methyl groups. Elemental analysis did not permit calculation of an empirical formula.

The remainder of the mixture was subjected to steam distillation to isolate volatile components. The steam distillate was extracted with methylene chloride and the combined extracts were dried over sodium sulfate. Filtration and concentration gave a light yellow oil which by VPC and NMR analyses was identified as unchanged **13**. No other volatile components could be isolated from the photolysate.

Ethyl 2-Cyano-5-methylhexa-2,4-dienoate (20). This compound was prepared in 15.1% yield according to a published procedure.[16] The NMR spectrum ($CDCl_3$) was interpreted in greater detail[23] than was reported in the literature:[16] δ 1.31 (t, 3, J = 7 Hz, CH_2CH_3), 2.04 [d, 6, J = 1.5 Hz, $(CH_3)_2C{=}C$], 4.28 (q, 2, J = 7 Hz, CH_2CH_3), 6.43 [d with secondary splitting, 1, J = 12, 1.5 Hz, $(CH_3)_2C{=}CH$], 8.10 [br d, J = 12 Hz, $(CH_3)_2C{=}CHCH{=}C$]. Sharpening of the doublet at δ 8.10 was observed on irradiating the peak at δ 2.04.

Irradiation of 13 in the Presence of Acetophenone. A solution of 0.524 g (0.0036 mol) of **13** and 52.8 g (0.44 mol) of acetophenone in 350 ml of *tert*-butyl alcohol was deoxygenated with UHP nitrogen for 30 min prior to irradiation through a Pyrex filter with 350-nm light. The relative concentrations were adjusted so that at this wavelength acetophenone absorbed 97% of the incident radiation.

After 1 h the irradiation was terminated and the solvents were removed under reduced pressure to give 0.48 g of an amber oil. Spectral analysis of the photolysate indicated the presence of **14** and **19**, in addition to unreacted **13**. No **22** was detected.

Registry No.—**11**, 54303-58-1; **12**, 59463-22-8; **13**, 55341-17-8; **13**, 2,4-DNPH, 59463-23-9; **14**, 59463-24-0; **16**, 59463-25-1; **19a**, 59463-26-2; **19b**, 59463-27-3; **20**, 28525-73-7; *isopropenyl acetate*, 108-22-5.

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(20) The same selectivity has been reported for two 3-methylspirodienones.[2b]
(21) Alternative mechanistic interpretations,[4b,4c] in which skeletal rearrangement and electron redistribution occur simultaneously, fail to account for the striking selectivity exhibited by 2,5-cyclohexadienones bearing C-3 substituents.
(22) Coupling constants were determined at 220 MHz.
(23) Coupling constants were determined from double irradiation experiments at 60 MHz.

Alicyclic Ring Closure. 1. Preferential Formation of Five-Membered over Seven-Membered Rings in Aldol Ring Closure Reactions

