Allylic Displacements and a Novel Ester-Ether Interchange in Fused Cyclobutanones[1]

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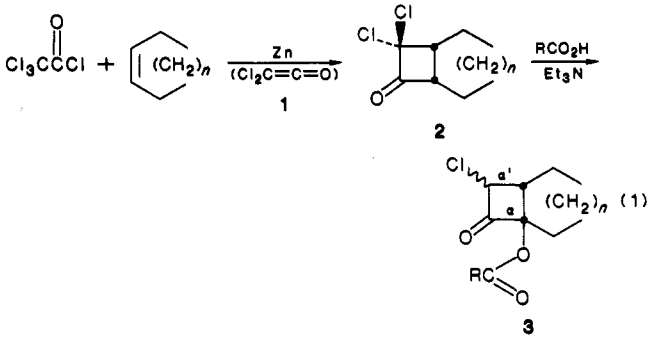
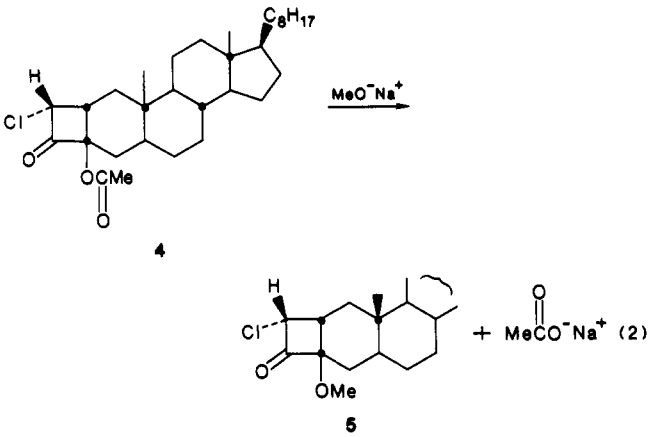
Chlorophenylcyclobutanone **11**, prepared by chlorophenylketene addition to cyclohexene, reacts readily with simple and hindered carboxylic acids in a cine substitution to produce keto esters **14**. The acyloxy and phenyl substituents in **14c** are shown by X-ray diffraction to be cis oriented; nevertheless **14** reacts with NaOMe at 20 °C by an unusual ester–ether interchange to produce **15** and the released carboxylate RCO_2^-. These reactions apparently proceed via an oxyallyl cation intermediate. The behaviors of related cyclobutanones **4**, **6**, and **11** with methoxide are contrasted.

Thermal [2 + 2] cycloaddition of halogenated ketenes to unsaturated substrates produces a wide array of four-membered ring systems of great value in synthetic and mechanistic studies.[2] For example, the cycloaddition of in situ generated dichloroketene (**1**) with cyclic olefins leads to the formation of fused dichlorocyclobutanones **2**, which can undergo ring contraction,[3] ring expansion,[4] ring opening,[5] or cine substitution reactions.[6] The latter class of reactions is particularly intriguing, due to the facility with which nucleophiles such as carboxylates add to the bicyclic framework to produce α-acyloxy-α'-chlorocyclobutanones **3** of stereochemical variability at the α'-carbon (eq 1). To differentiate the two substituents α to the

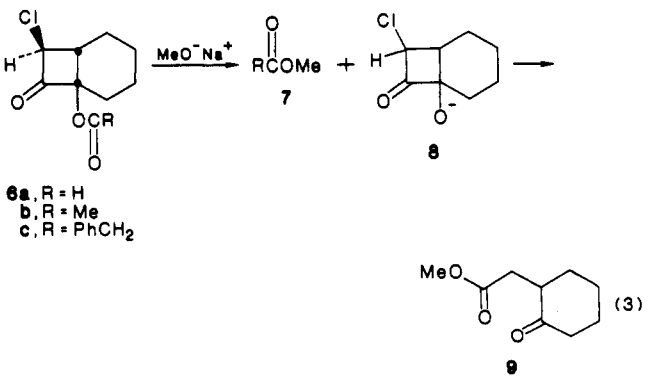


carbonyl group, we denote the bridgehead position as α and the other as α'.

In a preliminary report[6a] we described the contrasting reactivity of fused cyclobutanones of type **3** in the steroidal and bicyclo[4.2.0] series. This was dependent upon the stereochemical and conformational preferences of each system, unambiguously established by X-ray crystallographic analysis. Thus, reaction of steroidal cyclobutanone **4**, which possesses the trans configuration (chlorine and acyloxy trans), with sodium methoxide in MeOH–THF solution at 20 °C leads to the formation of the methyl ether **5** and acetic acid (eq 2). This ester–ether interchange is



an unusual occurrence and suggests a solvolysis reaction. On the other hand, under identical conditions as for **4**, reaction of the bicyclic counterpart **6**, either as the major isomer (Cl and acyloxy cis) or as a mixture of cis and trans isomers, produces ester cleavage products **7** and **8** (when R is H, Me, or $PhCH_2$) (eq 3). Product **8** is not isolated



but undergoes a fragmentation to yield keto acetate **9**. When R is hindered (mesityl, *t*-Bu) so that alcoholysis of the ester is slowed down, a cine substitution reaction analogous to that observed for steroid **4** takes place (eq 9).

The cine substitution reaction of steroid **4** leading to **5** is particularly noteworthy and provides strong evidence

(1) Stereochemistry. 75. For paper 74, see: Hassner, A.; Murthy, K. *Tetrahedron Lett.* **1986**, *27*, 1407.

(2) For a review, see: Brady, W. T. *Tetrahedron* **1981**, *37*, 2949.

