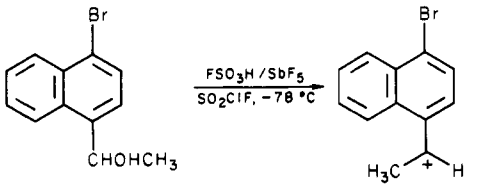

13 12

Conclusions

Obtaining ions **2a–c** and **6** upon ionization of precursors **1a–c** and **7** under stable ion conditions clearly indicates aryl participation of the 4-halophenyl as well as of the 10-bromoanthryl group. In ions **2a–c** the deshielding effect of the C_4 chemical shift increases as the electronegativity of halogen atoms decreases, indicating that n–π back donation is greater in fluoro than in chloro and bromo carbocations. Also the more electronegative the halogen atom, the more stable the carbocation formed. The present study thus extends our knowledge of "phenonium ions" to ring-halogenated systems.

Experimental Section

All the melting and boiling points are uncorrected. All the ^{13}C NMR spectra were recorded on a Varian FT-80 spectrometer equipped with a broad-band probe and a variable-temperature control. Proton NMR spectra were recorded on a Varian A-56/60A spectrometer. All the chlorides **1a–c** were prepared by thionyl chloride/pyridine reaction with the corresponding alcohols obtained from Aldrich Chemical Co., and their data are compared with literature.[6] Alcohol **4** was prepared by methyllithium reaction with *p*-bromobenzaldehyde, bp 126–128 °C (10 mm) (lit.[7] bp 128 °C (10 mm). 9-(2-Hydroxyethyl)-10-bromoanthracene (**7a**) was prepared by literature procedure.[9] Alcohol **13** was easily prepared from 1,4-dibromonaphthalene, *n*-butyllithium, and acetaldehyde reaction, mp 71–72 °C (lit.[14] mp 70–72 °C). All the new compounds **7**, **9**, **11**, **11a,b** gave satisfactory elemental analyses.

9-(β-Fluoroethyl)-10-bromoanthracene (7). Alcohol **7a** (10 mmol) was dissolved into 30 mL of methylene chloride at –78 °C under an inert atmosphere and (diethylamino)sulfur trifluoride (12 mmol) in 10 mL of methylene chloride was added dropwise. The reaction mixture was warmed up to room temperature and stirred overnight. Thereafter it was poured into cold water and extracted with methylene chloride. The organic layer washed with water, $NaHCO_3$ solution, and finally with brine solution. Drying and evaporation of solvent gave yellowish solid which was recrystallized with hexane–chloroform to give **7**, yield 90%; mp 126–127 °C; ^{13}C NMR ($CDCl_3$) $\delta_{^{13}C}$ 131.2, 130.4, 128.9, 126.9, 126.4, 126.0, 124.3, 123.4, 83.0 (d, J_{C-F} = 172.3 Hz), 29.1 (d, J_{C-F} = 21.4 Hz).

9-(α-Hydroxyethyl)-10-bromoanthracene (9). To a solution of 9,10-dibromoanthracene (10 mmol) in 50 mL of dry THF at –78 °C was added 12 mmol of *n*-butyllithium, and the reaction mixture was stirred at this temperature for additional 1 h. Acetaldehyde (10 mmol) in 10 mL of dry THF was added dropwise, and the reaction mixture was warmed up to room temperature and stirred an additional 1 h. Usual workup and recrystallization of the solid residue by chloroform–hexane gave **9** in 85% yield: mp 180–182 °C dec; ^{13}C NMR ($CDCl_3$) $\delta_{^{13}C}$ 23.0, 71.2, 122.9, 123.1, 124.9, 125.0, 125.3, 124.7, 126.1, 126.4, 127.0, 128.9, 131.0, 134.5.

1-(2-Hydroxyethyl)-4-bromonaphthalene (11). Alcohol **11** was conveniently prepared from 1,4-dibromonaphthalene, *n*-butyllithium, and ethylene oxide in 70% yield; bp 160–162 °C (0.4 mm), and analyzed by its ^{13}C NMR spectrum. ^{13}C NMR ($CDCl_3$) $\delta_{^{13}C}$ 138.3, 133.4, 127.8, 127.0, 126.7, 125.8, 125.5, 124.4, 123.6, 62.7, 36.1.

1-(2-Chloroethyl)-4-bromonaphthalene (11a). Chloride **11a** was prepared from alcohol **11** in the usual way by using thionyl chloride and pyridine in refluxed ether: yield 70%; bp 150–152 °C (0.4 mm); ^{13}C NMR ($CDCl_3$) δ 133.9, 132.0, 129.4, 128.0, 127.4, 127.0, 127.0, 126.2, 125.6, 123.5, 43.7, 36.0.

1-(2-Fluoroethyl)-4-bromonaphthalene (11b). Fluoride **11b** was conveniently prepared from alcohol **11** by using Middleton's procedure:[10] yield 87%; bp 130–132 °C (0.4 mm); ^{13}C NMR ($CDCl_3$) $\delta_{^{13}C}$ 132.5, 130.0, 129.3, 128.5, 127.8, 127.5, 126.6, 126.0, 124.3, 122.5, 83.5 (d, J_{C-F} = 170.4 Hz), 34.0 (d, J_{C-F} = 21.1 Hz).

General Procedure for Preparing the α-Ethylenehaloarenium Ions. In a carbon-13 NMR tube superacid (0.5 mL) is dissolved into 1–1.5 mL of SO_2ClF generally at –78 °C (or the temperatures indicated) with continuous stirring. The solid or liquid substrate to be ionized was added in portions to the cold acid solution in the tube while stirred on a Vortex mixer till a homogeneous ion solution was obtained.

Acknowledgment. Support of our work by the National Institutes of Health is gratefully acknowledged.

Registry No. **1a**, 332-43-4; **1b**, 32327-70-1; **1c**, 23386-17-6; **2a**, 90867-08-6; **2b**, 90867-09-7; **2c**, 90885-95-3; **3c**, 67595-65-7; **4**, 5391-88-8; **6**, 90867-07-5; **7**, 90867-01-9; **7a**, 90867-06-4; **8**, 90867-04-2; **9**, 90867-02-0; **10**, 90867-10-0; **11**, 90867-05-3; **11a**, 58149-81-8; **11b**, 90867-03-1; **12**, 90885-91-9; **13**, 58149-70-5; *p*-BrC_6H_4CHO, 1122-91-4; CH_3CHO, 75-07-0; 9,10-dibromoanthracene, 523-27-3; ethylene oxide, 75-21-8; 1,4-dibromonaphthalene, 83-53-4.

Medium-Ring Systems. 5.[1] Synthesis and Base-Catalyzed Isomerizations of Medium-Ring Cycloalkenones with Electron-Withdrawing Substituents[2]

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Medium-ring 3-cycloalkenones with electron-withdrawing substituents at the 3-position have been synthesized and subjected to base-catalyzed isomerizations. In a given ring size in the seven- and eight-membered carbocycles, the substituents studied caused similar shifts in the equilibria toward the 3-cycloalkenones relative to the unsubstituted cases. Steric effects of the substituents are therefore not significant. As the ring size is increased, the preference for the 3-cycloalkenone becomes more pronounced. In the nine- and ten-membered systems, an additional equilibrium involving formation of 4-cycloalkenones appears. Decreased effectiveness of conjugative interactions in endocyclic dienolates and in 2-cycloalkenones with increasing ring size is suggested.

The ability of a substituent to stabilize or destabilize a double bond has been quantitatively evaluated by Hine's[3] "double-bond stabilization parameters". In this approach, an equilibrium is established where the given substituent

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X is vinylic to the double bond in one component (1) and

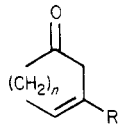
$$\underset{1}{trans\text{-}XCH{=}CHCH_2Y} \rightleftharpoons \underset{2}{trans\text{-}XCH_2CH{=}CHY}$$

allylic to the double bond in the other component (2) of the equilibration experiment. Hine observed that electron-withdrawing groups tend to destabilize double bonds, whereas electron-donating groups that are capable of donating their p electrons to the π system of the double bond tend to stabilize double bonds.

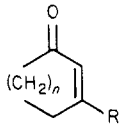
One of the difficulties in this method is the need to separate double-bond stabilizations in the vinylic system from homoconjugative interactions in the allylic system. A second difficulty, recognized by Hine, is the need to quantitatively evaluate the contribution of enhanced conjugation in the situation where one group on one side of the double bond is a resonance electron-donating group and the other side of the double bond contains a resonance electron-withdrawing group. This type of p–π interaction is analogous to those situations requiring Hammett σ^+ and σ^- scales.[4] A pertinent example of this phenomenon is the increased percentage[5] of 3-methoxy-2-cyclohexenone on equilibration with 3-methoxy-3-cyclohexenone relative to the unsubstituted cyclohexenones.[6]

A third difficulty is that similar electronic interactions at both ends of the double bond may provide an additional destabilization. For example, Taskinen[7] has reported that a 1,2-dialkoxyethylene system is about 4 kJ/mol less stable than a 1-alkoxyethylene system.

Medium-ring cycloalkenones (seven- to ten-membered rings) provide another system in which to study the effects of substituents on double bonds. In these systems the substituent might be placed on carbon-3 and an equilibrium might be established between the 3-cycloalkenone **3** and the 2-cycloalkenone **4**. In an isolated sense the



3 (Δ3), n = 3-6



4 (Δ2), n = 3-6

a, R = H; **b**, R = OCH_3; **c**, R = CO_2CH_3; **d**, R = C≡N; **e**, R = $COCH_3$; **f**, R = CH_2OAc

substituent interacts with the double bond in a similar manner in both isomers. The double bond is trisubstituted in both cases. The major difference between the isomers is the interaction of the carbonyl with the double-bond-substituent system. The substituent is at the β end of a conjugated framework in **4**, bringing into play possible enhanced conjugation with resonance electron-donating groups (see above) and possible destabilizations with resonance electron-withdrawing groups. In the 3-cycloalkenones **3**, the substituent is at the "nearer" end of a homoconjugative framework[8-10] if there indeed is significant interaction between the alkene and the carbonyl in these ring systems.

Table I. Equilibrations of 2- and 3-Cycloalkenones[6,11]

ring size	catalyst	composition, % Δ2	composition, % Δ3	$\Delta G^{80\,°C}$, kcal/mol
6	*p*-TsOH	99	1	3.2
7	*p*-TsOH	73	27	0.7
8	*p*-TsOH	20	80	-1.0
9	*p*-TsOH	>0.3	≪99.7	-3.7
10	*p*-TsOH	Δ2, Δ3 equilibrium not achieved[a]		

[a] Two isomers produced 96% *Z* isomer and 4% *E* isomer.[b] [b] Hirano[12] has reported formation of *Z*-Δ3 in 80% yield from hydrolysis of 2-cyclodecenone ethylene ketal.

Table II. Equilibration of 3-(Methoxycarbonyl)cycloalkenones[13]

ring size	catalyst	composition, % Δ2	composition, % Δ3	$\Delta G^{80\,°C}$, kcal/mol
7	DBN, *p*-TsOH	15	85	-1.2
8	DBN, *p*-TsOH	3.5	96.5	-2.3
9	DBN	>1	>99	>-3.2
10	DBN	trace	≫99[a]	≫-3.2

[a] Composed of 97.6% *E*-Δ3 and 2.4% *Z*-Δ3.

The medium-ring framework also provides more conformational freedom than smaller ring systems but limits the ring skeleton to the thermodynamically more stable cis configuration (up to n = 5) under normal conditions.

The unsubstituted cycloalkenones **3a** and **4a** exhibit equilibria which are significantly dependent on ring size[6,11] (Table I), reflecting the various conformational restraints on effective π orbital overlap in the Δ2 isomers **4a**. Whitham[6,11] utilized trends in ultraviolet spectra, infrared spectra, and especially proton magnetic resonance spectra for the 2-cycloalkenones **4a** to suggest that the effectiveness of conjugation between the carbonyl and the olefin decreased with increasing ring size. As conjugation decreases in effectiveness, the 2-cycloalkenones **4a** are destabilized relative to the 3-cycloalkenones **3a**, possibly from the juxtaposition of the relatively "electronegative" trigonal sp^2 carbon atom C-2 and the carbonyl carbon C-1 in a nonefficiently conjugated **4a**.

When we[13] equilibrated the 3-carbomethoxycycloalkenones **3c** and **4c**, more of the Δ3 isomer was obtained in each ring size than in the unsubstituted system (Table II). Molecular models suggested that the carbomethoxy group did not introduce nonbonded interactions or conformational restraints on the ring systems and could rotate freely in order to maximize electronic interactions with the electrons of the double bond in all isomers. The explanation offered[13] for this substituent effect was based on the premise that the Δ3 isomers **3c** could be more effectively conjugated while making fewer conformational demands on the ring system than the Δ2 isomers. In addition, the electronic stabilization of an enedione system **4c** is less than that of an analogous conjugated enone system as evidenced by the ability of acyclic enediones to readily rearrange.[14] Also, similar electronic interactions at both ends of a double bond tend to destabilize the double bond.[7]

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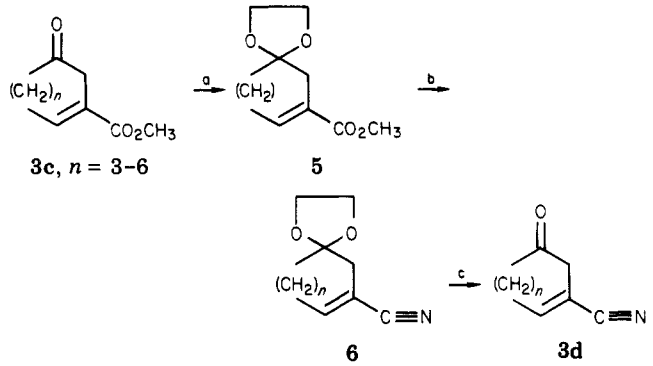
Scheme I[a]



3c, n = 3-6 5 6 3d

[a] (a) $(HOCH_2)_2$, PPTS,[19] toluene; (b) $(CH_3)_2AlNH_2$,[17] xylene; (c) p-TsOH, aqueous toluene.

In an attempt to better understand the substituent effects in medium-ring cycloalkenones, several additional 3-substituted-3-cycloalkenones have been synthesized (**3d**, **3e**, **3f**) with electron-withdrawing groups which differ in the relative importance of their inductive and resonance components and in the hybridization of the carbon atom directly attached to the ring.