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Received March 15, 1976

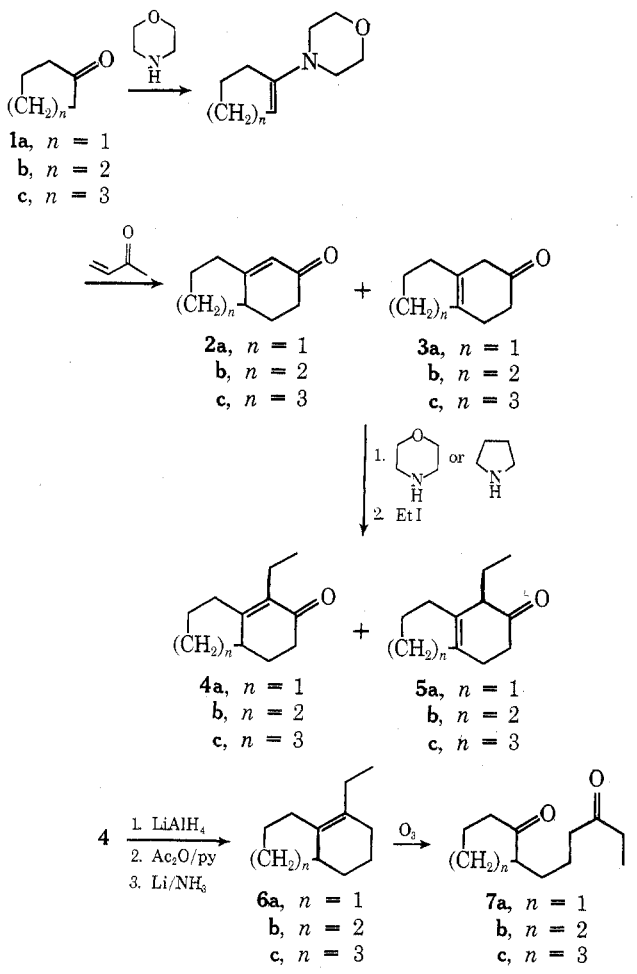
Diones **7a**, **7b**, and **7c**, synthesized from cyclopentanone, cyclohexanone, and cycloheptanone, respectively, were subjected to base-catalyzed aldol cyclization yielding principally an α,β-unsaturated ketone **8**, along with lesser amounts of the β,γ-unsaturated isomer **9**. No seven-membered ring unsaturated ketone **10** could be detected.

The closure of six-membered alicyclic rings has long been recognized as a facile process, particularly by enolate addition to a carbonyl group as in the ring closure step of the Robinson ring annelation procedure.[1] When a five- or seven-membered ring has to be closed, the same methods which work well in closing six-membered rings are usually employed. In the case of the five-membered rings, these are often successful, although sometimes they fail. When they do fail, that fact usually rates only passing mention, making systematic search of the literature for them all but impossible. Any attempt at explanation is usually confined to an inference of adverse steric interaction and/or strain. When the enolate addition methods are used in attempts to close a seven-membered ring, they often fail, although there are successful examples in the literature. Nevertheless, a large percentage of syntheses of compounds containing seven-membered rings, e.g., the hydroazulenic sesquiterpenoids, are actually achieved by ring expansion procedures, either chemical or, more often, photochemical. Nature herself appears to make the hydroazulenic compounds by cyclization of a ten-membered ring.[2] We, therefore, were interested to examine the products obtained from molecules able to close to give a five- or a seven-membered ring, but not a six-membered one. We have examined several such cyclizations where the reaction involved was an aldol reaction performed under conditions where both enolate ion formation and the first step of the aldol were reversible.

Results and Discussion

Diones **7a**, **7b**, and **7c** were synthesized by the route indicated in Scheme I. Robinson annelation reactions of methyl

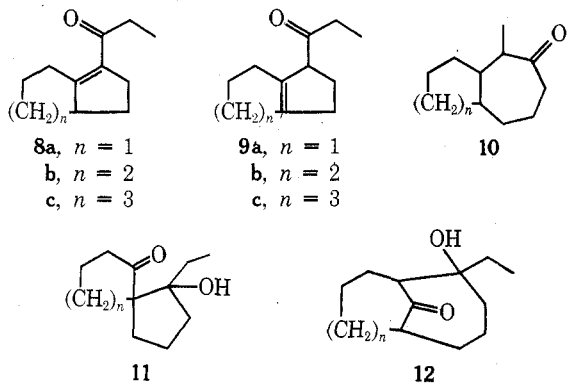
Scheme I



vinyl ketone on the morpholine enamine of the appropriate cycloalkanone **1** gave[3,4] the α,β-unsaturated ketones **2** together with some β,γ-unsaturated[5] isomers **3**. The morpholine or pyrrolidine enamines of **2** were monoalkylated[6] in the α position with 1 equiv of ethyl iodide to give the α,β-unsaturated ketones **4**, again accompanied by the β,γ-unsaturated[5] isomer **5**. No alkylated product could be obtained using ethyl bromide in place of the ethyl iodide. Each ketone mixture **4** and **5** was reduced with lithium aluminum hydride and acetylated, and the allylic acetate was reductively cleaved with lithium in liquid ammonia[7] to yield the alkene **6** together with traces of other isomers. The desired diones **7** were then obtained by ozonolysis, and purified by preparative GLC.

