Reductive Cyclization of Ketones Tethered to Activated Olefins Mediated by Magnesium in Methanol

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The reductive cyclizations of various ketones tethered to activated olefins such as α,β-unsaturated esters, nitriles, sulfoxides, and sulfides were mediated by magnesium in dry methanol in the presence of mercuric chloride. When treated with magnesium in dry methanol at −23 °C all of the ketones except nitrile **9** (42%) and 5-oxa-8-keto-2-enoate **5** (13%) gave excellent yields (79–98%) of mono- and bicyclic alcohol products resulting from carbon–carbon bond formation between the β-carbon of the activated olefin and the carbonyl carbon. The reaction was accelerated by the catalytic amount of mercuric chloride, although the stereoselectivity was not affected by the catalyst. For all the substrates except 8-keto-2-enoate **3** and 5-aza-8-keto-2-enoate **6**, the configuration of the major product was trans between the hydroxy and (methoxycarbonyl)methyl groups. The product isomer ratios were independent of the substrate geometry (*E* or *Z*). In contrast to the ketones, aldehydes tethered to α,β-unsaturated esters gave products of simple reduction of the double bond and/or saturated alcohols instead of the cyclized products. When the reaction temperature was lowered, the yields of cyclized product were significantly affected by the production of appreciable amounts of saturated product, but the stereoselectivity was not improved. Under the same reaction conditions α,β-unsaturated sulfoxide **16** gave deoxygenated sulfide **18** (85%) as the major product along with a small amount (9%) of cyclized product **19t**. In contrast, sulfone **17** underwent desulfonylation instead of cyclization to give olefin **20** (54%). With excess magnesium (15 equiv), however, α,β-unsaturated sulfoxide **16** gave cyclized sulfide **19t** (95%) *via* deoxygenated sulfide **18**. Both **16*Z*** and **16*E*** afforded product **19t** as a single isomer. It is suggested that the reductive cyclization of the α,β-unsaturated esters and nitriles proceed by means of nucleophilic attack of a β-carbon radical anion, formed by initial electron transfer from magnesium metal to the activated olefin, on the carbonyl group. The cyclization of the α,β-unsaturated sulfide proceeds by nucleophilic attack of the ketyl on the olefinic double bond.

Introduction

Although reductive cyclizations *via* carbon-centered free radicals are well documented,[1] the use of radical anions other than ketyl has received limited attention. Metalated ketyls derived from the corresponding ketones or aldehydes and low-valent metals such as Sm(II),[2] V(II),[3] Zn,[4] Na,[5] Li,[6] and $(n\text{-Bu})_3SnH$[7] in aprotic solvents have been added to suitable acceptors, for example, α,β-unsaturated esters and nitriles. There are only a few examples in the literature of intramolecular reductive cyclization reactions *via* radical anions other than ketyl. One of the examples is the electroreductive cyclization of ketones and aldehydes tethered to α,β-unsaturated esters and nitriles introduced by Little et al.[8] According to the mechanism proposed by them, the radical anion formed by initial transfer of an electron underwent a rapid reversible cyclization to the closed form of the radical anion. It was implied that the latter was formed from the linear radical anion with the negative charge at the β-carbon atom and the unpaired electron at the α-carbon atom. Subsequent irreversible protonation of the alkoxide, a second electron transfer, and rapid protonation led to the products. However, the radical anion species that underwent cyclization did not seem to be expressed properly[9] when its EPR measurements were compared with those of conjugated ketones reported by House et al.,[10] in which the major spin density was found to be localized on the β-carbon atom. Thus, it seems to be more reasonable to assume that irreversible protonation of the radical anion takes place on the oxygen atom of the ester enolate before cyclization rather than on the cyclized alkoxide. The net result of the electroreductive cyclization pathway looks the same as that of the ketyl pathway; however, reaction pathways A and B (see

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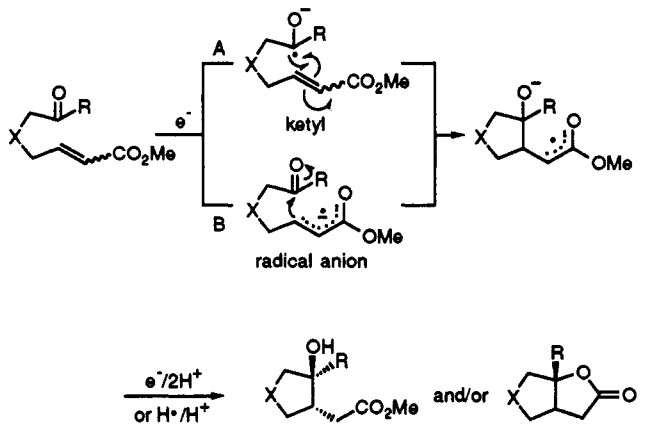
(9) Russell, G. A.; Lokensgard, J. *J. Am. Chem. Soc.* **1967**, *89*, 5059.

(10) (a) Bowers, K. W.; Giese, R. W.; Grimshaw, J.; House, H. O.; Kolodny, N. H.; Kronberger, K.; Roe, D. K. *J. Am. Chem. Soc.* **1970**, *92*, 2783. For a ketyl of enone (tetramethyl heptenone system) the equilibrium for isomerization of the double bond occurred at about −35 °C, whereas below −78 °C it was possible to freeze the original configuration. (b) House, H. O.; Giese, R. W.; Kronberger, K.; Kaplan, J. P.; Simeone, J. F. *J. Am. Chem. Soc.* **1970**, *92*, 2800.

0022-3263/94/1959-1428$04.50/0

Scheme 1



Scheme 1) seem to be quite different in that nucleophilic addition of the ketyl takes place in reversed fashion in the course of cyclization (Scheme 1). This notion was indirectly demonstrated with keto esters where the ketyl radical pathway gave the simple carbonyl reduction product[11] and the radical anion pathway produced the olefin reduction product as a byproduct.[8]

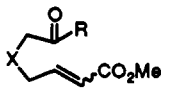
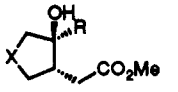
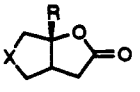
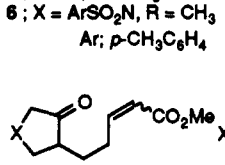
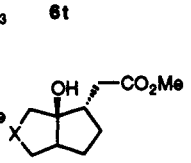
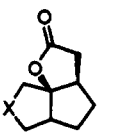
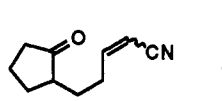
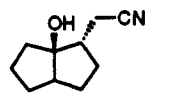
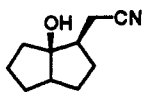
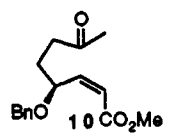
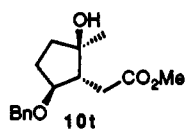
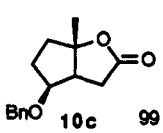
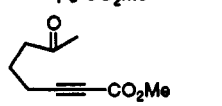
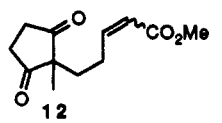
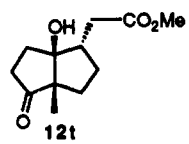
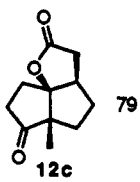
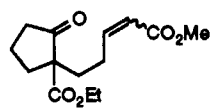
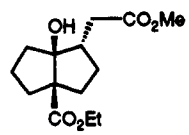
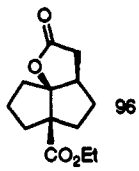
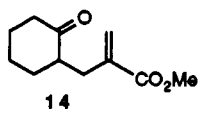
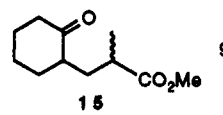
Another example of the radical anion pathway was the unexpected reductive coupling of two α,β-unsaturated nitrile groups placed in proximity to each other; the coupling occurred during an attempt to reduce double bonds selectively with magnesium in methanol.[12] The presence of a radical anion has also been strongly suggested for the magnesium in methanol reduction of α,β-unsaturated esters.[13] Very recently, Angle and Rainier conducted reductive cyclizations using quinone methide as the electron acceptor,[14] and the intermediacy of a quinone methide radical anion was suggested prior to cyclization onto a pendant olefin. We have recently suggested the presence of a radical anion, resembling the one generated from ketones by Sm(II),[15] in the magnesium-promoted reductive cleavage of γ-alkoxy α,β-unsaturated esters and nitriles and β-alkoxy halides.[16] The results discussed above, coupled with the propensity of magnesium in methanol to generate the radical anions of activated olefins, prompted the efforts described below. Herein we report a simple and facile method, which uses magnesium metal in dry methanol, for the intramolecular reductive cyclization of ketones tethered to activated olefins such as α,β-unsaturated esters and nitriles and for the cyclization of ketones, especially cyclopentanone derivatives, tethered to α,β-unsaturated sulfoxides and sulfides *via* a ketyl radical pathway.

Results and Discussion

Various substrates containing a ketone tethered to an activated olefin were reduced by magnesium in dry methanol to give the corresponding cyclized products in excellent yields (97–98%) as shown in Table 1. The cyclization reaction of ketones **1*E***, **7*E***, and **8*E*** tethered to α,β-unsaturated esters proceeded smoothly when the substrates were treated with 3 equiv of magnesium in dry methanol at −23 °C for 3 h. The cyclization gave mixtures of trans and cis isomers[17] in excellent yields along with trace amounts of simple reduction products (<2%). In all cases, trans isomers were predominant, and all cis products lactonized under the reaction conditions.

In order to examine temperature and catalyst effects on the stereoselectivity, *E* and *Z* isomers of **1**, **7**, and **8** were subjected to the same reaction conditions separately.

Table 1. Reductive Cyclization of Ketones Tethered to α,β-Unsaturated Esters and Nitriles with Mg/MeOH

substrate	cyclized product[a]	yield[b,c] (%)	
			
1; X = CH_2, R = CH_3	**1t**	**1c**	98 (4.32 : 1)
2; X = CH_2, R = H	**2t**	**2c**	- *d*
3; X = $(CH_2)_2$, R = CH_3	**3t**	**3c**	81 (0.88 : 1)
4; X = $(CH_2)_2$, R = H	**4t**	**4c**	- *d*
5; X = O, R = CH_3	**5t**	**5c**	13 (2.44 : 1)
6; X = $ArSO_2N$, R = CH_3 Ar; *p*-$CH_3C_6H_4$	**6t**	**6c**	97 (0.74 : 1)
			
7; X = CH_2	**7t**	**7c**	97 (10.1 : 1)
8; X = $(CH_2)_2$	**8t**	**8c**	98 (1.12 : 1)
			
9	**9t**	**9c**	42 (- *e*)
			
10	**10t**	**10c**	99 (3.80 : 1)
	**1t**	**1c**	95 (4.32 : 1)
11			
			79 (5.90 : 1)[f]
12	**12t**	**12c**	
			96 (5.23 : 1)[f]
13	**13t**	**13c**	
			99
14	**15**		

[a] t: trans, c: cis. [b] Isolated yields. [c] Ratios in the parentheses are t/c. [d] Only linear reduction products were obtained. [e] Ratio was not determined. [f] Ratios were determined by ^1H NMR.

(11) (a) Fukuzawa, S. I.; Nakanishi, A.; Fujinami, T.; Sakai, S. *J. Chem. Soc., Perkin Trans. 1* **1988**, 1669. (b) Fukuzawa, S. I.; Iida, M.; Nakanishi, A.; Fujinami, T.; Sakai, S. *J. Chem. Soc., Chem. Commun.* **1987**, 920. (c) Fukuzawa, S. I.; Nakanishi, A.; Fujinami, T.; Sakai, S. *J. Chem. Soc., Chem. Commun.* **1986**, 624. Reaction of ethyl 14-oxopentadec-2-enoate with an excess amount of SmI_2 (4 equiv) did not yield any cyclized product, but instead the simple carbonyl reduction product, ethyl 14-hydroxypentadec-2-enoate, was obtained as a single isolable product.

(12) Osborn, M. E.; Pegues, J. F.; Paquette, L. A. *J. Org. Chem.* **1980**, *45*, 167.

(13) Hudlicky, T.; Sinai-Zingde, G.; Natchus, M. G. *Tetrahedron Lett.* **1987**, *44*, 5287.

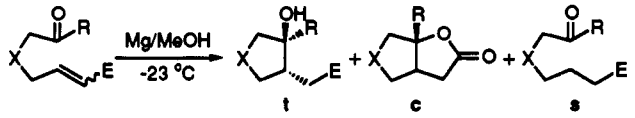
(14) Angle, S. R.; Rainier, J. D. *J. Org. Chem.* **1992**, *57*, 6883.

(15) Molander, G. A.; La Belle, B. E.; Hahn, G. *J. Org. Chem.* **1986**, *51*, 5259.

(16) Pak, C. S.; Lee, E.; Lee, G. H. *J. Org. Chem.* **1993**, *58*, 1523.

(17) Throughout the paper trans and cis were designated by the relationship between the hydroxy group and the functional group appendage.

Table 2. Reductive Cyclization of Ketones Tethered to α,β-Unsaturated Esters with Mg/MeOH System under Various Conditions[a]



E; CO_2Me

substrates	condns	time (h)	yield (t + c, %)	yield (s, %)	ratio (t/c)
1*Z* or 1*E*	−23 °C	3	98	<2	4.32/1
	cat. $HgCl_2$/−23 °C	2	98	<2	4.32/1
	−43 °C	no reaction			
	cat. $HgCl_2$/−43 °C	3	84	16	4.27/1
7*Z* or 7*E*	−23 °C	3	97	<2	10.1/1
	cat. $HgCl_2$/−43 °C	3	91	9	11.0/1
8*Z* or 8*E*	−23 °C	3	98	<2	1.12/1
	cat. $HgCl_2$/−43 °C	3	82	18	1.05/1

[a] t, trans; c, cis; and s, saturated product.

Regardless of the configuration of the double bond, identical product yields and isomer ratios were obtained (Table 2). This result is in sharp contrast with the stereochemical results of ketyl addition to α,β-unsaturated ester groups, in which the geometry of the double bond plays a critical role in determining the stereoselectivity.[3,18] Although the reaction did not occur at −43 °C, addition of a catalytic amount of mercuric chloride at the same temperature initiated[19] the reaction, and the products were obtained in nearly the same isomer ratio as in the −23 °C reaction. Lowering the reaction temperature caused a significant increase in the amount of the product of simple reduction of the olefinic double bond (16–18%), but the stereoselectivity remained the same. Although mercuric chloride played a role in initiating the reaction at −43 °C, its presence at −23 °C did not affect the results at all. When the substrate was not so soluble in methanol, as in the case of **6**, solvent such as dry THF or HMPA could be used as a cosolvent to improve the solubility.

These stereochemical outcomes imply that once the conjugated olefin becomes the corresponding radical anion, the original configuration of double bond is completely lost; that is, the incipient *E* or *Z* radical anion (**21′** and **22′**) must undergo a rapid equilibrium between the *E* and *Z* configurations under the reaction temperature limit. House et al.[10b] noted that reduction of *cis*-enone **21** or *trans*-enone **22** with sodium at −35 °C produced the corresponding radical anion, which underwent rapid equilibrium to form the more stable trans radical anion species **22′** because of the low rotation barrier around the C_α–C_β bond (see Figure 1). However, when the temperature was lowered to −78 °C, the interconversion of **21′** and **22′** was so slow that each radical anion afforded products originating from its original configuration. In the light of the electron transfer mechanism, reductive cyclizations mediated by electrolysis[20] and dissolving metals[21] have been intensively studied with α,β-unsaturated esters and nitriles. In these cases, the formation of a radical anion *via* a reversible electron transfer was proposed as the initial step. Subsequent irreversible protonation, if a proton source was present, afforded the allylic radical, as in the case of α,β-olefinic ketones. Another previously reported example implying the presence of an allylic radical is the formation of a coupling product from the reduction of methyl cinnamate and *p*-methoxycinnamate with aluminum amalgam in an aprotic solvent.[22] On the basis of these precedents, we postulate that the electronic distribution of either the radical anion or the allylic radical generated from the magnesium in methanol reduction of α,β-unsaturated esters is quite close to the distribution observed for electrolysis or dissolving metal reduction. In an attempt to equilibrate the substrate, 1*Z* was subjected to the reaction conditions, and then the reaction mixture was quenched when the reaction had proceeded approximately halfway to completion; however, we could not detect any 1*E* by GC. Since the isomerization of the double bond was controllable at lower temperatures,[10] the reaction was carried out at −78 °C in an effort to improve stereoselectivity; however, the reaction was so sluggish that it was not successful. These results indicate that irreversible, rapid protonation in the presence of excess methanol prohibits radical anion species from undergoing isomerization, as in the case of electrolysis in aqueous acetonitrile.[8b]

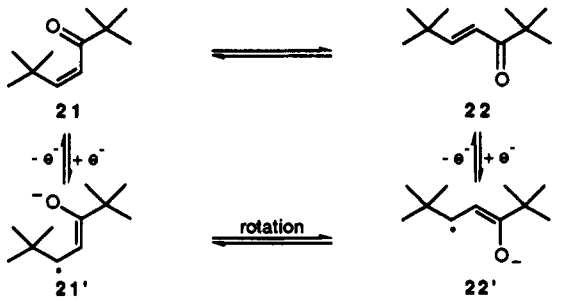


Figure 1.

In order to explain both the identical product isomer ratios for both substrate geometries and the failure to

(18) (a) Enholm, E. J.; Trivellas, A. *Tetrahedron Lett.* **1989**, *30*, 1063. (b) Enholm, E. J.; Satici, H.; Trivellas, A. *J. Org. Chem.* **1989**, *54*, 5841. (c) Enholm, E. J.; Trivellas, A. *J. Am. Chem. Soc.* **1989**, *111*, 6463.

(19) Hydrogen gas should be evolved as the reaction proceeded; otherwise, the reaction was not initiated.

(20) (a) Petrovich, J. P.; Anderson, J. D.; Baizer, M. M. *J. Org. Chem.* **1966**, *31*, 3897. (b) Anderson, J. D.; Baizer, M. M.; Petrovich, J. P. *J. Org. Chem.* **1966**, *31*, 3890. (c) Ingersoll, A. W. *Organic Syntheses*; Wiley: New York, 1944; Collect. Vol. I, p 311. (d) Gourley, R. N.; Grimshaw, J.; Miller, P. G. *J. Chem. Soc., Chem. Commun.* **1970**, 2318. (e) Baizer, M. M. *J. Org. Chem.* **1964**, *29*, 1670. (f) Baizer, M. M. *J. Org. Chem.* **1966**, *31*, 3847. (g) Jones, G. C.; Ledford, T. H. *Tetrahedron Lett.* **1967**, 615.

(21) (a) Coates, R. M.; Shaw, J. E. *J. Org. Chem.* **1970**, *35*, 2597. (b) Coates, R. M.; Shaw, J. E. *J. Org. Chem.* **1970**, *35*, 2601. (c) Zurqiyah, A.; Castro, C. E. *Org. Synth.* **1969**, *49*, 98.

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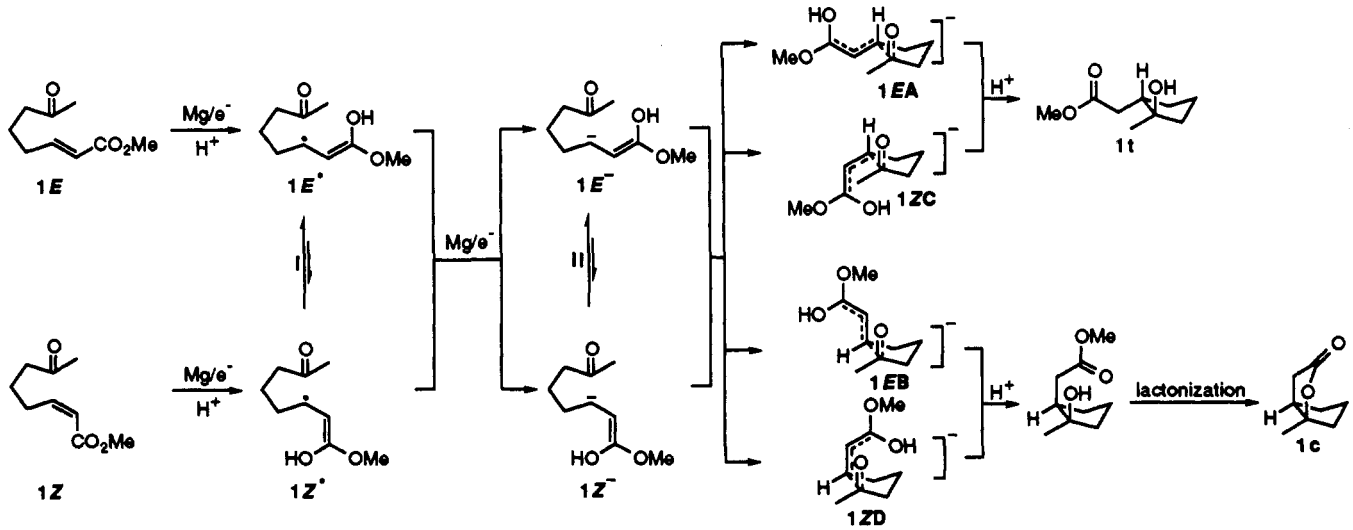
Scheme 2



1*EA*; electronically favorable & sterically unfavorable

1*EB*; electronically unfavorable & sterically favorable

1*ZC*; electronically favorable & sterically unfavorable

1*ZD*; electronically unfavorable & sterically favorable

isolate the equilibrium mixture of the substrate, we propose the mechanistic pathway illustrated in Scheme 2. The rapid equilibrium might occur at either the stage of allylic radical (stage I) or the stage of allylic anion (stage II). Since it is well known that the attack of a carbon-centered radical on a carbonyl group is an energetically unfavorable process[23] and, furthermore, the resulting alkoxide radical undergoes β-fragmentation[24] easily, it must be the allylic anion rather than the allylic radical that attacks the carbonyl group. It is reasonable to assume that by means of the rapid equilibria of geometrically isomeric allylic radicals 1*E*• and 1*Z*• and/or allylic anions 1*E*⁻ and 1*Z*⁻ formed from either isomers of 1, the sterically more favorable *E* allylic anion 1*E*⁻ would be the predominant species. These equilibria would lead to a mixture of the four possible transition state structures (1*EA*, 1*EB*, 1*ZC*, and 1*ZD*) illustrated in Scheme 2. Transition states 1*EA* and 1*ZC*, derived from *E* and *Z* allylic anions 1*E*⁻ and 1*Z*⁻, respectively, would lead to a trans product, whereas transition states 1*EB* and 1*ZD*, from 1*E*⁻ and 1*Z*⁻, would form a cis product, which eventually lactonizes under the reaction conditions. It is highly probable that, since the electronic repulsion between the C=O electron and the axial anion moiety C_β–C_α–C–O outweighs the nonbonded steric interaction between the CH_3 of acyl group and the C_α–C_β bond, transition states 1*EA* and 1*ZC* would be preferred relative to transition states 1*EB* and 1*ZD*.[18a,20] Because of the identical results obtained from *E* and *Z* isomers, it can be deduced that each isomer is converted to the same equilibrium mixture and that the favorable configuration of the allylic anion must be the thermodynamically favorable *E* form, formed through the fast rotation of the C_α–C_β bond of the α,β-unsaturated ester.

