Acknowledgment. Support from the National Science Foundation (Grant CHE-8003336) is gratefully acknowledged. Palladium chloride was obtained through the Johnson-Matthey metal loan program.

Registry No. 1, 22784-59-4; 3, 87305-64-4; 4, 87305-65-5; 5, 87305-66-6; 6, 87305-67-7; 6 (2-ene), 87305-73-5; 7, 29158-91-6; 9, 87305-68-8; 9 (acid), 87305-75-7; (*E*)-10, 86633-19-4; (*Z*)-10, 86633-18-3; (*E*)-11, 87305-69-9; (*E*)-11 (ethylene ketal), 87305-76-8; (*E*)-12, 87334-71-2; (*E*)-12 (silyl), 87305-77-9; $(PPh_3)_4Pd$, 14221-01-3; $4\text{-}NO_2C_6H_4COCl$, 122-04-3; $4\text{-}BrC_6H_4COCl$, 586-75-4; $Br(CH_2)_5COCl$, 22809-37-6; PhCOCl, 98-88-4; $Br(CH_2)_{10}COCl$, 15949-84-5; $Me_3SnCH_2CH{=}CH_2$, 762-73-2; Me_4Sn, 594-27-4; *n*-Bu_4Sn, 1461-25-2; $PhSnMe_3$, 934-56-5; PhSn-*n*-Bu_3, 960-16-7; $4\text{-}MeOC_6H_4Sn\text{-}n\text{-}Bu_3$, 70744-47-7; $3\text{-}CF_3C_6H_4Sn\text{-}n\text{-}Bu_3$, 53566-38-4; $Ph_2Sn\text{-}n\text{-}Bu_2$, 6452-61-5; $Me_3SnCH{=}CH_2$, 754-06-3; *n*-$Bu_3SnCH{=}CH_2$, 7486-35-3; (*E*)-*n*-$Bu_3SnCH{=}CHPh$, 66680-88-4; (*Z*)-*n*-$Bu_3SnCH{=}CHCH_3$, 66680-84-0; (*E*)-*n*-$Bu_3SnC(CH_3){=}CHCH_3$, 86633-14-9; (*Z*)-*n*-$Bu_3SnC(CH_3){=}CHCH_3$, 86633-15-0; (*E*)-*n*-$Bu_3SnCH{=}CHCH_2OSiMe_2Bu\text{-}t$, 86633-16-1; (*Z*)-*n*-$Bu_3SnCH{=}CHCH_2OSiMe_2Bu\text{-}t$, 86646-19-7; $Me_3SnC{\equiv}C\text{-}n\text{-}Pr$, 1118-50-9; $Me_3SnC{\equiv}CPh$, 1199-95-7; $Me_3SnCH_2OCH_3$, 4649-80-3; *n*-$Bu_3SnCH_2OCH_3$, 27490-32-0; Me_3SnCH_2Ph, 4314-94-7; *n*-Bu_3SnCH_2Ph, 28493-54-1; $Me_3SnCH_2CH{=}CHCH_3$, 43133-16-0; $4\text{-}NO_2C_6H_4COMe$, 100-19-6; $4\text{-}BrC_6H_4COMe$, 99-90-1; $Br(CH_2)_5COMe$, 50775-02-5; PhCOBu, 1009-14-9; $4\text{-}NO_2C_6H_4COPh$, 1144-74-7; $Br(CH_2)_5COPh$, 82777-11-5; $Br(CH_2)_{10}COPh$, 87305-70-2; $4\text{-}MeOC_6H_4COPh$, 611-94-9; $3\text{-}CF_3C_6H_4COPh$, 728-81-4; $PhCOCH{=}CH_2$, 768-03-6; $4\text{-}NO_2C_6H_4COCH{=}CH_2$, 22731-72-2; (*E*)-$PhCOCH{=}CHPh$, 614-47-1; (*E*)-$PhCOCH{=}CHCH_3$, 35845-66-0; (*Z*)-$PhCOCH{=}CHCH_3$, 35660-91-4; (*E*)-$PhCOC(CH_3){=}CHCH_3$, 20047-50-1; (*Z*)-$PhCOC(CH_3){=}CHCH_3$, 20047-49-8; (*E*)-$PhCOCH{=}CHCH_2OSiMe_2Bu\text{-}t$, 87305-71-3; (*Z*)-$PhCOCH{=}CHCH_2OSiMe_2Bu\text{-}t$, 87305-78-0; (*E*)-$PhCOCH{=}CHCO_2CH_2Ph$, 87305-72-4; $PhCOC{\equiv}C\text{-}n\text{-}Pr$, 65236-43-3; $PhCOC{\equiv}CPh$, 7338-94-5; $PhCOCH_2OCH_3$, 4079-52-1; $PhCOCH_3$, 98-86-2; $PhCOCH_2Ph$, 451-40-1; *n*-Bu_3SnH, 688-73-3; $PhC{\equiv}CH$, 536-74-3; $BrCH{=}CHCH_3$, 590-14-7; *n*-Bu_3SnCl, 1461-22-9; $CH_3CCl{=}CHCH_3$, 4461-41-0; $HC{\equiv}CCO_2CH_2Ph$, 14447-01-9; $HC{\equiv}CCH_2OSiMe_2Bu\text{-}t$, 76782-82-6; Me_3SnLi, 17946-71-3; CH_3OCH_2Cl, 107-30-2; *n*-Bu_3SnLi, 21308-48-5; $CH_3CHOH(CH_2)_2CO_2K$, 87305-74-6; γ-valerolactone, 108-29-2.

Organic Reactions at High Pressure. A Robinson Annulation Sequence Initiated by Michael Addition of Activated Cycloalkanones with Hindered Enones[1]

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Activated cycloalkanones (ring size = five, six, seven) undergo Michael addition to β,β-disubstituted enones and subsequent aldol cyclization at 15 kbar (1.5 GPa) pressure in acetonitrile containing triethylamine or 1,5-diazabicyclo[4.3.0]non-5-ene to afford 50–90% yields of bicyclic ketals. Rearrangement of these aldols under catalytic acid conditions gives >80% yields of the fused Robinson annulation products.

The classical Robinson annulation reaction[3] still remains an important method for fusing a cyclohexenone ring onto a preexisting cyclic ketone and has found extensive use in the synthesis of a variety of natural products.[4] The original procedure involved the sequential Michael addition of a ketone or keto ester enolate to a vinyl ketone, aldol ring closure of the intermediate 1,4-adduct, and dehydration of the resulting ketol (see eq 1). Despite subsequent modifications designed to overcome the limitations of the reaction,[4] a survey of the literature reveals that its applicability is confined to cases where the vinyl ketone possesses no more than one group in the β-position, and, indeed, in this limiting example only a low yield of product is obtained.

Recently, the use of elevated pressures to overcome steric inhibition in cycloaddition reactions has been demonstrated.[6] In light of this success, it was expected that the Robinson annulation of the enolates of doubly activated systems with hindered enones might be similarly accelerated since both the Michael reaction[7,8] and the aldol

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(2) National Institutes of Health Postdoctoral Fellow, 1981–1983. Present address: Department of Chemistry, Oklahoma State University, Stillwater, OK 74078.

(3) (a) Rapson, W. S.; Robinson, R. *J. Chem. Soc.* **1935**, 1285–1288. (b) Dufen, E. C.; McQuillin, F. J.; Robinson, R. *Ibid.* **1937**, 53–60.

(4) For two thorough reviews of the Robinson annulation, see (a) Gawley, R. E. *Synthesis* **1976**, 777–794. (b) Jung, M. E. *Tetrahedron* **1976**, *32*, 3–31.