These diones, as relatively dilute solutions, were each refluxed in methanol with ca. 2 equiv of sodium methoxide for 24 h. In each case, the only products detected were the α,β-unsaturated ketone **8** and the β,γ-unsaturated[5] isomer **9**. In the case of diones **7a** and **7b**, a number of different bases were tried, in protic and aprotic solvents, but the products were in each case the same as those obtained using sodium methoxide.

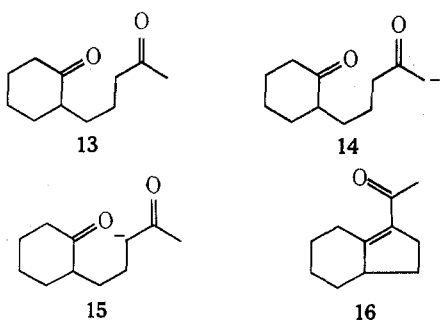
Diones **7** were chosen for this study as being the simplest diones in which opportunities for five- and seven-membered ring closure onto an existing ring are structurally and mechanistically equal, each of the possible enolate ions being C-alkylated. It is usual for the formation of aldols to be reversible.[8] Indeed, were it not for the intramolecular nature of the reaction, it would be expected that the equilibrium would favor the uncyclized diones. Even in these cases, it is not certain that the aldols would be predominant at equilibrium, but the essentially irreversible dehydration which follows serves to drive the reaction to completion. The keto alcohols **11** and **12**, if formed, cannot dehydrate into conjugation, and therefore only the conjugated ketones **8** and **9** are to be expected.



The use of ca. 2 equiv of base was determined to be the best compromise between the formation of by-products and the necessity of excessively long reaction times. The presence of large excesses of base, commonly used in aldol reactions to force the reaction quickly to completion, presumably promotes further (intermolecular) reactions of the various enolates possible.

We could detect no significant difference in the time or conditions required to effect cyclization of the three diones **7a**, **7b**, and **7c**. It is therefore concluded that the size of the ring (five, six or seven membered) *onto* which the new five-membered ring is fused has little influence on the ease of cyclization.

While we recognized at the outset that the bulk of the available evidence pointed to five-membered rings being easier to form than seven-membered ones, we were surprised to find none of the seven-membered ring product. Examination of models does not reveal any steric interaction which can be used to convincingly explain this complete lack of any seven-membered ring product. Interactions involving the terminal methyl groups (of the ethyl groups) in **7** would appear to be relatively unfavorable for formation of the seven-membered ring keto alcohol, yet Meyer and Wolfe[9] found the analogous exclusive formation of the five-membered ring unsaturated ketone **16** from dione **13**, even using a large excess



of base, which would favor the reaction of the kinetically formed[10] enolate **14**. The reaction was, however, slow, and doubtless the thermodynamically favored enolate **15** predominated. No significant unfavorable interaction can be seen to be created upon dehydration of the seven-membered ring keto alcohols, although reluctance of a seven-membered ring to adopt a conformation allowing a planar α,β-unsaturated carbonyl system has been observed[11,12] in monocyclic systems.

We also suppose that C-3 of the side chain comes into proximity of the ring carbonyl much more frequently than

C-5. There is no evidence that seven-membered rings once formed are any less thermodynamically stable than five-membered ones. The heats of combustion of the five-, six-, and seven-membered rings cycloalkanones and cycloalkenones do not, however, appear to have been determined.

Experimental Section[13]

Morpholine Enamines of Cycloalkanones.[14] A solution of 98 g (1.0 mol) of cyclohexanone in ca. 300 ml of benzene was refluxed for 30 h with 95 g (1.5 mol) of morpholine with continuous separation of water. Ca. 20 ml (theory 18 ml) of water was collected. The benzene and excess morpholine were removed under reduced pressure, and the residue distilled, yielding 134 g (80%) of 1-(1-morpholino)cyclohexene as a colorless liquid, bp 93–96 °C (6.0 mm).