(3) (a) Hassner, A.; Fletcher, V. *Tetrahedron Lett.* **1970**, 1071. (b) Garin, D. L.; Cammack, K. L. *J. Chem. Soc. Chem. Commun.* **1972**, 333. (c) Martin, P.; Greuter, H.; Rihs, G.; Wintler, T.; Bellus, D. *Helv. Chim. Acta* **1981**, *64*, 2571.

(4) (a) Stevens, H. C.; Reich, D. A.; Brandt, D. R.; Fountain, K. R.; Garghan, E. J. *J. Am. Chem. Soc.* **1965**, *87*, 5257. (b) Hassner, A.; Pinnick, H. W.; Ansell, J. M. *J. Org. Chem.* **1978**, *43*, 1774. (c) Vedejs, E.; Buchanan, R. A. *J. Org. Chem.* **1984**, *49*, 1840. (d) Greene, A. E.; Depres, J. P. *J. Am. Chem. Soc.* **1979**, *101*, 4003.

(5) (a) Conia, J. M.; Ripol, J. L. *Bull. Soc. Chim. Fr.* **1963**, 763. (b) Ghosez, L.; Montaigne, R.; Roussel, A.; Vanlierde, H.; Mallet, P. *Tetrahedron* **1971**, *27*, 615.

(6) (a) Hassner, A.; Dillon, J.; Krepski, L.; Onan, K.; *Tetrahedron Lett.* **1983**, 1135. (b) See ref 4a and: Harding, K.; Trotter, J.; May, L. *J. Org. Chem.* **1977**, *42*, 2715.

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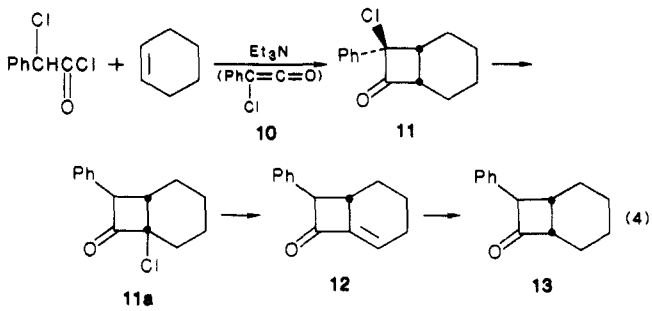
for the intermediacy of the controversial oxyallyl cation as opposed to a cyclopropanone[7] structure in this system. In order to observe the influence of substituents in these reactions we have examined **11**, the chlorophenylketene adduct of cyclohexene, because first a phenyl substituent is much larger than chlorine and if trans oriented it may provide a bicyclic system that behaves like steroid **4**. On the other hand, phenyl is better able to stabilize a positive charge and may lead to different substitution products. We now report the experimental details for the formation and reaction of **6** and the stereochemical and mechanistic consequences of introducing a phenyl substitutent in place of one of the chlorine substituents.

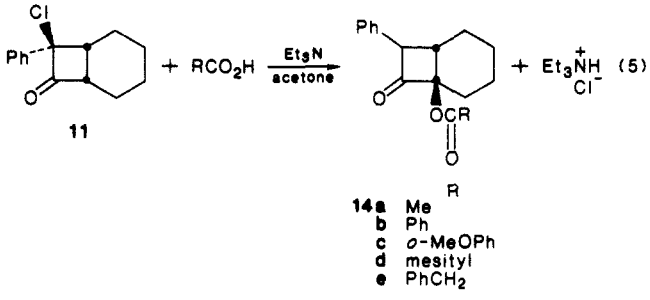
Results and Discussion

The [2 + 2] cycloaddition of chlorophenylketene (**10**) to cyclohexene was carried out by treatment of α-chloro-α-phenylacetyl chloride with triethylamine in cyclohexene solution. Though this had been shown[8a] to lead to formation of cyclobutanone **11**, in our hands attempted purification by vacuum distillation gave extensive decomposition and flash chromatography failed to effect good separation. We have discovered that thermal decomposition of **11** is due to a facile rearrangement leading to bicyclic olefin **12**, presumably via an unstable chlorocyclobutanone **11a** (eq 4). This rearrangement can be



minimized by addition of a small amount of the free radical trapping agent 2,6-di-*tert*-butyl-4-methylphenol followed by *rapid* vacuum distillation. In this manner **11** was obtained in 70% yield with only traces of the olefin **12**.[8b] Hydrogenation of **12** gave **13**, identical with the Zn reduction product of **11**.

Cyclobutanone **11** reacted with carboxylic acids, although more slowly than did chloro analogue **2**, to give crystalline α-acyloxy-α′-phenylcyclobutanones **14** in good to excellent yield (eq 5). Since even sterically encumbered



carboxylic acids such as mesitoic acid react to produce the cine substitution product in good yield, an S_N2' mechanism appears unlikely.

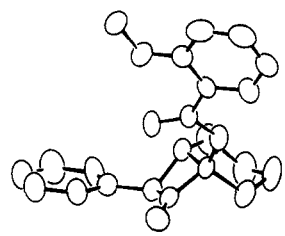
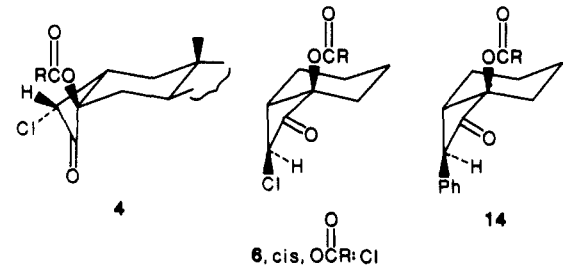


Figure 1. A perspective view of **14c** with 50% thermal ellipsoids.