(5) To date, only one report of successful (46%) base-catalyzed (2 N KOH in ethanol) Robinson annulation to mesityl oxide has appeared that employed the highly stabilized enolate of 2-hydroxycyclohexanone: Colonge, J.; Brison, P. *Bull. Soc. Chim. Fr.* **1962**, 98–101. This experiment, in our hands, failed to yield the Robinson-annulated product but gave instead a 52% yield of 7-acetyl-8,8-dimethyl-9-oxabicyclo[4.3.0]non-6-ene: bp 95–98 °C (1 mm); IR (thin film) 1650 cm^{-1}; ^1H NMR (90 MHz) δ 4.57 (dd, *J* = 7, 11 Hz, 1), 3.16 (m, 1), 2.33 (s, 3), 2.32–1.29 (complex, 7), 1.41 (s, 3), 1.34 (s, 3); UV (EtOH) 255 nm (ε 7040), 219 (5070); MS, *m/e* 194 (parent). Anal. Calcd for $C_{12}H_{18}O_2$: C, 74.22; H, 9.28. Found: C, 73.98; H, 9.21.

(6) (a) Dauben, W. G.; Baker, W. R. *Tetrahedron Lett.* **1982**, *23*, 2611–2614. (b) Dauben, W. G.; Bunce, R. A. *Ibid.* **1982**, *23*, 4875–4878. (c) Dauben, W. G.; Bunce, R. A. *J. Org. Chem.* **1982**, *47*, 5042–5044.

(7) Simple Michael additions are reported to have a negative $\Delta V^{\ddagger}$: (a) Isaacs, N. S. "Liquid Phase High Pressure Chemistry"; Wiley-Interscience: New York, 1981; p 339. (b) Scott, J. J.; Brower, K. R. *J. Am. Chem. Soc.* **1967**, *89*, 2682–2685.

(8) Several reports have appeared that demonstrate the use of elevated pressures in promoting Michael condensations; see the following: Matsumoto, K. *Angew. Chem., Int. Ed. Engl.* **1980**, *19*, 1013–1014. (b) Matsumoto, K. *Ibid.* **1981**, *20*, 770–771. (c) Matsumoto, K.; Uchida, T. *Chem. Lett.* **1981**, 1673–1676. (d) Dauben, W. G.; Gerdes, J. M. *Tetrahedron Lett.* **1983**, 3841–3844.

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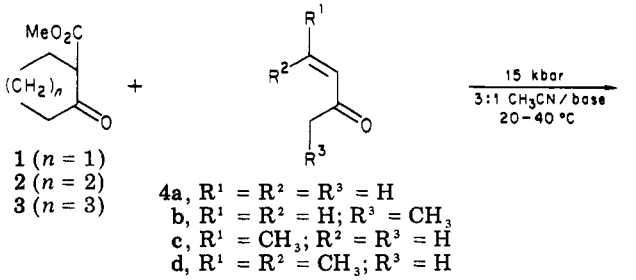
condensation[9] are known to exhibit negative volume and entropy profiles. The present study was, therefore, undertaken in connection with our ongoing investigations of high pressure in organic chemistry and its application to the synthesis of naturally occurring compounds.

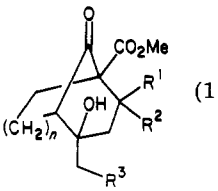
The results of our study on high-pressure cyclizations are depicted in eq 1–3 (see also Tables I–III in the Experimental Section). At 15-kbar (1.5 GPa) pressure in acetonitrile containing an excess of nonnucleophilic tertiary amine or amidine base as a cosolvent, cyclic β-keto esters **1–3** (ring size = five, six, seven) undergo condensative cyclization with a variety of enone Michael acceptors (**4a–d**, **9**, **10**), including even the normally unreactive mesityl oxide, to give, in synthetically useful yields, the bicyclic ketols **5–7**, having predominantly the indicated hydroxy stereochemistry. The only exception to this prevalence of bicyclic ketol formation resulted from reaction of 2-carbomethoxycycloheptanone (**3**) with mesityl oxide (**4d**), which afforded the fused ketol **8** as the major product accompanied by a minor amount of the bicyclic product **7d**. The analogous condensations of diones **15** and **16** are less general since they are only stable to conditions employing triethylamine as the base. Thus, reactions of **15** and **16** with **4a** and **4c** proceed smoothly at 15 kbar with triethylamine at 20 °C, while attempts with mesityl oxide (**4d**) and the 1-acetylcycloalkenes **9** and **10** even at 40 °C lead only to recovery of starting materials.

Although bicyclic ketols are not normally the desired product of the reaction, they are often crystalline, allowing for easy isolation and purification. These compounds also prove to be versatile synthetic intermedites since they can be readily dehydrated to the bicyclic enones[10] or converted to the fused Robinson products under mild acid conditions (vide infra). Finally, it is important to note that the bridgehead or angular carbomethoxy of the bicyclic or fused-ring compound, respectively, expands the possibilities for further synthetic transformations at this position.

With use of elevated pressures with mild heating in certain instances, triethylamine was generally found to be a sufficiently strong base for condensation of the more reactive five-membered ring[11] and the six-membered ring cases with unhindered enones. For the less reactive seven-membered ring[11] and the six-membered ring annulation with mesityl oxide, however, 1,5-diazabicyclo[4.3.0]non-5-ene (DBN) proved to be a superior base. Other bases explored—1,8-diazabicyclo[5.4.0]undec-7-ene (DBU), 1,4-diazabicyclo[2.2.2]octane (Dabco), *N*-ethylpiperidine, and *N*,*N*-diisopropylethylamine—generally afforded less satisfactory results.

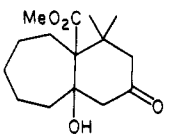
It was further noted that by careful selection of the thermal parameters, the reaction can, to an extent,[12] be controlled to give the simple Michael adduct, the bicyclic ketol or the fused enone (see eq 4). The six-membered



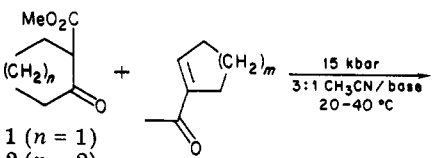


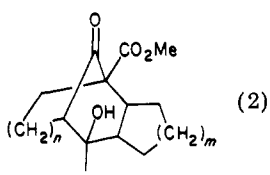
(1)

5a–d (*n* = 1)
6a–d (*n* = 2)
7a–d (*n* = 3)



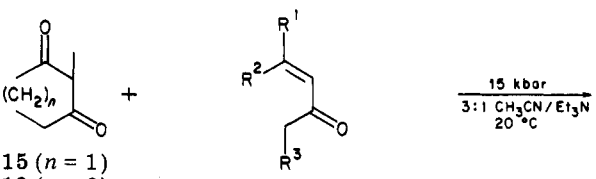
8

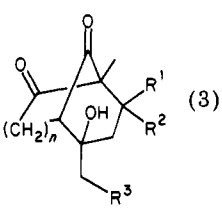




(2)

11 (*n* = 1, *m* = 1)
12 (*n* = 1, *m* = 2)
13 (*n* = 2, *m* = 1)
14 (*n* = 2, *m* = 2)





(3)

17a,c
18a,c

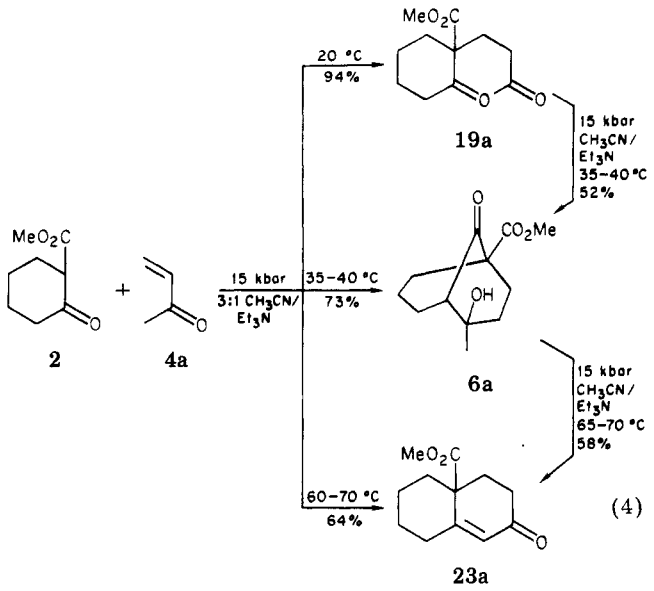
ring keto ester provides the best illustration of this control. in 3:1 acetonitrile/triethylamine at 20 °C (15 kbar) for 24 h, 2-carbomethoxycyclohexanone (**2**) and methyl vinyl ketone (**4a**) give 2-carbomethoxy-2-(3-oxobutyl)cyclohexanone (**19a**) in 94% yield. Under identical conditions at 35–40 °C, the bicyclic aldol, 1-carbomethoxy-4-hydroxy-4-methylbicyclo[3.3.1]nonan-9-one (**6a**), is obtained in 73% yield, and at 60–70 °C, the octalone product

(9) The aldol condensation has been shown to exhibit a negative ΔV^*: Monyoshi, T.; Mikami, K. *Rev. Phys. Chem. Jpn.* **1968**, *38*, 50–57. (b) The retroaldol reaction has a positive ΔV^* and should be retarded at high pressure; see Grønlund, F.; Andersen, B. *Acta Chem. Scand., Ser. A* **1979**, *33*, 329–334.