Using a similar procedure, 84 g (1.0 mol) of cyclopentanone when refluxed for 18 h with 126 g (2.0 mol) of morpholine gave 103.4 g (80%) of 1-(1- morpholino)cyclopentene, bp 60–64 °C (1.0 mm). Cycloheptanone (112 g, 1.0 mol) refluxed for 48 h with 95 g (1.5 mol) of morpholine and 0.5 g of *p*-toluenesulfonic acid gave 137 g (87%) of 1-(1-morpholino)cycloheptene, bp 125–130 °C (14 mm).

Addition of Methyl Vinyl Ketone to Cycloalkanone Enamines. Cyclohexanone Enamine. A solution of 67 g (0.40 mol) of 1-(1-morpholino)cyclohexene in 400 ml of freshly distilled dioxane was placed in a 3-l. three-necked flask equipped with a mechanical stirrer, condenser, and dropping funnel. A solution of 30 g (0.42 mol) of freshly distilled methyl vinyl ketone was added to the stirred enamine solution over 1 h. The mixture was refluxed for 4 h. Ca. 500 ml of water was added and the reflux continued for 15 h. After the solution cooled to room temperature, it was poured into 650 ml of water and extracted four times with ether (total 300 ml). The ethereal solution was washed with 3 N HCl, saturated sodium bicarbonate solution, and water, and dried over $MgSO_4$. The ether was removed under reduced pressure and the residue distilled, yielding 52 g (56%) of a mixture of ca. 80% $\Delta^{1(2)}$-bicyclo[4.4.0]decenone-3 (**2b**) and ca. 20% $\Delta^{1(6)}$-bicyclo[4.4.0]decenone-3 (**3b**): bp 120–125 °C (12 mm) [lit.[4] 55–60 °C (0.3 mm)]; uv max (EtOH) 239 nm (lit.[3] 238) due to **2b**; ir for **2b** 1680 cm^{-1}; ir for **3b** 1720 cm^{-1}; NMR of **2b** 5.68 ppm (s, vinyl hydrogen); MS *m/e* 150 29, M^+), 121 (100, M − 29).

Cyclopentanone Enamine. A solution of 54 g (0.77 mol) of methyl vinyl ketone was added over 1 h to 100 g (0.65 mol) of 1-(1-morpholino)cyclopentene in 150 ml of benzene. The mixture was refluxed for 6 h and the benzene removed by distillation. Ca. 200 ml of aqueous methanol was added and the solution refluxed overnight. Most of the methanol was distilled off, ca. 400 ml of water was added, and the mixture was extracted with ether. The ethereal solution was dried over $MgSO_4$, the ether removed under reduced pressure, and the residue distilled to yield 67.6 g (65%) of a mixture of $\Delta^{1(2)}$-bicyclo[4.3.0]nonenone-3 (**2a**) and $\Delta^{1(6)}$-bicyclo[4.4.0]nonenone-3 (**3a**), bp 112–116 °C (1.0 mm) [lit.[15] 80–81 °C (0.4 mm)]. The ratio of products varied, apparently depending largely on the length of the reflux with aqueous methanol, from 67% **2a**, 33% **3a** in the above preparation to virtually 100% **2a** when the reflux was extended to 48 h. Spectral details: uv max (EtOH) 237 nm (lit.[16] 237 nm) due to **2a**; ir 1655 cm^{-1} (**2a**), 1710 cm^{-1} (**3a**); NMR 5.73 ppm (s, or perhaps unresolved quartet, J = 2 Hz, vinyl H in **2a**); MS *m/e* 136 (19, M^+), 108 (100, M − 28), 107 (28, M − 29).