The higher trans stereoselectivities in the formations of five-membered rings from **5**, **7**, and **10–13** can also be explained in the same way. However, the poor stereoselectivity in the formations of the six-membered ring from **3** (47% trans) can be explained by the fact that in the six-membered ring transition state 1,3-diaxial interactions

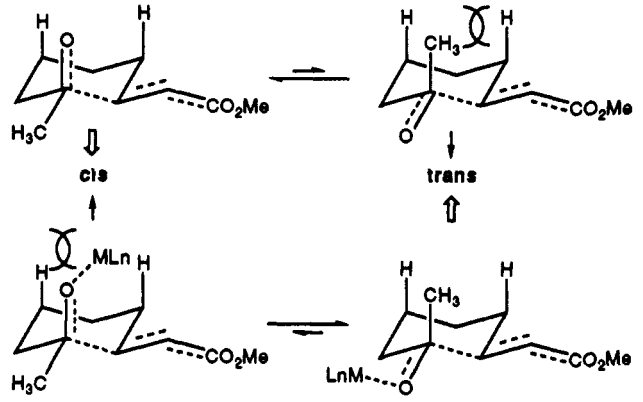


Figure 2.

become important and the electronic repulsion between C=O and C_β–C_α–C–O diminishes because of the proper 1,2-dihedral angle. According to Enholm's explanation,[18a] when electronic and steric effects are considered in five-membered ring transition states the relative stereochemistry between the (carbomethoxy)methyl group and the hydroxy group is controlled by the electronic effect, and the most favorable of the four possible transition states is 1*EA*, which leads to the trans product. In the six-membered ring transition state, however, the steric effect is the major factor controlling the relative stereochemistry of the product. In the six-membered ring transition state, which gives the cis major product, the steric repulsion between the 1,3-diaxial hydrogens and the methyl group seems to slightly exceed that between the 1,3-diaxial hydrogens and the carbonyl group; these 1,3-diaxial interactions are absent in the five-membered ring transition state. On the other hand, the steric repulsion between the carbonyl oxygen atom coordinated with metal and the 1,3-diaxial hydrogen atoms becomes an important factor in controlling stereoselectivity of the ketyl radical pathway (see Figure 2), and the trans isomer is the predominant product.

Thus, it is plausible to assume that in the magnesium in methanol reduction of cyclohexanone the critical factor determining the equilibrium position would be the difference in the 1,3-diaxial interactions of the C=O and

(23) (a) Knoll, H. *Z. Chem.* **1982**, *22*, 245. (b) Flies, F.; Lalande, R.; Maillard, B. *Tetrahedron Lett.* **1976**, 439.

(24) Brun, P.; Waegell, B. In *Reactive Intermediates*; Abramovitch, R. A., Ed.; Plenum Press: New York, 1983; Vol. 3, p 392.

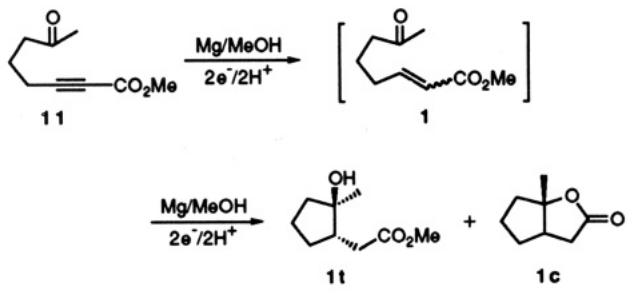


Figure 3.

methyl groups. The predominant formation of trans products from cyclopentanones **7**, **12**, and **13** can be rationalized in this way, but the cyclopentanones differ from the alicylic ketones in that the steric constraints of the cyclopentanone moiety should shift the equilibrium of the allylic anion far more toward the *E* configuration before the cyclization. Thus, the major contribution to the trans product must have come from transition state **1*E*A** since the contribution from transition state **1*Z*C** would be considerably reduced by the increased steric repulsion exerted by the cyclopentanone moiety.[18a] In contrast to the ketyl pathway, the radical anion pathway, wherein the thermodynamically favorable *E* isomer is equilibrated with the thermodynamically unfavorable *Z* isomer, gives rise to the electronically favorable and sterically unfavorable transition state **1*Z*C** and the electronically unfavorable and sterically favorable transition state **1*Z*D** to afford the trans and cis cyclized products, respectively. Thus, the stereoselectivity is higher in the ketyl pathway than in the radical anion pathway. Amplification of the steric constraint caused by the cyclohexanone moiety of **8** appears to be marginal (53% trans) compared to that caused by the cyclopentanone moiety of **7** (91% trans). In marked contrast, when coordination of the C=O group of the cyclohexanone moiety with a metal cation becomes possible, as in the ketyl pathway mediated by SmI_2,[18a] the strong steric repulsion of coordinated C=O cluster led to a predominantly trans product. The transition state of the radical anion pathway seems to be quite similar to that of the ketyl pathway, except for the coordination of the metal cation to the carbonyl oxygen atom. In cyclopentanone derivatives, the steric constraints of the cyclopentanone ring amplify the electronically favorable trans arrangement (**1*E*A**). Here also, the only determining factor is the steric environment of the carbanionic center that undergoes nucleophilic attack of the carbonyl group, as has been described for the electroreductive cyclization.[8] Since the cyclization of acetylenic ketone **11** resulted in the same product ratio as that of **1**, it might be that cyclization occurs after the reduction of the triple bond to a double bond *via* the same intermediate as in the case of **1**.[25] However, the possibility of reduction after the cyclization of the vinylic radical anion species cannot be excluded at the moment (see Figure 3).

For cyclic ketones **7**, **8**, **12**, and **13** the stereoselectivity changes dramatically depending on the ring size. Stereoselectivities of cyclopentanone derivatives **7**, **12**, and **13** are much higher than that of cyclohexanone derivative **8** for the reasons described above. Although the stereochemistry of the ring juncture could not be determined for **8t** and **8c**, the relative stereochemistry between the

(25) Shim, S. C.; Hwang, J.-T.; Kang, H.-Y.; Chang, M. H. *Tetrahedron Lett.* **1990**, *31*, 4765.

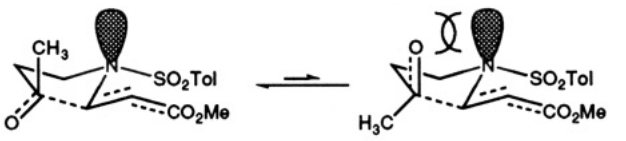


Figure 4.

(carbomethoxy)methyl and hydroxy groups was elucidated from the ^1H NMR peak for the α-methylene proton of lactone **8c**.[26] 5-Aza ketone **6** provided cyclized products in high yield (97%) but with poor stereoselectivity. In this case, dry THF was used as cosolvent because of substrate dissolved poorly in dry methanol. It is difficult to explain the poor stereoselectivity of aza ketone **6**, but it seems that a stereoelectronic interaction between the carbonyl oxygen atom and the nonbonding electron pair on nitrogen influenced on the transition state (see Figure 4).

In comparison with the stereoselectivity of the electroreductive cyclization reported by Little et al., the stereoselectivity for the same substrates was higher compared to that for the isomerization conditions, wherein malonate was used as the proton source, but slightly lower than that from the nonisomerization conditions, wherein water was used as the proton source. Except for substrate **5**, all of the 7-keto esters provided isomeric cyclized products in very high yields (95–99%) with only trace amounts (<2%) of simple saturated products derived from the reduction of α,β-olefinic bonds.[13] However, 8-keto ester **3** gave cyclized products **3t** and **3c** in 81% yield with a trans/cis ratio of 0.88:1 and 13% of the simple reduction product. Under the same reaction conditions, keto nitrile **9** gave 42% of cyclized products **9t** and **9c**, of which the isomer ratio could not be determined because of separation difficulties, 29% of the product of reduction of the olefinic double bond, and 27% of the corresponding saturated cyclopentanol. The product mixture indicates that protonation and cyclization of the carbanion species occurred competatively. Consequently, about half of the double bond reduction product was further reduced, probably *via* a ketyl intermediate, with residual magnesium. The possibility of ketyl formation before the reduction of the α,β-unsaturated nitrile group was excluded since cyclopentanol with an α,β-unsaturated nitrile group was not detected. In addition, according to the results reported by Hudlicky et al.,[13] it is highly unlikely that an isolated carbonyl group would be reduced prior to an α,β-unsaturated nitrile group. Even though our results look contradictory to theirs, in which the isolated ketone was inert in the presence of the α,β-unsaturated ester group, it is apparent that, in this case of the subsequently described cyclization of a vinyl sulfide, the formation of a cyclopentanone ketyl is possible. The formation of a cyclopentanone ketyl was further supported by the fact that isolated saturated keto nitrile **9s** (from **9**) and keto ester **7s** (from **7**) were reduced to the corresponding alcohols under the same reaction conditions.[27] The low yield of cyclized products **5t** and **5c** (13%) from oxa ketone **5** is attributed to the facile cleavage of the C_4–O bond. This cleavage produces methyl 3-butenoate as the major product. The formation of methyl 3-butenoate was confirmed by GC in comparison with an authentic sample

(26) Although in ref 18a stereochemistry of the ring juncture was expressed as the cis configuration without spectral data, it was not possible to assign the stereochemistry by 500-MHz ^1H NMR. However, ^1H and ^{13}C NMR spectra of **8t** and **8c** were identical with the reported value in ref 8b.

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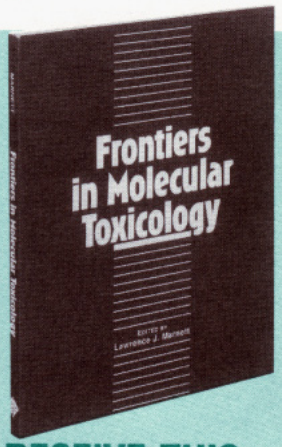

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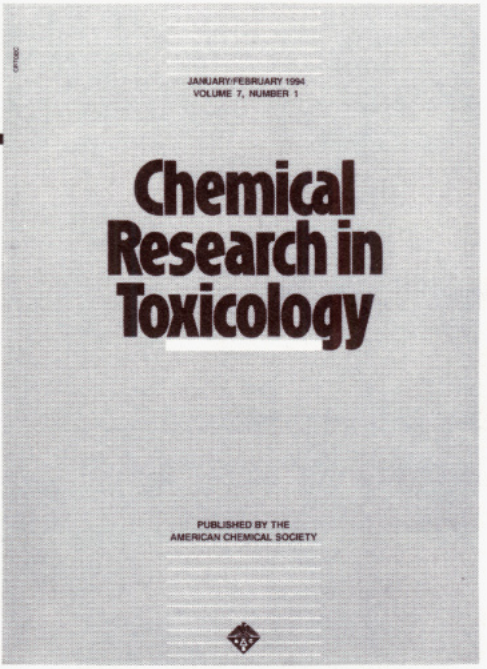

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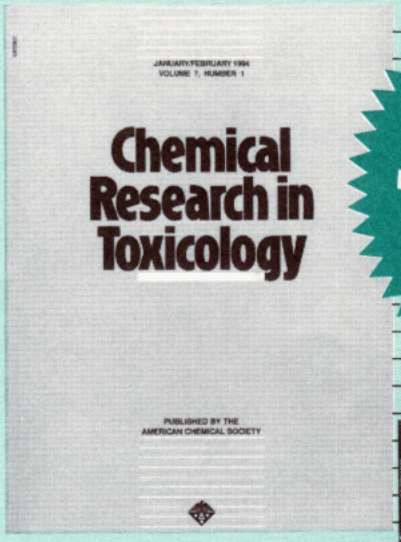

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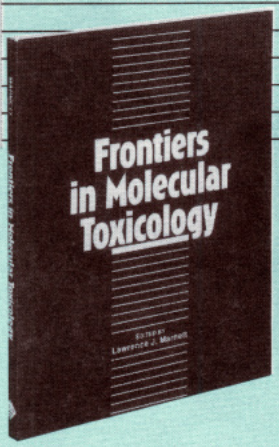

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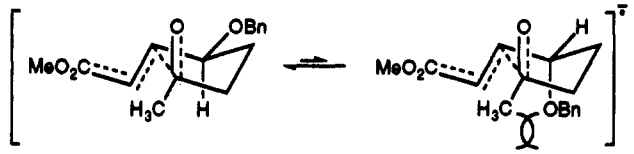


Figure 5.

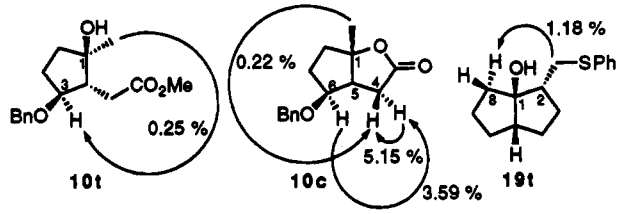


Figure 6.

prepared from vinylacetic acid and diazomethane. Cleavage of the alkoxy group indicates that carbanionic rather than radical character must have developed at the β-carbon.[28] The cleavage was not unexpected since our previous results[16] indicated that, once a carbanion formed, β-elimination proceeded quickly. In contrast to **5**, 4-(benzyloxy) ketone **10** gave cyclized products **10t** and **10c** in quantitative yield without any trace of cleavage product. The relative stereochemistry of **10t** and **10c** was established unequivocally by 2-D COSY experiments and 1-D NOE difference spectroscopy. Upon irradiation of the C_1-CH_3 resonance at 1.18 ppm, a 0.25% NOE at H-3α of **10t** was observed, and 0.22, 3.59, and 5.15% NOEs at H-5β, H-4α, and H-5β of **10c** were observed when the C_1-CH_3, H-6α, and H-4β resonances at 1.55, 3.76, and 2.93 ppm, respectively, were irradiated.[29] Examination of a Dreiding model revealed that the dramatic change in the amount of β-cleavage between these two compounds, which both have an alkoxy group at the same γ-position, must be due to the fact that, in the transition state of cyclization, the carbanion lobe of **5** is aligned with the C–O bond in the *syn*-periplanar position in such a way that severe electrostatic repulsion between the nonbonding electrons on the oxygen atom and the carbanion causes these two groups to swing into the *anti*-periplanar position, which makes E2-type elimination occur easily. In contrast, the benzyloxy group of **10** is at a 120° angle with the carbanion lobe in the transition state, and this dihedral angle is unfavorable for E2-type elimination. The trans relationships between the (carbomethoxy)methyl appendage and the benzyloxy group of **10t** and **10c** must stem from the most favorable transition state, wherein the bulky benzyloxy group is aligned in an equatorial position (see Figure 5).

Cyclopentanedione derivative **12** was cyclized at −43 °C to afford an inseparable mixture of **12t** and **12c** in 79% yield without any trace of simple reduction product. When the reaction temperature was raised to −23 °C, the yield of cyclized products was significantly decreased (40–50%), and a significant amount of intractable residue, probably the corresponding alcohols from futher reduction of the remaining carbonyl group, was obtained. The isomer ratio 5.90:1 of **12t** and **12c** was determined by integration of the OCH_3 proton (δ 3.71, singlet) and one of the characteristic α-methylene protons of the γ-lactone (δ 3.01, doublet of doublet) from the mixture of isomers. Even though the stereoselectivity of the Mg/MeOH reaction was slightly lower (81%) than that of the Zn–TMSCl-promoted cyclization (100%) the isolated yield of the cyclized products from **13** was much higher (96%) compared to that of Zn–TMSCl-mediated cyclization (76%).[4] Under the reaction conditions, transesterification did not occur.[13,30] In contrast to the *endo*-olefinic ester, *exo*-olefinic ester **14** underwent only the reduction of the olefinic bond to afford diastereomeric mixture **15** in quantitative yield. This result may be due to the relative stabilities of primary and secondary carbanions, protonation of which is much faster than cyclization for **14** compared to *endo*-analog **8**. In addition, the C–C bond distance the β-carbon and the carbonyl carbon is larger for **14** than for **8** in the transition state of cyclization. Instead of the expected cyclized products, aldehydes **2** and **4** provided two kinds of saturated, alicyclic reduction products: (1) the product of simple reduction of the olefinic double bond (47% for **2** and 48% for **4**) and (2) the fully reduced saturated alcohol (31% and 29% yields, respectively). It seems that the equilibrium between the free aldehyde and a hemiacetal in methanol solvent prohibits cyclization.[31] Thus, the olefinic double bond of the predominant hemiacetal species was reduced to give the corresponding saturated aldehyde after workup; after reduction of the olefinic double bond of the free aldehyde form, the aldehyde group was further reduced to afford the corresponding saturated alcohol.

When keto α,β-unsaturated sulfoxide **16** was used as an electron acceptor with 3 equiv of magnesium in dry methanol at −23 °C in the presence of a catalytic amount of mercuric chloride, only a small amount of the expected cyclized product was formed. Surprisingly, keto sulfoxide **16** (*Z* and *E*) underwent mostly deoxygenation to give the corresponding sulfide **18** (*Z* and *E*) in 85% yield along with cyclized sulfide **19t** in 9% yield. A mixture of *Z* and *E* isomeric keto sulfones **17*Z*** and **17*E*** was desulfonylated to give cleavage product **20** in 54% yield under the same reaction conditions as shown in Scheme 3.

Deoxygeneration of isomeric keto sulfoxides **16*E*** or **16*Z*** proceeded without isomerization of the olefinic double bond so that each of the isomeric keto sulfoxides gave a deoxygenated product retaining its original double bond configuration (**18*E*** or **18*Z***, respectively). From these results, it seems that, since the initially transferred electron is localized on the sulfoxide unit, the isomerization of the double bond through delocalization is not possible, and the subsequent transfer of an additional electron and deoxygenation resulted in sulfide **18**.[32] Similar deoxygenation of 1-alkenyl sulfoxides with ethylmagnesium bromide/cuprous iodide has been reported by Posner et

(27) The saturated keto ester **7s** and keto nitrile **9s** derived from **7** and **9** were subjected to the reaction conditions (0.12 mmol of substrate, 7 mL of MeOH, catalytic amount of $HgCl_2$, and 10 equiv of Mg at −23 °C). After 4 h, diastereomeric mixtures of cyclopentanols were obtained in 63% and 59% yields, respectively. Starting materials **7s** and **9s** were recovered in 36% ans 38% yields, respectively. Under the same reaction conditions, however, saturated keto esters **1s** and **14s** derived from **1** and **14** gave reduced products in trace amounts (<2%) and were recovered quantitatively.

(28) For α,β-epoxy radical C–O bond cleavage is not a favorable process [(a) Dickinson, J. M.; Murphy, J. A.; Patterson, C. W.; Wooster, N. F. *J. Chem. Soc., Perkin Trans. 1* **1990**, 1179], but contradictory results were also reported: (b) Hasegawa, E.; Ishiyama, K.; Hraguchi, T.; Shimizu, T. *J. Chem. Soc., Chem. Commun.* **1990**, 550.

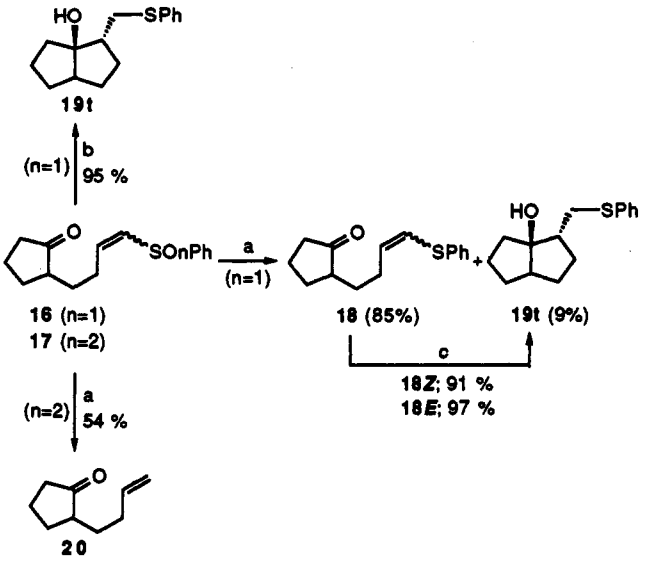
(29) NOE correlations and the numbering of **10t**, **10c**, and **19t** are illustrated in Figure 6.

(30) (a) Wei, Z.-Y.; Knaus, E. E. *Tetrahedron Lett.* **1993**, *34*, 4439. (b) Youn, I. K.; Pak, C. S. *Bull. Korean Chem. Soc.* **1987**, *8*, 434.

(31) Schmitz, E.; Eichhorn, I. In *The Chemistry of the Ether Linkage*; Patai, S., Ed.; Wiley: New York, 1967; Chapter 7, pp 311–319. Within 10 min the aldehydic proton peak completely disappeared at room temperature, while integration of the vinyl protons showed that they were still intact [^{1}H NMR (Mg/CD_3OD)]. Exchange of the ester group was also noticed by a disappearance of the $-OCH_3$ peak.

(32) (a) House, H. O. *Acc. Chem. Res.* **1976**, *9*, 59. (b) House, H. O. *Proc. Robert A. Welch Found. Conf. Chem. Res.* **1973**, *17*, 101.