(10) (a) Dauben, W. G.; McFarland, J. W.; Rogan, J. B. *J. Org. Chem.* **1961**, *26*, 297–300. (b) Liu, H.-J.; Ho, L.-K.; Lai, H. K. *Can. J. Chem.* **1981**, *59*, 1685–1688.

(11) (a) Rhoads, S. J.; Gilbert, J. C.; Decora, A. W.; Garland, T. R.; Spangler, R. J.; Urbigkit, M. J. *Tetrahedron* **1963**, *19*, 1625–1644. (b) Rhoads, S. J.; Decora, A. W. *Ibid.* **1963**, *19*, 1645–1659.

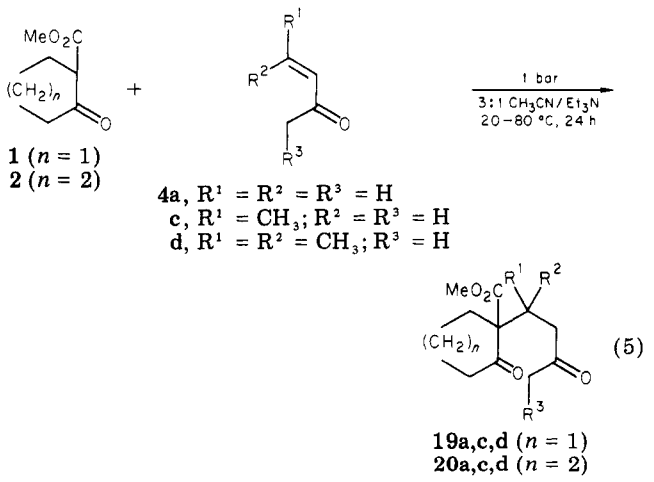
(12) The six- and seven-membered ring keto esters illustrate this control the best. The simple Michael adducts could not be intercepted in the reactions of the five-membered ring keto esters or reactions employing mesityl oxide for the range of conditions explored. In the absence of base, the five- and six-membered ring cases employing methyl vinyl ketone were observed to afford moderate yields of Michael adducts without subsequent closure.



(4)

23a can be isolated in 64% yield. It is additionally found that Michael adduct **19a** can be converted to the bicyclic ketol **6a** and this, in turn, can be carried on to **23a** simply by increasing the temperature under pressure.

Earlier reports from this laboratory[10a] and by other workers[10b] have demonstrated the utility of amine bases in Michael condensations of doubly activated cyclic systems with methyl vinyl ketone under standard pressure conditions. In the present study, control experiments performed at 1-bar pressure by allowing 2-carbomethoxycycloalkanones **1** and **2** to react with methyl vinyl ketone (**4a**), 3-penten-2-one (**4c**), and mesityl oxide (**4d**) at 20 and 80 °C in 3:1 acetonitrile/triethylamine illustrate the tremendous sensitivity of the initial Michael addition to the substitution at the β-position, the yields decreasing from 85–95% with **4a** down to ≤25% with **4c** and 0% with **4d** (see eq 5 and also Table IV in the Experimental Section).



1 (n = 1)
2 (n = 2)

4a, $R^1 = R^2 = R^3 = H$
c, $R^1 = CH_3$; $R^2 = R^3 = H$
d, $R^1 = R^2 = CH_3$; $R^3 = H$

(5)

19a,c,d (n = 1)
20a,c,d (n = 2)

tion). Furthermore, subsequent aldol condensation is never observed under these conditions. Similar results are obtained in control runs of the 1,3-diones **15** and **16** (see Table IV in the Experimental Section).

In the course of this investigation, it was noted that for all high-pressure condensations involving doubly stabilized enolates, 1,4-addition predominates even with mesityl oxide as the Michael acceptor. Preliminary studies allowing simple cycloalkanone enolates to react with mesityl oxide, on the other hand, have yielded primarily 1,2-addition products. Similar regioselectivities have also been observed under more classical conditions at ambient pressures[13] and have been readily rationalized on the basis of hard–soft acid–base theory,[14] the more delocalized "softer" carbanions adding preferentially at the "softer" β-position while the monostabilized enolates attack at the more electrophilic carbonyl carbon.

The fact that triethylamine and DBN may promote the ring-forming aldol condensation as well as the initial Michael addition suggests a substantial increase in the effective base strength at elevated pressures.[15] Since it is known that the volume change for $R_3N + H_2O \rightarrow R_3NH^+ + OH^-$ lies in the range of −25 to −30 cm^3 mol^{-1},[15a,b] it is reasonable to assume that a similar volume contraction should occur in the deprotonation of active methylene compounds. This negative contribution to the volume profile of the reaction involving amine protonation with electrostriction of the polar solvent around the charged species as they develop should, therefore, render the tertiary amine and amidine bases stronger at elevated pressures and deprotonation of the substrates should be accelerated.

Previous mechanistic reports[16] have observed that bicyclic ketols are often a major byproduct from hydroxide- and amine-catalyzed Michael-initiated cyclizations. Spencer[16b,c] has pointed out that amine bases capable of forming reactive enamines yield various mixtures of aldol products, while tertiary amines, which effect only general-base catalysis, give no detectable ketol formation. Thus, in the present investigation, the high selectivity favoring closure from the cycloalkanone enolate onto the side-chain carbonyl in the presence of triethylamine is noteworthy. This preference may derive from selective intramolecular enolate equilibration by a six-centered transfer of the activated transannular axial proton of **24b** to the side-chain enolate, resulting from the initial Michael addition[17] (see eq 6). Simple analysis of substituent A values[18] for the two chair conformations **24a** and **24b**, however, predicts a preponderance of **24a**, which does not possess the requisite geometry for proton transfer (or closure of the 1,3-equilibrated enolate **26** to give the generally observed cis-fused ketol[19]). Although conformer **24b** is less populated, NMR studies[20] have indicated that the application of pressure would accelerate the chair–chair interconversion (**24a** ⇄ **24b**), thereby making **24b** more accessible for reaction. The favorable alignment of the transannular

(13) Gasanov, A. G.; Mekhtiev, S. D.; Musaev, M. R. *Azerb. Khim. Zh.* **1975**, *3*, 6–10; (*Chem. Abstr.* **1976**, *84*, 58704h).

(14) Some representative illustrations of the concept of hard and soft bases in organic chemistry are presented: (a) Ho, T.-L. *J. Chem. Educ.* **1978**, *55*, 355–360. (b) Ho, T.-L. "Hard and Soft Acids and Bases Principle in Organic Chemistry"; Academic Press, New York, 1977; pp 93–99.

(15) (a) Ansano, T.; LeNoble, W. J. *Chem. Rev.* **1978**, *78*, 407–489. (b) See ref 7a, pp 155–164. (c) Hamann, S. D. "Volume Changes for the Ionization of Weak Electrolytes, and the Effects of Pressure on Ionization"; Division of Applied Chemistry Technical Paper No. 3 C.S.I.R.O. Australia, 1972. (d) The increase in base strength was further evidenced by a relatively violent reaction that occurred upon depressurization of one of the reactions attempted in CH_2Cl_2 with DBN as the base. Although little remained for analysis, a highly exothermic, HCl-forming reaction (carbene generation?) took place between DBN and this reaction solvent at 15 kbar, 40 °C.