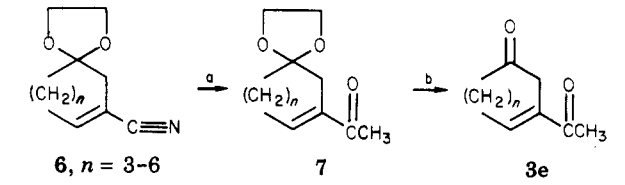
Synthesis

3-Carbomethoxycycloalkenones 3c. Cycloalkenones were ring-expanded by two carbons by using dimethyl acetylenedicarboxylate (DMAD) methodology as before.[1,13,15] Utilization of dioxane as the solvent[16] resulted in higher yields of products which were more difficult to purify by recrystallization. Double-bond configurations in the initial DMAD–enamine ring expansion products were reexamined and found to be identical with those assigned recently by Reinhoudt.[16]

3-Cyano-3-cycloalkenones 3d. The 3-cyano series has been obtained by utilizing Weinreb's[17] dimethylaluminum amide reagent (Scheme I). While Weinreb had previously reported[18] that this reagent was compatible with ketals when used in the conversion of esters to amides, no information was available on the compatibility of this reagent with aliphatic α,β-unsaturated esters or with other carbonyl groups. The basic nature of this reagent would probably make it incompatible with carbonyls, and treatment of methyl levulinate with dimethylaluminum amide in refluxing xylene indeed did produce a complicated mixture seemingly devoid of the desired 4-cyano-2-butanone. The ethylene ketal of ethyl levulinate produced the corresponding nitrile under Weinreb's conditions, suggesting that the reagent is compatible with ketals but not with simple carbonyls.

Accordingly, each 3-carbomethoxy-3-cycloalkenone **3c** was converted to the corresponding ethylene ketal **5** by the method of Sterzycki[19] and then refluxed with dimethylaluminum amide in xylene. The resulting cyano ketals **6** were hydrolyzed in refluxing aqueous toluene with p-toluenesulfonic acid to produce the desired 3-cyano-3-cycloalkenones **3d**. Ketal **6** was resistant to hydrolysis at lower temperature (refluxing acetone) and with the use of the less acidic catalyst pyridinium p-toluenesulfonate[19] (PPTS). The ten-membered-ring nitrile (**3d**, n = 6) was

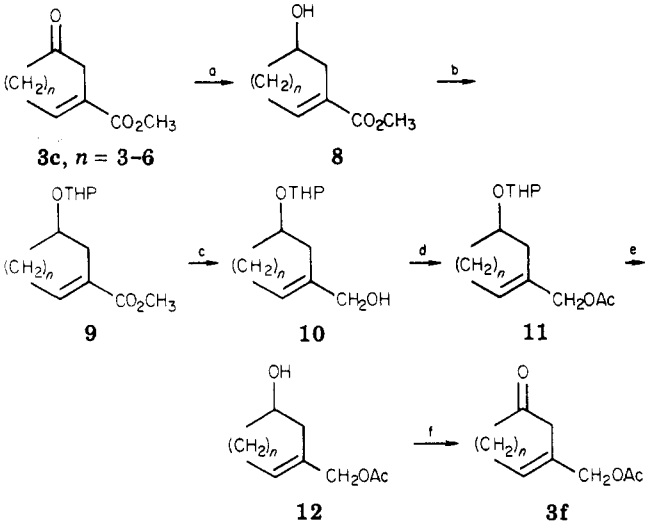
Scheme II[a]



6, n = 3-6 7 3e

[a] (a) CH_3Li,[20] ether; PPTS, H_2O; (b) p-TsOH, H_2O, toluene.

Scheme III[a]



3c, n = 3-6 8 9 10 11 12 3f

[a] (a) $NaBH_4$,[21] CH_3OH; (b) DHP, PPTS,[22] (c) Dibal,[23] Et_2O, KOH; (d) Ac_2O, pyr, DMAP;[24] (e) PPTS,[22] EtOH, H_2O; (f) PdC,[25] CH_2Cl_2.

obtained as an E/Z mixture which was separated chromatographically.

3-Acetyl-3-cycloalkenones 3e. The cyano ketals **6** obtained en route to the 3-cyano-3-cycloalkenones were utilized to prepare the 3-acetyl-3-cycloalkenones **3e** (Scheme II). The cyano ketals were converted with methyllithium to the imino ketals,[20] which were selectively hydrolyzed on workup to the acetyl ketals **7** by using PPTS. Production of the seven-membered acetyl ketal **7** (n = 3) was hindered by the predominant formation of Michael addition products. Subsequent hydrolysis of **7** with p-TsOH in aqueous toluene produced the desired 3-acetyl-3-cycloalkenones **3e**. The ten-membered-ring diketone **7** (n = 6) was isolated as a single isomer to which the E configuration was assigned (vinyl triplet at δ 6.9 with J = 8 Hz).

3-(Acetoxymethyl)-3-cycloalkenones 3f. Sodium borohydride reduction[21] of 3-carbomethoxy-3-cycloalkenone **3c** selectively produced the ester alcohol **8** (Scheme III), which was protected[22] as the tetrahydropyranyl ether **9**. Selective reduction[23] of the ester to the allyl alcohol **10** was accomplished by using diisobutyl aluminum hydride (Dibal). Alcohol **10** was acetylated[24] and the tetrahydropyranyl ether was selectively cleaved[22] by PPTS in aqueous ethanol. The alcohol **12** was then oxidized by the nearly neutral pyridinium dichromate[25] to the desired 3-(acetoxymethyl)-3-cycloalkenone **3f**. Close

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Table III. Equilibration of 3-(Methoxycarbonyl)cycloalkenones

ring size	catalyst	solvent	temp, °C	composition, % Δ2	composition, % Δ3	ΔG	ΔH	ΔS	r
7	DBN	benzene	25	9.9	90.1	−1.31	−1.8	−1.7	0.9999
			60	13.2	86.8	−1.25			
			80	15.1	84.9	−1.21			
7	DBN	toluene	27	7.7	92.3	−1.5	−3.5	−6.7	0.9888
			60	14.8	85.2	−1.2			
			80	16.8	83.2	−1.1			
			100	20.9	79.1	−1.0			
8	DBN	benzene	26	2.4	97.6	−2.20	−2.3	−1.0	0.9979
			60	3.7	96.3	−2.16			
			80[a]	4.5	95.5	−2.14			
8	DBN	toluene	27	1.5	98.5	−2.5	−4.1	−5.3	0.9921
			60	3.4	96.6	−2.3			
			80	4.2	95.8	−2.2			
			100	5.5	94.5	−2.1			

[a] Hirsch and Lin[13] reported 3.5% Δ2 and 96.5% Δ3.

to neutral conditions were necessary for this oxidation to prevent double-bond isomerization. Ten-membered **3f** (n = 6) was obtained as a single isomer assigned the E configuration.

Isomerizations

Equilibrations were performed by using 1,5-diazabicyclo[4.3.0]non-5-ene (DBN) as the base catalyst as before,[13] but toluene was substituted as the solvent. Equilibrations were performed at least in duplicate for each compound at each temperature. Equilibrium was approached from each side wherever enough of the Δ2 isomer was isolated to permit reequilibration. If this was not possible, one pure isomer and a mixture of isomers were used independently to approach equilibrium. Equilibrium products formed in greater than 0.5% were usually isolated by either column or preparative gas–liquid chromatographies or a combination of both. Toluene shifted the equilibria slightly toward the Δ2 isomers at higher temperatures (Table III) when compared to benzene. Values of ΔH and ΔS for various equilibria were obtained by linear least-squares analysis of plots of ln K, K = (Δ3/Δ2), against T^{-1}. Equilibration data accumulated at 80 °C and at other relevant temperatures (see below) are compiled in Tables IV and V.

Inspection of the data shows that compounds with electron-withdrawing conjugating groups have similar shifts toward the Δ3 isomers within the same ring size. Compounds with the same substituent also show increased preference for the Δ3 isomers with increasing ring size.

The similarity of the equilibrium product ratios for the conjugating electron-withdrawing substituents in the seven- and eight-membered-ring compounds indicate that the substituents are all influencing the equilibria in the same manner and that steric effects of the substituents are minimal, if existing at all.

The acetoxymethyl substituent had an interesting effect on the equilibria. At 33 °C, approaching the equilibrium from the seven-membered Δ3 isomer **3f**, (n = 3), only two isomers were apparently formed, the Δ3 and Δ2 isomers. Approach from the Δ2 isomer resulted in the production of four isomers; the Δ2, the Δ3, 22% of exocyclic isomer **13**,[26] and a small amount of unidentified high molecular weight material. At 80 °C approaching the equilibrium from both the Δ2 and Δ3 isomers yielded the same mixture of four products (17% of **13**) as in the 33 °C equilibration, plus a fifth unidentified material. Here, as in other instances (see below) where material other than 2- and 3-cycloalkenones are formed, the data may not be for true multicomponent equilibria.

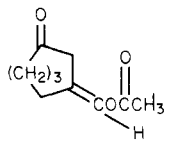

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Table IV. Isomerization of 3-Substituted Cycloalkenones Using DBN in Toluene

ring size	substituent	temp, °C	composition, % Δ2	composition, % Δ3	composition, % other	ΔG, kcal/mol
7	H	80	76.8	23.2		0.8
7	CO_2CH_3	80	16.8	83.2		−1.2
7	CN	80	15.1	84.9		−1.2
7	$COCH_3$	80	20.7	79.3		−0.9
7	$CH_2O(CO)CH_3$	80	47	21	6, 17, 9	
		33[a]	17.3	82.7		
		33[b]	50	24	4, 22	
8	CO_2CH_3	80	4.2	95.8		−2.2
8	CN	80	2.4	97.6		−2.6
8	$COCH_3$	80	3.3	96.7		−2.4
8	$CH_2O(CO)CH_3$	80		100		
		100	4.0	80.5	7, 8.5	
9	CO_2CH_3	80		99.9		
9	CN	80	0.3	97.3	2.4	
9	$COCH_3$	80		96.9	3.1	
9	$CH_2O(CO)CH_3$	80		99.9		

[a] Starting from Δ3 to obtain an apparent steady state. [b] Starting from Δ2.

Table V. Isomerization of 3-Substituted Cyclodecenones in Toluene

substituent	composition, % Δ2	composition, % Δ3(E)	composition, % Δ3(Z)	composition, % other
CO_2CH_3[a,b]		99.9		
$COCH_3$[b]		97.6		2.4[c]
CN[b]	3	83	9	1, 4
CN[d]		37	63	
CN[e]		44	56	
$CH_2O(CO)CH_3$		99.9		

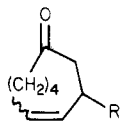
[a] Hirsch and Lin[13] reported an equilibrium composition of 97.6% E-Δ3 and 2.4% Z-Δ3 isomers. [b] Starting from E-Δ3. [c] GC analysis revealed an unsymmetrical peak. [d] Starting from Z-Δ3. [e] Starting from a mixture of 70% E-Δ3 and 30% Z-Δ3.

(26) The geometry of the double bond in **13** was determined by a difference nuclear Overhauser effect ^1H NMR study kindly performed by Dr. M. J. Shapiro of Sandoz, Inc.

The formation of exocyclic enone **13** appears to be dependent on the presence of a substantial amount of the Δ2 isomer **4f** (n = 3) in the equilibration. This is quite reasonable, since abstraction of an exocyclic proton is more likely when a dienolate is formed, as from **4f**, than when the proton is merely allylic, as from **3f**.

In the eight-membered acetoxymethyl compound **3f** (n = 4) a similar phenomenon is observed. At 80 °C no deviation from 100% Δ3 is observed; however, at 100 °C a mixture of 80.5% Δ3 isomer, 4.0% Δ2 isomer, and 15.5% of a mixture of two other materials was observed.

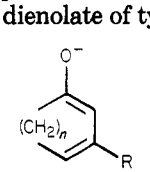
Equilibration of the nine-membered-ring carbomethoxy and acetoxymethyl compounds **3c** (n = 5) and **3f** (n = 5) yielded greater than 99% of the Δ3 isomer. The cyano compound **3d** (n = 5) yielded a small amount of the Δ2 isomer **4d**, (n = 5) and 2.4% of a third component **14**,



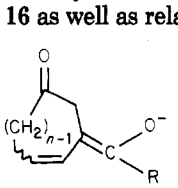
14, R = C≡N
15, R = C(O)CH$_3$

whereas the acetyl compound **3e** (n = 5) yielded no Δ2 isomer but 3.1% of another isomer **15**. Both **14** and **15** had 2 H multiplets at δ 5.8 and 5.7, respectively, in their ^{1}H NMR spectra, and two olefinic carbons characteristic of isolated olefins in their ^{13}C NMR spectra and have been assigned as the Δ4 isomers of unknown double-bond stereochemistry (but most likely Z). Such a Δ 4 isomer has been observed by Marchesini and Paronzini[27] in the DBN-catalyzed equilibration of cycloundecenone analogues **3c** and **4c** (n = 7), where the products were 5% Z-Δ3, 56% E-Δ3, and 39% E-Δ4 starting from E-Δ2 or any of the product isomers.

Formation of Δ4 isomers **14** and **15** in the nine-membered-ring system, which is competitive with or dominates formation of the Δ2 isomers **4**, may be explained on the basis of considerations of π orbital overlap. Whitham[6,11] has shown that cyclooctenones exhibit significant deuterium exchange at carbon-2 when refluxed under aqueous acid catalysis or under methoxide/dioxane conditions. If it is assumed that DBN can form dienolates corresponding to the intermediates postulated from Whitham's experiments, the interconversion of Δ2 and Δ3 isomers in a given ring size depends on the efficiency of overlap of the π orbitals in a dienolate of type **16** as well as relative product



16



17

stabilities. Inspection of molecular models suggests that the dienolate double bonds can be coplanar or nearly so in seven-membered rings but that increasing ring size permits such geometries only at the expense of increasingly severe steric interactions between hydrogens on carbons 5 and 6. In the larger medium ring sizes, therefore, abstraction of a C-2 hydrogen in a 3-cycloalkenone need not inevitably result in a delocalized dienolate, but might instead produce an enolate not conjugated with the adjacent alkene. More energy would then be required to achieve a dienolate conformation which is delocalized.