Chart I. Approximate Conformations of the Fused Cyclobutanone Rings in 4, 6, and 14c as Determined from X-ray Diffraction Data

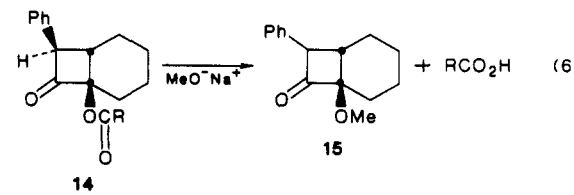


In order to understand more completely the mechanism of the reactions of these cyclobutanones with base, it was deemed important to define the stereochemical factors. Because stereochemical assignments in four-membered ring systems based on ^1H NMR coupling constants are ambiguous, an X-ray analysis of **14** became imperative. This was successfully accomplished for **14c**, whose structure is shown in Figure 1. It is seen to possess cis acyloxy and phenyl substituents which are quasi-equatorial to the four-membered ring.

Of interest are the endocyclic torsion angles in the cyclobutanone ring due to the cis relationship between the phenyl and ester substituents. The fused six-membered ring does not contribute to this flattening since a compound, analogous except with cis methyl groups instead of a fused ring,[9] also displays a mean endocyclic torsion angle of 16.7°. These rings are only slightly flatter than that in **6** (mean torsion angle 18.5°). All of these, however, are much flatter than the cyclobutanone ring in **4** which possesses trans substituents (24.2°) (see Chart I).[6a]

The slightly flattened conformation of the six-membered ring in **14c** is identical with that in **6** with C_s running through C(3) and C(6). In **4**, however, though the mean torsion angle is very similar, the C_s runs through C(4) and C(7).

Unexpectedly, in spite of the cis stereochemistry, adducts **14** behave, with sodium methoxide in MeOH–THF, like the trans isomer **4** rather than like the cis isomer **6**. The products of this reaction are the methyl ether **15** and the carboxylate (eq 6). No ester cleavage products of type



22 or an analogue of **9** were observed.

The facility with which carboxylic acids react with **11**, coupled with the ease of carboxylate generation with

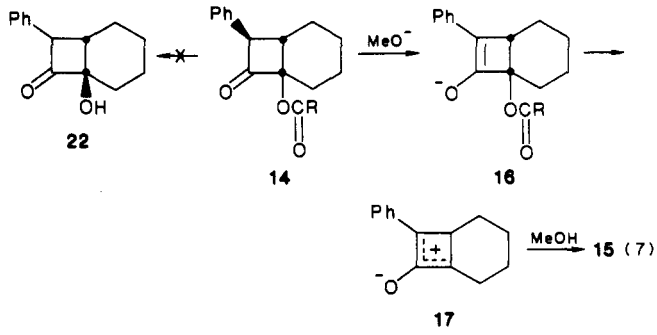
(7) (a) Fort, A. W. *J. Am. Chem. Soc.* **1962**, *84*, 2620, (b) 2625. (c) For entrapment of an oxyallyl intermediate in furan, see: Fort, A. W. *J. Org. Chem.* **1962**, *84*, 4979.

(8) (a) Brady, W. T.; Dorsey, E. D.; Parry, F. H. *J. Org. Chem.* **1969**, *34*, 3846. (b) The geometry of this cycloaddition has been shown to proceed in a manner which renders the larger substituent (phenyl) in the endo orientation. See: Rey, M.; Roberts, S.; Dieffenbacher, A.; Dreiding, A. S. *Helv. Chim. Acta* **1970**, *53*, 417.

(9) Hassner, A.; Dillon, J.; Onan, K. D., unpublished results.

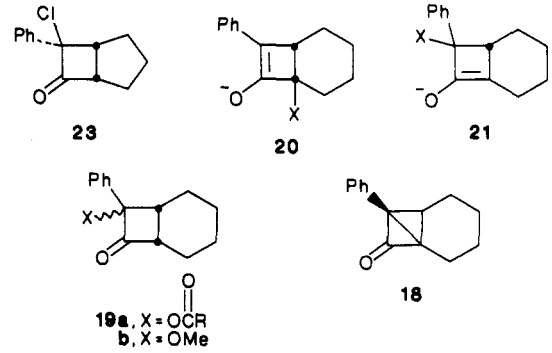
methoxide, suggests that 11 might have some application as a protecting group for the carboxylic acid function. This aspect is currently under study.

The conversion of esters 14 into methyl ether 15 can be rationalized by an enolization–ionization pathway. Thus the α'-hydrogen in 14 undergoes proton abstraction by base to produce enolate 16, which upon ionization of the allylic acyloxy substituent forms oxyallyl cation 17. The latter is trapped by methanol (eq 7). The transformation 11 →



14 and 14 → 15 are unique examples in which α-halo ketones or α-acetoxy ketones react exclusively via an oxyallyl cation and no products derived from a cyclopropanone (Favorskii ring contraction)[10] are observed. This, combined with the great strain expected in 18 leads us to rule out such a cyclopropanone intermediate.

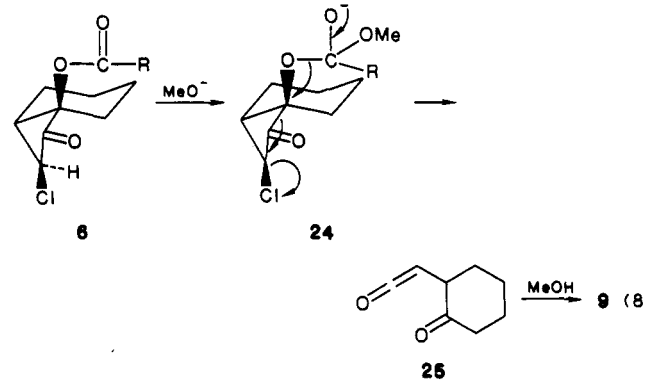
The fact that none of the isomeric ester 19a was found in the reaction of 11 with RCO_2^- nor was ether 19b observed in the conversion of 14 with methoxide can be explained by a preference of 17 to produce the more stable conjugated enolate 20 rather than the more strained 21.