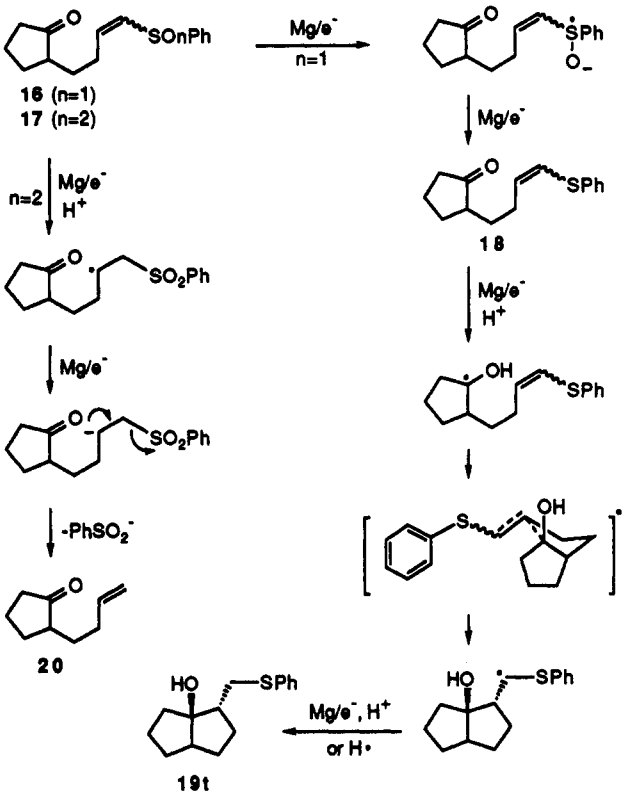
Scheme 3[a]



[a] Key: (a) 3 equiv of Mg/cat. $HgCl_2$, MeOH, −23 °C, 2 h; (b) 15 equiv of Mg/cat. $HgCl_2$, MeOH, −23 °C, 3 h; (c) 10 equiv of Mg/cat. $HgCl_2$, MeOH, −23 °C, 3 h.

al.[33] Surprisingly, the substrate's double-bond geometry did not affect the diastereoselectivity; the same cyclized product, **19t**, was obtained. This result contrasts with that of the SmI_2-mediated cyclization where a dramatic change in diastereoselectivity was observed depending on the substrate geometry. Interestingly, it was noticed that the yield of cyclized sulfide **19t** increased remarkably at the expense of deoxygenated product **18** as the amount of magnesium metal and the reaction time increased. When keto sulfoxide **16*Z*** and **16*E*** were treated with excess amount of magnesium metal (15 equiv), only cyclized sulfide **19t** was obtained in 95% yield as a single stereoisomer. The structure of **19t** was elucidated by 2-D COSY and 1-D NOE difference spectra. The configurational relationship between the hydroxy group and the (phenylthio)methyl group was determined as trans by an NOE experiment: a 1.18% NOE of H-8α was observed upon irradiation of diastereotopic H-9.[29] Regardless of substrate configuration, both **16*Z*** and **16*E*** afforded **19t** as a single isomer. The anticipated cyclized sulfoxide resulting from the direct cyclization of keto sulfoxide **16** was not formed; however, we were able to cyclize the isolated keto sulfides **18*E*** and **18*Z*** with 10 equiv of magnesium metal to afford cyclized sulfide **19t** in 97% and 91% yields, respectively. On the basis of these results, it is obvious that the cyclization of **16** occurs *via* keto sulfide **18** rather than by direct reductive cyclization of sulfoxide **16**. Consequently, by controlling the amount of magnesium metal added, we can perform either reduction or cyclization of sulfoxides conveniently under mild conditions.[34] In an effort to investigate the mechanistic pathway for ketyl generation, the possibility of the phenyl vinyl sulfide group of **18** accepting an electron was eliminated. Simple 1-alkenyl phenyl sulfide was inert to the same reaction conditions, even with excess magnesium in the presence of mercuric chloride.[35] This result reveals that an electron is transferred from magnesium metal to the carbonyl group of **18** rather than to the phenyl vinyl sulfide group. This electron transfer generates a ketyl radical, which undergoes nucleophilic attack by the olefinic double bond. The mechanism is similar to that of the SmI_2-mediated cyclization of ketones tethered to activated olefins and to the pinacol-type reaction of carbonyl compounds.[36] Other evidences for ketyl formation under the same reaction conditions was also obtained from the reduction of aldehydes **2** and **4** and keto nitrile **9**, in which alcohols were believed to be obtained from ketyl intermediates as minor products, as is the case for the reduction of carbonyl compounds with metals[37] or electronically.[38] It is clear that the cyclization of keto sulfoxide **16** proceeds *via* keto sulfide **18** as depicted in Scheme 4.

Scheme 4



The desulfonylation reaction mechanism may depend upon the type of substrate. Consequently, desulfonylation of keto sulfone **17** proceeds through the heterolytic β-cleavage of the β-sulfonyl carbanion derived from the one-electron transfer to the β-sulfonyl carbon radical, which resulted from one-electron transfer to the α,β-unsaturated sulfone and subsequent proton transfer, to give cleavage alkene **20** as described above. From the results of the previously reported desulfonylation mediated by SmI_2 of alkyl imidazolyl sulfone,[39] homolytic cleavage

(33) Posner, G. H.; Tang, P.-W. *J. Org. Chem.* **1978**, *43*, 4131.

(34) Various phenyl sulfoxides were easily reduced to the corresponding sulfide with magnesium metal (6 equiv) at −43 °C in quantitative yields. The paper for these results is in press (Lee, G. H.; Choi, E. B.; Lee, E.; Pak, C. S. *Tetrahedron Lett.*).

(35) Phenyl 4-phenyl-1-butenyl sulfide subjected to the same reaction condition with excess magnesium (>10 equiv) was recovered completely.

(36) (a) Corey, E. J.; Danheiser, R. L.; Chandrasekaran, S. *J. Org. Chem.* **1976**, *41*, 260. (b) Vigevani, A.; Pasqualucci, R.; Gallo, G. G.; Pifferi, G. *Tetrahedron* **1969**, *25*, 573. (c) Gourley, R. N.; Grimshaw, J. *J. Chem. Soc., Chem. Commun.* **1968**, 2388.

(37) (a) Wenkert, E.; Yoder, J. E. *J. Org. Chem.* **1970**, *35*, 2986. (b) Stocker, J. H.; Jenevein, R. M. *J. Org. Chem.* **1969**, *34*, 2807. (c) Huffman, J. W.; Charles, J. T. *J. Am. Chem. Soc.* **1968**, *90*, 6486. (d) Coulombeau, A.; Rassat, A. *J. Chem. Soc., Chem. Commun.* **1968**, *24*, 1587. (e) Greenwood, J. M.; Qureshi, I. H.; Sutherland, J. K. *J. Chem. Soc.* **1965**, 3154. (f) House, H. O.; Muller, H. C.; Pitt, C. G.; Wickham, P. P. *J. Org. Chem.* **1963**, *28*, 2407. (g) Beringer, F. M.; Galton, S. A.; Huang, S. J. *Tetrahedron* **1963**, *19*, 809.

(38) (a) Kabasakalian, P.; McGlotten, J.; Basch, A.; Yudis, M. D. *J. Org. Chem.* **1961**, *26*, 1738. (b) Mandell, L.; Powers, R. M.; Day, R. A., Jr. *J. Am. Chem. Soc.* **1958**, *80*, 5824.

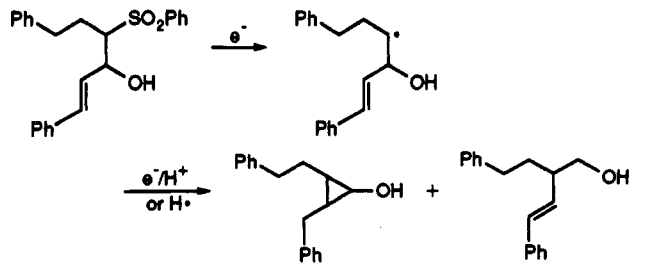


Figure 7.

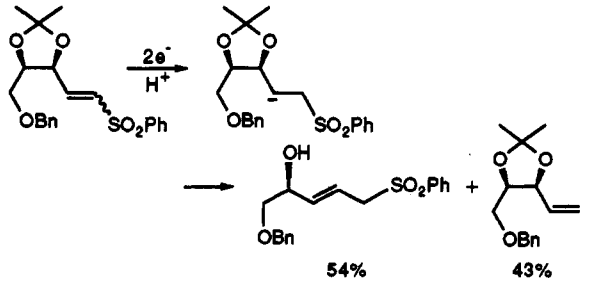


Figure 8.

of the radical anion was suggested by the isolation of a product stemming from radical species after extrusion of the sulfinate. Recently, desulfonylations of alkyl phenyl sulfones with magnesium in ethanol were reported; these desulfonylations imply homolytic cleavage of the carbon sulfur bond.[40,41] In the case of α,β-unsaturated sulfone, however, conclusive evidence for β-cleavage was obtained from product analysis of the reductive cleavage of dioxolane tethered to an α,β-unsaturated phenyl sulfone, in which a mixture of β-cleavage, C–O, and C–S products was obtained.[42] Combining these results allows us to conclude that desulfonylation of alkyl phenyl sulfones proceeds *via* the homolytic cleavage of the anion radical and that desulfonylation of α,β-unsaturated phenyl sulfones proceeds via heterolytic β-cleavage of the β-sulfonyl carbanion. Putting together all the results described above, we can state that an approximate order for electron-accepting ability from magnesium is C=CCO$_2$R, C=CCN, C=CSO$_2$Ph, C=CSOPh > C=O (cyclopentanone, aliphatic aldehyde > cyclohexanone, aliphatic ketone) ≫ C=CSPh.

In conclusion, this methodology provides an efficient, facile, and simple reductive cyclization of ketones tethered to activated olefins such as α,β-unsaturated esters and nitriles using magnesium powder in dry methanol in the presence of mercuric chloride as the selective electron transfer reagent. This method is a complementary to conventional ketyl type cyclization. This method is striking in that highly diastereoselective cyclization could be achieved with either an α,β-unsaturated sulfide or a sulfoxide. Further studies on the improvement of the stereoselectivity and the diversity of reactive electron acceptor groups are underway.

(39) Kende, A. S.; Mendoza, J. S. *Tetrahedron Lett.* **1990**, *31*, 7105.

(40) Desulfonylation of various benzenesulfones was easily performed with magnesium metal under the similar reaction condition. Lee, G. H.; Choi, E. B.; Lee, E.; Pak, C. S. *Tetrahedron Lett.* **1993**, *34*, 4541.

(41) In an attempt to demonstrate single electron transfer mechanism desulfonylation of (*E*)-1,6-diphenyl-4-(phenylsulfonyl)-1-hexen-3-ol was carried out to provide the homoallylic radical which in turn was either cyclized to form cyclopropanol *via* a 3-*exo*-*trig* mechanism or cleaved to the isomeric alcohol as in Figure 7.

(42) We have observed a mixture of β-cleavage products by treating dioxolane tethered to α,β-unsaturated phenyl sulfone with magnesium (3 equiv) in methanol at −43 °C in the presence of mercuric chloride as in Figure 8.

Experimental Section

General. Melting points were determined on a Thomas-Hoover capillary apparatus and are uncorrected. Infrared spectra were obtained on a Shimadzu IR-435 spectrophotometer. ^{1}H and ^{13}C NMR spectra were recorded using JEOL PMX60, Bruker AM-300, and AMX-500 NMR spectrometers, unless otherwise specified, in $CDCl_3$ solution using tetramethylsilane as internal standard. Mass spectra were obtained on a Shimadzu GCMS-QP1000 mass spectrometer. Microanalyses were performed in KRICT on a Perkin-Elmer 240C instrument. GC analyses were performed on a Schimadzu GC-8A flame ionization detector gas chromatograph fitted with a 1-m × 1/8-in. column (5% Dexil 300 on Gas Chrom W, 100–120 mesh) working in the range 50–230 °C (5–20 deg min^{-1}), with nitrogen as carrier gas, and the injector and detector temperature being 230 °C. Flash column chromatography was performed with Merck Kieselgel 60 (230–400 mesh ASTM) silica. Analytical thin-layer chromatography was performed on precoated silica gel plates (0.25-mm 60 F-254 E. Merck). All the reagent-grade chemicals, purchased from Aldrich, Fluka, Merck, and TCI, were used without further purification. All the organic solvents were obtained from Tedia, Oriental, Duksan, and Jin Chemical Co. and distilled prior to use. Methanol was dried over magnesium turnings, and THF was dried over sodium benzophenone prior to use. Triethylamine, methylene chloride, and dimethyl sulfoxide were distilled from calcium hydride. Magnesium, purchased from Aldrich (powder, −50 mesh, 99+%), was used without any special activation.

Compounds **1**, **2**, **4**, and **8**,[3b] and **3**[11a,b] were prepared using the known procedures.

Preparation of Methyl (*Z*)- and (*E*)-4-[(2-Oxopropyl)oxy]-2-butenoate (5*Z* and 5*E*). Preparation of 2-[(2-Propenyl)-oxy]ethanol. To a stirred mixture of ethylene glycol (12.41 g, 0.2 mol) and KOH (3.37 g, 60.0 mmol) in DMSO (50 mL) and water (10 mL) was added dropwise a solution of allyl bromide (6.05 g, 50.0 mmol) in DMSO (20 mL) over 30 min at 0 °C. After 1 h, the reaction mixture was allowed to warm to room temperature and stirred for an additional 5 h. The reaction mixture was diluted with ether (150 mL) and water (100 mL). The organic layer was separated, and the aqueous layer was extracted with ether (100 mL × 3). The combined organic layer was washed with brine (50 mL), dried ($MgSO_4$), filtered, and then concentrated *in vacuo* to afford a pale yellow oil. Flash column chromatography (SiO_2, hexane/ether (1/1)) gave the product (3.88 g, 86%) as a colorless oil: TLC R_f 0.27 (hexane/ether (1/1)); ^{1}H NMR (60 MHz) δ 5.53–6.37 (m, 1 H, CH=), 5.00–5.53 (m, 2 H, =CH$_2$), 3.87–4.23 (m, 2 H, OCH$_2$), 3.36–3.87 (m, 4 H, OCH$_2$CH$_2$O), 2.93 (br s, 1 H, OH); IR (neat) 3310 (OH), 3063, 2834, 1633 (C=C), 1338, 1095, 1055, 989, 921, 881 cm^{-1}; MS *m/e* (rel intensity) 89 (M$^+$ − 1, 1.4), 75 (9.6), 73 (74.2), 57 (100), 55 (29.8), 45 (78.1), 41 (35.4). Anal. Calcd for $C_5H_{10}O_2$: C, 58.80; H, 9.87. Found: C, 58.85; H, 9.81.

Preparation of Methyl (*Z*)- and (*E*)-4-[(2-Propenyl)oxy]-2-butenoate. To a stirred solution of oxalyl chloride (5.49 g, 44.0 mmol) in dry CH_2Cl_2 (90 mL) was added dropwise a solution of DMSO (6.8 mL, 88.0 mmol) in dry CH_2Cl_2 (20 mL) at −78 °C over 5 min. After 5 min, a solution of 2-[(2-propenyl)oxy]ethanol (3.61 g, 40.0 mmol) in dry CH_2Cl_2 (20 mL) was added within 5 min, and the stirring was continued for an additional 15 min. Dry triethylamine (28 mL, 200 mmol) was added, and the reaction mixture was stirred for 5 min and then allowed to warm to room temperature. After 5 min methyl (triphenylphosphoranylidene)-acetate (18.40 g, 55.0 mmol) was added, and the reaction mixture was refluxed for 30 min. The reaction mixture was cooled and concentrated *in vacuo* to afford a sticky material. The residue was diluted with ether (60 mL), the insoluble white solid was filtered, and then the filtrate was concentrated *in vacuo* to afford a pale brown oil as a mixture of *Z* and *E* isomers, which was purified by flash column chromatography (SiO_2, hexane/EtOAc, (4:1)) to give a mixture of *Z* and *E* isomers (6.01 g, 96%, *Z*/*E* = 1/3 was determined by ^{1}H NMR) as a colorless oil. Analytical samples of *Z* and *E* isomers were obtained by flash column chromatography (SiO_2, hexane/EtOAc (5/1)) of a small portion of the *Z* and *E* mixture.

***Z* isomer**: TLC R_f 0.61 (hexane/EtOAc, (5/1)); ^{1}H NMR (300 MHz) δ 6.41 (dt, J = 11.7, 4.9 Hz, 1 H, H-3), 5.93 (ddt, J = 17.2, 11.3, 5.6 Hz, 1 H, –CH=), 5.84 (dt, J = 11.7, 2.5 Hz, 1 H, H-2),

5.30 (dq, J = 17.2, ~1.6 Hz, 1 H, =CH), 5.21 (dq, J = 10.4, ~1.3 Hz, 1 H, =CH), 4.59 (dd, J = 4.9, 2.5 Hz, 2 H, H-4), 4.02 (dt, J = 5.6, 1.4 Hz, 2 H, OCH_2), 3.72 (s, 3 H, OCH_3); ^{13}C NMR (75.4 MHz) δ 166.38, 148.58, 134.31, 118.98, 117.31, 71.66, 68.23, 51.28; IR (neat) 3051, 2910, 1713 (CO), 1637 (C=C), 1426, 1398, 1215, 1181, 1086, 988, 922, 809, 733 cm^{-1}; MS m/e (rel intensity) 157 (M^+ + 1, 5.4), 125 (11.5), 115 (20.2), 99 (100), 85 (10.3), 83 (31.0), 71 (19.7), 68 (14.7), 55 (48.0), 41 (89.4). Anal. Calcd for $C_8H_{12}O_3$: C, 61.52; H, 7.74. Found: C, 61.49; H, 7.70.

***E* isomer**: TLC R_f 0.53 (hexane/EtOAc (5/1)); ^1H NMR (300 MHz) δ 6.97 (dt, J = 15.8, 4.2 Hz, 1 H, H-3), 6.10 (dt, J = 15.8, 2.0 Hz, 1 H, H-2), 5.91 (ddt, J = 17.2, 10.5, 5.5 Hz, 1 H, -CH=), 5.30 (dq, J = 17.2, ~1.7 Hz, 1 H, =CH), 5.21 (dq, J = 10.5, ~1.4 Hz, 1 H, =CH), 4.15 (dd, J = 4.2, 2.0 Hz, 2 H, H-4), 4.03 (dt, J = 5.5, 1.4 Hz, 2 H, OCH_2), 3.74 (s, 3 H, OCH_3); ^{13}C NMR (75.4 MHz) δ 166.52, 144.45, 134.03, 120.61, 117.10, 71.49, 68.35, 51.34; IR (neat) 3052, 2921, 2823, 1713 (CO), 1654 (C=C), 1425, 1339, 1257, 1162, 1023, 961, 920, 831, 742 cm^{-1}; MS m/e (rel intensity) 158 (M^+ + 2, 5.3), 157 (M^+ + 1, 42.3), 156 (M^+, 7.3), 127 (14.8), 125 (28.7), 115 (10.6), 99 (100), 85 (19.0), 71 (50.4), 68 (22.7), 55 (41.4), 41 (83.0). Anal. Calcd for $C_8H_{12}O_3$: C, 61.52; H, 7.74. Found: C, 61.56; H, 7.69.

Preparation of 5*Z* and 5*E*. A mixture of methyl 4-[(2-propenyl)oxy]-2-butenoate (5.47 g, 35.0 mmol), cuprous chloride (0.47 g, 3.5 mmol), and palladium chloride (0.27 g, 1.5 mmol) in DMF–H_2O (50:7, 57 mL) was stirred for 2 days under oxygen. The reaction mixture was diluted with ether (200 mL) and water (100 mL). The organic layers were separated, and the aqueous layer was extracted with ether (100 mL). The combined organic layer was washed with brine, dried ($MgSO_4$), filtered, and then concentrated *in vacuo* to afford a pale brown oil as a mixture of *Z* and *E* isomers. Flash column chromatography (SiO_2, hexane/EtOAc (3/1)) gave **5*Z*** (0.25 g, 4%) and **5*E*** (2.88 g, 48%) as colorless oils.

5*Z*: TLC R_f 0.32 (hexane/EtOAc (3/1)); ^1H NMR (300 MHz) δ 6.44 (dt, J = 11.7, 4.9 Hz, 1 H, H-3), 5.87 (dt, J = 11.7, 2.4 Hz, 1 H, H-2), 4.65 (dd, J = 4.9, 2.4 Hz, 2 H, H-4), 4.13 (s, 2 H, OCH_2), 3.77 (s, 3 H, OCH_3), 2.20 (s, 3 H, CH_3); IR (neat) 2924, 1704 (CO), 1645 (C=C), 1426, 1193, 1114, 809, 797 cm^{-1}; MS m/e (rel intensity) 173 (M^+ + 1, 0.8), 172 (M^+, 2.0), 171 (M^+ - 1, 12.6), 156 (3.4), 140 (11.4), 114 (27.9), 99 (65.9), 87 (18.3), 83 (25.4), 71 (12.6), 58 (27.9), 55 (28.0), 43 (100). Anal. Calcd for $C_8H_{14}O_4$: C, 55.81; H, 7.02. Found: C, 55.97; H, 6.97.

5*E*: TLC R_f 0.20 (hexane/EtOAc (3/1)); ^1H NMR (300 MHz) δ 6.96 (dt, J = 15.8, 4.3 Hz, 1 H, H-3), 6.11 (dt, J = 15.8, 2.2 Hz, 1 H, H-2), 4.24 (dd, J = 4.3, 2.2 Hz, 2 H, H-4), 4.12 (s, 2 H, OCH_2), 3.75 (s, 3 H, OCH_3), 2.18 (s, 3 H, CH_3); ^{13}C NMR (75.4 MHz) δ 205.76, 166.21, 143.21, 121.10, 75.62, 69.55, 51.36, 26.05; IR (neat) 2967, 1707 (CO), 1656 (C=C), 1427, 1266, 1166, 1128, 1033, 964, 858, 675 cm^{-1}; MS m/e (rel intensity) 173 (M^+ + 1, 4.7), 172 (M^+, 3.3), 171 (M^+ 1, 6.9), 142 (25.0), 115 (28.1), 113 (32.1), 99 (87.7), 87 (33.4), 83 (28.9), 71 (26.3), 58 (100), 45 (24.8). Anal. Calcd for $C_8H_{12}O_4$: C, 55.81; H, 7.02. Found: C, 55.79; H, 7.11.