Precedent for such inefficient conjugation in medium rings may be found in Whitham's work[6,11] and in Gardner's results[28] with cycloalkadienes. The latter group showed that 1,5-cyclooctadiene was quantitatively converted to 1,3-cyclooctadiene by using potassium *tert*-butoxide in Me_2SO, but that similar conditions in the cyclononadiene system produced 94% 1,5-cyclononadiene, 6% 1,3-cyclononadiene, and a trace of the 1,4-isomer. Clearly, conjugative stability in 1,3-cyclononadiene is significantly reduced from that in 1,3-cyclooctadiene.

When a 3-cycloalkenone possesses an electron-withdrawing conjugating substituent at carbon 3, exocyclic dienolates of type **17** formed by abstraction of an allylic proton may compete with formation of endocyclic dienolates of type **16**. Examination of molecular models of exocyclic dienolate **17** in the nine-membered ring suggests that steric interactions in coplanar or nearly coplanar systems of this type are much less severe than in endocyclic dienolate **16**. Formation of the Δ4 isomer then may be viewed simply as equilibration of α,β- and β,γ-unsaturated nitriles and ketones. Why this is not observed in the nine-membered ester system is puzzling.

The failure to observe 2-cyclononenones in these base-catalyzed reactions might, therefore, have no bearing on the question of the relative thermodynamic stabilities of the 3-substituted 2- and 3-cyclononenones. The corresponding 3-substituted 2-cyclononenones must be synthesized and subjected to these reaction conditions in order to definitively answer the question of whether our results in these nine-membered-ring systems represent equilibrium or not.

The cyclodecenones present an additional complication in the existence of reasonably stable E and Z isomers. As for the other rings, there is a marked preference for the Δ3 isomer **3** (n = 6) in each system (Table V). Ester (E)-**3c** in both toluene and benzene did not produce 2.4% of (Z)-**3c** as reported by Hirsch and Lin[13] (Table II), but they had used a longer column for their chromatographic analysis. We did not attempt to resolve this discrepancy.

Cyclodecenone ketone (E)-**3e** (n = 6) was only converted to 2.4% of an inseparable mixture, which was shown to be two compounds isomeric with starting material by GC–MS. From ^{1}H NMR at 200-MHz of this mixture, these compounds were determined to be the (Z)-**3e** isomer (triplet at δ 6.84 and singlet at δ 3.44 in 1:2 ratio characteristic of the vinyl hydrogen and C-2 hydrogens in Δ3 compounds) and a Δ4 isomer of unknown stereochemistry (multiplet at δ 5.3–5.6 and doublet at δ 3.67 in 1:1 ratio, analogous to the vinyl and C-2 hydrogens in **15**).

Ten-membered nitrile **3d** (n = 6) yielded different product ratios with different starting mixtures even after 1 month in toluene at 80 °C, suggesting that equilibrium may not have been reached (Table V). The E-Δ3 was predominantly unchanged but did provide 3% of a Δ2 isomer of unknown stereochemistry (δ 6.96 singlet), 9% of the Z-Δ3 isomer, 1% of a compound with a multiplet at δ 5.5, which suggests a Δ4 isomer related to **14** and 4% of more polar material, for which GC–MS indicated an isomer (m/e 177) and a compound with molecular ion 221, neither of which were further identified. The Z-Δ3 isomer as starting material produced an apparent steady state at 63% Z-Δ3 and 37% E-Δ3 which was unaffected by several weeks of treatment with DBN at 80 °C in toluene. A starting mixture of 70% E-Δ3 and 30% Z-Δ3 was converted to 44% E-Δ3 and 56% Z-Δ3, proportions not dissimilar to those starting from pure Z but which was

(27) Marchesini, A.; Paronzini, M. *Chem. Lett.* **1977**, 3.

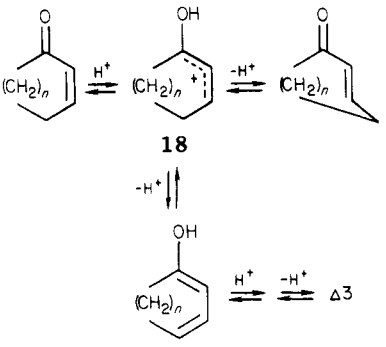
(28) Devaprabhakara, D.; Cardenas, C. G.; Gardner, P. D. *J. Am. Chem. Soc.* **1963**, *85*, 1553.

Table VI. Time To Reach Equilibrium or Apparent Steady State[a]

ring size	substituent	time
7	C≡N, CO_2CH_3, $COCH_3$	24 h
7	$CH_2O(CO)CH_3$	48 h
8	C≡N, CO_2CH_3, $COCH_3$	24–48 h
9	C≡N, CO_2CH_3, $COCH_3$	48 h
10	C≡N, CO_2CH_3, $COCH_3$	4 weeks

[a] DBN, toluene, 80 °C.

Scheme IV



changing composition so slowly that the isomerization was not continued.

The time required to reach equilibrium or an apparent steady state on treatment with DBN in toluene at 80 °C shows an interesting trend with ring size (Table VI). As the ring gets larger, the isomerization gets slower. This is consistent with increasing difficulty with increasing ring size to form an efficiently conjugated dienolate of type **16** (see above). It also suggests that formation of dienolate **17** is fairly efficient, at least in the nine-membered-ring system.

The apparent discrepancies between our cyclodecenone results and those of Whitham and Zaidlewicz[11] and Hirano[12] merit comment. Whitham[11] reported rapid interconversion of the *E*- and *Z*-Δ2 isomers **4a** (n = 6) using *p*-TsOH in benzene to an equilibrium mixture with 96% *Z*-Δ2, 4% *E*-Δ2, and no Δ3 isomers **3a** (n = 6). Starting with *E*-Δ3 **3a** (n = 6), a very slow and incomplete conversion to the equilibrium mixture of the Δ2 isomers **4a** was reported, while *Z*-Δ3 was totally unreactive. Evidence for formation of dienol intermediate from all of the isomers was suggested on the basis of deuterium incorporation data obtained for carbon-2 in aqueous acidic dioxane. Hirano[12] reported quantitative hydrolysis of 2-cyclodecenone ethylene ketal to 2-cyclodecenone (**4a**) on vigorous shaking in THF with 5% H_2SO_4 for 5 min, while longer reaction times (0.5–5 h) or stronger acid (30% H_2SO_4) produced (*Z*)-3-cyclodecenone ((*Z*)-**3a**). On the other hand, our 3-substituted 3-cyclodecenones **3c–e** (n = 6) produced little or no 2-cyclodecenones on treatment with base for a month.

In fact, these results may not be contradictory. Apparently, Whitham[11] equilibrated Δ2 isomers and Hirano hydrolyzed to form Δ2 isomers under milder reaction conditions than Whitham's deuterium incorporation study or Hirano's hydrolytic production of a Δ3 isomer. Under the milder acid conditions, an allylic cation **18** could be invoked to produce equilibration of Δ2 isomers without requiring formation of dienol **19** (Scheme IV). Analogously, hydrolysis of the ketal would, in its later stages, involve the same cation **18**. If efficient overlap between π orbitals in dienol **19** is indeed difficult, as discussed above, this dienol would form from cation **18** only under more vigorous reaction conditions. Whitham's reported *E*/*Z* isomerization in 2-cyclodecenone is then completely explicable when *p*-TsOH in benzene is used, where the solvent is nonnucleophilic.

Table VII. Olefinic ^{13}C NMR Chemical Shifts[29] of 3-Substituted-3-Cycloalkenones **3**

ring size	substituent	C-3	C-4
8	H[30]	124.31	131.64
8	CO_2CH_3	127.63	142.76
8	$COCH_3$	137.32	143.66
8	CN	109.50	148.77
9	CO_2CH_3	125.90	144.43
9	$COCH_3$	135.86	145.85
9	CN	108.28	150.28
10(*E*)	CO_2CH_3	127.95	144.92
10(*E*)	$COCH_3$	138.00	145.79
10(*E*)	CN	119.46	150.81

Table VIII. Olefinic ^{13}C NMR Chemical Shifts of Monosubstituted Ethylenes[31]

substituent	C_α	C_β
H	122.4	122.4
CHO	136.4	136.0
CO_2H	128.0	131.9
$COCH_3$	138.5	129.3
CO_2CH_3	128.7	129.9
CN	107.7	137.8

Under Whitham's more vigorous aqueous conditions for the deuterium incorporation study,[11] he presents evidence that the 2-cyclodecenones form a β-hydroxy ketone intermediate, so that *E*/*Z* isomerization in the 2-cyclodecenones proceeds by an addition–elimination sequence in aqueous media.

Since the substituted 3-cyclodecenones reported herein cannot be converted to the corresponding 2-cyclodecenones without invoking abstraction of a C-2 hydrogen by base to produce dienolate **16**, which presumably is not efficiently delocalized, and therefore should not form more easily than a simple enolate, the energy of activation in going from **18** to **19** probably is considerably different from the barrier for abstraction to produce **16** in our work. In addition, the 3-cyclodecenones substituted with conjugating electron-withdrawing groups have an additional option—formation of dienolate **17**—which is not available in the unsubstituted compound. Obviously further investigation of these cyclodecenones is warranted.

Only the nitrile system formed any Δ2 isomers among the nine- and ten-membered-ring systems studied, albeit in small amounts. One possible explanation for this substituent effect is that the cyano apparently polarizes the double bond in an α,β-unsaturated system to a greater extent than the other substituents studied. This is shown in the ^{13}C NMR chemical shifts of the olefinic carbons in the 3-substituted 3-cycloalkenones **3** (Table VII) as well as in monosubstituted ethylenes[31] (Table VIII).[32] This increased polarization could facilitate formation of dienolate **16**, leading to Δ2 isomers.

Summary

Electron-withdrawing substituents in the 3-position of medium-ring cycloalkenones shift equilibria toward the 3-cycloalkenones and away from the 2-cycloalkenones relative to the parent compounds. The electron-with-

(29) Kindly measured by Dr. M. J. Shapiro of Sandoz, Inc.
(30) Paquette, L. A.; Crouse, G. D.; Sharma, A. K. *J. Am. Chem. Soc.* **1982**, *104*, 4411.
(31) Miyajima, G.; Takahashi, K.; Nishimoto, K. *Org. Magn. Reson.* **1974**, *6*, 413.
(32) For studies of substituent effects on the spectra of such systems, see: Mease, R. C. Ph.D. Dissertation, Seton Hall University, 1984. Mease, R. C.; Hirsch, J. A., manuscript in preparation.

drawing groups cyano, acetyl, carbomethoxy, and acetoxymethyl effect similar shifts in a given ring size, suggesting that the substituents do not cause significant steric effects. Each of these substituents favors the 3-cycloalkenone to a greater extent as the ring becomes larger.

In the nine- and ten-membered rings, little or no 2-cycloalkenone is obtained when these 3-substituted 3-cycloalkenones are treated with base for extended periods of time. A different equilibrium becomes operative in these systems, producing small amounts of 4-cycloalkenone isomers. Dienolates relevant to 2-cycloalkenone/3-cycloalkenone equilibration become less stable in coplanar conformations as ring size increases, making them more difficult to form and leading to results which may be explicable only in terms of dienolate conformations where π overlap between enolate and adjacent alkene is inefficient.

Spectral data may assist in better understanding the above phenomena.[32]

Experimental Section

Melting points were determined by using open capillary tubes with a Mel-Temp Laboratory Devices apparatus and are uncorrected. Boiling points are also uncorrected. Infrared spectra were recorded on neat films on a Perkin-Elmer 567 grating infrared spectrophotometer. ^{1}H NMR spectra were recorded in $CDCl_3$ solutions on a Varian T-60 NMR spectrometer. High-field ^{1}H NMR spectra were obtained in $CDCl_3$ solutions on a Varian XC-200 NMR spectrometer. ^{13}C NMR spectra were similarly obtained on a JEOLCO 200-MHz NMR spectrometer. Ultraviolet spectra were measured on a Varian 219 UV–visible spectrophotometer. Mass spectral analyses were determined on a LKB Model 9000 spectrometer at 70 eV. Gas Chromatographic analyses were performed on a Varian 3700 gas chromatograph using a 6-ft. 10% DEGS or a 4-ft. 20% Carbowax 20M chromatography column. Elemental analyses were performed by Alfred Bernhardt Mikroanalytisches Laboratorium, Elbach, West Germany. Column chromatographic separations were performed by using a gravity flow of solvent and 70–230-mesh silica gel 60. Medium-pressure chromatographic separations[33] were performed on an Altex apparatus and 30–70-mesh silica gel 60. Thin-layer chromatography utilized Eastman Chromagram sheets and were visualized under 254-nm UV light and/or the use of a iodine chamber.

Dimethylaluminum Amide. The dimethylaluminum amide was prepared by following the procedure of Weinreb.[17] A solution consisting of 35 mL of a 25% solution of trimethylaluminum in hexane (Alfa) and 25 mL of dry methylene chloride was placed in a 100-mL, three-necked reaction flask. This flask was equipped with a dry ice condenser and a N_2 inlet and was cooled in a dry ice–isopropyl alcohol bath. In another three-neck flask equipped with a dry ice condenser, a N_2 inlet, and a tube leading to the reaction flask was placed a few pieces of sodium metal. The flask containing the sodium was also cooled in a dry ice–isopropyl alcohol bath. Ammonia gas was then introduced into this flask. When approximately 10 mL of the blue liquid ammonia solution accumulated in the flask, the addition of ammonia gas was stopped, and the stopcock between the liquid ammonia flask and the reaction flask was opened to allow the dried ammonia gas to slowly distill into the reaction flask. When half the addition of ammonia was complete, the cooling bath was removed from the reaction flask. When the addition was complete, the dry ice condenser was removed and the mixture was allowed to stir at room temperature overnight under a N_2 atmosphere until no more gas was evolved. This reagent was either used immediately or stored in the freezer for up to 2 weeks. According to Weinreb,[17] the reagent made by this procedure is approximately 1.2 M.