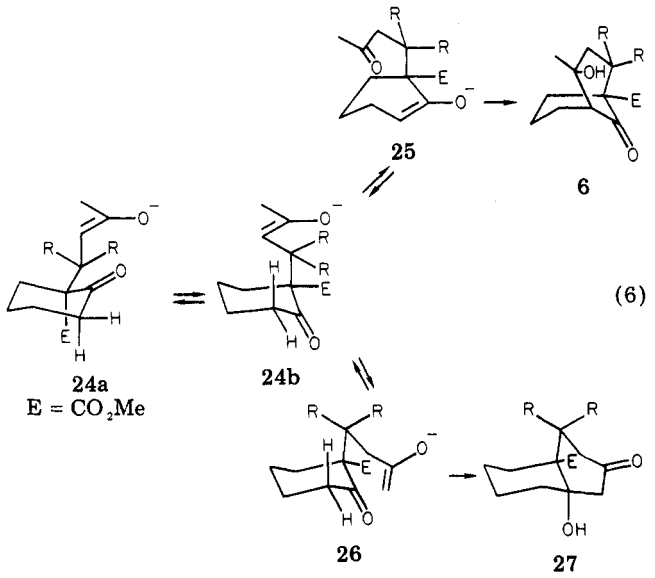
(16) (a) Johnson, W. S.; Korst, J. J.; Clement, R. A.; Dutta, J. *J. Am. Chem. Soc.* **1960**, *82*, 614–622. (b) Spencer, T. A.; Schmiegel, K. K. *Chem. Ind.* **1963**, 1765–1766. (c) Spencer, T. A.; Neel, H. S.; Flechtner, T. W.; Zayle, R. A. *Tetrahedron Lett.* **1965**, 3889–3897.

(17) This process has analogy with the enamine equilibration process described in Firrell, N. F.; Hickmott, P. W. *Chem. Commun.* **1969**, 544–546.

(18) Eliel, E. L.; Allinger, N. L.; Angyal, S. J.; Morrison, G. A. "Conformational Analysis"; Wiley-Interscience: New York, 1965; Chapter 7.

(19) Spencer, T. A.; Neel, H. S.; Ward, D. C.; Williamson, K. L. *J. Org. Chem.* **1966**, *31*, 434–436 and references cited therein.

(20) (a) Lüdemann, H.-D.; Rauchschwalbe, R.; Lang, E. *Angew. Chem., Int. Ed. Engl.* **1977**, *16*, 331–332. (b) See ref 7a, p 200.

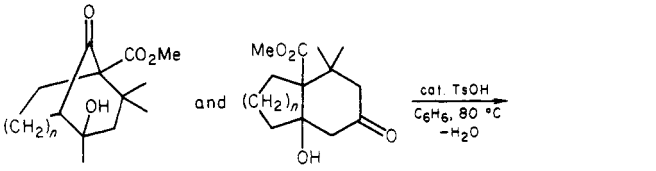


(6)

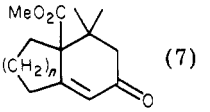
axial hydrogen in this conformer should then facilitate proton transfer over other competing processes. Following equilibration in this manner, the side-chain carbonyl is perfectly positioned for closure to the bicyclic system. This argument should also extend to five-membered derivatives where pseudoaxial and pseudoequatorial substituent orientations lie closer in energy and to the seven-membered ring cases where conformational energetics approximate those of the six-membered ring.[18]

The sole anomaly is seen in the reaction of 2-carbomethoxycycloheptanone (**3**) and mesityl oxide (**4d**), which afforded a 4:1 mixture of fused/bicyclic ketol (**8**/**7d**). This product ratio must reflect a unique combination of steric and conformational effects created by interaction of the adjacent carbomethoxy and *gem*-dimethyl groupings since no fused ketol is detected in the reaction of **3** with less substituted enones. Finally, although fused ketols were not observed in these cases or in the five-membered and six-membered ring series, the 5–8% of Robinson annulation product recovered from the crude reaction mixture presumably arises from this intermediate by amine-catalyzed dehydration[16,21,22] since control experiments have demonstrated the stability of the bicyclic ketols to the base and pressure conditions utilized for their preparation.

With bicyclic ketols now readily available and procedures already described for their conversion to unrearranged bicyclic enones,[10] a means for converting them to the fused Robinson products was desired. Rearrangement catalyzed by hydroxide or alkoxide base proceeds poorly, causing retro-Michael reaction or saponification and decarboxylation of the opened 2-carbomethoxy-2-(3-oxobutyl)cycloalkanone derivatives. It was discovered, however, that treatment with a catalytic amount of *p*-toluenesulfonic acid monohydrate in benzene with removal of water smoothly effects the retroaldol–aldol reactions and dehydration to give excellent yields of Robinson annulation products (see eq 7–9). The acid-catalyzed closure of 2-carbomethoxy-2-(3-oxobutyl)cycloalkanones has close analogy to a recent report by Liu and co-workers.[10b]

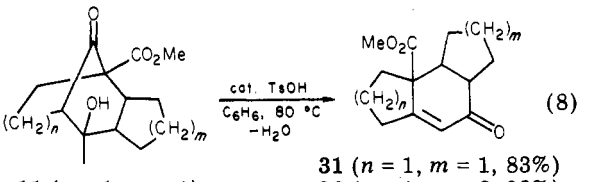


5d (n = 1)
6d (n = 2)
8 (n = 3)



(7)

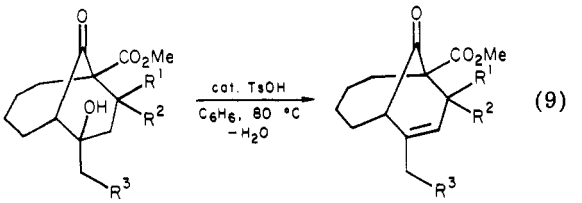
28d (n = 1, 86%)
29d (n = 2, 89%)
30d (n = 3, 92%)



(8)

11 (n = 1, m = 1)
12 (n = 1, m = 2)
13 (n = 2, m = 1)
14 (n = 2, m = 2)

31 (n = 1, m = 1, 83%)
32 (n = 1, m = 2, 89%)
33 (n = 2, m = 1, 85%)
34 (n = 2, m = 2, 87%)

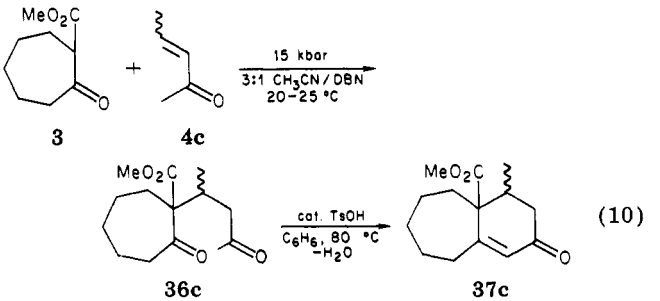


(9)

7c, $R^1 = CH_3$; $R^2 = R^3 = H$
7d, $R^1 = R^2 = CH_3$; $R^3 = H$

35c (79%)
35d (84%)

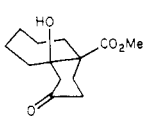
The ring strain inherent in the bicyclic ketol skeleton appears to control the course of the acid-catalyzed rearrangement. Thus, the [3.2.1] and [3.3.1] bicyclic systems, derived respectively from the five- and six-membered ring keto esters, undergo facile retroaldol ring opening, while the bicyclo[4.3.1] framework resulting from seven-membered ring condensations prefers to dehydrate without rearrangement. To prepare Robinson products in these cases, the initial high-pressure condensation is run at lower temperature, permitting isolation of the simple Michael adduct, and then treatment as before with catalytic acid produces the fused enone (see eq 10). Lastly, the fused ketol **8** is also readily converted to the Robinson-type product, using the identical acid conditions.[10b]



(10)

In conclusion, high-pressure conditions have been successfully applied to a general bicyclization and Robinson annulation sequence. Since ring-forming reactions initiated by Michael additions normally fail with mesityl oxide

(21) Compound **8** was also stable to repressurization with DBN at 40 °C and to treatment with amine bases at 1-bar pressure in refluxing benzene. Thus, i is expected to be the favored conformation since base



i

elimination occurs from a preferred trans diaxial geometry.