Preparation of Methyl (*Z*)- and (*E*)-4-[*N*-(2-Oxopropyl)-*N*-(*p*-toluenesulfonyl)amino]-2-butenoate (6*Z* and 6*E*). Preparation of [[(4-Methylphenyl)sulfonyl]amino]acetaldehyde Dimethyl Acetal. To a stirred solution of aminoacetaldehyde dimethyl acetal (2.63 g, 25.0 mmol) and dry triethylamine (7.0 mL, 50.0 mol) in dry CH_2Cl_2 (50 mL) was added dropwise a solution of *p*-toluenesulfonyl chloride (5.24 g, 27.5 mol) in dry CH_2Cl_2 (50 mL) over 30 min at 0 °C. After 30 min, the reaction mixture was diluted with water (200 mL). The organic layer was separated, and the aqueous layer was extracted with CH_2Cl_2 (100 mL). The combined organic layer was washed with 1 N HCl, water, and saturated aqueous $NaHCO_3$ solution, dried ($MgSO_4$), filtered, and then concentrated *in vacuo* to afford a pale yellow oil. Flash column chromatography (SiO_2, hexane/EtOAc (2/1)) gave the product (6.47 g, 100%) as a colorless oil: TLC R_f 0.29 (hexane/EtOAc (2/1)); ^1H NMR (300 MHz) δ 7.76 and 7.31 (AB quartet, J = 8.4 Hz, 4 H, aromatic), 4.92 (br t, J = 6.2 Hz, 1 H, NH), 4.34 (t, J = 5.6 Hz, 1 H, CH), 3.32 (s, 6 H, 2 OCH_3), 3.03 (t, J = ~5.9 Hz, 2 H, NCH_2), 2.42 (s, 3 H, CH_3); ^{13}C NMR (75.4 MHz) δ 143.45, 136.70, 129.65 (×2), 126.97 (×2), 102.48, 54.47 (×2), 44.42, 21.41; IR (neat) 3491 (NH), 3226, 2899, 1591 (C=C), 1301, 1152, 961, 880, 809 cm^{-1}; MS m/e (rel intensity) 258 (M^+ - 1, 0.3), 242 (4.5), 228 (11.8), 139 (7.8), 91 (6.6), 75 (100), 47 (17.2). Anal. Calcd for $C_{11}H_{17}NO_4S$: C, 50.95; H, 6.61; N, 5.40. Found: C, 60.02; H, 6.59; N, 5.43.

Preparation of *N*-Allyl-*N*-(2,2-dimethoxyethyl)-*p*-toluenesulfonamide. To a stirred solution of [[(4-methylphenyl)-sulfonyl]amino]acetaldehyde dimethyl acetal (5.84 g, 22.5 mmol) in dry DMSO (50 mL) was added portionwise NaH (60% dispersion in mineral oil, 0.95 g, 23.6 mmol) over 30 min at room temperature. After additional stirring for 30 min, allyl bromide (3.27 g, 27.0 mmol) was added dropwise over 10 min and further stirred for 1 h. The reaction mixture was diluted with ether (250 mL) and water (100 mL). The organic layer was separated, and the aqueous layer was extracted with ether (100 mL × 2). The combined organic layer was washed with brine, dried ($MgSO_4$), filtered, and then concentrated *in vacuo* to afford a pale yellow oil. Flash column chromatography (SiO_2, hexane/EtOAc (2/1)) gave the product (6.67 g, 99%) as a colorless oil: TLC R_f 0.57 (hexane/EtOAc (2/1)); ^1H NMR (300 MHz) δ 7.72 and 7.30 (AB quartet, J = 8.4 Hz, 4 H, aromatic), 3.02 (ddt, J = 17.0, 10.2, 6.4 Hz, 1 H, CCH=), 5.15 (dm, J = 17.0, 1 H, =CH), 5.12 (dm, J = 10.2 Hz, 1 H, =CH), 4.51 (t, J = 5.4 Hz, 1 H, CH), 3.93 (br d, J = 6.4 Hz, 2 H, NCH_2), 3.38 (s, 6 H, 2 OCH_3), 3.22 (d, J = 5.4 Hz, 2 H, NCH_2), 2.42 (s, 3 H, CH_3); ^{13}C NMR (75.4 MHz) δ 143.45, 136.70, 129.65 (×2), 126.97 (×2), 102.48, 54.47 (×2), 44.42, 21.41; IR (neat) 2900, 1592 (C=C), 1152, 1117, 1083, 981, 917, 810, 759, 657, 545 cm^{-1}; MS m/e (rel intensity) 298 (M^+ - 1, 0.3), 268 (33.7), 144 (2.5), 135 (2.1), 113 (8.9), 75 (100). Anal. Calcd for $C_{14}H_{21}NO_4S$: C, 56.17; H, 7.07; N, 4.68. Found: C, 56.22; H, 6.99; N, 4.69.

Preparation of Methyl (*Z*)- and (*E*)-4-[*N*-Allyl-*N*-(*p*-toluenesulfonyl)amino]-2-butenoate. A solution of 4-*N*-allyl-*N*-(2,2-dimethoxyethyl)-*p*-toluenesulfonamide (5.42 g, 17.5 mmol) in 80% acetic acid (50 mL) was heated for 1 h at 90 °C. The reaction mixture was cooled to room temperature, diluted with water (200 mL), and extracted with ether (200 mL × 2). The combined organic layer was washed with saturated aqueous $NaHCO_3$ solution and brine, respectively, dried ($MgSO_4$), filtered, and then concentrated *in vacuo* to afford a pale brown oil. Without further purification, a solution of methyl (triphenylphosphoranylidene)acetate (7.02 g, 21.0 mmol) in methanol (50 mL) was added dropwise to a solution of crude aldehyde in methanol (50 mL) over 20 min at room temperature. After additional stirring for 2 h, the solvent was removed *in vacuo*, and the residue was diluted with ether (30 mL). The insoluble white solid was filtered, and the filtrate was concentrated *in vacuo* to afford a pale brown oil as a mixture of *Z* and *E* isomers. Flash column chromatography (SiO_2, hexane/EtOAc (3/1)) gave a mixture of *Z* and *E* isomers (4.81 g, 86%, *Z*/*E* = 1.8/1 was determined by ^1H NMR) as a colorless oil. Analytical samples of *Z* and *E* isomers were obtained as a colorless oil and a white solid, respectively, by flash column chromatography (SiO_2, hexane/EtOAc (4/1)) of a small portion of the *Z* and *E* mixture.

***Z* isomer**: TLC R_f 0.37 (hexane/EtOAc (4/1)); ^1H NMR (300 MHz) δ 7.69 and 7.42 (AB quartet, J = 8.3 Hz, 4 H, aromatic), 6.21 (dt, J = 11.5, 5.8 Hz, 1 H, H-3), 5.85 (dt, J = 11.5, 2.1 Hz, 1 H, H-2), 5.65 (ddt, J = 17.1, 10.1, 6.2 Hz, 1 H, NCCH=), 5.17 (dd, J = 17.1, 1.5 Hz, 1 H, =CH), 5.12 (dd, J = 10.1, 1.5 Hz, 1 H, =CH), 4.24 (dd, J = 5.8, 2.1 Hz, 2 H, H-4), 3.78 (d, J = 6.2 Hz, 2 H, NCH_2), 3.62 (s, 3 H, OCH_3), 2.39 (s, 3 H, CH_3); ^{13}C NMR (75.4 MHz) δ 165.61, 146.39, 143.44, 135.97, 132.77, 129.92 (×2), 126.97 (×2), 120.17, 119.15, 51.22, 50.81, 45.69, 20.94; IR (neat) 2921, 1705 (CO), 1633 (C=C), 1591 (C=C), 1395, 1319, 1147, 1086, 982, 926, 808, 772, 718, 656, 579, 543 cm^{-1}; MS m/e (rel intensity) 311 (M^+ + 2, 0.4), 310 (M^+ + 1, 1.4), 309 (M^+, 0.4), 154 (100), 122 (18.4), 99 (7.7), 94 (33.5), 91 (5.8), 41 (13.3). Anal. Calcd for $C_{15}H_{19}NO_4S$: C, 58.23; H, 6.19; N, 4.53. Found: C, 58.19; H, 6.21; N, 4.59.

***E* isomer**: TLC R_f 0.27 (hexane/EtOAc (4/1)); mp 50–51 °C (ethanol); ^1H NMR (300 MHz) δ 7.41 and 7.72 (AB quartet, J = 8.3 Hz, 4 H, aromatic), 6.67 (dt, J = 15.7, 5.5 Hz, 1 H, H-3), 5.95 (dt, J = 15.7, 1.6 Hz, 1 H, H-2), 5.60 (ddt, 17.1, 10.1, 6.3 Hz, 1 H, N-C-CH=), 5.17 (dd, J = 17.1, 1.5 Hz, 1 H, =CH), 5.12 (dd, J = 10.1, 1.5 Hz, 1 H, =CH), 3.88 (dd, J = 5.5, 1.6 Hz, 2 H, H-4), 3.74 (d, J = 6.3 Hz, 2 H, NCH_2), 3.64 (s, 3 H, OCH_3), 2.39 (s, 3 H, CH_3); ^{13}C NMR (75.4 MHz) δ 165.51, 143.78, 143.44, 136.10, 132.69, 129.87 (×2), 127.02 (×2), 122.28, 119.22, 51.40, 50.58, 47.67, 20.93; IR (neat) 2910, 1702 (CO), 1651 (C=C), 1591 (C=C), 1278, 1170, 1085, 1003, 911, 885, 846, 816, 768, 722, 652, 593, 563 cm^{-1};

MS *m/e* (rel intensity) 311 (M^+ + 2, 0.6), 310 (M^+ + 1, 2.3), 309 (M^+, 1.0), 278 (4.2), 250 (1.4), 224 (1.0), 186 (0.8), 154 (100), 122 (8.7), 94 (17.1). Anal. Calcd for $C_{15}H_{19}NO_4S$: C, 58.23; H, 6.19; N, 4.53. Found: C, 58.22; H, 6.15; N, 4.54.

Preparation of 6*Z* and 6*E*. A mixture of 4-[*N*-allyl-*N*-(*p*-toluenesulfonyl)amino]-2-butenoate (4.64 g, 15.0 mmol), cuprous chloride (2.02 g, 1.5 mmol), and palladium chloride (0.14 g, 0.8 mmol) in DMF–H_2O (50:7, 30 mL) was stirred for 2 days under oxygen. The reaction mixture was diluted with ether (200 mL) and water (100 mL). The organic layer was separated, and the aqueous layer was extracted with ether (100 mL). The combined organic layer was washed with brine, dried ($MgSO_4$), filtered, and then concentrated *in vacuo* to afford a pale brown oil as a mixture of *Z* and *E* isomers. Flash column chromatography (SiO_2, hexane/EtOAc (1/1)) gave 6*Z* (1.08 g, 22%) as a colorless oil and 6*E* (1.12 g, 23%) as a white solid.

6*Z*: TLC R_f 0.53 (hexane/EtOAc (1/1)); ^1H NMR (300 MHz) δ 7.41 and 7.68 (AB quartet, J = 8.4 Hz, 4 H, aromatic), 6.28 (dt, J = 11.5, 5.8 Hz, 1 H, H-3), 5.84 (dt, J = 11.5, 2.1 Hz, 1 H, H-2), 4.24 (dd, J = 5.8, 2.1 Hz, 2 H, H-4), 4.17 (s, 2 H, NCH_2), 3.61 (s, 3 H, OCH_3), 2.39 (s, 3 H, CH_3), 2.06 (s, 3 H, $COCH_3$); ^{13}C NMR (75.4 MHz) δ 203.21, 165.68, 146.45, 143.42, 136.09, 129.80 (×2), 126.98 (×2), 120.06, 57.15, 51.22, 47.28, 26.78, 20.96; IR (neat) 2923, 1705 (CO), 1636 (C=C), 1591 (C=), 1394, 1315, 1146, 1096, 981, 919, 807, 770, 719, 653 cm^{-1}; MS *m/e* (rel intensity) 326 (M^+ + 1, 3.6), 325 (M^+, 3.5), 295 (14.8), 282 (33.5), 251 (34.9), 204 (27.6), 184 (20.4), 170 (65.8), 155 (86.5), 138 (20.9), 128 (37.8), 114 (34.5), 99 (34.6), 96 (96.6), 91 (100), 84 (25.2), 69 (30.5). Anal. Calcd for $C_{15}H_{19}NO_5S$: C, 55.37; H, 5.89; N, 4.30. Found: C, 55.45; H, 5.81; N, 4.28.

6*E*: TLC R_f 0.44 (hexane/EtOAc (1/1)); mp 89–90 °C (ethanol); ^1H NMR (300 MHz) δ 7.39 and 7.70 (AB quartet, J = 8.1 Hz, 4 H, aromatic), 6.66 (dt, J = 15.7, 5.7 Hz, 1 H, H-3), 5.92 (dt, J = 15.7, 1.4 Hz, 1 H, H-2), 4.12 (s, 2 H, NCH_2), 3.91 (dd, J = 5.7, 1.4 Hz, 2 H, H-4), 3.63 (s, 3 H, OCH_3), 2.38 (s, 3 H, CH_3), 2.04 (s, 3 H, $COCH_3$); ^{13}C NMR (75.4 MHz) δ 203.08, 165.56, 143.51, 143.40, 136.23, 129.72 (×2), 127.05 (×2), 122.31, 56.53, 51.39, 49.12, 26.78, 20.94; IR (neat) 2925, 1702 (CO), 1651 (C=C), 1591 (C=C), 1339, 1276, 1244, 1153, 1119, 975, 926, 803, 782, 719, 654, 581, 548 cm^{-1}; MS *m/e* (rel intensity) 327 (M^+ + 2, 2.0), 326 (M^+ + 1, 9.7), 294 (25.1), 282 (100), 170 (31.6), 155 (24.1), 99 (12.5), 96 (58.2), 91 (20.0). Anal. Calcd for $C_{15}H_{19}NO_5S$: C, 55.37; H, 5.89; N, 4.30. Found: C, 55.39; H, 5.91; N, 4.31.

Preparation of Methyl (*Z*)- and (*E*)-5-(2-Oxocyclopentyl)-2-pentenoate (7*Z* and 7*E*). Preparation of Ethyl 3-(2-Oxocyclopentyl)propionate. The pyrrolidine enamine was prepared from cyclopentanone (25.24 g, 0.3 mol) and pyrrolidine (23.47 g, 0.33 mol) in benzene (100 mL) under the usual conditions.[43] Removal of benzene and excess pyrrolidine *in vacuo* afforded the crude enamine as a brown oil. A solution of crude enamine and ethyl acrylate (36.04 g, 0.36 mol) in dry dioxane (100 mL) was refluxed for 1 h followed by addition of water (10 mL) and refluxing for an additional 30 min. The reaction mixture was allowed to cool to room temperature, and the solvent was concentrated *in vacuo* to afford a brown oil. The resulting residue was diluted with ether (200 mL) and water (100 mL). The organic layer was separated, and the aqueous layer was extracted with ether (150 mL × 2). The combined organic layer was washed with 2 N HCl and saturated aqueous $NaHCO_3$ solution, dried ($MgSO_4$), filtered, and then concentrated *in vacuo* to give on distillation the product (38.70 g, 70%) as a colorless oil: TLC R_f 0.57 (hexane/EtOAc (4/1)); bp 106–108 °C (1.2 mmHg); ^1H NMR (60 MHz) δ 4.15 (q, J = 7.0 Hz, 2 H, OCH_2), 1.20–2.75 (m, 11 H), 1.26 (t, J = 7.0 Hz, 3 H, CH_2); IR (neat) 2922, 1718 (CO), 1365, 1246, 1174, 1151, 1109, 1026 cm^{-1}; MS *m/e* (rel intensity) 185 (M^+ + 1, 2.8), 184 (M^+, 11.0), 139 (57.3), 138 (100), 110 (37.4), 83 (26.9), 82 (25.5), 68 (10.8), 55 (33.7). Anal. Calcd for $C_9H_{14}O_3$: C, 63.51; H, 8.29. Found: C, 63.49; H, 8.28.

Preparation of Ethyl 3-(2-Oxocyclopentyl)propionate Ethylene Ketal. A stirred solution of ethyl 3-(2-oxocyclopentyl)-propionate (36.85 g, 0.2 mol), ethylene glycol (18.62 g, 0.3 mol), and a catalytic amount *p*-TsOH in benzene (300 mL) was refluxed with azeotropic removal of water (Dean-Stark trap) for 5 h. The reaction mixture was allowed to cool to room temperature and washed with saturated $NaHCO_3$ solution, and the organic layer was dried ($MgSO_4$), filtered, and then concentrated *in vacuo* to afford to pale yellow oil. Distillation gave the product (39.72 g, 87%) as a colorless oil: TLC R_f 0.49 (hexane/EtOAc (5/1)); bp 120–121 °C (0.7 mmHg); ^1H NMR (60 MHz) δ 4.14 (q, J = 7.0 Hz, 2 H, OCH_2), 3.93 (s, 4 H, OCH_2CH_2O), 1.40–2.60 (m, 11 H), 1.25 (t, J = 7.0 Hz, 3 H, CH_3); IR (neat) 2925, 1725 (CO), 1362, 1173, 1025, 942 cm^{-1}; MS *m/e* (rel intensity) 230 (M^+ + 2, 2.2), 229 (M^+ + 1, 12.5), 228 (M^+, 14.9), 199 (28.7), 183 (22.3), 141 (44.6), 113 (25.2), 100 (28.7), 99 (100). Anal. Calcd for $C_{11}H_{18}O_4$: C, 61.66; H, 8.47. Found: C, 61.71; H, 8.45.

Preparation of 3-(2-Oxocyclopentyl)propanol Ethylene Ketal. To a stirred suspension of $LiAlH_4$ (3.42 g, 90.12 mmol) in dry THF (350 mL) was added ethyl 3-(2-oxocyclopentyl)-propionate ethylene ketal (34.25 g, 150.0 mmol) in dry THF (100 mL) dropwise for 3 min at 0 °C under the nitrogen atmosphere. After 1 h at 0 °C, the reaction mixture was quenched with water (10 mL) and then allowed to warm to room temperature. The reaction mixture was diluted with ether (400 mL), $MgSO_4$ (50 g) was added, and the resultant suspension was stirred for 1 h. Filtration and concentration *in vacuo* afforded a colorless oil. Flash column chromatography (SiO_2, hexane/EtOAc (1/2)) gave the product (27.66 g, 99%) as a colorless oil: TLC R_f 0.40 (hexane/EtOAc (1/1)); ^1H NMR (60 MHz) δ 3.93 (s, 4 H, OCH_2CH_2O), 3.63 (t, J = 6.0 Hz, 2 H, H-1), 1.00–2.20 (m, 11 H); IR (neat) 3364 (OH), 2909, 1311, 1201, 1141, 1100, 1026, 945 cm^{-1}; MS *m/e* (rel intensity) 187 (M^+ + 1, 0.4), 186 (M^+, 2.4), 155 (17.4), 141 (11.8), 113 (17.2), 100 (11.6), 99 (100). Anal. Calcd for $C_{10}H_{18}O_3$: C, 64.49; H, 9.74. Found: C, 64.50; H, 9.79.

Preparation of 3-(2-Oxocyclopentyl)propanal Ethylene Ketal. The product (22.99 g, 96%), which was purified by Kugelrohr distillation, was obtained as a pale yellow oil from 3-(2-oxocyclopentyl)propanol ethylene ketal (23.95 g, 0.13 mol) by using a Swern oxidation: TLC R_f 0.52 (hexane/ether (1/1)); bp 105–108 °C (0.5 mmHg, Kugelrohr); ^1H NMR (60 MHz) δ 9.80 (t, J = 1.8 Hz, CHO, 1 H), 3.90 (s, 4 H, OCH_2CH_2O), 2.50 (t, J = 6.5 Hz, 2 H, H-2), 1.10–2.20 (m, 9 H); IR (neat) 2917, 2696, 1714 (CO), 1498, 1145, 1099, 1026, 943 cm^{-1}; MS *m/e* (rel intensity) 185 (M^+ + 1, 5.9), 184 (M^+, 7.2), 141 (19.4), 140 (14.8), 125 (33.6), 124 (29.3), 113 (18.3), 100 (14.6), 99 (100), 55 (11.2). Anal. Calcd for $C_{10}H_{16}O_3$: C, 65.19; H, 8.75. Found: C, 65.21; H, 8.77.

Preparation of Methyl (*Z*)- and (*E*)-5-(2-Oxocyclopentyl)-2-pentenoate Ethylene Ketal. To a stirred solution of methyl (triphenylphosphoranylidene)acetate (33.44 g, 100.0 mmol) in dry MeOH (100 mL) was added dropwise a solution of 3-(2-oxocyclopentyl)propanal ethylene ketal (14.74 g, 80.0 mmol) in dry MeOH (30 mL) over 30 min at room temperature. After additional stirring for 2 h, the solvent was concentrated *in vacuo*, and the residue was diluted with ether (50 mL). The insoluble white solid was filtered, and the filtrate was concentrated *in vacuo* to afford a pale brown oil as a mixture of *Z* and *E* isomers. Flash column chromatography (SiO_2, hexane/EtOAc (9/1)) gave the *Z* isomer (6.46 g, 34%) and the *E* isomer (12.19 g, 63%) as colorless oils.

***Z* isomer**: TLC R_f 0.56 (hexane/EtOAc (9/1)); ^1H NMR (300 MHz) δ 6.24 (dt, J = 11.5, 7.5 Hz, 1 H, H-3), 5.77 (dt, J = 11.5, 1.7 Hz, 1 H, H-2), 3.81–4.00 (m, 4 H, OCH_2CH_2O), 3.71 (s, 3 H, OCH_3), 2.67 (qd, J = 7.5, 1.7 Hz, 2 H, H-4), 1.85–2.00 (m, 2H), 1.50–1.85 (m, 5 H), 1.25–1.50 (m, 2 H); ^{13}C NMR (75.4 MHz) δ 166.69, 150.78, 119.06, 118.00, 64.44, 64.31, 50.83, 45.61, 35.61, 29.20, 28.21, 27.51, 20.52; IR (neat) 2907, 1709 (CO), 1632 (C=C), 1427, 1157, 1019, 942, 814, 725 cm^{-1}; MS *m/e* (rel intensity) 241 (M^+ + 1, 0.7), 240 (M^+, 2.4), 239 (0.6), 197 (2.4), 181 (2.3), 167 (9.4), 141 (54.6), 125 (11.4), 99 (100). Anal. Calcd for $C_{13}H_{20}O_4$: C, 64.98; H, 8.39. Found: C, 64.95; H, 8.41.

***E* isomer**: TLC R_f 0.50 (hexane/EtOAc (9/1)); ^1H NMR (300 MHz) δ 6.99 (dt, J = 15.7, 7.0 Hz, 1 H, H-3), 5.83 (dt, J = 15.7, 1.6 Hz, 1 H, H-2), 3.81–4.00 (m, 4 H, OCH_2CH_2O), 3.72 (s, 3 H, OCH_3), 2.00–2.40 (m, 2 H, H-4), 1.82–2.00 (m, 2 H), 1.50–1.82 (m, 5 H), 1.23–1.50 (m, 2 H); ^{13}C NMR (75.4 MHz) δ 167.00, 149.60, 120.68, 117.86, 64.40, 64.32, 51.20, 45.29, 33.56, 30.67, 29.15, 27.14, 20.46; IR (neat) 2908, 1708 (CO), 1649 (C=C), 1426, 1257, 1165, 1025, 970, 846, 714 cm^{-1}; MS *m/e* (rel intensity) 241 (M^+ + 1, 0.7), 240 (M^+, 2.9), 239 (0.5), 197 (2.9), 167 (10.2), 141 (62.0), 125 (10.7), 119 (4.0), 113 (6.3), 99 (100). Anal. Calcd for $C_{13}H_{20}O_4$: C, 64.98; H, 8.39. Found: C, 64.99; H, 8.42.