Ethylene ketal of methyl 6-oxo-1-cycloheptenecarboxylate (5, n = 3) was prepared by the procedure of Sterzycki.[19] To a solution consisting of 6.6 g (39.0 mmol) of β-keto ester **3c** (n = 3) and 10 mL of ethylene glycol dissolved in 200 mL of toluene was added 1.0 g (3.9 mmol) of PPTS. This solution was refluxed for 4 h, and the water produced by the reaction was separated from the reaction mixture by use of a Dean–Stark trap. The reaction was cooled to room temperature, excess solvent removed by evaporation under reduced pressure, and the residue poured into 200 mL of CH_2Cl_2. This solution was first washed with 150 mL of a dilute $NaHCO_3$ solution and then with 200 mL of saturated brine and dried ($MgSO_4$), and the solvent was removed under reduced pressure to yield a green oil. The product was purified by column chromatography on silica gel by using a 4:1 hexane/ethyl ether mixture as eluant to yield 4.5 g (53%) of a clear colorless oil: IR 1700, 1640 cm^{-1}; NMR δ 7.27 (t, 1), 4.00 (s, 4), 3.73 (s, 3), 2.87 (s, 2), 2.6–1.4 (m, 6). Also isolated from the column chromatography was 0.5 g of a 1:1 mixture of the Δ2 isomer, the ethylene ketal of methyl 3-oxo-1-cycloheptenecarboxylate, and the Δ3 isomer **5** (n = 3): NMR δ 7.27 (t, 0.5), 6.85 (s, 0.5), 4.0 (s, 4), 3.73 (s, 3), 2.8–1.4 (m, 8).

Ethylene ketal of methyl 7-oxo-1-cyclooctenecarboxylate (5, n = 4) was prepared by the above procedure.[19] To a solution consisting of 8.0 g (44.0 mmol) of δ-keto ester **3c** (n = 4) and 10 g of ethylene glycol dissolved in 200 mL of toluene was added 1.1 g (4.0 mmol) of PPTS. This solution was refluxed for 3 h until no more H_2O was produced. Workup as above and evaporation of the solvent under reduced pressure yielded 8.6 g (86%) of a light yellow oil which crystallized in the freezer: IR 1730–1720, 1640 cm^{-1}; NMR δ 6.97 (t, 1), 3.93 (m, 4), 3.7 (s, 3), 2.7 (s, 2), 2.23 (s, 2), 1.6 (s, 6).

Ethylene Ketal of Methyl 8-Oxo-1-cyclononenecarboxylate (5, n = 5). Following the above procedure[19] a solution consisting of 9.9 g (51.0 mmol) of γ-keto ester **3c** (n = 5), 10.0 g of ethylene glycol, and 1.3 g (5 mmol) of PPTS dissolved in 150 mL of toluene was refluxed for 3 h. Workup and evaporation of the solvent under reduced pressure yielded 11.4 g (93%) of a light yellow oil which crystallized in the freezer: IR 1725–1710, 1645 cm^{-1}; NMR δ 6.88 (t, 1), 3.98 (m, 4), 373 (s, 3), 2.3 (s, 2), 1.6 (s, 8).

Ethylene Ketal of Methyl 9-Oxo-1-cyclodecenecarboxylate (5, n = 6). A 9:1 (E/Z) mixture of the ethylene ketal of methyl 9-oxo-1-cyclodecenecarboxylate (**5**, n = 6) was prepared by the above procedure.[19] To a solution consisting of 7.4 g (34.0 mmol) of a 1:1 (E/Z) mixture of γ-keto ester **3c** (n = 6) and 8.0 g of ethylene glycol dissolved in 150 mL of toluene was added 0.9 g (3.5 mmol) of PPTS. This solution was refluxed for 5 h with the H_2O produced being removed by a Dean–Stark trap. After workup as above, evaporation of the solvent under reduced pressure yielded 8.4 g (95%) of a light yellow oil which crystallized in the freezer: NMR δ 6.67 (t, 0.9), 6.3 (t, 0.1), 4.0 (m, 4), 3.80 (s) and 3.77 (s) (total of 3 H), 2.8 (s, 2), 2.6–2.3 (m, 2), 1.9–1.2 (s, 10).

Ethylene ketal of 7-oxo-1-cyanocyclooctene (6, n = 4) was prepared by the procedure of Weinreb.[17] A solution consisting of 10.9 g (48.0 mmol) of the ketal ester **5** (n = 4) dissolved in 200 mL of anhydrous xylene (refluxed and distilled over P_2O_5) was cooled to 0–2 °C under an N_2 atmosphere. To this solution was added 60 mL of an approximately 1.2 M solution of $(CH_3)_2AlNH_2$ (2 equiv). The reaction mixture was allowed to warm to room temperature and then refluxed for 72 h under an N_2 atmosphere. The reaction was monitored by NMR using the relative intensities of the proton chemical shifts of the protons that are α to both the ethylene ketal and the endocyclic double bond in the α,β-unsaturated amide vs. those in the α,β-unsaturated nitrile at δ 2.8 and 2.7, respectively. The orange reaction mixture was cooled to 0–2 °C and quenched by the dropwise addition of 20 mL of H_2O and CH_2Cl_2. The organic layer was separated from the filtrate, washed with 200 mL of a saturated NaCl solution, and dried ($MgSO_4$). The solvent was evaporated under reduced pressure to yield a gummy orange solid which was purified by column chromatography using a silica gel column and a 3:1 hexane/ethyl ether solution as eluant, yielding 4.2 g (45%) of a light green product: IR 2210, 1630 cm^{-1}; NMR δ 6.70 (t, 1), 4.03 (s, 4), 2.60 (s, 2), 2.33 (s, 2), 1.7 (s, 6). A sample of the chromatographed product was recrystallized from hexane, yielding a white solid with identical spectral properties as above, mp 60–62 °C.

Anal. Calcd for $C_{11}H_{15}O_2N$: C, 68.37; H, 7.82; N, 7.25. Found: C, 68.50; H, 7.91; N, 7.06.

Ethylene Ketal of 6-Oxo-1-cyano-1-cycloheptene (6, n = 3). This nitrile was prepared by the above procedure from 4.85 g (23.0 mmol) ketal ester **5** (n = 3), 40 mL of an approximate 1.2 M $(CH_3)_2AlNH_2$ solution, and 300 mL of dry xylene. The reaction

(33) Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.

was refluxed for 48 h under a N_2 atmosphere, cooled to 0–2 °C, quenched with 10 mL of H_2O, and worked up as above. Evaporation of the solvent under reduced pressure yielded a viscous green oil. Purification of this oil on a silica gel column using a 6:1 hexane/ethyl acetate solution as eluant yielded 1.7 g (41%) of clear colorless oil: IR 2210, 1635 cm^{-1}; NMR δ 6.77 (t, 1), 3.90 (s, 4), 2.53 (s, 2), 2.4–1.3 (m, 6).

Anal. Calcd for $C_{10}H_{13}O_2N$: C, 67.02; H, 7.31; N, 7.82. Found: C, 67.00; H, 7.20; N, 7.72.

Ethylene Ketal of 8-Oxo-1-cyano-1-cyclononene (6, n = 5). Following the above procedure of Weinreb,[17] a solution consisting of 6.7 g (28.0 mmol) of ketal ester **5** (n = 5), 45 mL of an approximate 1.2 M $(CH_3)_2AlNH_2$ solution, and 200 mL of dry xylene was refluxed for 96 h under an N_2 atmosphere. The reaction was cooled to 0–2 °C, quenched with H_2O, and worked up as above. Evaporation of the solvent under reduced pressure yielded 5.5 g of a gummy brown solid. Purification by column chromatography using a silica gel column and a 3:1 hexane/ethyl ether solution as eluant yielded 3.6 g (61%) of a light green solid: IR 2210, 1630 cm^{-1}; NMR δ 6.60 (t, 1), 4.00 (s, 4), 2.63 (s, 2), 2.33 (s, 2), 1.6 (s, 8). Recrystallization from hexane of a sample of the chromatographed nitrile yielded white needle-like crystals with identical spectral properties as above, mp 59–60 °C.

Anal. Calcd for $C_{12}H_{17}O_2N$: C, 69.54; H, 8.27; N, 6.76. Found: C, 69.39; H, 8.17; N, 6.70.

Ethylene ketal of 9-oxo-1-cyano-1-cyclodecene (6, n = 6) was prepared by the above procedure[17] from 8.2 g (32 mmol) of 1:1 (E/Z) mixtures of ketal ester **5** (n = 6), 60 mL of an approximate 1.2 M $(CH_3)_2AlNH_2$ solution, and 200 mL of dry xylene. The reaction was refluxed for 72 h under an N_2 atmosphere, cooled to 0–2 °C, and quenched with H_2O. After workup as above, evaporation of the solvent under reduced pressure yielded 5.8 g of a brown gummy solid. Purification by column chromatography using silica gel and a 3:1 mixture of hexane/ethyl ether as eluant yielded 4.4 g (61%) of light green crystals: IR 2210, 1630 cm^{-1}; NMR δ 6.47 (t, 1), 4.00 (s, 4), 2.60 (s, 2), 2.55–2.20 (m, 2), 1.7–1.3 (s, 10). Recrystallization from hexane of a sample of the chromatographed nitrile yielded white crystals with identical spectral properties as above, mp 81–83 °C.

Anal. Calcd for $C_{13}H_{19}O_2N$: C, 70.56; H, 8.65; N, 6.33. Found: C, 70.34; H, 8.50; N, 6.20.

6-Oxo-1-cyano-1-cycloheptene (3d, n = 3). To a solution consisting of 1.7 g (9.5 mmol) of γ-ketal nitrile **6** (n = 3) dissolved in 150 mL toluene was added 10 mL of H_2O and 0.5 g of p-TsOH. The reaction mixture was refluxed for 24 h, cooled to room temperature, and poured into 200 mL of CH_2Cl_2. This solution was first washed with 100 mL of $NaHCO_3$ solution and then with 200 mL of a saturated brine solution and dried over $MgSO_4$. Evaporation of the solvent under reduced pressure yielded 1.26 g (99%) of a yellow oil. Purification by column chromatography using silica gel and a 8:1 hexane/ethyl acetate solution as eluant yielded 0.95 g (75%) of a light yellow oil: IR 2210, 1710 cm^{-1}; NMR δ 6.70 (t, 1), 3.43 (s, 2), 2.8–1.8 (m, 6); UV λ $EtOH_{max}$ 212 (ϵ 10 000), 278 (160); ^{13}C NMR 204.98, 148.34, 119.3, 107.04, 43.58, 42.80, 30.24, 20.23.

Anal. Calcd for C_8H_9ON: C, 71.09; H, 6.71; N, 10.36. Found: C, 70.68; H, 6.72; N, 9.76.

7-Oxo-1-cyano-1-cyclooctene (3d, n = 4). To a solution consisting of 3.5 g (18 mmol) γ-ketal nitrile **6** (n = 4) dissolved in 75 mL of toluene was added 10 mL of H_2O and 0.5 g of p-TsOH. The reaction mixture was refluxed for 24 h, cooled to room temperature, and worked up as above. Evaporation of the solvent under reduced pressure yielded 2.4 g of a yellow oil. Purification of column chromatography on silica gel using a 3:1 hexane/ethyl ether mixture as eluant yielded 2.1 g (77%) of a light yellow oil: IR 2210, 1700, 1630 cm^{-1}; NMR δ 6.77 (t, 1), 3.33 (s, 2), 2.8–1.6 (m, 8). Distillation of the chromatographed nitrile yielded 1.5 g (57%) of a clear colorless oil with identical spectral properties as above: bp 100–102 °C (0.5 mmHg); UV λ_{max} EtOH 211 (ϵ 13 500), 285 (78); ^{13}C NMR δ 208.28, 148.77, 118.72, 109.50, 44.15, 40.65, 26.40, 25.32, 24.32.

Anal. Calcd for $C_9H_{11}ON$: C, 72.46; H, 7.43; N, 9.39. Found: C, 72.45; H, 7.37; N, 9.52.

8-Oxo-1-cyano-1-cyclononene (3d, n = 5). Following the above procedure 8-oxo-1-cyano-1-cyclononene was prepared from 1.9 g (9.0 mmol) of γ-ketal nitrile **6** (n = 5), 0.2 g of p-TsOH, 5 mL of H_2O, and 50 mL of toluene. The reaction mixture was refluxed for 24 h, cooled to room temperature, and worked up as above. Evaporation of the solvent under reduced pressure yielded light green crystals which were recrystallized from hexane to yield 1.4 g (94%) of white crystals: mp 55–56 °C; IR 2210, 1690, 1625 cm^{-1}; NMR δ 6.60 (t, 1), 3.33 (s, 2), 2.6–1.4 (m, 10); UV λ_{max} EtOH 209 (ϵ 10 000), 287 (45); ^{13}C NMR δ 208.36, 150.28, 119.20, 108.28, 43.25, 43.12, 26.21, 25.43, 25.04, 22.70.

Anal. Calcd for $C_{10}H_{13}ON$: C, 73.59; H, 8.03; N, 8.58. Found: C, 73.41; H, 8.10; N, 8.40.

9-Oxo-1-cyano-1-cyclodecene (3d, n = 6). To a solution consisting of 1.4 g (6.5 mmol) of γ-ketal **6** (n = 6) dissolved in 100 mL of toluene was added 0.5 g of p-TsOH and 5 mL of H_2O. The reaction mixture was refluxed for 48 h, cooled to room temperature, and worked up as above. Evaporation of the solvent under reduced pressure yielded 1.4 g (97%) of a yellow oil: IR 2210, 1710, 1630 cm^{-1}; NMR and TLC analysis suggested that the crude product was a two component mixture. Purification by column chromatography using silica gel and a 12:1 hexane/ethyl acetate mixture as eluant yielded 0.19 g (13%) of the less polar component, 0.19 g (13%) of a 9:1 mixture of less polar/more polar components, and 0.92 g (64%) of the more polar component. The less polar compound had an IR spectrum identical with that of the mixture and was assigned the Z configuration on the basis of NMR data: δ 6.40 (t, 1), 3.20 (s, 2), 2.8–2.2 (m, 4), 1.8–1.0 (m, 8); ^{13}C NMR δ 206.12, 153.02, 118.55, 106.72, 47.74, 37.07, 32.65, 27.84, 26.54, 23.61, 22.30.

Anal. Calcd for $C_{11}H_{15}ON$: C, 74.54; H, 8.53; N, 7.90. Found: C, 74.42; H, 8.43; N, 7.81.

The more polar fraction also had an IR spectrum identical with that of the mixture. Based on NMR data, it was assigned the E configuration: NMR δ 6.60 (t, 1), 3.33 (s, 2), 2.6–2.0 (m, 4), 1.9–1.1 (m, 8); UV λ_{max} EtOH 209 (ϵ 10 000), 287 (45); ^{13}C NMR δ 209.20, 150.81, 119.46, 109.90, 43.77, 38.37, 25.82, 25.69, 24.65, 23.22, 22.51.

Anal. Calcd for $C_{11}H_{15}ON$: C, 74.54; H, 8.53; N, 7.90. Found: C, 74.45; H, 8.51; N, 7.73.