(22) (a) Hupe, D. J.; Kendall, M. C. R.; Sinner, G. T.; Spencer, T. A. *J. Am. Chem. Soc.* **1973**, *95*, 2260–2270. (b) Brower, K. R.; Muhsin, M.; Brower, E. B. *Ibid.* **1976**, *98*, 779–782.

Table I. High-Pressure Cyclization of 2-Carbomethoxycycloalkanones with Acyclic Enones

keto ester	enone	base	T, °C	t, h	bicyclic ketol (yield)[a,b]
1	4a	Et_3N	20	24	5a (86)
	4b	Et_3N	20	24	5b (83)
	4c	Et_3N	20	24	5c (84)
	4d	Et_3N	20	24	5d (90)
2	4a	Et_3N	40	40	6a (73)
	4b	Et_3N	40	40	6b (65)
	4c	Et_3N	40	40	6c (84)
	4d	DBN	40	40	6d (74)
3	4a	DBN	40	40	7a (52)
	4c	DBN	40	40	7c (67)
	4d	DBN	40	40	7d (17) + 8 (68)

[a] Isolated yields, not optimized. [b] In reactions of 2 and 3, 5–8% each of uncyclized Michael adduct and fused Robinson enone product were also isolated.

Table II. High-Pressure Cyclizations of 2-Carbomethoxyalkanones with Cyclic Enones

keto ester	enone	base	T, °C	t, h	bicyclic ketol (yield)[a,b]
1	9	Et_3N	20	40	11 (67)
	10	Et_3N	20	40	13 (69)
2	9	DBN	40	40	12 (63)
	10	DBN	40	40	14 (64)

[a] Isolated yields, not optimized. [b] Small amounts (5–10%) of starting materials, uncyclized Michael adduct, and fused Robinson products are also isolated.

and proceed poorly with 3-penten-2-one and 1-acetylcycloalkenes,[4] the use of elevated pressures extends the scope and potential utility of the reaction while maintaining conditions mild enough to accommodate substrates possessing additional functionality. We are presently continuing our efforts to expand the applications of high pressure to organic synthesis.

Experimental Section[23]

General Procedure for High-Pressure Reactions. A 4-mL 3:1 v/v acetonitrile/triethylamine (3.6 equiv) or 1,5-diazabicyclo[4.3.0]non-5-ene (4.0 equiv) solution of 2.0 mmol of cyclo-

Table III. High-Pressure Cyclizations of 2-Methyl-1,3-cycloalkanediones with Acyclic Enones

dione	enone	base	T, °C	t, h	bicyclic ketol (yield)[a,b]
15	4a	Et_3N	20	38	17a (52)
	4c	Et_3N	20	40	17c (76)
	4d	Et_3N or DBN	20 or 40	40	17d (0)
16	4a	Et_3N	20	38	18a (60)
	4c	Et_3N	20	40	18c (67)
	4d	Et_3N or DBN	20 or 40	40	18d (0)

[a] Isolated yields, not optimized. [b] In reactions of 4a and 4c, small amounts of starting material and uncyclized Michael adduct were isolated. In reactions of 4d using Et_3N, starting materials were recovered; with DBN, mesityl oxide self-condensation products were isolated and the diones could not be recovered.

alkanone and 2.5 mmol of enone in a 12 cm × 1 cm Teflon tube (wall thickness = 0.038 cm) clamped at both ends was pressurized at 15-kbar (1.5 GPa) hydrostatic pressure for 24–40 h at 20–40 °C (see Tables I–III for exact conditions used for each substrate). The reactions were cooled (if necessary), depressurized, and concentrated in vacuo. The crude products were filtered through an 8.0 cm × 2.5 cm pad of silica gel with 10% ether in hexane to remove unreacted starting material followed by 75% ether in hexane. The latter solution was concentrated at reduced pressure to afford the bicyclic ketol products. Solid ketols were recrystallized from ether/hexane mixtures. The following compounds have been prepared by the above procedure.

1-Carbomethoxy-4-hydroxy-4-methylbicyclo[3.2.1]octan-8-one (5a): mp 105–107 °C; IR ($CHCl_3$) 3350, 1755, 1725 cm^{-1}; ^1H NMR (250 MHz) δ 3.78 (s, 3), 2.65–1.56 (complex, 10), 1.36 (s, 3). Anal. Calcd for $C_{11}H_{16}O_4$: C, 62.26; H, 7.55. Found: C, 61.98; H, 7.51.

1-Carbomethoxy-4-ethyl-4-hydroxybicyclo[3.2.1]octan-8-one (5b): IR (thin film) 3490, 1742, 1720 cm^{-1}; ^1H NMR (90 MHz) δ 3.75 (s, 3), 2.80–1.43 (complex, 12), 1.02 (minor) and 0.90 (2 t, J = 9 Hz, 3); mass spectrum, m/e (relative abundance) 226 (M^+, 3), 208 (1), 57 (100); exact mass calcd for $C_{12}H_{18}O_4$ m/e 226.1203, found m/e 226.1197.

1-Carbomethoxy-4-hydroxy-2,4-dimethylbicyclo[3.2.1]octan-8-one (5c): mp 139–140 °C; IR ($CHCl_3$) 3440, 1710 (br) cm^{-1}; ^1H NMR (90 MHz) δ 3.74 (s, 3), 3.02 (br s, 1), 2.93–1.37 (complex, 8), 1.32 (s, 3), 0.89 (d, J = 9 Hz, 3). Anal. Calcd for $C_{12}H_{18}O_4$: C, 63.72; H, 7.97. Found: C, 63.67; H, 7.82.

1-Carbomethoxy-4-hydroxy-2,2,4-trimethylbicyclo[3.2.1]-octan-8-one (5d): mp 123–124 °C; IR ($CHCl_3$) 3380, 1720 (br) cm^{-1}; ^1H NMR (250 MHz) δ 3.70 (s, 3), 2.54–1.38 (complex, 8), 1.36 (s, 3), 1.27 (s, 3), 1.07 (s, 3). Anal. Calcd for $C_{13}H_{20}O_4$: C, 65.00; H, 8.33. Found: C, 64.70; H, 8.00.

1-Carbomethoxy-4-hydroxy-4-methylbicyclo[3.3.1]nonan-9-one (6a): IR (thin film) 3450, 1730, 1708 cm^{-1}; ^1H NMR (90 MHz) δ 3.73 (s, 3), 3.09 (br s, 1), 2.90–1.22 (complex, 11), 1.35 (s, 3); mass spectrum, m/e (relative abundance) 226 (M^+, 4), 208 (6); exact mass calcd for $C_{12}H_{18}O_4$ m/e 226.1203, found m/e 226.1199.

1-Carbomethoxy-4-ethyl-4-hydroxybicyclo[3.3.1]nonan-9-one (6b): IR (thin film) 3440, 1705 (br) cm^{-1}; ^1H NMR (90 MHz) δ 3.73 (s, 3), 2.92–1.23 (complex, 14), 0.99 (minor) and 0.88 (2 t, J = 9 Hz, 3); mass spectrum, m/e (relative abundance) 240 (M^+, 3), 222 (39), 157 (100); exact mass calcd for $C_{13}H_{20}O_4$ m/e 240.1362, found m/e 240.1364.

1-Carbomethoxy-4-hydroxy-2,4-dimethylbicyclo[3.3.1]nonan-9-one (6c): IR (thin film) 3440, 1730, 1709 cm^{-1}; ^1H NMR (90 MHz) δ 3.73 (s, 3), 2.86–1.28 (complex, 11), 1.33 (major) and 1.22 (2 s, 3), 0.94 (minor) and 0.85 (2 d, J = 8 Hz, 3); mass spectrum, m/e (relative abundance) 240 (M^+, 5), 222 (7); exact mass calcd for $C_{13}H_{20}O_4$ m/e 240.1362, found m/e 240.1364.