(43) Stork, G.; Brizzolan, A.; Landesman, H.; Szumuszkovicz, J.; Terrel, R. *J. Am. Chem. Soc.* **1963**, *85*, 207.

Preparation of 7Z. A solution of methyl (*Z*)-5-(2-oxocyclopentyl)-2-pentenoate ethylene ketal (5.76 g, 24.0 mmol) in THF (40 mL) and 2 N HCl (40 mL) was stirred for 2 h at room temperature. The reaction mixture was diluted with EtOAc (200 mL) and water (100 mL). The organic layer was separated, and the aqueous layer was extracted with EtOAc (50 mL). The combined organic layer was washed with saturated aqueous $NaHCO_3$, dried ($MgSO_4$), filtered, and then concentrated *in vacuo* to afford a pale yellow oil, which was purified by flash column chromatography (SiO_2, hexane/EtOAc (3/1)) to give **7Z** (4.68 g, 99%) as a colorless oil: TLC R_f 0.63 (hexane/EtOAc (3/1)); ^{1}H NMR (300 MHz) δ 6.23 (dt, J = 11.5, 7.6 Hz, 1 H, H-3), 5.80 (dt, J = 11.5, 1.7 Hz, 1 H, H-2), 3.71 (s, 3 H, OCH_3), 2.62–2.84 (m, 2 H, H-4), 2.22–2.40 (m, 2 H), 1.87–2.20 (m, 4 H), 1.68–1.87 (m, 1 H), 1.51–1.66 (m, 1 H), 1.45–1.51 (m, 1 H); ^{13}C NMR (75.4 MHz) δ 220.81, 166.56, 149.59, 119.73, 50.90, 48.67, 37.97, 29.33, 28.73, 26.78, 20.56; IR (neat) 2909, 1709 (CO), 1633 (C=C), 1428, 1399, 1163, 1020, 1000, 924, 815, 724 cm^{-1}; MS *m/e* (rel intensity) 197 (M^+ + 1, 1.9), 196 (M^+, 2.9), 164 (47.2), 146 (13.7), 136 (14.8), 119 (19.6), 113 (56.7), 108 (15.4), 100 (30.6), 97 (33.2), 84 (100), 81 (55.7), 69 (11.7), 55 (13.2), 43 (13.7). Anal. Calcd for $C_{11}H_{16}O_3$: C, 67.32; H, 8.22. Found: C, 67.29; H, 8.24.

Preparation of 7E. The reaction was carried out as described in the preparation of **7Z**, using methyl (*E*)-5-(2-oxocyclopentyl)-2-pentenoate ethylene ketal (8.64 g, 36.0 mmol) to afford a pale yellow oil, which was purified by flash column chromatography (SiO_2, hexane/EtOAc (3/1)) to give **7E** (7.02 g, 99%) as a colorless oil: TLC R_f 0.55 (hexane/EtOAc (3/1)); ^{1}H NMR (300 MHz) δ 6.95 (dt, J = 15.7, 6.9 Hz, 1 H, H-3), 5.86 (dt, J = 15.7, 1.6 Hz, 1 H, H-2), 3.73 (s, 3 H, OCH_3), 1.70–2.40 (m, 9 H), 1.38–1.62 (m, 2 H); ^{13}C NMR (75.4 MHz) δ 220.37, 166.70, 148.31, 121.28, 51.21, 48.08, 37.83, 29.84, 29.41, 27.84, 20.46; IR (neat) 2913, 1715 (CO), 1649 (C=C), 1426, 1261, 1190, 1160, 1062, 1030, 978, 842, 713 cm^{-1}; MS *m/e* (rel intensity) 198 (M^+ + 2, 13.5), 197 (M^+ + 1, 100), 196 (M^+, 34.7), 165 (98.7), 146 (14.5), 136 (20.9), 119 (25.5), 113 (40.7), 108 (14.0), 87 (16.4), 84 (52.0), 81 (59.0), 71 (92.3), 43 (12.8). Anal. Calcd for $C_{11}H_{16}O_3$: C, 67.32; H, 8.22. Found: C, 67.37; H, 8.19.

Preparation of 5-(2-Oxocyclopentyl)-2-pentenenitrile (9). Preparation of 5-(2-Oxocyclopentyl)-2-pentenenitrile Ethylene Ketal. To a stirred mixture of NaH (0.72 g, 18.0 mmol, 60% dispersion in mineral oil) in dry THF (40 mL) at 0 °C was added dropwise a solution of dimethyl (cyanomethyl)phosphonate (2.69 g, 18.0 mmol) in dry THF (10 mL) over 10 min. The reaction mixture was allowed to warm to room temperature. After 10 min, the reaction mixture was cooled to 0 °C, and a solution of 3-(2-oxocyclopentyl)propanal ethylene ketal (2.77 g, 15.0 mmol) in dry THF (10 mL) was added dropwise over 10 min. After 1 h, the reaction mixture was allowed to warm to room temperature and stirred for an additional 30 min. The reaction mixture was poured into cold water and then extracted with EtOAc (100 mL × 2). The combined organic layer was washed with brine, dried ($MgSO_4$), filtered, and then concentrated *in vacuo* to afford a pale brown oil as a mixture of inseparable *Z* and *E* isomers. Flash column chromatography (SiO_2, hexane/EtOAc (4/1)) gave an inseparable mixture of *Z* and *E* isomers (2.92 g, 94%, *Z*/*E* = 1.43/1 was determined by ^{1}H NMR) as a colorless oil: TLC R_f 0.46 (hexane/EtOAc (4/1)); ^{1}H NMR (300 MHz) δ 6.74 (dt, J = 16.3, 6.9 Hz, 1 H, H-3 from *E* isomer), 6.47 (dt, J = 10.9, 7.7 Hz, 1 H, H-3 from *Z* isomer), 5.34 (dt, J = 16.3, 1.6 Hz, 1 H, H-2 from *E* isomer), 5.30 (dt, J = 10.9, 1.2 Hz, 1 H, H-2 from *Z* isomer), 3.80–4.30 (m, 8 H, 2 OCH_2CH_2O), 2.38–2.58 (m, 2 H, H-4 from *Z* isomer), 2.10–2.38 (m, 2 H), 1.80–2.10 (m, 4 H), 1.50–1.80 (m, 12 H), 1.20–1.50 (m, 2 H); IR (neat) 2913, 2196 (CN), 1624 (C=C), 1430, 1310, 1201, 1142, 1097, 1028, 960, 831, 739 cm^{-1}; MS *m/e* (rel intensity) 208 (M^+ + 1, 2.3), 207 (M^+, 4.1), 164 (5.1), 141 (75.3), 135 (21.7), 113 (11.4), 99 (100), 95 (17.6), 86 (10.6), 69 (13.6), 55 (16.7), 41 (9.8). Anal. Calcd for $C_{12}H_{17}NO$: C, 69.54; H, 8.27; N, 6.76. Found: C, 69.59; H, 8.31; N, 6.74.

Preparation of 9. The reaction was carried out as described in the preparation of **7Z**, using 5-(2-oxocyclopentyl)-2-pentenenitrile ethylene ketal (2.08 g, 10.0 mmol) to afford a pale yellow oil, which was purified by flash column chromatography (SiO_2, hexane/EtOAc (3/1)) to give to afford a pale yellow oil, which was purified by flash column chromatography (SiO_2, hexane/EtOAc (3/1)) to give an inseparable mixture of **9Z** and **9E** (1.58 g, 97%, **9Z**/**9E** = 1.51/1 was determined by ^{1}H NMR) as a colorless oil: TLC R_f 0.37 (hexane/EtOAc (3/1)); ^{1}H NMR (300 MHz) δ 6.72 (dt, J = 16.3, 6.8 Hz, 1 H, H-3 from **9E**), 6.50 (dt, J = 10.9, 7.0 Hz, 1 H, H-3 from **9Z**), 5.39 (dt, J = 16.3, 1.7 Hz, 1 H, H-2 from **9E**), 2.51 (m, 2 H, H-4 from **9Z**), 2.21–2.43 (m, 4 H), 1.70–2.21 (m, 12 H), 1.35–1.65 (m, 4 H); ^{13}C NMR (75.4 MHz) δ 220.17, 220.06, 154.92, 154.08, 117.19, 115.68, 100.15, 100.01, 48.22, 47.91, 37.80, 30.96, 29.69, 29.41, 29.30, 27.92, 27.46, 20.45; IR (neat) 2912, 2196 (CN), 1724 (CO), 1624 (C=C), 1440, 1398, 1149, 742 cm^{-1}; MS *m/e* (rel intensity) 165 (M^+ + 2, 0.4), 164 (M^+ + 1, 4.1), 163 (M^+, 3.7), 134 (5.5), 120 (7.6), 106 (6.9), 83 (100), 80 (16.9), 69 (28.5), 55 (47.0), 43 (27.5), 41 (70.6). Anal. Calcd for $C_{10}H_{13}NO$: C, 73.59; H, 8.03; N, 8.58. Found: C, 73.61; H, 8.05; N, 8.55.

Preparation of Methyl (Z)-7-Oxo-4-(benzyloxy)-2-octenoate (10Z). Preparation of 6-Oxo-1-hepten-3-ol Ethylene Ketal. To a sirred solution of oxalyl chloride (4.12 g, 33.0 mmol) in dry CH_2Cl_2 (70 mL) was added dropwise a solution of DMSO (5.1 mL, 66.0 mmol) in dry CH_2Cl_2 (15 mL) at −78 °C over 5 min. After 5 min, a solution of 4-oxopentanol ethylene ketal (4.93 g, 30.0 mmol) in dry CH_2Cl_2 (15 mL) was added within 5 min, and the stirring was continued for an additional 15 min. Dry triethylamine (21.0 mL, 150.0 mmol) was added, and the reaction mixture was stirred for 5 min and then allowed to warm to room temperature. Water (70 mL) was then added, and the aqueous layer was extracted with CH_2Cl_2 (100 mL). The combined organic layer was washed with 1 N HCl, brine, saturated aqueous $NaHCO_3$ solution, and brine, dried ($MgSO_4$), filtered, and then concentrated *in vacuo* to afford crude aldehyde as a pale yellow oil. Without further purification, to a stirred solution of crude aldehyde in dry THF (50 mL) was added dropwise vinylmagnesium bromide (1.0 M solution in THF, 40 mL, 40.0 mmol) over 20 min at −10 °C. After 1 h, the reaction mixture was allowed to warm to room temperature and quenched with saturated aqueous NH_4Cl solution (10 mL). The solvent was concentrated *in vacuo*, and the residue was diluted with ether (100 mL) and water (100 mL). The organic layer was separated, and the aqueous layer was extracted with ether (100 mL). The combined organic layer was washed with brine and then concentrated *in vacuo* to afford a pale brown oil. Flash column chromatography (SiO_2, hexane/EtOAc (1/1)) gave the product (3.48 g, 60%) as a colorless oil: TLC R_f 0.43 (hexane/EtOAc (1/1)); ^{1}H NMR (300 MHz) δ 5.85 (ddd, J = 17.2, 10.5, 6.1 Hz, 1 H, H-2), 5.22 (dt, J = 17.2, 1.5 Hz, 1 H, H-1), 5.09 (dt, J = 10.5, 1.4 Hz, 1 H, H-1), 4.09 (q, J = 6.1 Hz, 1 H, H-3), 3.95 (m, 4 H, OCH_2CH_2O), 2.92 (br s, 1 H, OH), 1.55–1.85 (m, 4 H, H-4, H-5), 1.32 (s, 3 H, H-7); ^{13}C NMR (75.4 MHz) δ 140.94, 114.26, 109.78, 72.51, 64.40 (×2), 34.55, 31.03, 23.63; IR (neat) 3378 (OH), 2905, 1368, 1211, 1054, 918, 885, 843 cm^{-1}; MS *m/e* (rel intensity) 171 (M^+ − 1, 0.6), 157 (20.5), 155 (14.9), 139 (15.6), 111 (69.4), 95 (23.2), 93 (19.2), 87 (100), 73 (20.1), 71 (15.7), 67 (21.0), 57 (24.2), 55 (27.6), 43 (100). Anal. Calcd for $C_9H_{16}O_3$: C, 62.77; H, 9.36. Found: C, 62.81; H, 9.35.

Preparation of 6-Oxo-3-(benzyloxy)-1-heptene Ethylene Ketal. To a mixture of NaH (60% dispersion in mineral oil, 0.96 g, 24.0 mmol) in dry THF (50 mL) was added dropwise a solution of 6-oxo-1-hepten-3-ol ethylene ketal (3.45 g, 20.0 mmol) in dry THF (10 mL) over 10 min at room temperature. After 30 min, benzyl bromide (4.11 g, 24.0 mmol) was added, and the reaction mixture was heated for 1 h at 50 °C. The reaction mixture was allowed to cool to room temperature, poured into cold water (100 mL), and extracted with ether (150 mL × 2). The combined organic layer was washed with brine, dried ($MgSO_4$), filtered, and then concentrated *in vacuo* to afford a pale yellow oil. Flash column chromatography (SiO_2, hexane/EtOAc (9/1)) gave the product (5.20 g, 99%) as a colorless oil: TLC R_f 0.38 (hexane/EtOAc (9/1)); ^{1}H NMR (300 MHz) δ 7.22–7.38 (m, 5 H, aromatic), 5.74 (ddd, J = 17.0, 10.6, 7.7 Hz, 1 H, H-2), 5.66–5.79 (m, 2 H, H-1), 4.58 and 4.36 (AB quartet, J = 11.9 Hz, 2 H, OCH_2Ph), 3.91 (m, 4 H, OCH_2CH_2O), 3.78 (m, 1 H, H-3), 1.57–1.89 (m, 4 H, H-4, H-5), 1.31 (s, 3 H, H-7); ^{13}C NMR (75.4 MHz) δ 138.81, 138.68, 128.24 (×2), 127.66 (×2), 127.34, 117.32, 109.90, 80.40, 69.95, 64.58 (×2), 34.74, 29.82, 23.84; IR (neat) 3040, 2906, 1366, 1202, 1047, 988, 925, 845, 732, 693 cm^{-1}; MS *m/e* (rel intensity) 264 (M^+ + 2, 0.4), 263 (M^+ + 1, 1.4), 247 (2.2), 171 (3.1), 155 (33.1), 115 (11.4), 111 (18.2), 94 (22.7), 87 (100), 59 (14.0), 43 (20.5). Anal. Calcd for $C_{16}H_{22}O_3$: C, 73.25; H, 8.45. Found: C, 73.29; H, 8.51.

Preparation of Methyl (Z)-7-Oxo-4-(benzyloxy)-2-octenoate Ethylene Ketal. A stirred solution of 6-oxo-3-(benzyloxy)-1-heptene ethylene ketal (3.94 g, 15.0 mmol) in MeOH

(50 mL) was ozonized at −78 °C. The reaction mixture was quenched with dimethyl sulfide (5 mL) and allowed to warm to room temperature. After 2 h, methyl (triphenylphosphoranylidene)acetate (8.36 g, 25.0 mmol) was added and stirred for 1 h. The solvent was concentrated *in vacuo* and diluted with ether (50 mL), the insoluble white solid was filtered, and the filtrate was concentrated *in vacuo* to afford a pale brown oil. Flash column chromatography (SiO_2, hexane/EtOAc (3/1)) gave the product (2.89 g, 60%) as a colorless oil: TLC R_f 0.45 (hexane/EtOAc (3/1)); ^{1}H NMR (300 MHz) δ 7.21–7.39 (m, 5 H, aromatic), 6.18 (dd, J = 11.7, 8.8 Hz, 1 H, H-3), 5.91 (dd, J = 11.7, 0.9 Hz, 1 H, H-2), 5.05 (m, 1 H, H-4), 4.52 and 4.42 (AB quartet, J = 11.6 Hz, 2 H, OCH_2Ph), 3.91 (m, 4 H, OCH_2CH_2O), 3.72 (s, 3 H, OCH_3), 1.60–1.90 (m, 4 H, H-5, H-6), 1.31 (s, 3 H, H-8); ^{13}C NMR (75.4 MHz) δ 166.10, 150.91, 138.38, 128.19 (×2), 127.67 (×2), 127.44, 120.91, 109.77, 74.66, 71.17, 64.54 (×2), 51.24, 34.31, 29.36, 23.75; IR (neat) 2913, 1711 (CO), 1635 (C=C), 1427, 1369, 1171, 1052, 847, 820, 733, 693 cm^{-1}; MS m/e (rel intensity) 322 (M^+ + 2, 1.5), 321 (M^+ + 1, 5.7), 320 (M^+, 2.6), 305 (2.1), 213 (15.8), 169 (15.4), 87 (100). Anal. Calcd for $C_{18}H_{24}O_3$: C, 67.48; H, 7.55. Found: C, 67.51; H, 7.60.

Preparation of Methyl 10*Z*. The reaction was carried out as described in the preparation of **7*Z***, using methyl (*Z*)-7-oxo-4-(benzyloxy)-2-octene ethylene ketal (2.25 g, 7.0 mmol) to afford a pale yellow oil, which was purified by flash column chromatography (SiO_2, hexane/EtOAc (3/1)) to give **10*Z*** (2.09 g, 99%) as a colorless oil: TLC R_f 0.40 (hexane/EtOAc (3/1)); ^{1}H NMR (300 MHz) δ 7.21–7.39 (m, 5 H, aromatic), 6.19 (dd, J = 11.7, 8.4 Hz, 1 H, H-3), 5.92 (dd, J = 11.7, 1.1 Hz, 1 H, H-2), 5.01 (m, 1 H, H-4), 4.52 and 4.39 (AB quartet, J = 11.6 Hz, 2 H, OCH_2Ph), 3.71 (s, 3 H, OCH_3), 2.45–2.70 (m, 2 H, H-6), 2.11 (s, 3 H, H-8), 1.75–2.00 (m, 2 H, H-5); ^{13}C NMR (75.4 MHz) δ 208.22, 166.10, 150,63, 138.15, 128.28 (×2), 127.74 (×2), 127.60, 121.19, 74.24, 71.31, 51.36, 39.41, 29.82, 28.69; IR (neat) 2911, 1703 (CO), 1637 (C=C), 1426, 1395, 1349, 1189, 1067, 988, 820, 733, 694 cm^{-1}; MS m/e (rel intensity) 278 (M^+ + 2, 1.5), 277 (M^+ + 1, 6.8), 276 (M^+, 1.7), 205 (1.1), 181 (2.1), 169 (100), 138 (19.0), 113 (5.3), 91 (11.0). Anal. Calcd for $C_{16}H_{20}O_4$: C, 69.55; H, 7.29. Found: C 69.48; H, 7.30.

Preparation of Methyl 7-Oxo-2-octynoate (11). Preparation of 6-Oxo-1-heptyne Ethylene Ketal. To a stirred suspension of lithium acetylide (ethylenediamine complex, 90%, 15.35 g, 0.15 mol) in dry THF (120 mL) was added dropwise a solution of 2-(3-chloropropyl)-2-methyl-1,3-dioxolane (16.47, g, 0.1 mol) in dry HMPA (30 mL) over 30 min at room temperature under the nitrogen atmosphere. After 12 h, the reaction mixture was quenched with water (5 mL) and concentrated *in vacuo* to afford a brown oil. The residue was diluted with ether (20 mL) and water (300 mL). The organic layer was separated, and the aqueous layer was extracted with ether (100 mL × 2). The combined organic layer was washed with brine (100 mL), dried ($MgSO_4$), filtered, and then concentrated *in vacuo* to give on distillation the product (13.11 g, 85%) as a colorless oil: TLC R_f 0.71 (hexane/ether (10/1)); bp 100–102 °C (25 mmHg); ^{1}H NMR (60 MHz) δ 3.93 (s, 4 H, OCH_2CH_2O), 1.70–2.20 (m, 7 H), 1.32 (s, 3 H, H-7). Anal. Calcd for $C_9H_{14}O_2$: C, 70.10; H, 9.15. Found: C, 70.17; H, 9.09.

Preparation of Methyl 7-Oxo-2-octynoate Ethylene Ketal. To a stirred solution of 6-oxo-1-heptyne ethylene ketal (1.93 g, 12.5 mmol) in dry THF (30 mL) was added dropwise *n*-butyllithium (2.5 M solution in hexane, 5.5 mL, 13.8 mmol) over 5 min at −78 °C under the nitrogen atmosphere. After 10 min, the reaction mixture was allowed to warm to 0 °C, and the stirring was continued for an additional 10 min. The reaction mixture was recooled to −78 °C, and methyl chloroformate (1.30 g, 13.8 mmol) was added in one portion. After 30 min, the reaction mixture was allowed to warm to room temperature and poured into water (100 mL). The aqueous layer was extracted with ether (100 mL × 2). The combined organic layer was washed with brine (100 mL), dried ($MgSO_4$), filtered, and then concentrated *in vacuo* to afford a yellow oil. Flash column chromatography (SiO_2, hexane/EtOAc (5/1)) gave the product (2.36 g, 89%) as a colorless oil: TLC R_f 0.33 (hexane/EtOAc (5/1)); ^{1}H NMR (300 MHz) δ 3.94 (m, 4 H, OCH_2CH_2O), 3.76 (s, 3 H, OCH_3), 2.38 (t, J = 6.8 Hz, 2 H, H-4), 1.63–1.82 (m, 4 H, H-5 and H-6), 1.32 (s, 3 H, H-8); ^{13}C NMR (75.4 MHz) δ 154.05, 109.44, 89.25, 72.93, 64.54 (×2), 52.39, 37.87, 23.74, 22.01, 18.58; IR (neat) 2918, 2206 (C≡C), 1697 (CO), 1424, 1367, 1237, 1124, 1098, 1055, 943, 912, 863, 801, 749 cm^{-1}; MS m/e (rel intensity) 214 (M^+ + 2, 0.5), 213 (M^+ + 1, 1.9), 197 (13.0), 111 (3.1), 99 (12.4), 87 (100), 43 (6.9). Anal. Calcd for $C_{11}H_{16}O_4$: C, 62.25; H, 7.60. Found: C, 62.28; H, 7.59.