Ethylene Ketal of 6-Oxo-1-acetyl-1-cycloheptene (7, n = 3). Following a procedure modified from that of House and Bare,[20] a solution consisting of 5.1 g (28 mmol) of γ-ketal nitrile **6** (n = 3) dissolved in 100 mL of anhydrous ethyl ether was cooled to 0–2 °C under an N_2 atmosphere. To this solution was slowly added 91 mL of a 1.25 M CH_3Li in ether solution (Aldrich); then the mixture was stirred at room temperature for 2 h. The reaction mixture was then again cooled to 0–2 °C and quenched by the dropwise addition of 5 mL of H_2O. After the quenched reaction was allowed to warm to room temperature, 0.2 g of PPTS was added and the reaction mixture was stirred overnight at room temperature. The reaction mixture was then poured in 300 mL of CH_2Cl_2, washed with 150 mL of $NaHCO_3$ solution and then with 200 mL of saturated brine, and dried ($MgSO_4$). Evaporation of the solvent under reduced pressure yielded a yellow oil. IR and NMR data of the crude material suggested that it was a mixture of ketal ketone **7** (n = 3) and side products: IR 2200, 1710, 1670-1660, 1640 cm^{-1}; NMR δ 7.4–7.0 (m), 6.7 (s), 4.0 (m), 2.8 (s), 2.7–0.6 (m). Purification of the crude material by column chromatography using silica gel and a hexane/ethyl acetate mixture as eluant yielded 1.02 g (19%) of the desired ketal–ketone **7** (n = 3); IR 1710, 1660 cm^{-1}; NMR δ 7.17 (t, 1), 3.95 (m, 4), 2.80 (s, 2), 2.5–1.6 (m, 9).

Anal. Calcd for $C_{11}H_{16}O_3$: 67.32; H, 8.22. Found: C, 67.20; H, 8.12.

Also isolated from the chromatography column was 0.2 g of a pure side product (TLC and GC) which was assigned the structure of the Michael addition product: IR 2210 cm^{-1}; NMR δ 3.97 (s, 4), 2.60 (m, 1), 1.77 (d, 2), 1.67 (m, 7), 1.17 (d, 3).

Anal. Calcd for $C_{11}H_{17}O_2N$: C, 67.66; H, 8.78; N, 7.17. Found: C, 67.84; H, 8.66; N, 6.61.

Ethylene Ketal of 7-Oxo-1-acetyl-1-cyclooctene (7, n = 4). Following the above procedure, a solution consisting of 2.7 g (14 mmol) of γ-ketal nitrile **6** (n = 4) dissolved in 75 mL of anhydrous ethyl ether was cooled to 0–2 °C under an N_2 atmosphere. To this solution was slowly added 45 mL of a 1.25 M CH_3Li solution in ethyl ether. The reaction mixture was stirred under an N_2 atmosphere for 1 h at 0–2 °C, then warmed to room temperature, and stirred for an additional 2 h. The reaction mixture was again

cooled to 0–2 °C and quenched by the dropwise addition of 5 mL of H_2O. To the quenched reaction mixture was added 0.2 g of PPTS, and the mixture was stirred overnight at room temperature. After workup as above, evaporation of the solvent under reduced pressure yielded 2.7 g (90%) of a light yellow oil which crystallized in the freezer: IR 1670, 1635 cm^{-1}; NMR δ 6.90 (t, 1), 4.0 (m, 4), 2.73 (s, 2), 2.3 (m, 5), 1.67 (s, 6). Recrystallization from hexane of a sample of product yielded white crystals with identical spectral properties as above, mp 38–39 °C.

Anal. Calcd for $C_{12}H_{18}O_3$: C, 68.55; H, 8.63. Found: C, 68.38; H, 8.61.

Ethylene ketal of 8-oxo-1-acetyl-1-cyclononene (7, n = 5) was prepared by the above procedure from 3.0 g (15 mmol) of γ-ketal nitrile **6** (n = 5) dissolved in 125 mL of anhydrous ethyl ether and 50 mL of a 1.25 M solution of CH_3Li. After the reaction mixture was quenched with 5 mL of H_2O, 0.4 g of PPTS was added to the reaction mixture, and this mixture was stirred overnight. After workup as above, the solvent was evaporated under reduced pressure to yield 2.9 g (90%) of a yellow oil which crystallized in the freezer: IR 1670, 1640 cm^{-1}; NMR δ 6.72 (t, 1), 3.93 (m, 4), 2.83 (s, 2), 2.53–2.13 (m, 5), 1.67 (s, 8). Recrystallization from hexane of a sample of product yielded white crystals with identical spectral properties as above, mp 38–40 °C.

Anal. Calcd for $C_{13}H_{20}O_3$: C, 69.61; H, 8.99. Found: C, 69.53; H, 8.88.

Ethylene Ketal of 9-Oxo-1-acetyl-1-cyclodecene (7, n = 6). Following the above procedure the ethylene ketal of 9-oxo-1-acetyl-1-cyclodecene (**7**, n = 6) was prepared from 2.2 g (10 mmol) of γ-ketal nitrile **6** (n = 6) dissolved in 150 mL of anhydrous ethyl ether and 32 mL of a 1.25 M solution of CH_3Li in ethyl ether. After being quenched with 5 mL of H_2O, 0.5 g of PPTS was added, and the mixture was stirred overnight at room temperature. The reaction mixture was worked up as above and the solvent evaporated under reduced pressure to yield 2.3 g (97%) of a light yellow oil which crystallized in the freezer: IR 1670, 1630 cm^{-1}; NMR δ 6.50 (t, 1), 4.00 (m, 4), 2.80 (s, 2), 2.33 (m, 5), 1.6 (s, 10). A sample of product was recrystallized from hexane to yield white crystals with identical spectral properties as above, mp 95–96 °C.

Anal. Calcd for $C_{14}H_{22}O_3$: C, 70.56; H, 9.34. Found: C, 70.77; H, 9.20.

6-Oxo-1-acetyl-1-cycloheptene (3e, n = 3). To a solution consisting of 1.02 g (5.20 mmol) of γ-ketal ketone **7** (n = 3) dissolved in 150 mL of toluene was added 5 mL of H_2O and 0.2 g of p-TsOH. This mixture was refluxed overnight, cooled to room temperature, and poured into 150 mL of CH_2Cl_2. This solution was washed with 100 mL of a dilute $NaHCO_3$ solution and with 200 mL of a saturated brine solution and dried ($MgSO_4$). Evaporation of the solvent under reduced pressure yielded 0.69 g (98%) of a yellow oil: IR 1710, 1665, 1635 cm^{-1}; NMR δ 7.07 (t, 1), 3.60 (s, 2), 2.8–1.9 (m, 9). Purification by column chromatography using silica gel and a 6:1 hexane/ethyl acetate mixture as eluant yielded 0.42 g (60%) of a clear colorless oil with identical spectral properties as above: UV λ_{max} EtOH 223 (ϵ 7300), 233 (7500), 290 (100); ^{13}C NMR δ 208.59, 197.21, 142.93, 135.13, 43.09, 39.40, 29.00, 25.21, 21.42;

Anal. Calcd for $C_9H_{12}O_2$: C, 71.03; H, 7.95. Found: C, 70.90; H, 7.84.

7-Oxo-1-acetyl-1-cyclooctene (3e, n = 4). Following the above procedure 2.7 g (14 mmol) γ-ketal ketone **7** (n = 4) was dissolved in 100 mL of toluene, and to this solution was added 5 mL of H_2O and 0.2 g of p-TsOH. The reaction mixture was refluxed for 12 h, cooled to room temperature, poured into 150 mL of CH_2Cl_2, and worked up as above. Evaporation of the solvent under reduced pressure yielded a yellow oil which was purified on a silica gel chromatography column using a 4:1 hexane/ethyl ether mixture as eluant: IR 1695, 1660, 1635 cm^{-1}; NMR δ 7.03 (t, 1), 3.47 (s, 2), 2.6–1.7 (m, 11). Distillation of the chromatographed material yielded 1.76 g (77%) of a clear colorless oil with spectral properties identical with those above: bp 112 °C (4 mmHg); UV λ_{max} EtOH 228 (ϵ 10 000), 283 (110); ^{13}C NMR δ 212.25, 197.44, 143.66, 137.32, 41.06, 40.35, 26.71, 25.49, 24.97, 24.82;

Anal. Calcd for $C_{10}H_{14}O_2$: C, 72.26; H, 8.49. Found: C, 72.08; H, 8.43.

8-Oxo-1-acetyl-1-cyclononene (3e, n = 5). Following the above procedure 8-oxo-1-acetyl-1-cyclononene (**3e**, n = 5) was prepared from 2.9 g (13 mmol) of keto ketal **7** (n = 5) and 0.5 g of p-TsOH dissolved in 150 mL of toluene and 10 mL of H_2O. The solution was refluxed for 24 h, cooled to room temperature, and worked up as above. Evaporation of the solvent under reduced pressure yielded 2.1 g of a yellow oil which was purified on a silica gel chromatography column using a 3:1 hexane/ethyl ether mixture as eluant, yielding 1.7 g of a light yellow oil: IR 1700, 1665, 1635 cm^{-1}; NMR δ 6.92 (t, 1), 3.55 (s, 2), 2.4–2.2 (m, 7), 2.0–1.4 (m, 6). Distillation under reduced pressure of the chromatographed material yielded 1.2 g (51%) of clear colorless oil which had identical spectral properties with those above: bp 101 °C (0.5 mmHg); UV λ_{max} EtOH 226 (ϵ 10 400), 292 (115); ^{13}C NMR δ 213.30, 197.51, 145.85, 135.86, 41.99, 41.41, 27.18, 26.48, 26.40, 24.32, 25.02.

Anal. Calcd for $C_{11}H_{16}O_2$: C, 73.30; H, 8.95. Found: C, 73.15; H, 8.85.

(*E*)-9-Oxo-1-acetyl-1-cyclodecene (3e, n = 6). Following the above procedure (*E*)-9-oxo-1-acetyl-1-cyclodecene (**3e**, n = 6) was prepared from 2.96 g (12.4 mmol) of a 1:1 (*E*/*Z*) mixture of ketal ketone **7** (n = 6) and 0.5 g of p-TsOH dissolved in 300 mL of toluene and 10 mL of H_2O. The reaction mixture was refluxed for 8 h, cooled to room temperature, and worked up as above. Evaporation of the solvent under reduced pressure yielded 2.14 g (89%) of a brown oil. Purification by column chromatography using silica gel and a 3:1 hexane/ethyl ether mixture as eluant yielded a light orange oil which crystallized in the freezer: IR 1700, 1660, 1635 cm^{-1}; NMR δ 6.90 (t, 1), 3.47 (s, 2), 2.5–2.1 (m, 7), 2.8–1.2 (m, 8). Recrystallization from hexane of the chromatographed product yielded 0.91 g (38%) of white crystals with identical spectral properties as above: mp 30–31 °C; UV λ_{max} EtOH 235 (ϵ 10 000), 291 (100); ^{13}C NMR δ 212.02, 198.38, 145.79, 138.00, 41.49, 36.32, 29.25, 25.78, 25.02, 24.38, 22.37, 22.17.

Anal. Calcd for $C_{12}H_{18}O_2$: C, 74.19; H, 9.34. Found: C, 74.38; H, 9.18.

Methyl 6-Hydroxy-1-cycloheptenecarboxylate (8, n = 3). This reduction was accomplished by the procedure of House as modified by Meresak.[21] A solution consisting of 12.0 g (0.07 mol) of methyl 6-oxo-1-cycloheptenecarboxylate (**3c**, n = 3) dissolved in 300 mL of anhydrous methanol was cooled to 0–2 °C. To this solution was added 1.35 g (0.035 mol) of $NaBH_4$. This mixture was stirred for 20 h at 0–2 °C and warmed to room temperature, and the pH adjusted to approximately 6 by the dropwise addition of 10% HCl. This solution was concentrated to one-half of its original volume under reduced pressure, poured into CH_2Cl_2, and washed with 200 mL of water. The aqueous layer was washed with 2 × 100 mL of CH_2Cl_2. The organic layers were combined, washed with 200 mL of saturated brine, dried (Na_2SO_4), and evaporated under reduced pressure to yield 11.2 g (93%) of a light yellow colored oil which was distilled under reduced pressure to yield 10.9 g (90%) of a clear colorless oil: bp 102–104 °C (0.5 mmHg); IR 1685–1715, 3400 cm^{-1}; NMR δ 7.27 (t, 1), 3.73 (s, 4), 3.67 (s, 1), 3.2–1.4 (m, 8).

Anal. Calcd for $C_9H_{14}O_3$: C, 63.51; H, 8.29. Found: C, 63.99; H, 8.26.

Methyl 7-hydroxy-1-cyclooctenecarboxylate (8, n = 4) was prepared by the above procedure as a yellow oil from 7.0 g (0.04 mol) of methyl 7-oxo-1-cyclooctenecarboxylate (**3c**, n = 4), 0.73 g (0.02 mol) of $NaBH_4$, and 140 mL of anhydrous methanol. Reduced pressure distillation of the crude product yielded 6.5 g (93%) of a clear colorless viscous oil: IR 3450, 1710, 1645 cm^{-1}; NMR δ 7.1 (t, 1), 4.0 (s, 1), 3.8 (s, 3), 2.9 (s, 1), 2.7 (t, 2), 2.4–2.2 (m, 2), 2.0–1.4 (m, 6).

Anal. Calcd for $C_{10}H_{16}O_3$: C, 65.19; H, 8.75. Found: C, 64.96; H, 8.78.

Methyl 8-Hydroxy-1-cyclononenecarboxylate (8, n = 5). This reduction was accomplished by the above procedure[21] from 13.4 g (0.068 mol) of methyl-8-oxo-1-cyclononenecarboxylate (**3c**, n = 4) and 1.3 g (0.034 mol) of $NaBH_4$ in 140 mL of anhydrous methanol. After workup, evaporation of solvent under reduced pressure yielded 13.0 g (96%) of a viscous, light yellow-colored oil: IR 3450, 1680–1700 cm^{-1}; NMR δ 7.0 (t, 1), 4.0 (s, 1), 3.77 (s, 3), 3.27 (s, 1), 2.8 (s, 1), 2.7 (s, 1), 2.33 (s, 2), 1.6 (s, 8). A small sample was distilled under reduced pressure, bp 118–120 °C (1 mmHg), to yield a clear colorless oil with identical spectral characteristics as above.