1-Carbomethoxy-4-hydroxy-2,2,4-trimethylbicyclo[3.3.1]-nonan-9-one (6d): mp 144–145 °C; IR ($CHCl_3$) 3480, 1730, 1708 cm^{-1}; ^1H NMR (250 MHz) δ 3.68 (s, 3), 2.64–1.46 (complex, 10), 1.31 (s, 3), 1.28 (s, 3), 1.18 (s, 3). Anal. Calcd for $C_{14}H_{22}O_4$: C, 66.14; H, 8.66. Found: C, 66.35; H, 8.48.

1-Carbomethoxy-7-hydroxy-7-methylbicyclo[4.3.1]decan-10-one (7a): IR (thin film) 3470, 1728, 1700 cm^{-1}; ^1H NMR (90 MHz) δ 3.70 (s, 3), 2.85 (br s, 1), 2.81–1.43 (complex, 13), 1.27 (s,

(23) The construction and use of the high-pressure apparatus employed in the present study has been described previously.[24] The 2-methyl-1,3-cyclopentanedione (Roussel-Uclaf) and 2-methyl-1,3-cyclohexanedione (Parke-Davis) were recrystallized before use. The 2-carbomethoxycyclopentanone (Aldrich), 2-carbomethoxycyclohexanone,[25] 2-carbomethoxycycloheptanone,[26] methyl vinyl ketone (Aldrich), ethyl vinyl ketone (Aldrich), mesityl oxide (Eastman), 1-acetylcyclohexene (Aldrich), and 1-acetylcyclopentene[27] were distilled prior to use. The triethylamine (Aldrich) was distilled from calcium hydride; the 1,5-diazabicyclo-[4.3.0]non-5-ene (Aldrich) was distilled from barium oxide; and the acetonitrile, stored over 4-Å sieves, was used without further purification. Infrared spectra were obtained as neat films or $CHCl_3$ solutions as indicated with a Perkin-Elmer 281 spectrometer. Nuclear magnetic resonance spectra were recorded as solutions in $CDCl_3$ with internal Me_4Si on a Varian EM 390 or the UCB-250 superconducting FT instrument. Splitting patterns are reported as follows: s, singlet; br s, broad singlet; d, doublet; dd, doublet of doublets; t, triplet; q, quartet; or m, multiplet. Ultraviolet spectra were recorded on a Hewlett-Packard 8450-A spectrophotometer. Mass spectra were measured at 70 eV on an AEI-MS-12 (low resolution) or a Du Pont CEC 21-110B (high resolution) instrument. Elemental analyses were performed by the Microanalytical Laboratory, University of California, Berkeley. Melting points were obtained with a Büchi melting point apparatus and are uncorrected.

(24) Dauben, W. G.; Krabbenhoft, H. O. *J. Org. Chem.* **1977**, *42*, 282–287.

(25) This compound was prepared in 62% yield by employing an adaptation of the procedure described by Corey et al. for 3-carbomethoxy-7,7-dimethylbicyclo[4.2.0]octan-2-one. See Corey, E. J.; Mitra, R. B.; Uda, H. *J. Am. Chem. Soc.* **1964**, *86*, 485–492.

(26) This compound was prepared in 80% yield by employing an adaptation of the procedure of Krapcho et al.: Krapcho, A. P.; Diamanti, J.; Cayen, C.; Bingham, R. "Organic Syntheses"; Baumgarten, H. E., Ed.; Wiley: New York, 1973; Collect. Vol. V, pp 198–201.

(27) Casals, P.-F. *Bull. Soc. Chim. Fr.* **1963**, 253–264.

Table IV. Control Runs of Activated Ketones with Michael Acceptors at 1-bar Pressure

activated ketone	enone	base	T, °C	t, h	Michael adduct (yield)[a]
1	4a	Et_3N	20	12	19a (93)
	4c	Et_3N	80	24	19c (25)
	4d	Et_3N	20 or 80	48	19d (0)
2	4a	Et_3N	20	24	20a (86)
	4c	Et_3N or DBN	20 or 80	24	20c (<5)
	4d	DBN	80	24	20d (0)
15	4a	Et_3N	20	24	21a (50)[b]
	4c	Et_3N	80	24	21c (31)
	4d	Et_3N or DBN	20 or 80	36	21d (0)
16	4a	Et_3N	20	24	22a (67)[b]
	4c	Et_3N	80	24	22c (23)
	4d	Et_3N or DBN	20 or 80	36	22d (0)

[a] Isolated yields, not optimized. [b] For spectral data, see ref 28.

3); mass spectrum, *m/e* (relative abundance) 240 (M^+, 2), 222 (7); exact mass calcd for $C_{13}H_{20}O_4$ *m/e* 240.1362, found *m/e* 240.1356.

1-Carbomethoxy-7-hydroxy-7,9-dimethylbicyclo[4.3.1]decan-10-one (7c): IR (thin film) 3440, 1722, 1698 cm^{-1}; ^1H NMR (90 MHz) δ 3.75 (s, 3), 2.88–1.47 (complex, 13), 1.30 (major) and 1.24 (2 s, 3), 0.94 (major) and 0.87 (2 d, *J* = 8 Hz, 3); mass spectrum, *m/e* (relative abundance) 254 (M^+, 2), 236 (4); exact mass calcd for $C_{14}H_{22}O_4$ *m/e* 254.1519, found *m/e* 254.1522.

1-Carbomethoxy-7-hydroxy-7,7,9-trimethylbicyclo[4.3.1]decan-10-one (7d): mp 95–97 °C; IR ($CHCl_3$) 3400, 1725, 1705 cm^{-1}; ^1H NMR (90 MHz) δ 3.71 (s, 3), 2.62 (m, 1), 2.22 and 1.28 (AB q, *J* = 16 Hz, 2), 2.10 (m, 3), 1.61 (m, 6), 1.30 (s, 3), 1.25 (s, 3), 1.01 (s, 3); mass spectrum, *m/e* (relative abundance) 268 (M^+, 4), 250 (8); exact mass calcd for $C_{15}H_{24}O_4$ *m/e* 268.1675, found *m/e* 268.1675.

1-Carbomethoxy-7-hydroxy-11,11-dimethylbicyclo[5.4.0]undecan-9-one (8): mp 127–128 °C; IR ($CHCl_3$) 3400, 1698 (br) cm^{-1}; ^1H NMR (250 MHz) δ 3.69 (s, 3), 2.74 and 2.21 (AB q, *J* = 13.2 Hz, 2), 2.36–1.24 (complex, 13), 1.13 (s, 3), 0.86 (s, 3). Anal. Calcd for $C_{15}H_{24}O_4$: C, 67.16; H, 8.96. Found: C, 67.12; H, 8.89.

1-Carbomethoxy-7-hydroxy-7-methyltricyclo[6.2.1.0^{2,6}]undecan-11-one (11): mp 172–173 °C; IR ($CHCl_3$) 3420, 1724 (br) cm^{-1}; ^1H NMR (90 MHz) δ 3.78 (s, 3), 2.90–1.27 (complex, 14), 1.27 (s, 3). Anal. Calcd for $C_{14}H_{20}O_4$: C, 66.63; H, 8.00. Found: C, 66.34; H, 7.87.

1-Carbomethoxy-8-hydroxy-8-methyltricyclo[7.2.1.0^{2,7}]dodecan-12-one (12): mp 156–157 °C; IR ($CHCl_3$) 3410, 1730 (br) cm^{-1}; ^1H NMR (90 MHz) δ 3.77 (s, 3), 2.82–1.32 (complex, 16), 1.32 (s, 3). Anal. Calcd for $C_{15}H_{22}O_4$: C, 67.67; H, 8.27. Found: C, 67.26; H, 8.13.

1-Carbomethoxy-7-hydroxy-7-methyltricyclo[6.3.1.0^{2,6}]dodecan-12-one (13): IR (thin film) 3450, 1730, 1705 cm^{-1}; ^1H NMR (90 MHz) δ 3.78 (s, 3), 3.00–1.26 (complex, 16), 1.32 (s, 3); mass spectrum, *m/e* (relative abundance) 266 (M^+, 25), 248 (32); exact mass calcd for $C_{15}H_{22}O_4$ *m/e* 266.1519, found *m/e* 266.1515.