Preparation of 11. The reaction was carried out as described in the preparation of **7*Z***, using methyl 7-oxo-2-octynoate ethylene ketal (2.12 g, 10.0 mmol) to afford a pale yellow oil, which was purified by flash column chromatography (SiO_2, hexane/EtOAc, (3/1)) to give **11** (1.63 g, 97%) as a colorless oil: TLC R_f 0.30 (hexane/EtOAc (3/1)); ^{1}H NMR (300 MHz) δ 3.77 (s, 3 H, OCH_3), 2.61 (t, J = 7.1 Hz, 2 H, H-4), 2.40 (t, J = 6.9 Hz, 2 H, H-6), 2.17 (s, 3 H, H-8), 1.85 (m, 2 H, H-5); ^{13}C NMR (75.4 MHz) δ 207.41, 153.88, 88.45, 73.27, 52.42, 41.55, 29.85, 21.10, 17.69; IR (neat) 2919, 2206 (C≡C), 1691 (CO), 1416, 1349, 1238, 1181, 1153, 1070, 940, 800, 749 cm^{-1}; MS m/e (rel intensity) 170 (M^+ + 2, 4.8), 169 (M^+ + 1, 38.1), 168 (M^+, 6.9), 137 (67.2), 121 (18.6), 111 (18.3), 109 (10.4), 98 (18.3), 94 (29.1), 79 (23.3), 43 (100). Anal. Calcd for $C_9H_{12}O_3$: C, 64.27; H, 7.19. Found: C, 64.31; H, 7.15.

Preparation of Methyl 5-(2-Methyl-1,3-dioxocyclopent-2-yl)-2-pentenoate (12). A suspension of 2-methyl-1,3-cyclopetanedione (2.24 g, 20.0 mmol) and acrolein (1.68 g, 30.0 mmol) in distilled water (30 mL) was stirred for 12 h at room temperature under the nitrogen atmosphere. The reaction mixture was concentrated *in vacuo* to afford the crude product as a pale orange oil. The residue was dissolved in ethanol (30 mL), and methyl (triphenylphosphoranylidene)acetate (8.02 g, 24.0 mmol) was added at room temperature. After 1 h, the reaction mixture was concentrated *in vacuo*, and the residue was purified by flash column chromatography (SiO_2, hexane/EtOAc (2/1)) to give an inseparable mixture of **12*Z*** and **12*E*** (4.17 g, 93%, **12*Z*/12*E*** = 1/2.06 was determined by ^{1}H NMR) as a colorless oil: TLC R_f 0.22 (hexane/EtOAc (3/1)); IR (neat) 2898, 1703 (CO), 1641 (C=C), 1426, 1259, 1186, 1065, 1031, 986, 817 cm^{-1}; MS m/e (rel intensity) 225 (M^+ + 1, 0.9), 224 (M^+, 1.9), 192 (8.9), 125 (100), 113 (100), 100 (37.1), 97 (43.5), 81 (100), 69 (58.3), 43 (18.0). Anal. Calcd for $C_{12}H_{16}O_4$: C, 64.27; H, 7.19. Found: C, 64.20; H, 7.21.

12*Z*: ^{1}H NMR (300 MHz) δ 6.10 (dt, J = 11.4, 7.6 Hz, 1 H, H-3), 5.76 (dt, J = 11.4, 1.6 Hz, 1 H, H-2), 3.70 (s, 3 H, OCH_3), 2.65–2.95 (m, 4 H, $COCH_2CH_2CO$), 2.54 (m, 2 H, H-4), 1.74–1.87 (m, 2 H, H-5), 1.15 (s, 3 H, CH_3); ^{13}C NMR (75.4 MHz) δ 216.04 (×2), 166.26, 147.88, 120.24, 56.17, 50.99, 35.03 (×2), 33.67, 24.20, 19.49.

12*E*: ^{1}H NMR (300 MHz) δ 6.80 (dt, J = 15.7, 6.9 Hz, 1 H, H-3), 5.78 (dt, J = 15.7, 1.6 Hz, 1 H, H-2), 3.71 (s, 3 H, OCH_3), 2.65–2.95 (m, 4 H, $COCH_2CH_2CO$), 2.02–2.18 (m, 2 H, H-4), 1.74–1.87 (m, 2 H, H-5), 1.16 (s, 3 H, CH_3); ^{13}C NMR (75.4 MHz) δ 215.73 (×2), 166.43, 147.12, 121.67, 55.90, 51.34, 34.88 (×2), 32.52, 27.07, 19.65.

Preparation of Methyl (*Z*)- and (*E*)-5-[2-(Ethoxycarbonyl)-1-oxocyclopent-2-yl]-2-pentenoate (13*Z* and 13*E*). A mixture of ethyl 2-oxocyclopentanecarboxylate (3.13 g, 20.0 mmol), acrolein (1.68 g, 30.0 mmol), and triethylamine (0.5 mL) in ether (30 mL) was stirred for 2 h at room temperature under the nitrogen atmosphere. The reaction mixture was concentrated *in vacuo* to afford a pale orange oil. The residue was dissolved in ethanol (30 mL) and methyl (triphenylphosphoranylidene)-acetate (8.02, g, 24.0 mmol) was added at room temperature. After 1 h, the reaction mixture was concentrated *in vacuo*, and the residue was purified by flash column chromatography (SiO_2, hexane/EtOAc (3/1)) to give **13*Z*** (1.73 g, 32%) and **13*E*** (3.34 g, 61%) as colorless oils.

13*Z*: TLC R_f 0.45 (hexane/EtOAc (3/1)); ^{1}H NMR (300 MHz) δ 6.22 (dt, J = 12.4, 7.6 Hz, 1 H, H-3), 5.79 (dt, J = 12.4, 1.6 Hz, 1 H, H-2), 4.17 (q, J = 7.1 Hz, 2 H, OCH_2), 3.70 (s, 3 H, OCH_3), 2.60–2.75 (m, 2 H, H-4), 2.35–2.60 (m, 2H), 2.20–2.35 (m, 1 H), 1.90–2.20 (m, 4 H), 1.62–1.67 (m, 1 H), 1.26 (t, J = 7.1 Hz, 3 H, CH_3); ^{13}C NMR (75.4 MHz) δ 214.52, 170.59, 166.39, 148.88, 119.74, 61.31, 60.01, 50.91, 37.76, 32.50, 32.33, 24.36, 19.50, 13.92; IR (neat) 2928, 1739 (CO), 1708 (CO), 1635 (C=C), 1430, 1398, 1222, 1165, 1111, 1022, 817 cm^{-1}; MS m/e (rel intensity) 270 (M^+ + 2, 2.5), 269 (M^+ + 1, 17.4), 268 (M^+, 3.1), 237 (9.3), 191 (13.5), 169 (21.1), 163 (14.4), 156 (100), 141 (14.8), 128 (10.7), 127 (10.7), 123 (33.3), 113 (20.9), 110 (46.0), 95 (24.6), 81 (65.9) 68 (12.7), 55 (10.0), 43 (34.6). Anal. Calcd for $C_{14}H_{20}O_5$: C, 61.74; H, 7.40. Found: C, 61.69; H, 7.41.

13E: TLC R_f 0.36 (hexane/EtOAc (3/1)); ^{1}H NMR (300 MHz) δ 6.93 (dt, J = 15.7, 6.6 Hz, 1 H, H-3), 5.84 (dt, J = 15.7, 1.5 Hz, 1 H, H-2), 4.17 (q, J = 7.1 Hz, 2 H, OCH_2), 3.72 (s, 3 H, OCH_3), 1.82–2.60 (m, 9 H), 1.65–1.82 (m, 1 H), 1.26 (t, J = 7.1 Hz, 3 H, CH_3); ^{13}C NMR (75.4 MHz) δ 214.16, 170.55, 166.69, 147.85, 121.27, 61.38, 59.66, 51.28, 37.69, 33.07, 31.81, 27.44, 19.45, 13.92; IR (neat) 2913, 1735 (CO), 1700 (CO), 1649 (C=C), 1426, 1140, 1021, 976, 914, 848, 727 cm^{-1}; MS m/e (rel intensity) 270 (M^+ + 2, 2.0), 269 (M^+ + 1, 14.7), 268 (M^+, 3.1), 237 (9.5), 191 (13.5), 169 (13.1), 163 (11.5), 156 (100) 141 (11.0), 123 (19.5), 113 (15.2), 110 (37.8), 95 (18.7), 81 (43.8), 68 (7.5), 55 (7.2). Anal. Calcd for $C_{14}H_{20}O_5$: C, 61.74; H, 7.40. Found: C, 61.69; H, 7.41.

Preparation of Methyl 2-[(2-Oxocyclohexyl)methyl]propenoate (14). To a stirred solution of dry diisopropylamine (2.8 mL, 20.0 mmol) in dry THF (30 mL) was added dropwise *n*-BuLi (2.5 M solution in hexane, 8 mL, 20.0 mmol) over 5 min. After 10 min, the reaction mixture was allowed to warm to 0 °C and stirred for an additional 10 min. The reaction mixture was recooled to −78 °C, and a solution of cyclohexanone (1.96 g, 20.0 mmol) in dry THF (10 mL) was added dropwise over 10 min. After 20 min, the reaction mixture was allowed to warm to 0 °C, the stirring was continued for 10 min, and methyl 2-(bromomethyl)propenoate (3.58 g, 20.0 mmol) was added in one portion. After 30 min, the reaction mixture was concentrated in vacuo and the residue was diluted with water (100 mL) and ether (100 mL). The organic layer was separated, and the aqueous layer was extracted with ether (50 mL × 2). The combined organic layer was washed with brine (50 mL), dried ($MgSO_4$), filtered, and then concentrated *in vacuo* to give a colorless oil. Cyclohexanone was removed in reduced pressure (Kugelrohr), and the residue was purified by flash column chromatography (SiO_2, hexane/EtOAc (4/1)) to give **14** (2.54 g, 65%) as a colorless oil: TLC R_f 0.39 (hexane/EtOAc (4/1)); ^{1}H NMR (300 MHz) δ 6.02 (d, J = 1.4 Hz, 1 H, H-3), 3.59 (m, 1 H, H-3), 3.74 (s, 3 H, OCH_3), 2.92 (ddd, J = 14.3, 5.5, 1.1 Hz, 1 H, CHC=), 2.50–2.65 (m, 1 H, CHCO), 2.25–2.50 (m, 2 H, CHC= and CHCO), 2.00–2.20 (m, 3 H), 1.78 (m, 1 H), 1.57–1.78 (m, 2 H), 1.23–1.40 (m, 1 H); ^{13}C NMR (75.4 MHz) δ 211.90, 167.30, 138.06, 126.90, 51.65, 48.98, 42.02, 33.47, 31.96, 27.91, 24.89; IR (neat) 2905, 1703 (CO), 1622 (C=C), 1428, 1291, 1193, 1142, 942, 811 cm^{-1}; MS m/e (rel intensity) 197 (M^+ + 1, 2.6), 196 (M^+, 8.3), 165 (22.0), 164 (54.3), 136 (100), 122 (24.9), 119 (16.0), 100 (35.9), 97 (54.1), 93 (21.6), 79 (31.0), 67 (266.6), 55 (30.9), 41 (28.0). Anal. Calcd for $C_{11}H_{16}O_3$: C, 67.32; H, 8.22. Found: C, 67.39; H, 8.18.

Preparation of (*Z*)- and (*E*)-4-(2-Oxocyclopentyl)-1-butenyl Phenyl Sulfoxide (16*Z* and 16*E*). Preparation of (*Z*)- and (*E*)-4-(2-Oxocyclopentyl)-1-butenyl Phenyl Sulfoxide Ethylene Ketal. To a stirred solution of dimethyl (phenylsulfinyl)methylphosphonate (8.57 g, 34.52 mmol) in dry THF (150 mL) was added dropwise n-BuLi (2.5 M in hexane, 13.8 mL, 34.50 mmol) over 10 min at −78 °C. After 30 min, a solution of 3-(2-oxocyclopentyl)propanal ethylene ketal (5.53 g, 30.02 mmol) in dry THF (20 mL) was added dropwise over 20 min, and the stirring was continued for an additional 30 min. The reaction mixture was allowed to warm to room temperature, stirred for an additional 1 h, and then diluted with EtOAc (250 mL) and water (200 mL). The organic layer was separated, and the aqueous layer was extracted with EtOAc (100 mL × 2). The combined organic layer was washed with brine, dried ($MgSO_4$), filtered, and then concentrated *in vacuo* to afford a pale yellow oil, which was purified by flash column chromatography (SiO_2, hexane/ether (1/1)) to give the *E* isomer (5.02 g, 50%) and the *Z* isomer (4.81 g, 41%) as colorless oils.

***E* isomer**: TLC R_f 0.40 (hexane/EtOAc, (1/1)); ^{1}H NMR (300 MHz) δ 7.42–7.68 (m, 5 H, aromatic), 6.64 (dt, J = 15.2, 6.7 Hz, 1 H, H-2, from major), 6.53–6.67 (m, 1 H, H-2, from minor), 6.27 (dt, J = 15.1, 1.4 Hz, 1 H, H-1, from minor), 6.25 (dt, J = 15.2, 1.4 Hz, 1 H, H-1, from major), 3.80–3.98 (m, 4 H, OCH_2CH_2O), 2.10–2.40 (m, 2 H), 1.79–2.00 (m, 2 H), 1.49–1.79 (m, 5 H), 1.20–1.49 (m, 2 H); IR (neat) 3027, 2916, 1609 (C=C), 1435, 1301, 1197, 1137, 1078, 1035, 955, 744, 686 cm^{-1}; MS m/e (rel intensity) 308 (M^+ + 2, 10.3), 307 (M^+ + 1, 46.6), 306 (M^+, 6.5), 289 (41.8), 263 (19.7), 141 (61.9), 99 (100), 77 (14.9), 55 (24.8), 41 (17.4). Anal. Calcd for $C_{17}H_{22}O_3S$: C, 66.64; H, 7.24. Found: C, 66.71; H, 7.26.

***Z* isomer**: TLC R_f 0.35 (hexane/EtOAc (1/1)); ^{1}H NMR (300 MHz) δ 7.42–7.68 (m, 5 H, aromatic), 6.15–6.32 (m, 2 H, H-1 and H-2), 3.82–4.02 (m, 4 H, OCH_2CH_2O), 1.30–2.86 (m, 11 H); IR (neat) 3024, 2902, 1607 (C=C), 1435, 1301, 1197, 1137, 1078, 1028, 943, 833, 739, 686 cm^{-1}; MS m/e (rel intensity) 308 (M^+ + 2, 17.2), 307 (M^+ + 1, 80.3), 306 (M^+, 31.3), 289 (61.8), 263 (26.7), 141 (50.7), 109 (19.0), 99 (100), 77 (34.2), 55 (29.7), 51 (15.5), 41 (23.9). Anal. Calcd for $C_{17}H_{22}O_3S$: C, 66.64; H, 7.24. Found: C, 66.70; H, 7.21.

Preparation of 16*Z*. The reaction was carried out as described in the preparation of **7*Z***, using (*Z*)-4-(2-oxocyclopentyl)-1-butenyl phenyl sulfoxide ethylene ketal (3.37 g, 10.01 mmol) to afford a pale yellow oil, which was purified by flash column chromatography (SiO_2, CH_2Cl_2/MeOH (10/1)) to give **16*Z*** (2.92 g, 100%) as a colorless oil: TLC R_f 0.25 (hexane/EtOAc (1/1)); ^{1}H NMR (300 MHz) δ 7.42–7.68 (m, 5 H, aromatic), 6.13–6.29 (m, 2 H, H-1 and H-2), 2.52–2.84 (m, 2 H), 2.23–2.42 (m, 2 H, H-3), 1.72–2.23 (m, 5 H), 1.42–1.68 (m, 2 H); ^{13}C NMR (75.4 MHz) δ 219.98, 219.90, 143.97, 141.16, 140.80, 137.19, 136.78, 130.35, 128.92, 123.62, 48.13, 47.82, 37.62, 37.55, 29.36, 29.00, 28.65, 28.42, 27.18, 26.66, 20.24; IR (neat) 2038, 2908, 1717 (CO), 1651 (C=C), 1435, 1148, 1078, 1029, 739, 686 cm^{-1}; MS m/e (rel intensity) 264 (M^+ + 2, 9.1), 263 (M^+ + 1, 49.3), 262 (M^+, 7.5), 245 (100), 179 (40.6), 149 (48.8), 135 (76.0), 129 (24.7), 123 (21.8), 115 (38.1), 109 (40.8), 97 (28.8), 91 (36.9), 85 (22.9), 77 (78.6), 69 (23.0), 67 (32.6), 55 (64.9), 51 (47.5), 41 (70.3). Anal. Calcd for $C_{15}H_{18}O_2S$: C, 68.67; H, 6.91. Found: C, 68.65; H, 6.89.

Preparation of 16*E*. The reaction was carried out as described in the preparation of **7*Z***, using (*E*)-4-(2-oxocyclopentyl)-1-butenyl phenyl sulfoxide ethylene ketal (3.37 g, 10.01 mmol) to afford a pale yellow oil, which was purified by flash chromatography (SiO_2, CH_2Cl_2/MeOH (10/1)) to give **16*E*** (2.92 g, 100%) as a colorless oil: TLC R_f 0.30 (hexane/EtOAc (1/1)); ^{1}H NMR (300 MHz) δ 7.42–7.66 (m, 5 H, aromatic), 6.61 (dt, J = 15.1, 6.7 Hz, 1 H, H-2), 6.60 (dt, J = 15.1, 6.7 Hz, 1 H, H-2), 6.28 (dt, J = 15.1, 1.4 Hz, 1 H, H-1), 1.83–2.40 (m, 8 H), 1.66–1.83 (m, 1 H), 1.35–1.58 (m, 2 H); ^{13}C NMR (75.4 MHz) δ 220.10, 143.77, 139.42, 135.26, 130.58, 128.99, 124.03, 47.93, 47.87, 37.65, 29.54, 29.46, 29.23, 27.70, 20.29; IR (neat) 2037, 2905, 1721 (CO), 1620 (C=C), 1435, 1149, 1078, 1036, 962, 746 cm^{-1}; MS m/e (rel intensity) 264 (M^+ + 2, 11.3), 263 (M^+ + 1, 63.0), 245 (32.2), 279 (14.2), 135 (32.5), 130 (50.6), 115 (32.7), 109 (35.5), 97 (22.9), 91 (33.1), 85 (20.0), 83 (20.1), 77 (69.0), 67 (31.9), 55 (78.2), 51 (51.7), 41 (100). Anal. Calcd for $C_{15}H_{18}O_2S$: C, 68.67; H, 6.91. Found: C, 68.65; H, 6.98.

Preparation of 4-(2-Oxocyclopentyl)-1-butenyl Phenyl Sulfone (17). Preparation of 4-(2-Oxocyclopentyl)-1-butenyl Phenyl Sulfone Ethylene Ketal. To a stirred solution of dimethyl (phenylsulfonyl)methylphosphonate (4.56 g, 17.26 mmol) in dry THF (150 mL) was added dropwise n-BuLi (2.5 M in hexane, 6.9 mL, 17.25 mmol) over 10 min at −78 °C. After 30 min, a solution of 3-(2-oxocyclopentyl)propanal ethylene ketal (2.77 g, 15.01 mmol) in dry THF (20 mL) was added dropwise over 20 min, and the stirring was continued for an additional 30 min. The reaction mixture was allowed to warm to room temperature, stirred for an additional 1 h, and then diluted with EtOAc (200 mL) and water (100 mL). The organic layer was separated, and the aqueous layer was extracted with EtOAc (50 mL × 2). The combined organic layer was washed with brine, dried ($MgSO_4$), filtered, and then concentrated *in vacuo* to afford a pale yellow oil, which was purified by flash column chromatography (SiO_2, hexane/EtOAc (1/1)) to give an inseparable mixture of *Z* and *E* (5.13 g, 97%, *Z*/*E* = 1/3 was determined by ^{1}H NMR) as a colorless oil: TLC R_f 0.57 (hexane/EtOAc (1/1)); ^{1}H NMR (300 MHz) δ 7.82–7.97 (m, 2 H, aromatic), 7.46–7.68 (m, 3 H, aromatic), 7.01 (dt, J = 15.1, 6.7 Hz, 1 H, H-2, from *E* isomer), 6.35 (dt, J = 15.1, 1.6 Hz, 1 H, H-1), 6.22–6.41 (m, 2 H, H-1 and H-2, from *Z* isomer), 3.78–3.98 (m, 4 H, OCH_2CH_2O), 2.60–2.80 (m, 2 H, H-3, from *Z* isomer), 2.13–2.40 (m, 2 H, H-3, from *E* isomer), 1.79–1.98 (m, 2 H), 1.48–1.79 (m, 5 H), 1.20–1.48 (m, 2 H); ^{13}C NMR (75.4 MHz) δ 147.42, 147.10, 141.56, 140.46, 133.04, 132.98, 129.98, 128.98, 127.23, 126.92, 117.61, 117.50, 64.19, 64.11, 45.30, 45.07, 35.40, 35.27, 29.91, 29.04, 27.76, 26.61, 26.20, 20.36, 20.31; IR (neat) 3025, 2906, 1615 (C=C), 1436, 1279, 1198, 1134, 1080, 1020, 960, 815, 749, 684, 591, 543 cm^{-1}; MS m/e (rel intensity) 324 (M^+ + 2, 21.7), 323 (M^+ + 1, 100), 322 (M^+, 30.8), 181 (23.5), 141 (85.1), 99 (83.5), 77 (13.1). Anal. Calcd for $C_{17}H_{22}O_4S$: C, 63.33; H, 6.88. Found: C, 63.40; H, 6.85.

Preparation of 17*Z* and 17*E*. The reaction was carried out as described in the preparation of **7*Z***, using 4-(2-oxocyclopentyl)-

1-butenyl phenyl sulfone ethylene ketal (3.52 g, 10.02 mmol) to afford a colorless oil, which was purified by flash column chromatography (SiO_2, hexane/EtOAc (1/1)) to give an inseparable mixture of 17*Z* and 17*E* (3.08 g, 100%, 17*Z*/17*E* = 1/3 was determined by ^1H NMR) as a colorless oil: TLC R_f 0.47 (hexane/EtOAc (1/1)); ^1H NMR (300 MHz) δ 7.83–7.95 (m, 2 H, aromatic), 7.50–7.68 (m, 3 H, aromatic), 6.98 (dt, J = 15.1, 6.7 Hz, 1 H, H-2, from 17*E*), 6.36 (dt, J = 15.1, 1.5 Hz, 1 H, H-1, from 17*E*), 6.20–6.36 (m, 2 H, H-1 and H-2, from 17*Z*), 2.67–2.87 (m, 2 H, H-3, from 17*Z*), 1.32–2.42 (m, 16 H); ^{13}C NMR (75.4 MHz) δ 220.43, 220.16, 146.26, 145.99, 141.46, 140.39, 133.30, 133.21, 130.80, 129.15, 127.42, 127.08, 48.51, 48.06, 37.87, 37.81, 29.44, 29.31, 29.20, 28.41, 27.43, 25.69, 20.46; IR (neat) 3025, 2909, 1719 (CO), 1615 (C=C), 1437, 1278, 1079, 813, 750, 712, 684, 588, 544 cm^{-1}; MS m/e (rel intensity) 280 (M^+ + 2, 16.2), 279 (M^+ + 1, 88.6), 278 (M^+, 14.9), 195 (54.4), 137 (51.7), 125 (49.5), 97 (29.8), 84 (100), 77 (45.2), 67 (15.2), 55 (29.4), 51 (17.0), 41 (35.9). Anal. Calcd for $C_{15}H_{18}O_3S$: C, 64.72; H, 6.52. Found: C, 67.79; H, 6.49.