This notion receives some validity from the fact that when we attempted the cine substitution on 23, the chlorophenylketene adduct of cyclopentene, no reaction occurred with acetic acid–triethylamine, even under reflux. It appears that enolization of 23 toward the bridgehead is much less favorable here than in 11 because of the additional strain created.

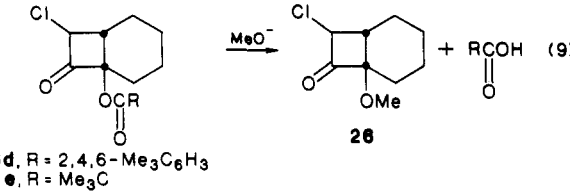
With the correct stereochemical assignments and preferred conformations for keto esters 4, 6 and 14 now in hand from X-ray data (Chart I), it is possible to assess the factors governing the contrasting reactivity in these compounds. Steroidal cyclobutanone 4 is ideally suited for enol or enolate anion formation due to the nonsterically encumbered β-configuration of the α'-hydrogen as well as the quasi-axial nature of this hydrogen with respect to the four-membered ring, which allows for better p-orbital overlap with the carbonyl system. In this case oxyallyl cation formation results by *loss of the quasi-axial acyloxy substituent* followed by entrapment with MeOH to form methyl ether 5. Stereoisomerization of trans 4 to its cis isomer is unfavorable because it gives rise to 1,3-diaxial interactions of Cl and RCO_2 which cannot be relieved by ring flipping of the cyclohexane ring to another chain conformer.

On the other hand, ring flipping permits the bicyclic cis chloro ester 6 to exist with a quasi-equatorial chlorine, the more stable stereoisomer in this system. Since 6 contains an α'-hydrogen which is sterically encumbered, enolization is slowed so that nucleophilic attack at the ester carbonyl now becomes more competitive. More importantly, the stereochemical alignment in this compound offers the possibility for a unique fragmentation reaction where all bonds undergoing cleavage are antiperiplanar (see 24). This produces ketene intermediate 25, which can be trapped by methanol (eq 8). This conversion is not possible in steroid 4.



While the phenyl cyclobutanone 14 shares the same stereochemistry and conformation as the chloro ketone 6, it does not possess the good leaving group (Cl) present in 6. Furthermore, the strong tendency to form the highly conjugated enolate promotes the formation of an oxyallyl cation and hence leads to ether 15.

When ester 6 possesses a bulky R substituent (i.e. 6d, R = mesityl, or 6e, R = *t*-butyl) then attack at the ester carbonyl is slowed down considerably, and enolization to the oxyallyl cation takes place leading, as in the steroid 14, to ester–ether exchange (formation of 26) (eq 9).



In conclusion, cyclobutanones 2 (n = 2) react readily with carboxylate anions to produce cine substitution products 4, 6, or 14. The behavior of these esters toward methoxide ion depends on the nature and stereochemistry of the substituents on the cyclobutanone ring. Attack by methoxide at the ester carbonyl leading to cleavage takes place in 6a–c where cis–trans equilibration is possible. On the other hand, when such attack is hindered by bulky substituents (6d,e) or in the rigid steroidal system 4, which possesses only the trans acyloxy–Cl configuration, as well as in the phenyl case 14, where a halogen leaving group is absent, an unusual ester–ether exchange occurs which most likely proceeds via an oxyallyl cation intermediate.

Experimental Section

Melting points were taken on a Fisher-Johns apparatus and are uncorrected. Infrared spectra were recorded on a Perkin-Elmer

(10) See ref 7a and: (a) Bordwell, F. G.; Carlson, M. W. *J. Am. Chem. Soc.* **1970**, *92*, 3377. (b) Hoffman, H. M. R. *Angew. Chem., Int. Ed. Engl.* **1973**, *12*, 819. (c) Edelson, S. S.; Turro, N. J. *J. Am. Chem. Soc.* **1970**, *92*, 2770.

283B spectrometer either neat or in CCl_4. Nuclear magnetic resonance spectra were recorded on a Varian EM360 spectrometer in ca. 10% w/v solutions with deuterated chloroform as solvent and tetramethylsilane as internal standard. Carbon-13 spectra were obtained on a Varian FT80A spectrometer using deuterated chloroform as solvent and tetramethylsilane as internal standard, unless otherwise noted. Gas chromatography/mass spectra were obtained on a Hewlett-Packard 5993 spectrometer using a capillary column and a flow rate of 1 cm^3/min. Gas chromatographic separations were performed on a Varian Aerograph GC using a column packed with SE-32 as a stationary phase and a flow rate of 1 cm^3/min.

General Procedure for Reaction of 2 (n = 3) with Acids. Formation of 6. To a flame-dried two-neck flask flushed with argon were added 1.0 g (5.2 mmol) of 7,7-dichloro-*cis*-bicyclo-[4.2.0]octane-8-one[11] and 10 mL of anhydrous acetone followed by 1 equiv of carboxylic acid. To this stirred mixture was added 0.52 g (5.2 mmol) of triethylamine all at once. An immediate precipitate of triethylammonium chloride ($Et_3N^+HCl^-$) was produced. The mixture was stirred 15 min and quenched with dilute HCl. Ether (50 mL) was added and washed successively with water, 5% HCl, sodium bicarbonate solution, and sodium chloride and dried over anhydrous $MgSO_4$. Removal of ether gave the adduct generally in quantitative yield.