1-Carbomethoxy-8-hydroxy-8-methyltricyclo[7.3.1.0^{2,7}]tridecan-13-one (14): IR (thin film) 3470, 1732, 1710 cm^{-1}; ^1H NMR (90 MHz) δ 3.78 (s, 3), 2.86–1.06 (complex, 18), 1.35 (s, 3); mass spectrum, *m/e* (relative abundance) 280 (M^+, 1), 262 (4); exact mass calcd for $C_{16}H_{24}O_4$ *m/e* 280.1675, found *m/e* 280.1668.

4-Hydroxy-1,4-dimethylbicyclo[3.2.1]octane-7,8-dione (17a): mp 163–164 °C; IR ($CHCl_3$) 3455, 1758, 1721 cm^{-1}; ^1H NMR (90 MHz) δ 2.95–2.54 (m, 3), 2.34 (br s, 1), 2.08–1.61 (m, 4), 1.44 (s, 3), 1.10 (s, 3). Anal. Calcd for $C_{10}H_{14}O_3$: C, 65.92; H, 7.69. Found: C, 65.69; H, 7.37.

4-Hydroxy-1,2,4-trimethylbicyclo[3.2.1]octane-7,8-dione (17c): mp 184–185 °C; IR ($CHCl_3$) 3370, 1758, 1712 cm^{-1}; ^1H NMR (90 MHz) δ 2.80–1.42 (complex, 7), 1.24 (s, 3), 0.88 (s, 3), 0.79 (d, *J* = 10 Hz, 3). Anal. Calcd for $C_{11}H_{16}O_3$: C, 67.35; H, 8.16. Found: C, 67.05; H, 8.03.

6-Hydroxy-1,6-dimethylbicyclo[3.3.1]nonane-2,9-dione (18a): isolated containing a trace of cis-fused ketol; mp 106–109 °C (lit.[19] mp 115–116 °C); IR[19] ($CHCl_3$) 3410, 1722, 1699 cm^{-1}; ^1H NMR[19] (90 MHz) δ 2.93 (br s, 1), 2.90–1.62 (complex, 9), 1.41 (s, 3), 1.15 (s, 3); methyl of cis-fused ketol at 1.31. Anal. Calcd for $C_{11}H_{16}O_3$: C, 67.35; H, 8.16. Found: C, 67.13; H, 8.10.

6-Hydroxy-1,6,8-trimethylbicyclo[3.3.1]nonane-2,9-dione (18c): mp 131–132 °C; IR ($CHCl_3$) 3495, 1728, 1698 cm^{-1}; ^1H NMR (90 MHz) δ 2.77–1.61 (complex, 8), 2.75 (br s, 1), 1.42 (s, 3), 1.21 (s, 3), 0.92 (d, *J* = 8.5 Hz, 3). Anal. Calcd for $C_{12}H_{18}O_3$: C, 68.53; H, 8.63. Found: C, 68.28; H, 8.86.

General Procedure for Acid-Catalyzed Rearrangement of the Bicyclic Ketols to Fused-Ring Enones. A benzene solution of 1.00 mmol of ketol and *p*-toluenesulfonic acid monohydrate (20% of ketol by weight) was refluxed for 6–36 h with Dean-Stark removal of water until TLC revealed complete consumption of starting material. The reaction was cooled, concentrated in vacuo, and chromatographed on a 20 cm × 0.5 cm silica gel column using 5% ether in hexane. The following compounds have been prepared by the above procedure.

1-Carbomethoxy-2,2-dimethylbicyclo[4.3.0]non-5-en-4-one (28d). This compound was prepared in 86% yield from **5d**: IR (thin film) 1720, 1654 cm^{-1}; ^1H NMR (250 MHz) δ 5.98 (s, 1), 3.67 (s, 3), 2.60 and 2.04 (AB q, *J* = 9.3 Hz, 2), 2.58–2.30 (m, 2), 1.90–1.52 (m, 4), 0.99 (s, 3), 0.97 (s, 3); UV (ethanol) 240 nm (ε 9550); mass spectrum, *m/e* (relative abundance) 222 (M^+, 28), 163 (24); exact mass calcd for $C_{13}H_{18}O_3$ *m/e* 222.1256, found *m/e* 222.1257.

1-Carbomethoxy-2,2-dimethylbicyclo[4.4.0]dec-5-en-4-one (29d). This compound was obtained in 89% yield from **6d**: mp 94–95 °C; IR ($CHCl_3$) 1720, 1660, 1626 cm^{-1}; ^1H NMR (90 MHz) δ 5.92 (s, 1), 3.74 (s, 3), 2.54 and 2.10 (AB q, *J* = 16 Hz, 2), 2.59–1.18 (complex, 8), 1.06 (s, 3), 0.97 (s, 3); UV (ethanol) 240 nm (ε 9250); mass spectrum, *m/e* (relative abundance) 236 (M^+, 31), 180 (45), 177 (22), 152 (100); exact mass calcd for $C_{14}H_{20}O_3$ *m/e* 236.1412, found *m/e* 236.1404.

1-Carbomethoxy-11,11-dimethylbicyclo[5.4.0]undec-7-en-9-one (30d). This compound was isolated in 92% yield from **8**: IR (thin film) 1719, 1662, 1620 cm^{-1}; ^1H NMR (90 MHz) δ 5.96 (s, 1), 3.71 (s, 3), 2.47 and 2.21 (AB q, *J* = 16 Hz, 2), 2.56–1.31 (complex, 10), 1.04 (s, 3), 0.97 (s, 3); UV (ethanol) 243 nm (ε 9100); mass spectrum, *m/e* (relative abundance) 250 (M^+, 35), 191 (20), 166 (100); exact mass calcd for $C_{15}H_{22}O_3$ *m/e* 250.1569, found *m/e* 250.1569.

1-Carbomethoxytricyclo[7.3.0.0^{2,6}]dodec-8-en-7-one (31). This compound was prepared in 83% yield from **11**: mp 93–94 °C; IR ($CHCl_3$) 1720, 1660 cm^{-1}; ^1H NMR (90 MHz) δ 5.93 (s, 1), 3.71 (s, 3), 2.80–1.23 (complex, 14); UV (ethanol) 237 nm (ε 9570); mass spectrum, *m/e* (relative abundance) 234 (M^+, 7), 175 (100); exact mass calcd for $C_{14}H_{18}O_3$ *m/e* 234.1256, found *m/e* 234.1256.

1-Carbomethoxytricyclo[8.3.0.0^{2,7}]tridec-9-en-8-one (32). This compound was obtained in 89% yield from **12**: mp 85–86 °C; IR ($CHCl_3$) 1720, 1655 cm^{-1}; ^1H NMR (250 MHz) δ 5.98 (s, 1), 3.72 (s, 3), 2.82–2.16 (complex, 5), 1.94–1.59 (complex, 6), 1.50–0.95 (complex, 5); UV (ethanol) 239 nm (ε 9730); mass spectrum, *m/e* (relative abundance) 248 (M^+, 41), 189 (100); exact mass calcd for $C_{15}H_{20}O_3$ *m/e* 248.1412, found *m/e* 248.1400.

1-Carbomethoxytricyclo[7.4.0.0^{2,6}]tridec-8-en-7-one (33). This compound was isolated in 85% yield from **13**: mp 119–120 °C; IR ($CHCl_3$) 1720, 1665, 1630 cm^{-1}; ^1H NMR (250 MHz) δ 5.94 (s, 1), 3.77 (s, 3), 2.74–1.14 (complex, 16); UV (ethanol) 239 nm (ε 9550); mass spectrum, *m/e* (relative abundance) 248 (M^+, 59), 189 (100); exact mass calcd for $C_{15}H_{20}O_3$ *m/e* 248.1412, found *m/e* 248.1411.