Anal. Calcd for $C_{11}H_{18}O_3$: C, 66.64; H, 9.15. Found: C, 66.56; H, 9.07.

Methyl 9-hydroxy-1-cyclodecenecarboxylate (8, n = 6) was prepared by the above procedure from 7.1 g (0.033 mol) of a 4:1 (E/Z) mixture of methyl 9-oxo-1-cyclodecenecarboxylate, 0.64 g (0.016 mol) of $NaBH_4$, and 300 mL of anhydrous methanol. After workup, evaporation of the solvent under reduced pressure yielded 5.3 g (77%) of a light yellow oil: IR 3450, 1700, 1635 cm^{-1}; NMR δ 6.93 (t, 1), 4.2–3.8 (m, 5), 2.8–1.2 (m, 14). A sample of crude product was distilled under reduced pressure, bp 119–120 °C (0.5 mmHg), to yield a clear colorless oil with identical spectral properties as above.

Anal. Calcd for $C_{12}H_{20}O_3$: C, 67.89; H, 9.50. Found: C, 67.70; H, 9.40.

Tetrahydropyranyl Ether of Methyl 7-Hydroxy-1-cyclooctenecarboxylate (9, n = 4). (Following the procedure of Miyoshita, Yoshikoshi, and Grieco,[22] 2.5 g (13.6 mmol) of methyl 7-hydroxy-1-cyclooctenecarboxylate (8, n = 4) was stirred for 5.5 h with 2 mL (21.9 mmol) of DHP, 0.34 g (1.36 mmol) of PPTS, and 20 mL of dry CH_2Cl_2. The solution was diluted with 100 mL of $CHCl_3$ and washed with 150 mL of a half-saturated brine solution. The solution was evaporated under reduced pressure to yield a yellow oil. TLC analysis showed two components. The product mixture was separated by column chromatography using silica gel and a 20:1 CCl_4/ethyl acetate solution as eluant to yield 3.5 g (96%) of a clear colorless oil: IR 1710, 1640 cm^{-1}; NMR δ 7.1 (t, 1), 4.8 (d, 1), 4.1–3.4 (m, 6), 2.9–2.6 (m, 2), 2.5–2.1 (m, 2), 2.1–2.0 (s, 2).

Anal. Calcd for $C_{15}H_{24}O_4$: C, 67.14; H, 9.01. Found: C, 67.05; H, 9.07.

Tetrahydropyranyl ether of methyl 6-hydroxy-1-cycloheptenecarboxylate (9, n = 3) was prepared by the method of Miyoshita.[22] To a solution consisting of 10.9 g (0.064 mol) of methyl 6-hydroxy-1-cycloheptene (8, n = 3) and 9 mL of DHP dissolved in 300 mL of CH_2Cl_2 was added 0.8 g (0.3 mmol) of PPTS. This solution was stirred at room temperature for 24 h and then worked up as before. Evaporation of the solvent under reduced pressure yielded 16.0 g (98%) of an orange oil. Distillation of this oil at reduced pressure, bp 118–122 °C (0.5 mmHg), yielded 14.4 g (89%) of a clear colorless oil: IR 1710, 1640 cm^{-1}; NMR δ 7.23 (t, 1), 4.73 (s, 1), 4.0–3.4 (m, 6), 3.0–1.2 (m, 14).

Anal. Calcd for $C_{14}H_{22}O_4$: C, 66.12; H, 8.72. Found: C, 65.94; H, 8.62.

Tetrahydropyranyl ether of methyl 8-hydroxy-1-cyclononenecarboxylate (9, n = 5) was prepared by the method of Miyoshita[22] from 12.0 g (0.061 mol) of methyl 8-hydroxy-1-cyclononenecarboxylate (8, n = 5), 8.3 mL of DHP, 40 mL of CH_2Cl_2, and 1.5 g (6 mmol) of PPTS. After workup as above, evaporation of the solvent under reduced pressure yielded 14.5 g (84%) of a yellow colored oil: IR 1720–1710, 1640 cm^{-1}; NMR δ 7.0 (t, 1), 4.9–4.7 (d, 1), 4.2–3.4 (m, 6), 2.9–2.7 (t, 2), 2.4–2.1 (s, 2), 2.0–1.2 (m, 14); TLC analysis of the crude product revealed a three component mixture. Distillation of a 1.0-g sample of crude product resulted in the cleavage of the THP ether: bp 120–123 °C 1.0 mmHg: NMR δ 7.0 (t, 1), 4.0 (s, 1), 3.8 (s, 3), 3.27 (s, 1), 2.8 (s, 1), 2.7 (s, 1), 2.6–2.1 (m, 2), 1.6 (s, 8). Purification of a sample of the ether by column chromatography on silica gel using a 3:1 mixture of hexane/ethyl ether as eluant proved unsuccessful. The crude product was then dissolved in 200 mL of CH_2Cl_2, washed exhaustively with 3 × 150 mL of saturated $NaHCO_3$, and then dried ($MgSO_4$). After evaporation of the solvent, distillation of the product, bp 145–148 °C (1.0 mmHg), yielded a clear colorless oil, which was one component from TLC analysis. The purified product had spectral characteristics identical with the crude product.

Anal. Calcd for $C_{16}H_{26}O_4$: C, 68.06; H, 9.28. Found: C, 68.10; H, 9.15.

Tetrahydropyranyl ether of methyl 9-hydroxy-1-cyclodecenecarboxylate (9, n = 6) was prepared by the above method from 5.4 g (0.025 mol) of alcohol 8 (n = 6), 4 mL of DHP, and 0.32 g (1.27 mmol) of PPTS dissolved in 150 mL of dry CH_2Cl_2. Workup and evaporation of solvent under reduced pressure yielded 7.48 g of a light yellow oil. TLC analysis revealed four components. Distillation under pressure of a small sample resulted in the partial cleavage of the THP ether. Purification by column chromatography on silica gel using a 15:1 hexane/ethyl acetate mixture as eluant yielded 6.4 g (86%) of a clear colorless oil: IR 1710, 1635 cm^{-1}; NMR analysis showed evidence of the product being a 4:1 (E/Z) mixture δ 6.8 (t, 0.8), 6.38 (t, 0.2), 4.3–3.3 (m, 7), 2.8–1.2 (m, 20).

Anal. Calcd for $C_{17}H_{28}O_4$: C, 68.89; H, 9.52. Found: C, 68.71; H, 9.37.

Tetrahydropyranyl Ether of 6-Hydroxy-1-(hydroxymethyl)-1-cycloheptene (10, n = 3). This reduction was accomplished by the method of Corey[23] as modified by Eskola.[34] A solution consisting of 4.9 g (0.019 mol) of the unsaturated ester 9 (n = 3) dissolved in 250 mL of anhydrous ethyl ether was cooled to 0–2 °C under an N_2 atmosphere. To this solution was added 60 mL (in excess of 3 equiv) of a 1 M diisobutyl aluminumhydride (Dibal) solution in ethyl ether (Aldrich). This mixture was stirred at 0–2 °C under an N_2 atmosphere for 2 h. The reaction mixture was quenched by the dropwise addition of 10 mL of a 30% KOH solution and aged overnight. The aluminum salts were then filtered and washed extensively with 300 mL of ethyl acetate. The filtrate was washed with 200 mL of a 30% KOH solution, dried ($MgSO_4$), and evaporated under reduced pressure to yield 3.9 g (89%) of a viscous light yellow oil: IR 3400 cm^{-1}; NMR δ 5.93 (t, 1), 4.77 (s, 1), 4.2–3.0 (m, 6), 2.6–1.2 (m, 14). A sample of crude product was chromatographed on silica gel by using a 3:1 hexane/ethyl acetate mixture as eluant and then distilled to yield a clear colorless oil with identical spectral characteristics as above, bp 125–127 °C (0.5 mmHg).

Anal. Calcd for $C_{13}H_{22}O_3$: C, 68.99; H, 9.80. Found: C, 68.74; H, 9.87.

Tetrahydropyranyl ether of 7-hydroxy-1-(hydroxymethyl)-1-cyclooctene (10, n = 4) was reduced by the procedure of Corey[23] as modified by Eskola[34] using 14.8 g (0.055 mol) of 9 (n = 4) dissolved in 600 mL of anhydrous ethyl ether and 166 mL of a 1 M solution of Dibal. After workup, evaporation of the solvent under reduced pressure yielded a light yellow oil. Distillation of the oil yielded 8.5 g (64%) of a clear colorless oil: IR 3475 cm^{-1}; NMR δ 5.83 (t, 1), 4.77 (d, 1), 4.2–3.4 (m, 6), 2.7–2.4 (m, 2), 2.4–2.1 (m, 2), 2.0–1.1 (s, 12).

Anal. Calcd for $C_{14}H_{24}O_3$: C, 69.96; H, 10.06. Found: C, 69.77; H, 9.90.

Tetrahydropyranyl Ether of 8-Hydroxy-1-(hydroxymethyl)-1-cyclononene (10, n = 5). This reduction was accomplished by the above procedure from 7.8 g (0.028 mol) of ester 9 (n = 5) dissolved in 500 mL of anhydrous ethyl ether and 83 mL of 1 M Dibal in ethyl ether. After workup, evaporation of the solvent under reduced pressure yielded a cloudy oil: IR 3410 cm^{-1}; NMR δ 5.70 (t, 1), 4.50 (d, 1), 4.1–3.4 (m, 6), 2.7–1.1 (m, 18). Distillation of the product under reduced pressure yielded 5.0 g (70%) of a clear colorless oil, bp 148–152 °C (1.0 mmHg), with identical spectral characteristics as above.

Anal. Calcd for $C_{15}H_{26}O_3$: C, 70.83; H, 10.30. Found: C, 70.73; H, 10.14.

Tetrahydropyranyl Ether of 9-Hydroxy-1-(hydroxymethyl)-1-cyclodecene (10, n = 6). This reduction was accomplished by the above procedure from 5.7 g (0.019 mol) of a 4:1 (E/Z) mixture of ester 9 (n = 6) dissolved in 250 mL of anhydrous ethyl ether and 60 mL of 1 M Dibal in ethyl ether. After workup, evaporation of the solvent under reduced pressure yielded 4.8 g (94%) of a cloudy viscous oil: IR 3400 cm^{-1}; NMR δ 5.53 (t, 1), 4.83 (d, 1), 4.2–3.4 (m, 6), 2.7–1.3 (m, 20). A sample was purified on a silica gel column by using a 3:1 hexane/ethyl acetate mixture as eluant to yield a clear colorless oil with identical spectral properties as above.

Anal. Calcd for $C_{16}H_{28}O_3$: C, 71.60; H, 10.52. Found: C, 70.94; H, 10.49.

Tetrahydropyranyl Ether of 7-Hydroxy-1-(acetoxymethyl)-1-cyclooctene (11, n = 4). This acetylation was accomplished by use of the procedure of Höfle, Steglich, and Vorbruggen.[24] To a mixture of 3.1 g (12.8 mmol) of allyl alcohol 10 (n = 4), 13 mL of pyridine, and a few crystals of 4-(dimethylamino)pyridine (DMAP) was added in a dropwise manner a solution consisting of 1.3 g (12.8 mmol) acetic anhydride in 3 mL of pyridine. This mixture was heated with stirring at 50–70 °C for 4.5 h. The mixture was cooled to room temperature, poured into 150 mL of diethyl ether, and washed with 100 mL of a 10% HCl solution. The organic layer was dried with anhydrous $MgSO_4$,

(34) P. Eskola, unpublished observations.

and the solvent was evaporated under reduced pressure to yield a yellow oil. The IR spectrum of the crude product had no OH band at 3450 cm^{-1}. The oil was purified by column chromatography using silica gel and 3:1 mixture of toluene/ethyl acetate as eluant to yield 2.7 g (74%) of a light yellow oil: IR 1745 cm^{-1}; NMR δ 5.77 (t, 1), 4.75 (s, 1), 4.6 (s, 2), 4.2–3.4 (m, 3), 2.6–1.2 (m, 19).

Anal. Calcd for $C_{16}H_{26}O_4$: C, 68.06; H, 9.28. Found: C, 68.01, H, 9.25.

Tetrahydropyranyl Ether of 6-Hydroxy-1-(acetoxymethyl)-1-cycloheptene (11, n = 3). This acetylation was accomplished by using the procedure of Höfle, Steglich, and Vorbruggen[24] from a solution of 3.6 g (16 mmol) of allyl alcohol **10** (n = 3) and a few crystals of DMAP dissolved in 40 mL of dry pyridine. To this solution was added in a dropwise manner 1.6 g (16 mmol) of acetic anhydride dissolved in 10 mL of pyridine. This solution was stirred at 50–70 °C for 6 h, cooled to room temperature, and worked up as above. Evaporation of the solvent under reduced pressure yielded 4.1 g (95%) of a yellow oil: IR 1730 cm^{-1}; NMR δ 6.00 (t, 1), 4.70 (s, 1), 4.50 (s, 2), 4.2–3.4 (m, 3), 2.6–1.4 (m, 17). A sample was purified by column chromatography using silica gel and a 20:1 toluene/ethyl acetate mixture as eluant to yield a very light yellow oil with identical spectral properties as above. Distillation of a portion of the chromatographed sample caused partial THP ether cleavage.

Anal. Calcd for $C_{15}H_{24}O_4$: C, 67.14; H, 9.01. Found: C, 67.04; H, 9.01.

Tetrahydropyranyl Ether of 8-Hydroxy-1-(acetoxymethyl)-1-cyclononene (11, n = 5). This acetylation was accomplished by using the above procedure[24] from 5.0 g (19.5 mmol) of allyl alcohol **10** (n = 5), 0.1 g of DMAP, 25 mL of dry pyridine, and 2.0 g (19.6 mmol) of acetic anhydride in 5 mL of dry pyridine. This mixture was heated at 50–70 °C for 5 h, cooled to room temperature, and worked up as before. Evaporation of the solvent under reduced pressure yielded 4.7 g (81%) of a light yellow oil: IR 1735 cm^{-1}; NMR δ 5.67 (t, 1), 4.73 (s, 1), 4.57 (s, 2), 4.1–3.4 (m, 3), 2.6–1.3 (m, 21). Purification of a small sample by column chromatography using silica gel and a 9:1 mixture of hexane/ethyl acetate as eluant yielded a clear colorless oil with identical spectral properties as above.