Cycloheptanone Enamine. The procedure described for the cyclohexanone enamine was employed. 1-(1-Morpholino)cycloheptene (95 g, 0.52 mol) yielded 67 g of a compound, bp 95–98 °C (0.1 mm), which spectral data, especially the singlet at 2.09 ppm in the NMR, indicated was 2-(oxobutyl)cycloheptanone, the product of the initial Michael step of the Robinson annelation. This dione (65 g) in anhydrous methanol was refluxed overnight under dry nitrogen with ca. 5 g of sodium methoxide. Ether and water were added and the ether separated, washed with 5% HCl, water, and dried over $MgSO_4$. The ether was removed under reduced pressure and the residue distilled, yielding 60 g (70%) of a mixture of $\Delta^{1(11)}$-bicyclo[5.4.0]undecenone-10 (**2c**) and $\Delta^{1(7)}$-bicyclo[5.4.0]undecenone-10 (**3c**): bp 96–98 °C (0.5 mm); uv max (EtOH) 240 nm **2c** [lit.[17] 240 nm (EtOH)]; ir 1660 (**2c**), 1720 cm^{-1} (**3c**); NMR 5.73 ppm (s, vinyl H in **2c**); MS *m/e* 164 (56, M^+), 136 (100, M − 28), 122 (64, M − 42), 108 (66, M − 58).

Alkylation of Unsaturated Ketones 2. Ketone 2b. A solution of 52 g (0.35 mol) of ketone **2b** in 500 ml of toluene was refluxed with 64 g (1.05 mol) of morpholine for 40 h with continuous separation of water. Slightly more than the theoretical quantity of water was obtained. The toluene and excess morpholine were distilled off and the residue distilled yielding 60 g (78%) of the morpholine enamine of **2b**, bp 130–135 °C (0.28 mol). A mixture of 59 g (0.27 mol) of the enamine, 42 g (0.27 mol) of iodoethane, and ca. 250 ml of dry dioxane was refluxed for ca. 50 h. Dilute HCl was added and the solution refluxed overnight. the product was extracted with ether; the ethereal solution was washed with saturated $NaHCO_3$ and water, dried over $MgSO_4$, and evaporated under reduced pressure and the residue was distilled to yield 14.4 g (30%) of a mixture of ca. 70% 2-ethyl-$\Delta^{1(2)}$-bicyclo[4.4.0]decenone-3 (**4b**) and its β,γ isomer 2-ethyl-$\Delta^{1(5)}$-bicyclo[4.4.0]-decenone-3 (**5b**) and ca. 30% starting ketone **2b** and its β,γ isomer **3b**. Fractions of almost exclusively alkylated ketones **4b** and **5b** were obtained by distillation on a spinning column, bp 86–92 °C (0.8 mm). **4b** showed uv max (EtOH) 242 nm; ir 1670 cm^{-1}; NMR 0.88 ppm (t, J = 7 Hz, methyl H); MS *m/e* 178 (56, M^+), 163 (6, M − 15), 150 (100, M − 28), 149 (98, M − 29). **5b** showed uv end absorption; ir 1710 cm^{-1}; NMR 0.88 ppm (t, J = 7 Hz, methyl H); MS *m/e* 178 (M^+).

Ketone 2a. A solution of 330 g (2.42 mol) of ketone **2a** in ca. 3 l. of toluene was refluxed with 320 g (4.5 mol) of pyrrolidine for ca. 48 h with continuous separation of water. A total of 50 ml (theory 43 ml) was obtained. The toluene and excess pyrrolidine were distilled off and the enamine distilled, yielding 357 g (78%), bp 120–130 °C (0.50 mm). A mixture of 357 g (1.89 mol) of the enamine and 296 g (1.90 mol) of iodoethane was refluxed in 1 l. of dioxane for 72 h. The mixture was acidified with dilute HCl and refluxed overnight. The mixture was distilled until much of the dioxane had been removed. Water was added, and the mixture extracted with ether. The ethereal extract was washed with water, dried over magnesium sulfate, and distilled to yield a mixture of 2-ethyl-$\Delta^{1(2)}$-bicyclo[4.3.0]nonenone-3 (**4a**), 2-ethyl-$\Delta^{1(5)}$-bicyclo[4.3.0]nonenone-3 (**5a**), and starting ketone **2a**. Fractions of almost exclusively alkylated ketones **4a** and **5a** were obtained by spinning band distillation, bp 78–84 °C (0.07 mm). **4a** showed uv max (EtOH) 227 nm, with shoulder 283 nm; ir 1655 cm^{-1}; NMR 0.91 ppm (t, J = 7 Hz, methyl H); MS *m/e* 164 (47, M^+), 149 (6, M − 15), 136 (100, M − 28), 135 (52, M − 29).