***cis*- and *trans*-1-(Formyloxy)-7-chloro-*cis*-bicyclo-[4.2.0]octan-8-one (6a).** The adduct of formic acid was purified as a mixture of isomers by bulb-to-bulb distillation to give a clear oil: bp 100 °C (0.03 mmHg); ^1H NMR ($CDCl_3$) δ 8.0 (s, 1 H), 5.3 (d, J = 10 Hz), 4.6 (d, J = 9 Hz, together with δ 5.3 peak = 1 H), 3.2 (m, 1 H), 2.3–1.2 (m, 8 H); IR (CCl_4) 1780, 1730 cm^{-1}. Anal. Calcd for $C_9H_{11}ClO_2$: C, 53.34; H, 5.47. Found: C, 53.50; H, 5.55.

***cis-exo*-1-Acetoxy-*exo*-7-chloro-*cis*-bicyclo[4.2.0]octan-8-one (6b).** The mixture of isomers obtained from reaction of **2** with acetic acid was dissolved in a small amount of ether and placed in a dry ice–acetone bath. The resulting solid was filtered and recrystallized from hexane to give the cis isomer as fine cotton-like needles: ^1H NMR ($CDCl_3$) δ 4.5 (d, J = 9 Hz, 1 H), 3.2 (m, 1 H), 2.1 (s, 3 H), 2–1 (m, 8 H); IR (CCl_4) 1780, 1725 cm^{-1}. Anal. Calcd for $C_{10}H_{13}ClO_3$: C, 55.43; H, 6.06. Found: C, 55.69; H, 6.12.

***trans-exo*-1-Acetoxy-*endo*-7-chloro-*cis*-bicyclo[4.2.0]octan-8-one (6b).** The mother liquor obtained from **6b** was distilled in vacuo, giving a pale yellow viscous oil. NMR showed this to contain approximately 30% of cis isomer **6b** and 70% of trans isomer, bp 150 °C (bath) (0.02 mmHg). trans isomer: ^1H NMR ($CDCl_3$) δ 5.2 (d, J = 10 Hz, 1 H), 3.15 (m, 1 H), 2.15 (s, 3 H), 2–1 (m, 8 H); IR (neat) 1780, 1725 cm^{-1}. Anal. Calcd for $C_{10}H_{13}ClO_3$: C, 55.43; H, 6.06. Found: C, 55.62; H, 6.24.

***cis-exo*-1-(Phenylacetoxy)-7-chloro-*cis*-bicyclo[4.2.0]octan-8-one (6c).** The mixture of isomers obtained from phenylacetic acid was separated as for **6b**. *cis*-**6c** was obtained as fine cotton-like needles: mp 107–108 °C; ^1H NMR ($CDCl_3$) δ 7.3 (s, 5 H), 4.5 (d, J = 9 Hz, 1 H), 3.68 (s, 2 H), 3.2 (m, 1 H), 2.3–1.2 (m, 8 H); IR (CCl_4) 1783, 1730 cm^{-1}; mass spectrum; m/e (relative intensity) 293 (M^+), 157, 91 (100). Anal. Calcd for $C_{16}H_{17}O_3Cl$ (292.8): C, 65.63; H, 5.86. Found: C, 65.69; H, 5.90.

***trans-exo*-1-(Phenylacetoxy)-*endo*-7-chloro-*cis*-bicyclo-[4.2.0]octan-8-one (6c).** The mixture was separated as for **6b**. *trans*-**6c** was obtained as a pale yellow viscous oil: bp 200 °C (bath) (0.01 mmHg); ^1H NMR ($CDCl_3$) δ 7.3 (s, 5 H), 5.2 (d, J = 10 Hz, 1 H), 3.68 (s, 2 H), 3.1 (m, 1 H), 2–1.1 (m, 8 H); IR (neat) 1780, 1728 cm^{-1}; mass spectrum, m/e (relative intensity) 293 (M^+), 157, 91 (100). Anal. Calcd for $C_{16}H_{17}O_3Cl$ (292.8): C, 65.63; H, 5.86. Found: C, 65.43; H, 5.92.

***cis-exo*-1-[(2,4,6-Trimethylbenzoyl)oxy]-*exo*-7-chloro-*cis*-bicyclo[4.2.0]octan-8-one (6d).** The procedure of Harding[6b] was modified. The crude mixture of esters was dissolved in hot hexane, and only cis isomer **6d** crystallized as cotton-like needles, which compared in all ways to the compound previously reported: mp 116–117 °C (lit.[6b] mp 118 °C); ^1H NMR ($CDCl_3$) δ 6.75 (s, 2 H), 4.5 (d, J = 9 Hz, 1 H), 3.25 (m, 1 H), 2.3 (s, 9 H), 2.1–1.0 (m, 8 H); IR (CCl_4) 1795, 1700 cm^{-1}.

***trans-exo*-1-[(2,4,6-Trimethylbenzoyl)oxy]-*endo*-7-chloro-*cis*-bicyclo[4.2.0]octan-8-one (6d).** The mother liquor of **6d** was recrystallized from ethanol to give colorless prisms, which compared in all ways to the compound previously reported: mp 122–123 °C (lit.[6b] mp 123 °C); ^1H NMR ($CDCl_3$) δ 6.75 (s, 2 H), 5.25 (d, J = 10 Hz), 3.3 (m, 1 H), 2.3 (s, 9 H), 2–1 (m, 8 H); IR (CCl_4) 1800, 1720 cm^{-1}.