Reaction of Ketones or Aldehydes Tethered to α,β-Unsaturated Esters (or Nitrile) with Mg in MeOH. General Procedure: Method A. A mixture of ketones (or aldehydes) (4.0 mmol) and magnesium powder (292 mg, 12.0 mmol) in dry methanol (15 mL) in the presence of a catalytic amount of mercuric chloride was stirred for 2 h at −23 °C under the nitrogen atmosphere. The reaction mixture was poured into 0.5 N HCl (80 mL) and then extracted with ethyl acetate (100 mL × 2). The combined organic layer was washed with saturated aqueous $NaHCO_3$ solution, dried over $MgSO_4$, filtered, and then concentrated *in vacuo*. The residue was purified by flash column chromatography (SiO_2).

Method B. This method is identical to method A except dry methanol (10 mL) and dry THF (5 mL) are used as the solvent because of the solubility of the substrate.

Method C. This method is identical to method A except the reaction temperature is −43 °C.

Method D. This method is identical to method A except (a) the amount of substrate used is 2.0 mmol and (b) 15 equiv of magnesium powder (729 mg, 30.0 mmol) and 30 mL of dry methanol are used.

Method E. This method is identical to method D except 10 equiv of magnesium powder (486 mg, 20.0 mmol) and 20 mL of dry methanol are used.

Reaction of 1*Z* or 1*E*. 1-Methyl-2-oxabicyclo[3.3.0^{1,5}]-octan-3-one (1c) (124 mg, 18%), **methyl 7-oxooctanoate (1s)** (7 mg, 1%), and ***trans*-2-[(methoxycarbonyl)methyl]-1-methylcyclopentan-1-ol (1t)** (551 mg, 80%) as colorless oils were obtained from 1*Z* or 1*E* by method A.

1c: TLC R_f 0.61 (hexane/CH_2Cl_2/ether (10/10/1)); ^1H NMR (500 MHz) δ 2.84 (dd, J = 18.4, 9.9 Hz, 1 H, H-4β), 2.42 (m, 1 H, H-5), 2.27 (ddd, J = 18.4, 2.4, 0.3 Hz, 1H, H-4α), 2.01–2.07 (m, 1 H, H-8), 1.88–1.96 (m, 1 H, H-6), 1.54-1.74 (m, 3 H, H-7, H-8′), 1.45–1.52 (m, 1 H, H-6′), 1.45 (s, 3 H, CH_3); ^{13}C NMR (125.7 MHz) δ 177.10 (C-3), 95.35 (C-1), 43.64 (C-5), 39.62 (C-8), 36.61 (C-4), 34.14 (C-6), 25.32 (C-9), 24.15 (C-7); IR (neat) 2925, 1752 (CO), 1261, 1220, 1107, 1144, 1017, 944 cm^{-1}; MS m/e (rel intensity) 142 (M^+ + 2, 6.4), 141 (M^+ + 1, 56.2), 140 (M^+, 10.3), 112 (14.8), 97 (100), 81 (46.2), 69 (18.1), 58 (22.1), 55 (33.0), 43 (50). Anal. Calcd for $C_8H_{12}O_2$: C, 68.55; H, 8.63. Found: C, 68.61; H, 8.60.

1s: TLC R_f 0.52 (hexane/CH_2Cl_2/ether (10/10/1)); ^1H NMR (500 MHz) δ 3.57 (s, 3 H, OCH_3), 2.35 (t, J = 7.4 Hz, 2 H, H-6), 2.22 (t, J = 7.4 Hz, 2 H, H-2), 2.04 (s, 3 H, H-8), 1.52 (m, 4 H, H-4, H-5), 1.23 (m, 2 H, H-3); ^{13}C NMR (125.7 MHz) δ 208.73, 173.89, 51.31, 43.24, 33.66, 29.73, 28.43, 24.51, 23.19; IR (neat) 2910, 1725 (CO), 1349, 1193, 1164 cm^{-1}; MS m/e (rel intensity) 174 (M^+ + 2, 0.9), 173 (M^+ + 1, 3.8), 172 (M^+, 2.6), 115 (75.7), 87 (27.0), 83 (24.9), 73 (22.9), 58 (22.0), 55 (22.2), 43 (100). Anal. Calcd for $C_9H_{16}O_3$: C, 62.77; H, 9.63. Found: C, 62.72; H, 9.42.

1t: TLC R_f 0.15 (hexane/CH_2Cl_2/ether (10/10/1)); ^1H NMR (500 MHz) δ 3.58 (s, 3 H, OCH_3), 2.88 (br s, 1 H, OH), 2.37 (m, 1 H, $CHCO_2Me$), 2.18 (dd, J = 15.5, 7.6 Hz, 1 H, $CHCO_2Me$), 2.13 (m, 1 H, H-2), 1.88 (m, 1 H, H-3), 1.70 (m, 1 H, H-4), 1.57–1.67 (m, 2 H, H-4′, H-5), 1.43–1.53 (m, 1 H, H-5′), 1.10–1.19 (m, 1 H, H-3′), 1.04 (s, 3 H, CH_3); ^{13}C NMR (125.7 MHz) δ 174.54 (CO), 79.16 (C-1), 51.59 (OCH_3), 46.19 (C-2), 40.77 (C-4), 34.85 (CH_2CO_2), 29.97 (C-3), 22.74 (CH_3), 20.26 (C-5); IR (neat) 3371 (OH), 2927, 1714 (CO), 1428, 1251, 1199, 1145, 1006 cm^{-1}; MS m/e (rel intensity) 173 (M^+ + 1, 1.1), 172 (M^+, 1.5), 155 (20.0), 140 (31.8), 129 (61.8), 125 (33.3), 112 (63.9), 97 (69.3), 81 (45.8), 71 (49.3), 58 (31.4), 43 (100). Anal. Calcd for $C_9H_{16}O_3$: C, 62.77; H, 9.36. Found: C, 62.82; H, 9.33.

Reaction of 2*E*: Methyl 7-oxoheptanoate (297 mg, 47%) and **methyl 7-hydroxyheptanoate** (199 mg, 31%) as colorless oils were obtained from 2*E* by method A.

Methyl 7-oxoheptanoate: TLC R_f 0.52 (hexane/EtOAc (3/1)); ^1H NMR (300 MHz) δ 9.71 (t, J = 1.7 Hz, 1 H, CHO), 3.61 (s, 3 H, OCH_3), 2.40 (td, J = 1.7, 7.2 Hz, 2 H, H-6), 2.27 (t, J = 7.5 Hz, 2 H, H-2), 1.59 (m, 4 H, H-3 and H-5), 1.32 (m, 2 H, H-4); ^{13}C NMR (75.4 MHz) δ 202.46, 173.95, 51.43, 43.53, 33.68, 28.48, 24.52, 21.57; IR (neat) 2913, 2699, 1719 (CO), 1426, 1242, 1195, 1168, 1090, 1003, 981 cm^{-1}; MS m/e (rel intensity) 156 (M^+ − 2, 4.2), 143 (27.3), 128 (38.8), 125 (23.6), 124 (41.8), 115 (66.0), 114 (42.3), 101 (15.3), 97 (15.3), 96 (21.2), 87 (18.5), 83 (35.4), 74 (100), 68 (20.8). Anal. Calcd for $C_8H_{14}O_3$: C, 60.74; H, 8.92. Found: C, 60.79; H, 9.00.

Methyl 7-hydroxyheptanoate: TLC R_f 0.21 (hexane/EtOAc (3/1)); ^1H NMR (300 MHz) δ 3.67 (s, 3 H, OCH_3), 3.64 (t, J = 6.5 Hz, 2 H, H-7), 2.29 (t, J = 7.5 Hz, 2 H, H-2), 1.50–1.85 (m, 5 H, OH, H-3, and H-6), 1.30–1.48 (m, 4 H, H-4 and H-5); ^{13}C NMR (75.4 MHz) δ 174.30, 62.75, 51.62, 33.94, 32.46, 28.83, 25.51, 24.81; IR (neat) 3341 (OH), 2897, 1724 (CO), 1426, 1199, 1162, 1032, 1011 cm^{-1}; MS m/e (rel intensity) 163 (M^+ + 3, 0.4), 162 (M^+ + 2, 1.0), 161 (M^+ + 1, 8.8), 160 (M^+, 2.2), 129 (19.2), 111 (11.6), 101 (11.3), 87 (59.2), 84 (20.0), 82 (21.4), 74 (100), 69 (35.7), 68 (29.9), 59 (19.3), 55 (39.4), 43 (39.5). Anal. Calcd for $C_8H_{16}O_3$: C, 59.98; H, 10.07. Found: C, 59.91; H, 9.99.

Reaction of 3*E*. Methyl 8-oxononanoate (3s) (97 mg, 13%), **1-methyl-2-oxabicyclo[3.3.0^{1,5}]nonanan-3-one (3c)** (265 mg, 43%), and ***trans*-2-[(methoxycarbonyl)methyl]-1-methylcyclohexan-1-ol (3t)** (283 mg, 38%) were obtained from 3*E* by method A.

3s: TLC R_f 0.48 (hexane/EtOAc (3/1)); ^1H NMR (300 MHz) δ 3.62 (s, 3 H, OCH_3), 2.38 (t, J = 7.4 Hz, 2 H), 2.26 (t, J = 7.5 Hz, 2 H), 2.09 (s, 3 H, H-9), 1.46–1.68 (m, 4 H, H-3 and H-6), 1.20–1.35 (m, 4 H, H-4 and H-5); ^{13}C NMR (75.4 MHz) δ 209.10, 174.13, 51.41, 43.55, 33.91, 29.81, 28.81, 28.70, 24.67, 23.51; IR (neat) 2908, 1730 (CO), 1708 (CO), 1454, 1350, 1192, 1164, 1090, 1008 cm^{-1}; MS m/e (rel intensity) 187 (M^+ + 1, 0.9), 155 (4.6), 129 (12.5), 109 (6.7), 97 (17.2), 87 (16.2), 83 (8.3), 74 (5.8), 69 (22.0), 59 (12.9), 58 (18.9), 55 (24.3), 43 (100), 41 (23.7). Anal. Calcd for $C_{10}H_{18}O_3$: C, 64.49; H, 9.74. Found: C, 64.51; H, 9.71.

3c: TLC R_f 0.44 (hexane/EtOAc (3/1)); ^1H NMR (300 MHz) δ 2.54 (dd, J = 17.1, 7.6 Hz, 1 H, H-9), 2.32 (dd, J = 17.1, 7.9 Hz, 1 H, H-9′), 2.19 (m, 1 H, H-1), 1.36 (s, 3 H, CH_3), 1.20–1.80 (m, 8 H); ^{13}C NMR (75.4 MHz) δ 176.54, 84.89, 40.08, 35.03, 34.52, 26.28, 25.36, 21.74, 21.03; IR (neat) 2906, 1769 (CO), 1420, 1375, 1241, 1209, 1167, 1097, 938 cm^{-1}; MS m/e (rel intensity) 156 (M^+ + 2, 0.6), 155 (M^+ + 1, 3.8), 154 (M^+, 4.9), 139 (28.3), 121 (7.8), 111 (53.3), 95 (10.4), 83 (10.2), 81 (12.3), 71 (16.6), 68 (26.5), 67 (27.8), 58 (15.0), 55 (54.1), 43 (100), 41 (53.3). Anal. Calcd for $C_9H_{14}O_3$: C, 70.10; H, 9.74. Found: C, 70.18; H, 9.73.

3t: TLC R_f 0.30 (hexane/EtOAc (3/1)); ^1H NMR (300 MHz) δ 3.63 (s, 3 H, OCH_3), 2.66 (dd, J = 14.8, 4.5 Hz, 1 H, $CHCO_2Me$), 1.97 (dd, J = 14.8, 9.0 Hz, 1 H, $CHCO_2Me$), 1.80–1.93 (m, 1 H, H-2), 1.85 (s, 1 H, OH), 1.52–1.79 (m, 4 H, ring protons), 1.10–1.43 (m, 3 H, ring protons), 1.06 (s, 3 H, CH_3); ^{13}C NMR (75.4 MHz) δ 174.64, 72.34, 51.57, 45.10, 42.49, 35.34, 30.14, 25.48, 24.03, 20.13; IR (neat) 3386 (OH), 2901, 1712 (CO), 1429, 1362, 1278, 1166, 1123, 983, 952, 886 cm^{-1}; MS m/e (rel intensity) 186 (M^+, 0.6), 169 (3.1), 154 (4.2), 139 (7.7), 126 (9.4), 111 (24.8), 97 (12.3), 95 (16.2), 87 (23.1), 71 (36.9), 67 (12.2), 59 (19.6), 58 (20.4), 55 (35.2), 43 (100), 41 (39.8). Anal. Calcd for $C_{10}H_{18}O_3$: C, 64.49; H, 9.74. Found: C, 64.52; H, 9.71.

Reaction of 4*E*. Methyl 8-oxooctanoate (308 mg, 48%) and **methyl 8-hydroxyoctanoate** (188 mg, 29%) were obtained as colorless oils from 4*E* by method A.

Methyl 8-oxooctanoate: TLC R_f 0.48 (hexane/EtOAc, (3/1)); ^1H NMR (300 MHz) δ 9.70 (t, J = 1.8 Hz, 1 H, CHO), 3.61 (s, 3 H, OCH_3), 2.37 (td, J = 1.8, 7.3 Hz, 2 H, H-7), 2.25 (t, J = 7.5 Hz, 2 H, H-2), 1.50–1.70 (m, 4 H, H-3 and H-6), 1.20–1.40 (m, 4 H, H-4 and H-5); ^{13}C NMR (75.4 MHz) δ 202.64, 174.06, 51.37, 43.65, 33.81, 28.70, 28.63, 24.56, 21.71; IR (neat) 2907, 1727 (CO), 1433, 1237, 1193, 1166, 1095, 1008 cm^{-1}; MS m/e (rel intensity) 174 (M^+ + 2, 1.5), 173 (M^+ + 1, 11.1), 172 (M^+, 2.0), 141 (38.9), 129 (19.6), 101 (11.2), 97 (26.5), 95 (30.5), 87 (58.7), 86 (16.7), 81

(13.7), 74 (64.6), 69 (55.1), 68 (24.6), 67 (20.9), 59 (41.5), 55 (78.2), 43 (74.8), 41 (100). Anal. Calcd for $C_9H_{16}O_3$: C, 62.77; H, 9.36. Found: C, 62.81; H, 9.35.

Methyl 8-hydroxyoctanoate: TLC R_f 0.19 (hexane/EtOAc (3/1)); ^{1}H NMR (300 MHz) δ 3.67 (s, 3 H, OCH_3), 3.63 (t, J = 6.6 Hz, 2 H, H-8), 2.31 (t, J = 7.5 Hz, 2 H, H-2), 1.89 (s, 1 H, OH), 1.50–1.72 (m, 4 H, H-3 and H-7), 1.22–1.47 (m, 6 H, H-4, H-5, and H-6); ^{13}C NMR (75.4 MHz) δ 174.30, 62.76, 51.40, 33.96, 32.56, 28.97, 28.93, 25.45, 24.75; IR (neat) 3333 (OH), 2893, 1727 (CO), 1427, 1238, 1192, 1164, 1049 cm^{-1}; MS m/e (rel intensity) 176 (M^+ + 2, 11.7), 175 (M^+ + 1, 100), 174 (M^+, 5.5), 157 (23.0), 143 (32.5), 125 (31.2), 124 (16.2), 97 (12.2), 96 (17.5), 82 (11.9), 74 (20.6), 55 (14.5), 43 (13.0). Anal. Calcd for $C_9H_{18}O_3$: C, 62.04; H, 10.41. Found: C, 62.08; H, 10.39.

Reaction of 5*Z* or 5*E*. 1-Methyl-2,7-dioxabicyclo[3.3.0^{1,5}]-octan-3-one (5c) (22 mg, 4%) and ***trans*-4-[(methoxycarbonyl)methyl]-3-methyltetrahydrofuran-3-ol (5t)** (63 mg, 9%) as colorless oils were obtained from **5*Z*** or **5*E*** by method A.

5c: TLC R_f 0.62 (CH_2Cl_2/ether (2/1)); ^{1}H NMR (300 MHz) δ 4.09 (d, J = 10.5 Hz, 1 H, H-8), 3.93 (dd, J = 9.7, 6.7 Hz, 1 H, H-6), 3.79 (dd, J = 9.7, 3.1 Hz, 1 H, H-6′), 3.49 (d, J = 10.5 Hz, 1 H, H-8′), 2.95 (dd, J = 18.4, 10.0 Hz, 1 H, H-4), 2.69 (ddt, J = 10.0, 6.7, 3.1 Hz, 1 H, H-5), 2.51 (dd, J = 18.4, 3.1 Hz, 1 H, H-4′), 1.56 (s, 3 H, CH_3); ^{13}C NMR (75.4 MHz) δ 175.64, 92.85, 77.91, 75.20, 44.64, 35.20, 22.02; IR (neat) 2903, 1758 (CO), 1429, 1376, 1233, 1135, 1059, 1024, 954, 917, 841, 787, 707, 660, 580, 536, 513 cm^{-1}; MS m/e (rel intensity) 144 (M^+ + 2, 0.6), 143 (M^+ + 1, 0.9), 142 (M^+, 6.7), 113 (3.1), 99 (9.3), 83 (12.0), 69 (15.9), 68 (10.6), 55 (20.8), 45 (26.3), 43 (100), 41 (53.7). Anal. Calcd for $C_7H_{10}O_3$: C, 59.14; H, 7.09. Found: C, 59.21; H, 7.03.

5t: TLC R_f 0.29 (CH_2Cl_2/ether (2/1)); ^{1}H NMR (300 MHz) δ 4.17 (dd, J = 8.8, 7.5 Hz, 1 H, H-3), 3.70 (d, J = 8.9 Hz, 1 H, H-5), 3.65 (s, 3 H, OCH_3), 3.54 (d, J = 8.9 Hz, 1 H, H-5′), 3.41 (dd, J = 8.8, 7.2 Hz, 1 H, H-3′), 3.10 (br s, 1 H, OH), 2.52 (m, 1 H, H-2), 2.44 (dd, J = 16.3, 7.8 Hz, 1 H, $CHCO_2$), 2.26 (dd, J = 16.3, 7.2 Hz, 1 H, $CHCO_2$), 1.21 (s, 3 H, CH_3); ^{13}C NMR (75.4 MHz) δ 173.41, 79.05, 78.11, 72.72, 51.93, 45.90, 33.13, 20.88; IR (neat) 3382 (OH), 2919, 1724 (CO), 1428, 1365, 1254, 1166, 1132, 1051, 992, 920 cm^{-1}; MS m/e (rel intensity) 176 (M^+ + 2, 1.0), 175 (M^+ + 1, 1.2), 143 (8.4), 131 (24.6), 125 (22.5), 112 (31.8), 101 (77.8), 100 (55.8), 84 (39.0), 83 (49.3), 74 (17.9), 71 (28.5), 69 (22.7), 59 (61.4), 43 (100), 41 (20.7). Anal. Calcd for $C_8H_{14}O_4$: C, 55.16; H, 8.10. Found: C, 55.19; H, 8.08.

Reaction of 6*Z* or 6*E*. 1-Methyl-2-oxa-7-(*p*-toluenesulfonyl)-7-azobicyclo[3.3.0^{1,5}]octan-3-one (6c) (661 mg, 56%) and ***trans*-4-[(methoxycarbonyl)methyl]-3-methyl-1-(*p*-toluenesulfonyl)pyrrolidin-3-ol (6t)** (536 mg, 41%) were obtained as white crystals from **6*Z*** or **6*E*** by method B.

6c: TLC R_f 0.69 (CH_2Cl_2/ether (2/1)); mp 159–160 °C (ethanol); ^{1}H NMR (300 MHz) δ 7.65 and 7.46 (AB quartet, J = 8.1 Hz, 4 H, aromatic), 3.49 (d, J = 11.1 Hz, 1 H, H-8), 3.17 (dd, J = 10.1, 8.1 Hz, 1 H, H-6), 3.04 (dd, J = 10.1, 3.5 Hz, 1 H, H-6′), 2.99 (dd, J = 18.2, 9.5 Hz, 1 H, H-4), 2.73 (d, J = 11.1 Hz, 1 H, H-8′), 2.67 (m, 1 H, H-5), 2.47 (dd, J = 18.2, 2.2 Hz, 1 H, H-4′), 2.40 (s, 3 H, CH_3), 1.35 (s, 3 H, CH_3); ^{13}C NMR (75.4 MHz) δ 175.46, 143.92, 131.11, 129.92 (×2), 127.81 (×2), 90.98, 58.24, 54.18, 42.09, 34.57, 22.04, 21.02; IR (neat) 2949, 1759 (CO), 1591 (C=C), 1331, 1297, 1238, 1152, 1122, 1085, 1030, 971, 944, 830, 662, 626, 581, 546 cm^{-1}; MS m/e (rel intensity) 298 (M^+ + 3, 0.3), 297 (M^+ + 2, 1.2), 296 (M^+ + 1, 4.2), 295 (M^+, 12.1), 198 (2.0), 155 (3.8), 140 (100), 112 (28.4), 105 (2.0), 98 (4.5), 91 (6.9), 83 (4.6), 68 (8.5), 42 (76.2). Anal. Calcd for $C_{14}H_{17}NO_4S$: C, 56.93; H, 5.80; N, 4.74. Found: C, 56.99; H, 5.82; N, 4.75.