Ketone 2c. A solution of 64 g (0.39 mol) of ketone **2c** in 200 ml of toluene was refluxed with 42 g (0.59 mol) of pyrrolidine for 24 h with continuous separation of water. The toluene and excess pyrrolidine were distilled off and the enamine distilled, yielding 64.2 g (76%), bp 130–135 °C (0.18 mm). A mixture of 64 g (0.39 mol) of the enamine and 96 g (0.615 mol) of iodoethane was refluxed in 500 ml of dioxane for 24 h. Two layers formed, the lower of which contained the enamines. The mixture was acidified with dilute HCl and refluxed overnight. The mixture was extracted with chloroform, and the chloroform extracts washed with saturated $NaHCO_3$ and water and dried over $MgSO_4$. The chloroform was removed under reduced pressure and the residue distilled yielding a mixture of 11-ethyl-$\Delta^{1(11)}$-bicyclo[5.4.0]undecenone-10 (**4c**), 11-ethyl-$\Delta^{1(6)}$-bicyclo[5.4.0]undecenone-10 (**5c**), and starting ketone **2c**. Fractions rich in the alkylated ketone **4c** were obtained by spinning band distillation, bp 115–125 °C (0.28 mm). **4c** showed uv max (EtOH) 243 nm; ir 1670 cm^{-1}; NMR 0.89 ppm (t, J = 7 Hz, methyl H); MS *m/e* 192 (3, M^+), 175 (34, M − 17), 148 (26, M − 54), 77 (100, M − 115).

Partially purified samples of all alkylated ketones were obtained by preparative GLC on a 12 ft Carbowax 20M column at 150 °C. Satisfactory analyses could not be obtained, apparently because the ketones were not particularly stable compounds.

Conversion of Ketones 4 into Alkenes 6. Ketone 4b. A solution of 1.05 g (0.0059 mol) of ketone **4b** in 30 ml of anhydrous ether was added dropwise, under nitrogen, to a cooled (0 °C) suspension of 0.123 g (0.00324 mol) of lithium aluminum hydride in 20 ml of ether. The mixture was allowed to warm to room temperature and stirred for 1.5 h. Water (0.12 ml) was carefully added, followed by 0.12 ml of 15% NaOH and 0.36 ml of water. The salts which precipitated were removed by filtration. The ether solution was separated, dried over $MgSO_4$, and evaporated under reduced pressure to yield 0.60 g (56%) of 2-ethyl-$\Delta^{1(2)}$-bicyclo[4.4.0]decenol-3: ir 3320, 1660 cm^{-1}; NMR 0.97 (t, J = 7, methyl H), 5.4 ppm (broad, CHOH); MS *m/e* 180 (10, M^+), 163 (27, M − 17), 90 (100, M − 90). The crude alcohol, which rapidly oxidized in air, was immediately dissolved in 10 ml of dry pyridine and 2 ml of freshly distilled acetic anhydride added. The mixture was allowed to stand at room temperature overnight. Water was added and the product extracted with chloroform. The chloroform extract was dried over $MgSO_4$, and evaporated under reduced pressure to yield 0.43 g (58%) of 2-ethyl-3-acetoxy-$\Delta^{1(2)}$-bicyclo[4.4.0]decene: ir 1740 cm^{-1}; NMR 0.92 (t, J = 7 Hz, methyl H), 1.99 (s, CH_3CO–), 5.28 ppm (d?, CHOAc); MS *m/e* 222 (0.5, M^+), 162 (65, M − 60), 133 (100, M − 89). The acetate (0.42 g), without further purification, was dissolved in ca. 15 ml of liquid ammonia, and 1.0 g of lithium added. After 2 min, the mixture turned blue. Ether (25 ml) was added, and the ammonia allowed to evaporate. Water was carefully added, followed by dilute HCl. The ether layer was separated, dried over $MgSO_4$, and evaporated to yield 0.32 g (ca. 100%) of crude 2-ethyl-$\Delta^{1(2)}$-bicyclo[4.4.0]decene (**6b**). Pure samples were obtained by preparative GLC

on a 12 ft Carbowax 20M column at 150 °C. In **6b**, ir does not show the double bond stretch; NMR 0.92 (t, J = 7 Hz, methyl H), 1.88 ppm (q, J = 7 Hz, CH_2CH_3), no vinyl signal; MS m/e 164 (27, M^+), 122 (100, M − 42).