1-Carbomethoxytricyclo[8.4.0.0^{2,7}]tetradec-9-en-8-one (34). This compound was prepared in 87% yield from **14**: mp 123–124

°C; IR ($CHCl_3$) 1710, 1664, 1628 cm^{-1}; ^1H NMR (250 MHz) δ 5.98 (s, 1), 3.78 (s, 3), 2.78 (d, J = 8.0 Hz, 1), 2.53–1.02 (complex, 17); UV (ethanol) 238 nm (ϵ 9960); mass spectrum, m/e (relative abundance) 262 (M^+, 71), 203 (100); exact mass calcd for $C_{16}H_{22}O_3$ m/e 262.1569, found m/e 262.1569.

1-Carbomethoxy-7,9-dimethylbicyclo[4.3.1]dec-7-en-10-one (35c). This compound was isolated in 79% yield from **7c**: IR (thin film) 1736, 1708 cm^{-1}; ^1H NMR (250 MHz) δ 5.32 (s, 1), 3.78 (s, 3), 3.19 (br s, 1), 2.84 (br s, 1), 2.28 (dd, J = 7.5, 15.0 Hz, 1), 2.13 (br d, J = 15.0 Hz, 1), 1.88 (m, 1), 1.78 (br d, J = 15.0 Hz, 1), 1.71 (s, 3), 1.62–1.02 (complex, 4), 0.98 (d, J = 8.0 Hz, 3); UV (ethanol) 222 nm (ϵ 1310), 255 (145), 261 (145), 273 (116); mass spectrum, m/e (relative abundance) 236 (M^+, 36), 177 (38); exact mass calcd for $C_{14}H_{20}O_3$ m/e 236.1412, found m/e 236.1419.

1-Carbomethoxy-7,9,9-trimethylbicyclo[4.3.1]dec-7-en-10-one (35d). This compound was obtained in 84% yield from **7d**: mp 114–115 °C; IR ($CHCl_3$) 1735, 1703 cm^{-1}; ^1H NMR (90 MHz) δ 5.35 (s, 1), 3.77 (s, 3), 2.86 (m, 1), 2.39–1.12 (complex, 8), 1.67 (s, 3), 1.17 (s, 3), 1.10 (s, 3); UV (ethanol) 201 nm (ϵ 4100), 284 (87); mass spectrum, m/e (relative abundance) 250 (M^+, 31), 191 (37); exact mass calcd for $C_{15}H_{22}O_3$ m/e 250.1569, found m/e 250.1570.

2-Carbomethoxy-2-(1-methyl-3-oxobutyl)cycloheptanone (36c). A 3:1 v/v acetonitrile/DBN solution of 340 mg (2.00 mmol) of 2-carbomethoxycycloheptanone and 210 mg (2.50 mmol) of 3-penten-2-one was pressurized at 15-kbar pressure in a sealed Teflon tube for 40 h at 20–25 °C. The reaction was depressurized, concentrated in vacuo, and purified on a 25 cm × 1 cm silica gel column to afford 386 mg (1.52 mmol, 76%) of pure 2-carbomethoxy-2-(1-methyl-3-oxobutyl)cycloheptanone: IR (thin film) 1725, 1708 cm^{-1}; ^1H NMR (90 MHz) δ 3.73 (s, 3), 3.10–1.18 (complex, 13), 2.08 (s, 3), 0.91 and 0.83 (2 d, J = 7.5 Hz, 3); mass spectrum, m/e (relative abundance) 254 (M^+, 3), 170 (100); exact mass calcd for $C_{14}H_{22}O_4$ m/e 254.1519, found m/e 254.1516.

1-Carbomethoxy-11-methylbicyclo[5.4.0]undec-7-en-9-one (37c). By employing the general conditions described above for acid-catalyzed conversion of bicyclic ketols to fused enones; this compound was prepared in 90% yield: IR (thin film) 1720, 1660 cm^{-1}; ^1H NMR (90 MHz) δ 5.92 (s, 1), 3.74 (s, 3), 3.04–1.09 (complex, 13), 1.00 and 0.96 (2 d, J = 7.5 Hz, 3); UV (ethanol) 241 nm (ϵ 9645); mass spectrum, m/e (relative abundance) 236 (M^+, 36), 177 (39); exact mass calcd for $C_{14}H_{20}O_3$ m/e 236.1412, found m/e 236.1411.

General Procedure for Ambient Pressure Control Runs. The control runs were performed at 1-bar pressure and 20–80 °C, using conditions otherwise identical in each case with those described for the high-pressure runs (see Table IV). Purifications were effected on 25 cm × 1 cm silica gel columns eluted with ether/hexane mixtures. The following new compounds were prepared.

2-Carbomethoxy-2-(3-oxobutyl)cyclopentanone (19a): IR (thin film) 1710 (br) cm^{-1}; ^1H NMR (90 MHz) δ 3.69 (s, 3), 2.74–1.76 (complex, 10), 2.10 (s, 3); mass spectrum, m/e 212 (M^+, 4).

2-Carbomethoxy-2-(1-methyl-3-oxobutyl)cyclopentanone (19c): IR (thin film) 1730, 1715 cm^{-1}; ^1H NMR (90 MHz) δ 3.77 (s, 3), 3.04–1.75 (complex, 9), 2.18 (s, 3), 0.91 (d, J = 8.0 Hz, 3); mass spectrum, m/e 226 (M^+, 2).

2-Carbomethoxy-2-(3-oxobutyl)cyclohexanone (20a): IR (thin film) 1712 (br) cm^{-1}; ^1H NMR (90 MHz) δ 3.72 (s, 3), 2.71–1.40 (complex, 12), 2.09 (s, 3); mass spectrum, m/e 226 (M^+, 3).

2-Methyl-2-(1-methyl-3-oxobutyl)-1,3-cyclopentanedione (21c): IR (thin film) 1730, 1700 cm^{-1}; ^1H NMR (90 MHz) δ 3.10–1.77 (complex, 7), 2.11 (s, 3), 1.14 (s, 3), 0.83 (d, J = 8.5 Hz, 3); mass spectrum, m/e 196 (M^+, 8).

2-Methyl-2-(1-methyl-3-oxobutyl)-1,3-cyclohexanedione (22c): IR (thin film) 1715, 1694 cm^{-1}; ^1H NMR (90 MHz) δ 3.30–1.51 (complex, 9), 2.14 (s, 3), 1.09 (s, 3), 0.80 (d, J = 8.5 Hz, 3); mass spectrum, m/e 210 (M^+, 6).

Registry No. **1**, 10472-24-9; **2**, 41302-34-5; **3**, 52784-32-4; **4a**, 78-94-4; **4b**, 1629-58-9; **4c**, 625-33-2; **4d**, 141-79-7; **5a**, 87307-39-9; **5b**, 87307-40-2; **5c**, 87307-41-3; **5d**, 87307-42-4; **6a**, 87307-43-5; **6b**, 87307-44-6; **6c**, 87307-45-7; **6d**, 87307-46-8; **7a**, 87307-47-9; **7c**, 87307-48-0; **7d**, 87307-49-1; **8**, 87307-50-4; **9**, 16112-10-0; **10**, 932-66-1; **11**, 87307-51-5; **12**, 87307-52-6; **13**, 87307-53-7; **14**, 87307-54-8; **15**, 765-69-5; **16**, 1193-55-1; **17a**, 55790-69-7; **17c**, 87307-55-9; **18a**, 6134-90-3; **18c**, 87307-56-0; **19a**, 31208-52-3; **19c**, 87307-57-1; **20a**, 87307-58-2; **20c**, 87307-59-3; **21a**, 25112-78-1; **21c**, 87307-60-6; **22a**, 5073-65-4; **22c**, 87307-61-7; **28d**, 87307-62-8; **29d**, 87307-63-9; **30d**, 87307-64-0; **31**, 87307-65-1; **32**, 87307-66-2; **33**, 87307-67-3; **34**, 87307-68-4; **35c**, 87307-69-5; **35d**, 87307-70-8; **36c**, 87307-71-9; **37c**, 87307-72-0; 7-acetyl-8,8-dimethyl-9-oxabicyclo-[4.3.0]non-6-ene, 87307-73-1.

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