6t: TLC R_f 0.59 (CH_2Cl_2/ether (2/1)); mp 100–101 °C (toluene); ^{1}H NMR (300 MHz) δ 7.66 and 7.43 (AB quartet, J = 8.1 Hz, 4 H, aromatic), 4.97 (s, 1 H, OH), 3.56 (s, 3 H, OCH_3), 3.48 (dd, J = 10.0, 7.3 Hz, 1 H, H-3), 3.10 (d, J = 9.8 Hz, 1 H, H-5), 3.02 (d, J = 9.8 Hz, 1 H, H-5′), 2.89 (dd, J = 10.0, 7.0 Hz, 1 H, H-3′), 2.39 (s, 3 H, CH_3), 2.32 (dd, J = 15.8, 10.6 Hz, 1 H, $CHCO_2$), 2.12 (m, 1 H, H-2), 1.95 (dd, J = 15.8, 4.0 Hz, 1 H, $CHCO_2$), 0.89 (s, 3 H, CH_3); ^{13}C NMR (75.4 MHz) δ 172.23, 143.30, 133.33, 129.75 (×2), 127.24 (×2), 75.98, 58.75, 51.45, 51.23, 44.45, 32.18, 20.93 (2); IR (neat) 3468 (OH), 2923, 1718 (CO), 1594 (C=C), 1428, 1371, 1322, 1265, 1217, 1148, 1126, 1084, 1054, 1030, 993, 925, 890, 866, 808, 707, 663, 632, 588, 543 cm^{-1}; MS m/e (rel intensity) 329 (M^+ + 2, 0.8), 328 (M^+ + 1, 4.5), 310 (4.6), 296 (2.6), 278 (2.8), 236 (3.1), 198 (3.4), 184 (9.9), 172 (100), 154 (25.9), 140 (39.5), 112 (20.5), 94 (36.6), 42 (64.3). Anal. Calcd for $C_{15}H_{21}NO_5S$: C, 55.03; H, 6.46; N, 4.28. Found: C, 55.00; H, 6.52; N, 4.25.

Reaction of a Mixture of 9*Z* and 9*E*. 5-(2-Oxocyclopentyl)pentanonitrile (192 mg, 29%), **2-(cyanomethyl)-1-hydroxybicyclo[3.3.0^{1,5}]octane (9s and 9t)** (278 mg, 42%), and **5-(2-hydroxycyclopentyl)pentanonitrile** (181 mg, 27%) were obtained as colorless oils from a mixture of **9*Z*** and **9*E*** by method A.

5-(2-Oxocyclopentyl)pentanonitrile: TLC R_f 0.53 (hexane/EtOAc (2/1)); ^{1}H NMR (300 MHz) δ 2.37 (t, J = 7.0 Hz, 2 H, H-2), 2.21–2.40 (m, 2 H), 1.97–2.20 (m, 3 H), 1.62–1.90 (m, 4 H), 1.45–1.62 (m, 3 H), 1.21–1.40 (m, 1 H); ^{13}C NMR (75.4 MHz) δ 220.85, 119.51, 48.70, 37.91, 29.39, 28.62, 26.47, 25.21, 20.54, 16.86; IR (neat) 2901, 2218 (CN), 1718 (CO), 1419, 927, 819 cm^{-1}; MS m/e (rel intensity) 166 (M^+ + 1, 0.8), 165 (M^+, 1.9), 164 (1.1), 122 (2.4), 108 (3.6), 97 (8.2), 94 (3.6), 84 (100), 55 (13.2). Anal. Calcd for $C_{10}H_{15}NO$: C, 72.69; H, 9.51; N, 8.48. Found: C, 72.74; H, 9.47; N, 8.45.

9s and 9t: TLC R_f 0.42 (hexane/EtOAc (2/1)); ^{1}H NMR (300 MHz) δ 2.26 (dd, J = 16.5, 5.7 Hz, 1 H, CHCN), 2.29 (dd, J = 16.5, 7.3 Hz, 1 H, CHCN), 2.05–2.60 (m, 11 H), 1.20–2.00 (m, 25 H), 1.03–1.20 (m, 2 H); ^{13}C NMR (75.4 MHz) δ 119.71, 119.51, 91.16, 74.20, 51.17, 47.00, 45.19, 35.80, 34.63, 34.54, 29.69, 29.07, 28.49, 28.09, 27.43, 25.49, 25.38, 21.47, 16.86, 16.81; IR (neat) 3395 (OH), 2905, 2221 (CN), 1454, 1316, 1004, 977, 897 cm^{-1}; MS m/e (rel intensity) 166 (M^+ + 1, 0.7), 165 (M^+, 2.2), 164 (1.5), 148 (3.7), 135 (5.8), 125 (12.2), 110 (27.1), 97 (100), 83 (39.0), 69 (12.5), 55 (12.8). Anal. Calcd for $C_{10}H_{15}NO$: C, 72.69; H, 95.1; N, 8.48. Found: C, 72.73; H, 9.52; N, 8.50.

5-(2-Hydroxycyclopentyl)pentanonitrile: TLC R_f 0.32 (hexane/EtOAc (2/1)); ^{1}H NMR (300 MHz) δ 3.78 (q, J = ~6.2 Hz, 1 H, CHOH), 2.36 (t, J = 7.0 Hz, 2 H, H-2), 2.34 (s, 1 H, OH), 1.80–1.99 (m, 2 H), 1.35–1.80 (m, 9 H), 1.07–1.30 (m, 2 H); ^{13}C NMR (75.4 MHz) δ 119.69, 78.70, 47.48, 34.38, 32.66, 29.66, 27.08, 25.27, 21.52, 16.65; IR (neat) 3353 (OH), 2902, 2221 (CN), 1408, 1063, 1019 cm^{-1}; MS m/e (rel intensity) 167 (M^+, 0.4), 166 (M^+ – 1, 1.1), 165 (M^+ – 2, 0.5), 150 (24.4), 138 (6.9), 124 (17.1), 110 (22.7), 97 (100), 82 (47.3), 69 (21.7), 57 (16.9). Anal. Calcd for $C_{10}H_{17}NO$: C, 71.81; H, 10.24; N, 8.37. Found: C, 71.87; H, 10.21; N, 8.41.

Reaction of 10*Z*. 6β-(Benzyloxy)-1β-methyl-2-oxabicyclo[3.3.0^{1,5}]octan-3-one (10c) (277 mg, 23%) and **3β-(benzyloxy)-2α-[(methoxycarbonyl)methyl]-1α-methylcyclopentan-1-ol (10t)** (846 mg, 76%) were obtained as colorless oils from **10*Z*** by method A.

10c: TLC R_f 0.50 (hexane/EtOAc (4/1)); ^{1}H NMR (300 MHz) δ 7.23–7.42 (m, 5 H, aromatic), 4.51 and 4.38 (AB quartet, J = 11.86 Hz, 2 H, CH_2O), 3.76 (m, 1 H, H-6α), 2.93 (dd, J = 18.68, 11.02 Hz, 1 H, H-4β), 2.55 (m, 1 H, H-5β), 2.34 (dd, J = 18.68, 3.33 Hz, H-4α), 1.90–2.15 (m, 3 H, H-7, H-8α), 1.75–1.90 (m, 1 H, H-8β), 1.55 (s, 3 H, CH_3); ^{13}C NMR (75.4 MHz) δ 176.19 (C-3), 137.93, 128.42 (×2), 127.69, 127.42 (×2), 94.56 (C-1), 86.53 (C-6), 70.60 ($PhCH_2O$), 50.51 (C-5), 36.61 (C-6), 34.02 (C-4), 29.45 (C-7), 25.96 (CH_3); IR (neat) 3005, 2927, 2846, 1751 (CO), 1348, 1233, 1189, 1167, 1104, 1061, 1022, 948, 735, 694 cm^{-1}; MS m/e (rel intensity) 248 (M^+ + 2, 1.3), 247 (M^+ + 1, 8.0), 246 (M^+, 2.3), 229 (5.8), 168 (5.1), 155 (3.3), 142 (4.3), 139 (7.7), 137 (8.7), 109 (3.3), 104 (5.3), 91 (100), 43 (10.7). Anal. Calcd for $C_{15}H_{18}O_3$: C, 73.15; H, 7.37. Found: C, 73.19; H, 7.33.

10t: TLC R_f 0.32 (hexane/EtOAc (4/1)); ^{1}H NMR (300 MHz) δ 7.22–7.40 (m, 5 H, aromatic), 4.54 and 4.45 (AB quartet, J = 11.73 Hz, 2 H, CH_2O), 3.80 (br s, 1 H, OH), 3.66 (s, 3 H, OCH_3), 3.59 (q, J = ~5.7 Hz, 1 H, H-3α), 2.35–2.50 (m, 3 H, CH_2CO_2, H-2), 1.92–2.08 (m, 2 H, H-5β, H-4), 1.76–1.92 (m, 1 H, H-4′), 1.61–1.76 (m, 1 H, H-5α), 1.18 (s, 3 H, CH_3); ^{13}C NMR (75.4 MHz) δ 174.10 (CO), 138.02, 128.23 (×2), 127.56 (×2), 127.50, 83.61 (C-3), 78.18 (C-1), 71.01 ($PhCH_2O$), 51.81 (C-2), 51.73 (OCH_3), 38.13 (C-5), 33.20 (CH_2CO_2), 28.21 (C-4), 23.92 (CH_3); IR (neat) 3390 (OH), 3036, 2927, 1714 (CO), 1427, 1341, 1251, 1200, 1080, 1021, 923, 734, 694 cm^{-1}; MS m/e (rel intensity) 279 (M^+ + 1, 13.1), 278 (M^+, 1.4), 261 (100), 271 (25.9), 153 (96.1), 137 (7.9), 127 (6.0), 111 (5.0), 94 (12.8), 91 (27.1), 81 (10.5), 43 (9.0). Anal. Calcd for $C_{16}H_{22}O_4$: C, 69.04; H, 7.97. Found: C, 68.98; H, 7.93.

Reaction of a Mixture of 12*Z* and 12*E*. 8-Methyl-2-oxatricyclo[6.3.0^{1,5}.0^{1,3}]undecane-3,9-dione (12c) and 5α-hydroxy-1α-methyl-6β-[(methoxycarbonyl)methyl]bicyclo[3.3.0^{1,5}]octan-2-one (12t) (718 mg, 79%, **12c/12t** = 1/5.90 was

determined by ^{1}H NMR) were obtained as a colorless oil from a mixture of **12Z** and **12E** by method C.

12c and 12t: TLC R_f 0.32 (hexane/EtOAc (3/1)); ^{1}H NMR (300 MHz) δ 3.71 (s, 3 H, OCH_3), 3.57 (br s, 1 H, OH), 3.01 (dd, J = 15.6, 8.9 Hz, 1 H, H-4 from **12c**), 2.22–2.90 (m, 7 H), 1.68–2.18 (m, 6 H), 1.48–1.68 (m, 4 H), 1.15–1.34 (m, 4 H), 1.10 (s, 6 H, $2CH_3$); IR (neat) 3420 (OH), 2916, 1772 (CO from **12c**), 1721 (CO from **12t**), 1428, 1255, 1166, 1115, 1072, 1029, 960 cm^{-1}; MS *m/e* (rel intensity) 227 (M^+ + 1, 3.9), 226 (M^+, 28.1), 208 (10.4), 194 (49.2), 181 (19.4), 180 (18.9), 171 (30.1), 170 (27.5), 167 (30.5), 166 (28.8), 154 (42.0), 153 (69.7), 152 (65.6), 138 (100), 126 (38.6), 125 (38.2), 112 (38.4), 107 (46.2), 97 (23.1), 93 (39.9), 82 (17.3), 69 (22.1), 55 (16.2). Anal. Calcd for $C_{12}H_{18}O_4$: C, 63.70; H, 8.02. Found: C, 63.74; H, 7.99.

12c: ^{13}C NMR (75.4 MHz) δ 218.87, 176.02, 99.34, 59.13, 44.78, 36.29, 35.82, 35.19, 31.32, 30.21, 16.44.

12t: ^{13}C NMR (75.4 MHz) δ 221.91, 174.44, 87.89, 58.27, 51.81, 44.00, 35.64, 33.78, 33.33, 28.74, 27.70, 17.15.

Reaction of 13Z or 13E. 8-(Ethoxycarbonyl)-2-oxatricyclo[6.3.0^{1,5}.0^{1,5}]undecanone (13c) and *trans*-8-(ethoxycarbonyl)-2-[(ethoxycarbonyl)methyl]-1-hydroxybicyclo[3.3.0^{1,5}]octane (13t) (779 mg, 96%, **13c/13t** = 1/5.23 was determined by ^{1}H NMR) as a colorless oil were obtained from **13Z** or **13E** by method C.

13c and 13t: TLC R_f 0.49 (hexane/EtOAc (3/2)); ^{1}H NMR (300 MHz) δ 4.18 (q, J = 7.1 Hz, 2 H, OCH_2 from **13t**), 4.17 (q, J = 7.1 Hz, 2 H, OCH_2 from **13c**), 3.68 (s, 3 H, OCH_3), 3.22 (br s, 1 H, OH), 2.76 (dd, J = 15.6, 8.8 Hz, 1 H, H-4 from **13c**), 2.20–2.67 (m, 9 H), 1.15–2.20 (m, 16 H), 1.28 (t, J = 7.1 Hz, 3 H, CH_3 from **13t**), 1.27 (t, J = 7.1 Hz, 3 H, CH_3 from **13c**); IR (neat) 3445 (OH), 2920, 1774 (CO), 1715 (CO), 1429, 1359, 1266, 1185, 1118, 1017, 954, 919 cm^{-1}; MS *m/e* (rel intensity) 272 (M^+ + 3, 2.8), 272 (M^+ + 2, 18.3), 271 (M^+ + 1, 100), 270 (M^+, 4.7), 253 (14.3), 224 (10.2), 207 (16.2), 196 (13.6), 192 (33.6), 179 (40.4), 165 (58.8), 164 (50.5), 156 (17.8), 137 (14.3), 119 (20.4), 105 (11.5). Anal. Calcd for $C_{14}H_{22}O_5$: C, 62.20; H, 8.20. Found: C, 62.27; H, 8.19.

13c: ^{13}C NMR (75.4 MHz) δ 175.78, 173.03, 105.02, 61.71, 60.05, 45.69, 38.13, 35.71, 34.42, 34.21, 31.41, 23.53, 13.96.

13t: ^{13}C NMR (75.4 MHz) δ 176.14, 173.86, 92.79, 61.54, 60.65, 51.56, 46.59, 37.71, 36.05, 34.91, 34.21, 28.49, 24.71, 14.10.

Reaction of 14. Methyl 2-[(2-oxocyclohexyl)methyl]propanoate (15) (785 mg, 99%) was obtained as a colorless oil from **14** by method A.

15: TLC R_f 0.54 (hexane/EtOAc (3/1)); ^{1}H NMR (300 MHz) δ 3.67 and 3.66 (two singlets, 3 H, OCH_3), 2.47–2.65 (m, 1 H), 1.98–2.45 (m, 6 H), 1.20–1.95 (m, 5 H), 1.16 (d, J = 7.0 Hz, 3 H, CH_3); ^{13}C NMR (75.4 MHz) δ 212.70, 212.37, 177.21, 176.70, 51.41, 51.37, 48.57, 48.16, 42.14, 41.87, 37.36, 36.65, 34.73, 33.96, 33.65, 33.21, 28.07, 27.89, 25.03, 24.86, 17.68, 17.50; IR (neat) 2906, 1713 (CO), 1702 (CO), 1427, 1193, 1162, 1134, 1080, 834 cm^{-1}; MS *m/e* (rel intensity) 200 (M^+ + 2, 1.3), 199 (M^+ + 1, 10.8), 198 (M^+, 15.2), 167 (100), 139 (46.9), 138 (93.6), 124 (29.5), 111 (100), 101 (33.3), 98 (100), 88 (100), 83 (74.7), 69 (81.2), 55 (100), 41 (50.1). Anal. Calcd for $C_{11}H_{18}O_3$: C, 66.64; H, 9.15. Found: C, 66.70; H, 9.13.

Reaction of 16Z. (Z)-1-(Phenylthio)-4-(2-oxocyclopentyl)-1-butene (18Z) (838 mg, 85%) and ***trans*-1-hydroxy-2-(phenylthio)methylbicyclo[3.3.0^{1,5}]octane (19t)** (89 mg, 9%) were obtained as colorless oils from **16Z** by method A.

18Z: TLC R_f 0.48 (hexane/EtOAc (4/1)); ^{1}H NMR (300 MHz) δ 7.15–7.38 (m, 5 H, aromatic), 6.22 (dt, J = 9.2, 1.3 Hz, 1 H, H-1), 5.78 (dt, J = 9.2, 7.2 Hz, 1 H, H-2), 2.20–2.40 (m, 4 H), 1.86–2.20 (m, 4 H), 1.67–1.86 (m, 1 H), 1.47–1.63 (m, 1 H), 1.32–1.47 (m, 1 H); ^{13}C NMR (75.4 MHz) δ 221.10, 136.09, 132.23, 128.90 (×2), 128.66 (×2), 126.14, 123.60, 48.59, 38.05, 29.48, 28.76, 27.02, 20.64; IR (neat) 3031, 2903, 1724 (CO), 1575, 1471, 1147, 1082, 1019, 735, 685 cm^{-1}; MS *m/e* (rel intensity) 247 (M^+ + 1, 5.6), 246 (M^+, 28.4), 245 (M^+ − 1, 8.8), 162 (91.4), 147 (23.5), 134 (25.9), 129 (84.2), 116 (46.0), 115 (43.4), 109 (31.3), 91 (21.4), 85 (100), 77 (35.1), 65 (23.8), 55 (21.7), 45 (20.0), 43 (36.5), 41 (37.2). Anal. Calcd for $C_{15}H_{18}OS$: C, 73.13; H, 7.36. Found: C, 73.16; H, 7.33.

19t: TLC R_f 0.41 (hexane/EtOAc (4/1)); ^{1}H NMR (500 MHz) δ 7.14–7.37 (m, 5 H, aromatic), 3.03 (dd, J = 12.9, 8.1 Hz, 1 H, H-9), 2.97 (dd, J = 12.9, 7.2 Hz, 1 H, H-9′), 2.06–2.25 (m, 3 H, H-5, H-2, H-6β), 2.15 (s, 1 H, OH), 1.77–1.88 (m, 2 H, H-3β, H-4β), 1.64–1.73 (m, 3 H, H-7, H-8β), 1.43-1.53 (m, 1 H, H-8α), 1.19–1.31 (m, 2 H, H-4α, H-3α), 0.99–1.09 (m, 1 H, H-6α); ^{13}C NMR (125.7 MHz) δ 136.33, 128.95 (×2), 128.86 (×2), 125.91, 92.26 (C-1), 51.45 (C-5), 49.56 (C-2), 36.61 (C-8), 34.77 (C-6), 34.20 (C-9), 30.59 (C-4), 29.51 (C-3), 25.66 (C-7); IR (neat) 3359 (OH), 3033, 2916, 1575, 1472, 1291, 1207, 1083, 1020, 974, 914, 734, 686 cm^{-1}; MS *m/e* (rel intensity) 249 (M^+ + 1, 12.8), 248 (M^+, 71.3), 231 (33.1), 139 (88.1), 123 (13.1), 121 (62.9), 110 (100), 97 (29.3), 93 (21.6), 79 (19.1), 69 (41.3), 55 (42.3), 43 (33.4). Anal. Calcd for $C_{15}H_{20}OS$: C, 72.54; H, 8.12. Found: C, 72.61; H, 8.09.

Reaction of 16E. (E)-1-(Phenylthio)-4-(2-oxocyclopentyl)-1-butene (18E) (838 mg, 85%) and **19t** (89 mg, 9%) were obtained as colorless oils from **16E** by method A.

18E: TLC R_f 0.48 (hexane/EtOAc (4/1)); ^{1}H NMR (300 MHz) δ 7.12–7.36 (m, 5 H, aromatic), 6.18 (dt, J = 14.9, 1.3 Hz, 1 H, H-1), 5.92 (dt, J = 14.9, 6.9 Hz, 1 H, H-2), 2.17–2.38 (m, 4 H), 1.83–2.17 (m, 4 H), 1.68–1.83 (m, 1 H), 1.32–1.60 (m, 2 H); ^{13}C NMR (75.4 MHz) δ 220.89, 136.01, 135.49, 128.85 (×2), 128.57 (×2), 126.11, 121.90, 48.26, 37.99, 30.84, 29.47, 28.95, 20.61; IR (neat) 3032, 2903, 1721 (CO), 1575, 1469, 1147, 1084, 1019, 941, 736, 686 cm^{-1}; MS *m/e* (rel intensity) 247 (M^+ + 1, 13.8), 246 (M^+, 54.6), 245 (M^+ − 1, 2.5), 162 (85.7), 147 (27.6), 137 (34.8), 129 (78.8), 115 (52.3), 109 (36.5), 91 (21.3), 85 (100), 77 (41.5), 65 (25.4), 55 (30.6), 51 (30.1), 45 (27.1), 41 (71.9). Anal. Calcd for $C_{15}H_{18}OS$: C, 73.13; H, 7.36. Found: C, 73.18; H, 7.29.

Reaction of 16Z. From **16Z** by method D was obtained **19t** (472 mg, 95%) as a colorless oil after flash column chromatography (SiO_2).

Reaction of 16E. From **16E** by method D was obtained **19t** (472 mg, 95%) as a colorless oil after flash column chromatography (SiO_2).

Reaction of 18Z. From **18Z** by method E was obtained **19t** (452 mg, 91%) as a colorless oil after flash column chromatography (SiO_2).

Reaction of 18E. From **18E** by method D was obtained **19t** (482 mg, 97%) as a colorless oil after flash column chromatography (SiO_2).

Reaction of a Mixture of 17Z and 17E. 2-(3-Butenyl)-cyclopentanone (20) (299 mg, 54%) was obtained as a colorless oil from an inseparable mixture of **17Z** and **17E** by method A.

20: TLC R_f 0.71 (pentane/ether (4/1)); ^{1}H NMR (300 MHz) δ 5.71–5.88 (m, 1 H, –CH=C), 4.93–5.10 (m, 2 H, C=CH_2), 1.95–2.38 (m, 7 H), 1.69–1.95 (m, 2 H), 1.44–1.61 (m, 1 H), 1.25–1.44 (m, 1 H); ^{13}C NMR (75.4 MHz) δ 221.15, 137.91, 114.92, 48.31, 38.10, 31.49, 29.43, 28.71, 20.59; IR (neat) 2895, 1730 (CO), 1632 (C=C), 1433, 1399, 1263, 1146, 990, 906, 819 cm^{-1}; MS *m/e* (rel intensity) 139 (M^+ + 1, 4.7), 138 (M^+, 11.0), 84 (100), 67 (25.8), 55 (32.0), 53 (17.0), 43 (16.4), 41 (81.5). Anal. Calcd for $C_9H_{14}O$: C, 78.21; H, 10.21. Found: C, 78.29; H, 10.18.

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Supplementary Material Available: ^{1}H NMR spectra of **1(t, c, s)**, **2s**, **3(t, c, s)**, **4s**, **6(t, c)**, **7(t, c)**, **8(t, c)**, **[9t + 9c]**, **9b**, **10(t, c)**, **[12t + 12c]**, **15**, **18(Z, E)**, **19**, and **20** and ^{13}C–^{1}H 2D NMR spectra of **1(t, c)**, **6(t, c)**, **10(t, c)**, and **19** (35 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.