***cis*- and *trans-exo*-1-(Pivaloyloxy)-7-chloro-*cis*-bicyclo-[4.2.0]octan-8-one (6e).** The adduct of pivalic acid was obtained as a mixture of isomers and as a pale yellow oil: ^1H NMR ($CDCl_3$) δ 5.2 (d, J = 10 Hz), 4.5 (d, J = 9 Hz, combined with δ 5.2 = 1 H), 3.3 (m, 1 H), 2.3–1.5 (m, 8 H), 1.2 (s, 9 H); IR (neat) 1803, 1730 cm^{-1}. This compound could not be obtained sufficiently pure for satisfactory elemental analysis.

Reaction of Compounds 6a–c with Sodium Methoxide. To 500 mg of a mixture of **6** in 10 mL of anhydrous methanol and 5 mL of anhydrous THF (to dissolve the ester) was added 1 equiv of sodium methoxide in 5 mL of anhydrous MeOH [prepared by addition of sodium metal (1 equiv) to methanol] all at once. The mixture was stirred for 2 h, water (25 mL) was added, and the mixture was extracted with three 25-mL portions of ether. The ether was washed with water and dried over anhydrous $MgSO_4$. Removal of ether left a yellow oil. In the case of **6a,b** a single compound was obtained by preparative VPC (SE30, t = 180 °C). This was shown to be keto acetate **9** by comparison of spectra with those of an authentic sample as well as GC coinjection: ^1H NMR ($CDCl_3$) δ 3.63 (s, 3 H), 3.5–1.2 (m, 11 H); IR (neat) 1740, 1712 cm^{-1}. In the case of **6c** two compounds were obtained in 96% yield which were separted by preparative VPC (SE 30, t = 180 °C). The first compound was shown to be the methyl ester of phenylacetic acid [δ 7.15 (s), 3.62 (s), 3.5 (s); 1740 cm^{-1}] by comparison with an authentic sample, and the second was keto acetate **9**.

Reaction of Compounds 6d,e with Sodium Methoxide. To 250 mg of a mixture of **6** in 5 mL of anhydrous MeOH and 3 mL of anhydrous THF was added 1 equiv of sodium methoxide in 1.5 mL of anhydrous MeOH all at once. The mixture was stirred at 20 °C for 2 h, water (15 mL) was added, and the mixture was extracted with three 15-mL portions of ether. The ether was washed with water and dried over anhydrous magnesium sulfate. Removal of ether left a pale yellow oil. This was shown to be one compound by VPC. Preparative VPC gave a clear oil shown to be methyl ether **26**, the spectra of which were identical with those previously reported:[6b] ^1H NMR ($CDCl_3$) δ 4.5 (d, J = 9 Hz, 1 H), 3.32 (s, 3 H), 2.8 (m, 1 H), 2.2–1 (m, 8 H); IR (neat) 1795 cm^{-1}.

General Procedure for Cycloaddition of Phenylchloroketene with Olefins. Formation of 23 and 11. To a dry three-necked flask under argon and equipped with reflux condenser and addition funnel were added 70 mL of olefin and 0.053 mol of α-chlorophenylacetyl chloride. To this refluxing mixture a solution containing 0.053 mol of triethylamine in 30 mL of olefin was added over a period of 1 h. The mixture was heated an additional half hour at reflux and the $Et_3NH^+Cl^-$ filtered. The filtrate was washed successively with water, 5% HCl, saturated sodium bicarbonate, and saturated sodium chloride and dried over ($MgSO_4$) anhydrous magnesium sulfate. Removal of olefin in vacuo gave a yellow-brown oil or solid which was purified by distillation or recrystallization.

***exo*-7-Chloro-*endo*-7-phenyl-*cis*-bicyclo[4.2.0]octan-8-one (11).** The adduct from cyclohexene was obtained as a yellow-brown oil, which could be purified in two ways. Purification with silica gel by fast elution with EtOAc–petroleum ether (1:24) gave a pale yellow oil. For larger quantities distillation at reduced pressure was accomplished by addition of a small amount of 2,6-di-*tert*-butyl-4-methylphenol and *rapid* distillation. This produced a pale yellow oil in 70% yield: ^1H NMR ($CDCl_3$) δ 7.47 (m, 5 H), 4.2 (m, 1 H), 3.03 (m, 1 H), 2.2–0.2 (m, 8 H); ^{13}C NMR 189.2, 136.6, 128.6, 128.5, 127.8, 79.2, 54.0, 40.0, 27.7, 22.2, 20.7 ppm; IR (CCl_4) 1790 cm^{-1}. Anal. Calcd for $C_{14}H_{15}ClO$ (234.77): C, 71.62; H, 6.46. Found: C, 71.78; H, 6.46.

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(13) All calculations were carried out on a VAX 11/780 computer. The least-squares program was based on FMLS (Ganzel, P. L., Sparks, R. A., Trueblood, K. N., UCLA) and modified by McPhail, A. T., Duke University. Figure 1 was drawn with ORTEP, crystallographic illustration programs: Johnson, C. K. ORNL-3794; Oak Ridge National Laboratory: Oak Ridge, TN.

***exo*-6-Chloro-*endo*-6-phenyl-*cis*-bicyclo[3.2.0]heptan-7-one (23).** The adduct from cyclopentene was obtained as a yellow solid in 60% yield. Recrystallization from ethanol or methanol gave colorless prisms: mp 88.5–86.5 °C; ^{1}H NMR ($CDCl_3$) δ 7.35 (m, 5 H), 4.1 (d, 1 H), 3.4 (m, 1 H), 2.4–1.1 (m, 6 H); IR (CCl_4) 1793 cm^{-1}; mass spectrum; *m/e* (relative intensity) 220 (M^+, 21), 192 (34), 157 (59), 129 (100), 115 (53), 91 (34), 77 (15), 63 (19), 51 (16), 39 (25). Anal. Calcd for $C_{13}H_{13}ClO$ (220.71): C, 70.74; H, 5.95.