Tetrahydropyranyl Ether of 9-Hydroxy-1-(acetoxymethyl)-1-cyclodecene (11, n = 6). This acetylation was accomplished by the above procedure. To a solution consisting of 4.3 g (16.0 mmol) allyl alcohol **10** (n = 6) and a few crystals of DMAP dissolved in 50 mL of pyridine was added dropwise 1.64 g (16.0 mmol) of acetic anhydride. This solution was stirred at 50–70 °C for 8 h, cooled to room temperature, and worked up as before. Evaporation of the solvent under reduced pressure yielded 4.8 g (98%) of a yellow oil: IR 1730 cm^{-1}; NMR δ 5.53 (t, 1), 4.80 (s, 1), 4.63 (s, 2), 4.2–3.4 (m, 3), 2.6–1.2 (m, 23). A sample was purified by column chromatography using silica gel and a 15:1 hexane/ethyl acetate mixture as eluant to give a clear colorless oil with identical spectral properties. Distillation of a portion of the chromatographed sample caused partial cleavage of the THP ether.

Anal. Calcd for $C_{18}H_{30}O_4$: C, 69.64; H, 9.74. Found: C, 69.59; H, 9.63.

6-Hydroxy-1-(acetoxymethyl)-1-cycloheptene (12, n = 3). The cleavage of THP ether **11** (n = 3) was accomplished by the method of Miyoshita, Yoshikoshi, and Grieco.[22] A solution consisting of 3.3 g (0.012 mol) of the THP ether, 2 mL of H_2O, and 0.3 g (1.2 mmol) of PPTS dissolved in 150 mL of absolute ethyl alcohol was stirred at 50–70 °C for 6 h. The reaction mixture was cooled to room temperature, poured into 200 mL of CH_2Cl_2, washed with 300 mL of saturated $NaHCO_3$, and dried ($MgSO_4$), and the solvent was evaporated under reduced pressure to yield 2.2 g of crude product. The crude product was chromatographed on a silica gel column by using a 20:1 toluene/ethyl ether mixture as eluant, yielding a yellow oil. This oil was distilled under reduced pressure to yield 1.46 g (66%) of a clear colorless oil: bp 122 °C (2 mmHg); IR 3400, 1735 cm^{-1}; NMR δ 6.0 (t, 1), 4.97 (s, 2), 3.9–3.4 (m, 1), 3.1 (s, 1), 2.5–1.2 (m, 11).

Anal. Calcd for $C_{10}H_{16}O_3$: C, 65.19; H, 8.75. Found: C, 65.04; H, 8.73.

7-Hydroxy-1-(acetoxymethyl)-1-cyclooctene (12, n = 4). The THP ether cleavage was accomplished by the above procedure. A solution consisting of 8.7 g (31.0 mmol) of THP ether **11** (n = 4), 0.78 g (3.1 mmol) of PPTS, and 3 mL of H_2O dissolved in 100 mL of absolute ethyl alcohol was stirred for 4 h at 55 °C. The solution was cooled to room temperature and worked up as above. Evaporation of the solvent under reduced pressure yielded 7.1 g of a yellow oil. The crude product was distilled under reduced pressure to give 4.44 g (72%) of a clear colorless oil: bp 118–129 °C (0.5 mmHg); IR 3400, 1730 cm^{-1}; NMR δ 5.77 (t, 1), 4.57 (s, 2), 4.1–3.7 (m, 1), 2.9 (s, 1), 2.5–1.2 (m, 13).

Anal. Calcd for $C_{11}H_{18}O_3$: C, 66.54; H, 9.15. Found: C, 66.52; H, 9.20.

8-Hydroxy-1-(acetoxymethyl)-1-cyclononene (12, n = 5). The THP ether **11** (n = 5) was cleaved by the above procedure. A solution consisting of 9.7 g (34.0 mmol) of THP ether, 0.8 g (3.2 mmol) of PPTS, and 3 mL of H_2O dissolved in 100 mL of absolute ethyl alcohol was stirred at 60–70 °C overnight. The reaction mixture was cooled to room temperature and worked up as above. Evaporation of the solvent under reduced pressure yielded a yellow oil which was purified on a silica gel column by using a 3:1 hexane/ethyl acetate mixture as the eluant to yield 4.2 g (58%) of a light yellow oil: IR 3415, 1710–1730 cm^{-1}; NMR δ 5.6 (t, 1), 4.5 (s, 2), 3.83 (m, 1), 2.6–1.2 (m, 16). Distillation under reduced pressure of a sample of the chromatographed oil yielded a clear colorless oil with identical spectral properties as above, bp 126–128 °C (0.5 mmHg).

Anal. Calcd for $C_{12}H_{20}O_3$: C, 67.89; H, 9.50. Found: C, 67.74; H, 9.40.

9-Hydroxy-1-(acetoxymethyl)-1-cyclodecene (12, n = 6). The cleavage of THP ether **11** (n = 6) was accomplished by the above method. A solution consisting of 4.5 g (14.0 mmol) of THP ether, 0.2 g (0.8 mmol) of PPTS, and 5 mL of H_2O dissolved in 250 mL of absolute ethyl alcohol was stirred at 50–70 °C for 5 h. The solvent was evaporated under reduced pressure to yield 2.9 g of a light yellow oil. TLC analysis of the crude product revealed a two-component mixture. NMR analysis of the crude product showed a 10:1 mixture of E/Z isomers. Separation on a silica gel column by using a 3:1 mixture of hexane/ethyl acetate yielded 1.6 g (50%) of the E isomer; IR 3450, 1740–1715 cm^{-1}; NMR δ 5.57 (t, 1), 4.60 (s, 2), 4.2–3.9 (m, 1), 2.6–1.2 (m, 18).

Anal. Calcd for $C_{13}H_{22}O_3$: C, 68.99; H, 9.80. Found: C, 68.77; H, 9.75.

Also isolated from the chromatography column was 0.46 g of an approximate 1:1 mixture of E/Z isomers: NMR δ 5.73 (t, 0.5), 5.57 (t, 0.5), 4.67 (s, 1), 4.2–3.9 (m, 1), 2.6–1.2 (m, 18).

6-Oxo-1-(acetoxymethyl)-1-cycloheptene (3f, n = 3). This oxidation was performed by the method of Corey and Schmidt.[25] To a solution of 1.35 g (7.34 mmol) of alcohol **12** (n = 3) dissolved in 60 mL of dry CH_2Cl_2 was added 2.8 g (7.34 mmol) of pyridinium dichromate (PDC). This suspension was stirred at room temperature for 29 h. The reaction mixture was then gravity filtered through a fritted glass Buchner funnel filled with anhydrous $MgSO_4$. The $MgSO_4$ was exhaustively washed with CH_2Cl_2. Concentration of the filtrate under reduced pressure yielded a light brown liquid which was chromatographed on a silica gel column by using an 8:1 mixture of hexane/ethyl acetate as eluant to yield 1.04 g (78%) of a clear colorless oil: IR 1735, 1710 cm^{-1}; ^1H NMR δ 5.85 (t, 1), 4.45 (s, 2), 3.2 (s, 2), 2.6–1.4 (m, 9); UV λ_{max} EtOH 286 (ϵ 88); ^{13}C NMR δ 207.98, 170.71, 130.00, 127.46, 69.59, 43.79, 43.45, 28.56, 21.99, 20.75.

Anal. Calcd for $C_{10}H_{14}O_3$: C, 65.92; H, 7.74. Found: C, 65.77; H, 7.74.

7-Oxo-1-(acetoxymethyl)-1-cyclooctene (3f, n = 4). This oxidation was accomplished by using the above procedure.[25] A suspension of 3.34 g (17.0 mmol) of alcohol **12** (n = 4) and 6.3 g (17.0 mmol) of PDC in 60 mL of dry CH_2Cl_2 was stirred overnight. Gravity filtration through $MgSO_4$ and concentration of the filtrate under reduced pressure yielded a brown liquid which was chromatographed on a silica gel column by using 12:1 hexane/ethyl acetate as eluant to yield a light yellow oil. Distillation under reduced pressure yielded 1.37 g (41%) of clear colorless oil: bp 100–102 °C (0.5 mmHg): IR 1735, 1695 cm^{-1}; ^1H NMR δ 5.87 (t, 1), 4.53 (s, 2), 3.17 (s, 2), 3.17 (s, 2), 2.6–1.4 (m, 11); UV λ_{max} EtOH 275 (ϵ 105); ^{13}C NMR δ 211.52, 170.34, 130.58, 68.92, 44.33, 41.52, 26.83, 25.91, 24.50, 20.55.

Anal. Calcd for $C_{11}H_{16}O_3$: C, 67.32; H, 8.22. Found: C, 67.24; H, 8.20.

8-Oxo-1-(acetoxymethyl)-1-cyclononene (3f, n = 5). Following the above procedure a suspension of 3.7 g (17.6 mmol) of alcohol **12** (n = 5) and 6.0 g of PDC in 100 mL of dry CH_2Cl_2 was stirred at room temperature for 2 days. Workup as before and chromatography on a silica gel column by using a 7:1 hexane/ethyl acetate mixture as eluant yielded a yellow oil. Distillation under reduced pressure yielded 2.6 g (70%) of a clear colorless oil: bp 110–112 °C (0.5 mmHg): IR 1735, 1695 cm^{-1}; ^1H NMR δ 5.70 (t, 1), 4.63 (s, 2), 3.13 (s, 2), 2.6–1.4 (m, 13); UV λ_{max} EtOH 293 (ϵ 79); ^{13}C NMR δ 211.43, 170.34, 131.31, 128.56, 68.68, 43.33, 41.82, 26.34, 26.08, 25.85, 23.87, 20.65.

Anal. Calcd for $C_{12}H_{18}O_3$: C, 68.55; H, 8.63. Found: C, 68.48; H, 8.52.

(*E*)-9-Oxo-1-(acetoxymethyl)-1-cyclodecene ((*E*)-3f, n = 6). Following the above procedure, a suspension of 2.0 g (8.9 mmol) of alcohol **12** (n = 6) and 3.4 g (8.9 mmol) of PDC in 200 mL of dry CH_2Cl_2 was stirred at room temperature for 24 h. Workup as before and chromatography on a silica gel column by using a 12:1 hexane/ethyl acetate mixture as eluant yielded 1.38 g (69%) of a light yellow oil: IR 1740, 1700, 1665 cm^{-1}; NMR δ 5.57 (t, 1), 4.57 (s, 2), 3.10 (s, 2), 2.6–1.2 (m, 15); UV λ_{max} EtOH 290 (ϵ 43); ^{13}C NMR δ 211.87, 169.80, 130.19, 131.88, 68.94, 43.64, 37.33, 26.08, 25.33, 24.64, 23.09, 21.53, 20.16.

Anal. Calcd for $C_{13}H_{20}O_3$: C, 69.61; H, 8.99. Found: C, 69.51; H, 8.94.

Base-Catalyzed Isomerizations of Cycloalkenones. A typical isomerization was conducted as follows. To a solution consisting of 100 mg of the starting isomer dissolved in 5 mL of freshly distilled toluene was added 45 μL (approximately $^2/_3$ of a equivalent) of DBN. (The DBN was periodically distilled and was stored under an N_2 atmosphere.) The flask containing the isomerization mixture was then fitted with a condenser, and the solution was stirred at the appropriate temperature under an N_2 atmosphere. The appropriate temperature was maintained by a Matheson Lab-Stat apparatus. The isomerization was continued until no further change in the product ratio was observed by gas–liquid chromatography. The isomerization mixture was then poured into 100 mL of a 10% HCl solution and was extracted with 3 × 100 mL of CH_2Cl_2. The organic layers were combined and dried ($MgSO_4$), and the solvent was evaporated under reduced pressure. The final isomerization ratio was then determined by the average of at least three gas chromatograms. The area under each peak was determined by the height multiplied by the width at one-half the peak height.

Methyl 3-oxo-1-cycloheptenecarboxylate (4c, n = 3) was prepared as the minor component in a 20.9%/79.1% $\Delta2/\Delta3$ mixture from the DBN-catalyzed double-bond equilibration of methyl 6-oxo-1-cycloheptenecarboxylate (**3c**, n = 3) at 100 °C in toluene. The $\Delta2$ isomer was isolated by column chromatography using silica gel and a hexane/ethyl ether mixture as eluant: IR 1715, 1665 cm^{-1}; NMR δ 6.90 (s, 1), 3.8 (s, 3), 2.9–2.5 (m, 4), 2.0–1.7 (m, 4) (lit.[8] δ 6.78 (s, 1), 3.75 (s, 3), 2.83–1.72 (m, 8); UV λ_{max} EtOH 237 (ϵ 5000), 320 (72); ^{13}C NMR δ 203.57, 167.51, 144.10, 136.71, 52.30, 42.17, 24.85, 24.56, 21.03.

Methyl 3-oxo-1-cyclooctenecarboxylate (4c, n = 4) was prepared as the minor component in a 5.5%/94.5% $\Delta2/\Delta3$ mixture from the DBN-catalyzed double-bond equilibration at 100 °C in toluene of methyl 7-oxo-1-cyclooctenecarboxylate (**3c**, n = 4). The minor component was isolated by column chromatography using silica gel and a hexane/ethyl ether mixture as eluant: IR 1715, 1680, 1655 cm^{-1}; NMR δ 6.90 (s, 1), 3.77 (s, 3), 2.9–2.5 (m, 4), 2.1–1.5 (m, 6); UV λ_{max} EtOH 206 (ϵ 7000), 231 (6400), 300 (145); ^{13}C NMR δ 206.79, 167.87, 139.28, 136.13, 52.44, 43.34, 28.27, 26.48, 22.83, 22.17.

3-Oxo-1-cyano-1-cycloheptene (4d, n = 3). The $\Delta2$ isomer 3-oxo-1-cyano-1-cycloheptene (**4d**, n = 3) was prepared as the minor component in a 16.1%/83.9% $\Delta2/\Delta3$ mixture from the DBN-catalyzed double-bond equilibration at 100 °C in toluene of 6-oxo-1-cyano-1-cycloheptene (**3d**, n = 3). The minor component was isolated by column chromatography using silica gel and a hexane/ethyl acetate mixture as eluant: IR 2210, 1675, 1605 cm^{-1}; NMR δ 6.57 (s, 1), 2.9–2.3 (m, 4), 2.3–1.5 (m, 4); UV λ_{max} EtOH 237 (ϵ 12000), 336 (70); ^{13}C NMR δ 201.01, 142.67, 127.22, 118.81, 42.84, 32.03, 25.25, 21.06.

