff, W. D. *J. Organomet. Chem.* **1987**, *334*, 9.

(15) 1,5-Hexadiyne was deprotonated with 1.0 equiv of *n*-butyllithium in THF at –78 °C, then treated with 1.0 equiv of triflate **5**,[6d] and upon warming to 0 °C gave a 55% yield of triyne **4a**. The triyne **4a** was converted to complexes **3a** and **3b** in 66 and 52% yields, respectively, according to procedures for related alkynyl carbene complexes.[16]

(16) Chan, K. S.; Wulff, W. D. *J. Org. Chem.* **1986**, *108*, 5239.

(17) Lecker, S. H.; Nguyen, N. H.; Vollhardt, K. P. C. *J. Am. Chem. Soc.* **1986**, *108*, 856.

Free Radical Ring Expansion of Fused Cyclobutanones: A New Ring Expansion Annulation Stratagem

Paul Dowd* and Wei Zhang

Department of Chemistry, University of Pittsburgh
Pittsburgh, Pennsylvania 15260

Received August 21, 1991

The Diels–Alder reaction is highly valued because it can be employed to append four carbons stereospecifically to an alkene to form a new six-membered ring. Similar stereospecific annulation strategies have been developed for fusing one, two, and three carbons to alkenes to synthesize three-, four-, and five-membered rings. So too, it would be useful to append five, six, or more carbons to appropriate alkenes to form seven-, eight-, or higher-membered rings in stereospecific fashion. We have discovered a new synthetic method which accomplishes this goal.

The procedure is straightforward. An ω-bromoalkyl ketene is generated from an appropriate ω-bromo acid in the presence of an alkene to form a cyclobutanone[1,2] (Scheme I). Free radical reaction[3] of the adduct yields the ring-expanded[4] annulation product (Scheme I).

The reaction sequence leading to the ring fusion is stereospecific; the cis stereochemistry is enforced by the requirements of the cyclobutanone ring and is then translated to the ring-expansion product. Further examples are shown in Table I.

In the ketene cycloaddition, a mixture of exo and endo products is observed. The cycloadducts with exo side chains undergo smooth ring expansion. Cyclobutanones with endo side chains are prone to undergo direct reduction as a consequence of steric hindrance to ring-closure.

In a typical example (Table I, entry 1) the exo adduct **1** of cyclopentadiene and bromopropyl ketene was treated under slow addition conditions with tri-*n*-butyltin hydride and AIBN in refluxing benzene. The product of ring annulation **2** was obtained in 74% yield together with minor amounts of the alternative ring-opening product **3** and the product **4** of cyclization to the double bond.

In designing this sequence, we anticipated that the initial primary radical in **5** would attack the four-membered ketone to give the alkoxy radical[4,5] (Scheme II). The latter would then open in either of two ways (to **7** or **8**) to yield the ring-expanded annulation product **2** accompanied by the minor product of ring attachment **3**. The driving force is provided by the relief of strain in the four-membered ring. In every instance, ring expansion is the major path in the sequence.

Entry 2 in Table I shows that annulation of eight-membered rings is also possible following this strategy. Annulation to cy-

---

(1) Snider, B. B. *Chem. Rev.* **1988**, *88*, 793. Ghosez, L.; O'Donnell, M. J. *Pericyclic Reactions*; Marchand, A. P., Lehr, R. E., Eds.; Academic: New York, 1977; Vol. II, pp 79–140.

(2) Regio- and stereoselectivity of ketene–olefin cycloadditions: Wang, X.; Houk, K. N. *J. Am. Chem. Soc.* **1990**, *112*, 1754. Valenti, E.; Pericas, M. A.; Moyano, A. *J. Org. Chem.* **1990**, *55*, 3582. Bernardi, F.; Bottoni, A.; Robb, M. A.; Venturini, A. *J. Am. Chem. Soc.* **1990**, *112*, 2106.

(3) For recent reviews of free radical reactions, see: Curran, D. P. *Synthesis* **1988**, *417*, 489. Ramaiah, M. *Tetrahedron* **1987**, *43*, 3541.

(4) For free radical ring-expansions, see: Dowd, P.; Choi, S.-C. *Tetrahedron* **1991**, *47*, 4847 and references therein.

(5) Intramolecular addition of alkyl radicals to carbonyl groups: Walton, R.; Fraser-Reid, B. *J. Am. Chem. Soc.* **1991**, *113*, 5791. Beckwith, A. L. J.; Hay, B. P. *J. Am. Chem. Soc.* **1989**, *111*, 2674. Beckwith, A. L. J.; Hay, B. P. *J. Am. Chem. Soc.* **1989**, *111*, 230.

0002-7863/91/1513-9875$02.50/0