Rearrangement of 11 to 7-Phenylbicyclo[4.2.0]-1-octen-8-one (12). To 1.0 g of 11 (1.3 mmol) and 5 mL of toluene was added 0.43 g (4.3 mmol) of triethylamine. The mixture was refluxed for 12 h. TlC examination revealed the mixture to contain some starting material as well as a new compound at lower R_f. Separation was accomplished by using flash chromatography to give the olefin in 80% yield: ^{1}H NMR ($CDCl_3$) δ 7.15 (s, 5 H), 6.28 (5, J = 3 Hz, 1 H), 3.8 (d, J = 7 Hz, 1 H), 2.83 (m, 1 H), 2.3, 1.9–0.8 (m, 6 H); ^{13}C NMR 195.4, 147.5, 137.2, 128.6, 127.2, 126.9, 126.4, 67.0, 40.2, 28.2, 25.3, 21.7 ppm; IR (neat) 1751, 1654 cm^{-1}; mass spectrum, *m/e* (relative intensity) 198 (M^+, 100); UV (EtOH) 207.5 (A = 0.68), 240 (A = 0.67) nm [ϵ 8980 for c 7.57 × 10^{-5} M]. [An elemental analysis was not possible due to traces of chloro ketone **11a** present which had an R_f value identical with that of 12].

Attempted Reaction of 23 with Carboxylic Acid. To 1.0 g (4.5 mmol) of **23** in 10 mL of anhydrous acetone was added 1 equiv each of acetic acid and triethylamine. The mixture was stirred 12 h, at which time no precipitate was observed. The mixture was refluxed 12 h and worked up as usual. The residue obtained from the organic phase was shown by NMR to be unreacted **23**.

General Procedure for Reaction of 11 with Nucleophiles. Formation of 14. To a flame dried three-neck flask flushed with argon and equipped with an argon inlet were added 1.0 g (4.3 mmol) of 11, 10 mL of anhydrous acetone, and 1 equiv of the appropriate acid. To this stirred mixture was added 1 equiv of triethylamine. The mixture was stirred overnight, and a few milliliters of 5% hydrochloric acid were added. Ether (50 mL) was added and the ether washed successively with water, sodium bicarbonate solution, and sodium chloride solution and dried over anhydrous magnesium sulfate. Removal of ether in vacuo gave the adducts, which were recrystallized. Crude yields were quantitative except for the mesityl compound **14d**, which was obtained in 82% crude yield.

***exo*-1-Acetoxy-7-phenyl-*cis*-bicyclo[4.2.0]octan-8-one (14a).** Treatment of 11 with acetic acid gave **14a** as a yellow powder, which was recrystallized from hexane to give a white powder in 82% yield: mp 87–87.5 °C; ^{1}H NMR ($CDCl_3$) δ 7.2 (s over m, 5 H), 4.1 (d, J = 10 Hz, 1 H), 3.3 (m, 1 H), 2.2 (s, 3 H), 2.1–1.5 (m, 8 H); ^{13}C NMR 188.5, 169.7, 136.0, 128.7, 128.0, 127.2, 85.2, 58.0, 38.1, 28.5, 21.6, 20.8, 20.3 ppm; IR (CCl_4) 1800, 1750 cm^{-1}; mass spectrum, *m/e* (relative intensity) 216 (100), 198 (40), 188 (25), 129 (16), 118 (64), 115 (22), 97 (22), 91 (53), 43 (48). Anal. Calcd for $C_{16}H_{18}O_3$ (258.3): C, 74.39; H, 7.01. Found: C, 74.37; H, 7.02.

***exo*-1-(Benzoyloxy)-7-phenyl-*cis*-bicyclo[4.2.0]octan-8-one (14b).** Treatment of 11 with benzoic acid gave **14b** as a pale yellow solid. Recrystallization from methanol gave colorless crystals in 81% yield: mp 120–122 °C; ^{1}H NMR ($CDCl_3$) δ 8.0, 7.4 (m, 10 H), 4.1 (d, J = 10 Hz, 1 H), 3.4 (m, 1 H), 2.3–1.4 (m, 8 H); ^{13}C NMR 188.8, 165.1, 136.0, 133.1, 130.0, 129.9, 129.5, 128.8, 128.7, 128.5, 128.4, 128.3, 128.2, 128.1, 127.3, 85.4, 58.1, 38.1, 28.7, 21.7, 20.5, 20.3 ppm; IR (CCl_4) 1800, 1729 cm^{-1}; mass spectrum; *m/e* (relative intensity) 105 (100), 77 (19). Anal. Calcd for $C_{21}H_{20}O_3$ (320.4): C, 78.72; H, 6.30. Found: C, 78.77; H, 6.30.

***exo*-1-[(*o*-Methoxybenzoyl)oxy]-7-phenyl-*cis*-bicyclo[4.2.0]octan-8-one (14c).** Treatment of 11 with *o*-methoxybenzoic acid gave **14c** as a yellow solid, which was recrystallized from methanol (82% yield): mp 99.5–100.5 °C; ^{1}H NMR δ 7.85, 7.4, 7.0 (m, 9 H), 4.15 (d, J = 10 Hz, 1 H), 3.9 (s, 3 H), 1.8 (m, 8 H); IR 1795, 1733 cm^{-1}; mass spectrum, *m/e* (relative intensity) 135 (100).