3-Oxo-1-cyano-1-cyclooctene (4d, n = 4). The $\Delta2$ isomer 3-oxo-1-cyano-1-cyclooctene (**4d**, n = 4) was prepared as the minor component in a 2.9%/97.1% $\Delta2/\Delta3$ mixture from the DBN-catalyzed double-bond equilibration at 100 °C in toluene of 7-oxo-1-cyano-1-cyclooctene (**3d**, n = 4). The minor component was isolated by column chromatography using silica gel and a hexane/ethyl acetate mixture as eluant: IR 2210, 1690, 1660 cm^{-1}; NMR δ 6.60 (s, 1), 2.8–2.4 (m, 4), 2.0–1.5 (m, 6); UV λ_{max} EtOH 215 (ϵ 4700), 228 (4000), 290 (180); ^{13}C NMR δ 203.70, 141.18, 122.60, 118.00, 43.04, 31.92, 26.25, 22.33, 21.87.

3-Oxo-1-acetyl-1-cycloheptene (4e, n = 3). The $\Delta2$ isomer 3-oxo-1-acetyl-1-cycloheptene (**4e**, n = 3) was prepared as the minor component in a 20.7%/79.3% $\Delta2/\Delta3$ mixture from the DBN-catalyzed double-bond equilibration of 6-oxo-1-acetyl-1-cycloheptene (**3e**, n = 3) at 80 °C in toluene. The minor component was isolated by column chromatography using silica gel and a hexane/ethyl acetate mixture as eluant: IR 1675 cm^{-1}; NMR δ 6.75 (s, 1), 2.9–2.6 (m, 4), 2.43 (s, 3), 2.0–1.6 (m, 4); UV λ_{max} EtOH 244 (ϵ 8400), 315 (122); ^{13}C NMR δ 205.07, 200.20, 151.37, 136.86, 42.26, 26.16, 25.35, 24.73, 21.41.

3-Oxo-1-acetyl-1-cyclooctene (4e, n = 4). The $\Delta2$ isomer 3-oxo-1-acetyl-1-cyclooctene (**4e**, n = 4) was prepared as the minor component in a 4.9%/95.1% $\Delta2/\Delta3$ mixture from the DBN-catalyzed double-bond equilibration of 7-oxo-1-acetyl-1-cyclooctene (**3e**, n = 4) at 100 °C in toluene. The minor component was concentrated by column chromatography using silica gel and a hexane/ethyl acetate mixture as eluant and isolated by preparative gas–liquid chromatography: IR 1680 cm^{-1}; NMR δ 6.70 (s, 1), 2.8–2.4 (m, 4), 2.33 (s, 3), 2.0–1.4 (m, 6); UV λ_{max} EtOH 207 (end absorption) (ϵ 6000), 234 (5000), 298 (225); ^{13}C NMR δ 206.67, 200.29, 146.97, 136.57, 43.32, 26.41, 26.15, 25.89, 23.29, 22.51.

3-Oxo-1-cyano-1-cyclononene (4d, n = 5). The $\Delta2$ isomer 3-oxo-1-cyano-cyclononene (**4d**, n = 5) was prepared as a minor component in a 0.5%/96.7%/2.8% $\Delta2/\Delta3/\Delta4$ mixture from the DBN-catalyzed double-bond isomerization of 8-oxo-1-cyano-1-cyclononene (**3d**, n = 5) at 100 °C in toluene. A small amount of the $\Delta2$ isomer (5 mg) was isolated by column chromatography using silica gel and a hexane/ethyl acetate mixture as eluant: IR 2200, 1705, 1670 cm^{-1}; NMR δ 6.7 (s), 2.8–2.5 (m).

3-Cyano-4-cyclononenone (14). The $\Delta4$ isomer 3-cyano-4-cyclononenone (**14**) was prepared as a minor component in a 0.5%/96.7%/2.8% $\Delta2/\Delta3/\Delta4$ mixture from the DBN-catalyzed double-bond isomerization of 8-oxo-1-cyano-1-cyclononene (**3d**, n = 5) at 100 °C in toluene. The $\Delta4$ isomer was isolated by preparative gas–liquid chromatography: IR 2230, 1710 cm^{-1}; NMR δ 5.80 (m, 2), 3.88 (t, 1), 3.0 (q, 1), 2.6–1.5 (m, 9); UV λ_{max} EtOH 205 (end absorption) (ϵ 14000), 276 (44); ^{13}C NMR δ 212.40, 134.14, 125.50, 121.35, 44.53, 43.89, 27.60, 27.30, 25.59, 20.39.

3-Acetyl-4-cyclononenone (15). The $\Delta4$ isomer 3-acetyl-4-cyclononenone (**15**) was prepared as the minor component in a 96.4%/3.6% $\Delta3/\Delta4$ mixture from the DBN-catalyzed double-bond isomerization at 100 °C in toluene of 8-oxo-1-acetyl-1-cyclononenone (**3e**, n = 5). The minor component was isolated by preparative gas–liquid chromatography as above: IR 1720, 1700 cm^{-1}; NMR δ 5.70 (m, 2), 3.65 (m, 1), 2.7–1.5 (m, 13); UV λ_{max} EtOH 205 (end absorption) (ϵ 10000), 275 (101); ^{13}C NMR δ 216.46, 207.81, 133.62, 127.31, 49.79, 44.82, 41.73, 28.24, 27.74, 25.81, 20.74.

3-Oxo-1-(acetoxymethyl)-1-cycloheptene (4f, n = 3). The $\Delta2$ isomer 3-oxo-1-(acetoxymethyl)-1-cycloheptene (**4f**, n = 3) was prepared as the major component (47%) in a five-component isomerization mixture from the DBN-catalyzed double-bond isomerization of 6-oxo-1-(acetoxymethyl)-1-cycloheptene (**3f**, n = 3) at 80 °C in toluene. The major component was isolated by preparative gas–liquid chromatography: IR 1730, 1650–1635 cm^{-1}; NMR δ 6.05 (s, 1), 4.62 (s, 2), 2.63 (m, 2), 2.36 (m, 2), 2.13 (s, 3), 1.85 (m, 4); UV λ_{max} EtOH 232 (ϵ 11500), 314 (80); mass spectrum, molecular ion m/e 182, base peak 43; ^{13}C NMR δ 203.34, 170.20, 153.44, 128.01, 66.61, 42.40, 29.55, 24.88.

(*Z*)-3-(Acetoxymethylene)cycloheptanone (13). The exocyclic isomer (*Z*)-3-(acetoxymethylene)cycloheptanone (**13**) was isolated as a minor component (17%) in an isomerization mixture from the DBN-catalyzed double-bond isomerization of 6-oxo-1-(acetoxymethyl)-1-cycloheptene (**3f**, n = 3) at 80 °C in toluene by preparative gas–liquid chromatography: mass spectrum molecular ion m/e 182, base peak 43; NMR δ 7.10 (s, 1), 3.30 (s, 2), 2.5 (m, 2), 2.25 (m, 2), 2.15 (s, 3), 1.75 (m, 4). The *Z* configuration was determined by a difference NOE experiment.[26] The vinyl

hydrogen was irradiated, causing an enhancement of the signal at δ 2.25 and not the hydrogens at δ 3.30; ^{13}C NMR δ 210.11, 167.84, 132.79, 118.55, 44.29, 43.71, 33.50, 31.29, 24.39, 20.68.

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Registry No. **3a** (*n* = 3), 1121-64-8; **3c** (*n* = 3), 42205-56-1; **3c** (*n* = 4), 17606-95-0; **3c** (*n* = 5), 42205-59-4; (*E*)-**3c** (*n* = 6), 42205-61-8; **3d** (*n* = 3), 90743-12-7; **3d** (*n* = 4), 90743-15-0; **3d** (*n* = 5), 90743-18-3; (*E*)-**3d** (*n* = 6), 90743-22-9; (*Z*)-**3d** (*n* = 6), 90762-82-6; **3e** (*n* = 3), 90743-13-8; **3e** (*n* = 4), 90743-16-1; **3e** (*n* = 5), 90743-19-4; (*E*)-**3e** (*n* = 6), 90743-21-8; **3f** (*n* = 3), 90743-14-9; **3f** (*n* = 4), 90743-17-2; **3f** (*n* = 5), 90743-20-7; (*E*)-**3f** (*n* = 6), 90743-23-0; **4a** (*n* = 3), 1121-66-0; **4c** (*n* = 3), 42205-57-2; **4c** (*n* = 4), 90743-28-5; **4d** (*n* = 3), 90743-25-2; **4d** (*n* = 4), 90743-29-6; **4d** (*n* = 5), 90743-32-1; **4d** (*n* = 6), 90743-24-1; **4e** (*n* = 3), 90743-26-3; **4e** (*n* = 4), 90743-30-9; **4f** (*n* = 3), 90743-27-4; **4f** (*n* = 4), 90743-31-0; **5** (*n* = 3), 90743-33-2; Δ²-**5** (*n* = 3), 90743-37-6; **5** (*n* = 4), 90743-34-3; **5** (*n* = 5), 90743-35-4; (*E*)-**5** (*n* = 6), 90743-36-5; (*Z*)-**5** (*n* = 6), 90743-38-7; **6** (*n* = 3), 90743-40-1; **6** (*n* = 4), 90743-39-8; **6** (*n* = 5), 90743-41-2; **6** (*n* = 6), 90743-42-3; **7** (*n* = 3), 90743-43-4; **7** (*n* = 4), 90743-45-6; **7** (*n* = 5), 90743-46-7; **7** (*n* = 6), 90743-47-8; **8** (*n* = 3), 90743-48-9; **8** (*n* = 4), 90743-49-0; **8** (*n* = 5), 90743-50-3; **8** (*n* = 6), 90743-51-4; **9** (*n* = 3), 90743-53-6; **9** (*n* = 4), 90743-52-5; **9** (*n* = 5), 90743-54-7; (*E*)-**9** (*n* = 6), 90743-55-8; (*Z*)-**9** (*n* = 6), 90743-56-9; **10** (*n* = 3), 90743-57-0; **10** (*n* = 4), 90743-58-1; **10** (*n* = 5), 90743-59-2; **10** (*n* = 6), 90743-60-5; **11** (*n* = 3), 90743-61-6; **11** (*n* = 4), 90743-62-7; **11** (*n* = 5), 90743-63-8; **11** (*n* = 6), 90743-64-9; **12** (*n* = 3), 90743-65-0; **12** (*n* = 4), 90743-66-1; **12** (*n* = 5), 90743-72-9; (*E*)-**12** (*n* = 6), 90743-67-2; (*Z*)-**12** (*n* = 6), 90743-68-3; **13**, 90743-71-8; **14**, 90743-69-4; **15**, 90743-70-7; DBN, 3001-72-7; dimethylaluminum amide, 24758-44-9; trimethylaluminum, 75-24-1; ammonia, 7664-41-7; 2-methyl-6-oxo-1-cyanocycloheptane ethylene ketal, 90743-44-5.

The Search for Long Range Aryl Migration in the Solvolysis of Suitably Positioned Monoaryl Derivatives in the Tricyclo[3.2.1.0^{2,4}]octane and Bicyclo[3.2.1]octane Skeletal Systems[1,2]

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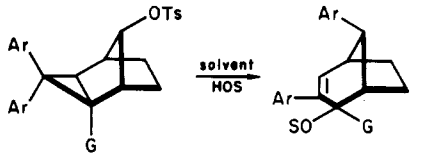
Previous work has established that long range aryl migration (LRAM) and electrocyclic ring opening (ERO) combine (LRAMERO) to rearrange the *exo*-3,3-diaryltricyclo[3.2.1.0^{2,4}]oct-*anti*-8-yl system in solvolysis. Left uninvestigated in the earlier work were the necessity of the second ("stationary") aryl group and the extent and need that ERO contribute to the process. The present study involved the synthesis, characterization, and solvolytic behavior of substrates designed to investigate these aspects of reaction. It has been determined that a second aryl group is not necessary in order to observe LRAMERO, although the proximate positioning of the migrating aryl group and the leaving group center remains critical. The *syn*-3-phenyl and *syn*-3-*p*-tolyl (note *mono*aryl) analogues of the previously studied *di*aryl systems exhibit undiminished LRAMERO, whereas the *anti*-3-phenyl epimer is inert. The kinetics exhibited by the syn compounds, coupled with the rearranged products observed, additionally support the view that ERO occurs in concert with LRAM. Regretably, the question of the necessity of ERO remains unanswered. The bicyclo[3.2.1]octane substrate chosen to decide the question eschewed LRAM, presumably because of a conformational bias, and instead underwent solvolysis via σ-participation in exactly the same manner as its parent, the solvolysis of which was reported some time ago.

Introduction

Rearrangement via long range aryl migration (LRAM) coupled with electrocyclic ring opening (ERO) characterizes the solvolysis of certain substrates, as shown in eq 1.[5]

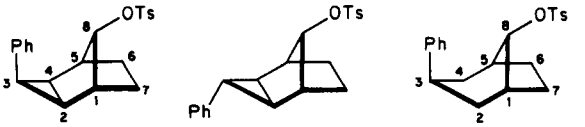


(1)

In spite of the considerable information gained in earlier studies, two items of mechanistic interest remained. First, what role in the solvolysis, if any, is played by the stationary aryl group? Second, is ERO necessary, so that the rare transannular aryl migration observed is restricted to tricyclics as in eq 1 or might other substrates with suitable geometry but lacking the possibility of ERO nonetheless exhibit LRAM? The present study investigated these aspects of the reaction.

Results

Tosylates *syn*-1-OTs, its *p*-tolyl analogue, *anti*-1-OTs, and 2-OTs have been synthesized.[6]



syn-1-OTs *anti*-1-OTs 2-OTs

(1) Electrocyclic Effects in Solvolysis. 6. Part 5. Wilt, J. W.; Curtis, V. A.; O-Yang, C. *J. Org. Chem.* **1982**, *47*, 3721.

(2) Taken in part from the M.S. Thesis of L.N.C., Loyola University of Chicago, June, 1983.

(3) Present address: Department of Chemistry, Northeastern Illinois State University, Chicago, IL.

(4) Undergraduate Research Scholar, 1983.

(5) A summary of earlier work may be found in Part 5 of this series (ref 1).

(6) Our use of syn and anti corresponds, respectively, to the endo and exo prefixes occasionally employed for such substituents. The former terms (to us) better convey the stereochemical relationship of the phenyl group to its migration terminus in LRAM observed in some of these substances.

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