***exo*-1-[(2,4,6-Trimethylbenzoyl)oxy]-7-phenyl-*cis*-bicyclo[4.2.0]octan-8-one (14d).** Treatment of 11 with mesitoic acid yielded **14d** as a yellow oil in 82% yield, which was crystallized from 95% EtOH to give white crystals in 60% yield: mp 106.5–107.5 °C; ^{1}H NMR δ 6.95 (s, 2 H), 4.2 (d, J = 10 Hz, 11 H), 2.35 (s, 9 H), 3.6 (m, 1 H), 2.2–1.3 (m, 8 H); IR 1796, 1730 cm^{-1}; mass spectrum, *m/e* (relative intensity) 147 (100).

***exo*-1-(Phenylacetoxy)-7-phenyl-*cis*-bicyclo[4.2.0]octan-8-one (14l).** The adduct obtained from phenylacetic acid was a pale yellow oil: ^{1}H NMR ($CDCl_3$) δ 7.3 (2 s, 10 H), 4.05 (d, J = 10 Hz, 1 H), 3.6 (s, 2 H), 3.1 (m, 1 H), 2.1–1.2 (m, 8 H). IR (neat) 1795, 1740 cm^{-1}.

Reactions of Esters 14a–e with NaOMe To Give *exo*-1-Methoxy-7-phenyl-*cis*-bicyclo[4.2.0]octan-8-one (15). To 1.0 g (4.3 mmol) of 14 in 20 mL of anhydrous MeOH and 10 mL of THF was added a solution containing 4.3 mmol of NaOMe in 5 mL of methanol. The mixture was stirred for 2 h at 25 °C and the methanol removed in vacuo. The resulting oil was dissolved in 50 mL of ether, washed successively with water, saturated $NaHCO_3$, and saturated NaCl, and dried ($MgSO_4$). Removal of ether left a yellow oil in 90% yield: ^{1}H NMR ($CDCl_3$) δ 7.3 (s, 5 H), 4.1 (d, J = 10 Hz, 1 H), 3.4 (s, 3 H), 2.1–1.4 (m, 8 H); IR (neat) 1765 cm^{-1}. Attempts to obtain crystalline **15** by chromatography were unsuccessful, hence it was converted to its semicarbazone. Anal. Calcd for $C_{16}H_{21}N_3O_2$: C, 66.87; H, 7.38. Found: C, 66.94; H, 7.39.

The reaction was carried out as shown above for **15**, and the bicarbonate layer was acidified with concentrated HCl and extracted with three 25-mL portions of CH_2Cl_2. The CH_2Cl_2 was washed to neutrality with water, followed by saturated NaCl. Removal of CH_2Cl_2 left the carboxylic acids in quantitative yield, which were identified by comparison with spectra of authentic samples.

Catalytic Hydrogenation of 12 to 7-Phenyl-*cis*-bicyclo-[4.2.0]octan-8-one. A mixture of 500 mg (2.5 mmol) of **12**, 50 mg of 10% palladium-on-carbon catalyst, and 10 mL of ethyl acetate was hydrogenated in a Parr apparatus at 7 atm. for 24 h. Filtration and removal of solvent left a pale yellow oil, which was distilled bulb-to-bulb to give a clear oil in 56% yield: bp 100 °C (bath) (0.1 mmHg); ^{1}H NMR ($CDCl_3$) δ 7.2 (m, 5 H), 4.3 (m, 1 H), 3.2 (m, 1 H), 2.7 (m, 1 H), 2.4–1.2 (m, 8 H); IR (neat) 1775 cm^{-1}.

Zinc Reduction of 11 To Give 13. A mixture of 500 mg (2.2 mmol) of 11, 10 mL of acetic acid, and 0.69 g of zinc was stirred at 50 °C for 1 H. The mixture was filtered on a pad of Celite and the filtrate taken up in 50 mL of ether. The ether was washed successively with water, 5% $NaHCO_3$, and saturated NaCl and dried ($MgSO_4$). Removal of ether in vacuo gave a pale yellow oil, which was purified by bulb-to-bulb distillation to give a clear oil in 90% yield, the NMR and IR of which were superimposable with those of the compound obtained by catalytic hydrogenation of **12**.

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Registry No. **2** (n = 2), 32166-29-3; **6a** (trans), 86477-36-3; **6a** (cis), 86496-74-4; **6b** (cis), 62653-14-9; **6b** (trans), 62653-13-8; **6c** (trans), 86477-37-4; **6d** (cis), 62653-12-7; **6d** (trans), 62609-28-3; **6e** (cis), 86496-76-6; **6e** (trans), 86477-38-5; **7** (R = $PhCH_2$), 101-41-7; **9**, 13672-64-5; **11**, 103150-19-2; **12**, 103150-20-5; **13**, 103238-77-3; **14a**, 103150-21-6; **14b**, 103150-23-8; **14c**, 103150-24-9; **14d**, 103150-26-1; **14e**, 103150-25-0; **15**, 103150-22-7; **15** semicarbazone, 103150-28-3; **23**, 103150-27-2; **26**, 62609-26-1; $PhCHClCOCl$, 2912-62-1; t-$BuCO_2H$, 75-98-9; o-$MeOC_6H_4CO_2H$, 579-75-9; $PhCO_2H$, 65-85-0; 2,4,6-$Me_3C_6H_2CO_2H$, 480-63-7; HCO_2H, 64-18-6; CH_3CO_2H, 64-19-7; $PhCH_2CO_2H$, 103-82-2; cyclohexene, 110-83-8; cyclopentene, 142-29-0.

Supplementary Material Available: Tables I–V listing atomic coordinates, anisotropic thermal parameters for non-hydrogen atoms, hydrogen atom parameters, bond lengths, valency angles, and torsion angles for **14c**, all with estimated standard deviations (9 pages). Ordering information is given on any current masthead page.