Anal. Calcd for $C_{12}H_{20}$: C, 87.73; H, 12.27. Found: C, 87.94; H, 12.10.

Ketone 4a. Lithium aluminum hydride (0.07 mol) reduction of 11.4 g of ketone **4a**, using the above procedure, gave 11.87 g (ca. 100%) of 2-ethyl-$\Delta^{1(2)}$-bicyclo[4.3.0]nonenol-3: ir 3300 cm^{-1}; NMR 0.96 (t, J = 8 Hz, methyl H), 5.4 ppm (d?, J = 7 Hz, CHOH); MS m/e 166 (15, M^+), 165 (16, M − 1), 148 (38, M − 18), 147 (47, M − 19), 137 (47, M − 29), 119 (100, M − 47). This crude alcohol was acetylated in 83% yield to give 2-ethyl-3-acetoxy-$\Delta^{1(2)}$-bicyclo[4.3.0]nonene: ir 1735 cm^{-1}; NMR 0.94 ppm (t, J = 7 Hz, methyl H); MS m/e 208 (0.5, M^+), 176 (10, M − 32), 148 (35, M − 60), 147 (35, M − 61), 133 (9, M − 75), 119 (100, M − 89). The crude acetate was reduced with Li/NH_3 to give, *after distillation*, a 50% yield of 2-ethyl-$\Delta^{1(2)}$-bicyclo[4.3.0]nonene (**6a**): bp 51–55 °C (0.25 mm); ir does not show the double bond stretch; NMR 0.95 ppm (t, J = 7 Hz, methyl H); MS m/e 150 (53, M^+), 121 (100, M − 29), 107 (17, M − 43), 93 (50, M − 57).

Anal. Calcd for $C_{11}H_{18}$: C, 87.93, H, 12.07. Found: C, 87.99; H, 12.02.

Ketone 4c. Lithium aluminum hydride reduction of 44 g of ketone **4c** gave 39 g (85%) of 11-ethyl-$\Delta^{1(11)}$-bicyclo[5.4.0]undecenol-10: ir 3350 cm^{-1}; NMR 1.00 (t?, J = 7 Hz, methyl H), signals at 6.23 (s) and 6.82 ppm (d) are assigned to the –CHOH protons in the two epimeric alcohols possible; MS m/e 194, (4, M^+), 193 (10, M − 1), 176 (46, M − 18), 175 (100, M − 19), 150 (84, M − 44), 135 (71, M − 59). Acetylation of the alcohol gave 11-ethyl-10-acetoxy-$\Delta^{1(11)}$-bicyclo[5.4.0]undecene; ir 1735 cm^{-1}; NMR the methyl triplet appears to be at 0.93 ppm, but is obscured by other signals; the CH_3CO signal at 1.93 ppm is split, presumably due to the two epimers present, signals at 6.22 (s) and 6.83 ppm (d) are assigned to the CHOAc protons in the two epimers; MS parent ion is not seen convincingly, m/e 174 (61, M − 62), 149 (100, M − 85). The crude acetate (10 g) was reduced with Li/NH_3 to yield 12 g (ca. 100%) of 2-ethyl-$\Delta^{1(11)}$-bicyclo[5.4.0]undecene (**6c**): ir double bond stretch does not show; NMR 0.96 ppm (t, J = 7 Hz, methyl H); MS 178 (46, M^+), 163 (8, M − 15), 149 (100, M − 29), 135 (46, M − 43), 122 (24, M − 56).

Anal. Calcd for $C_{13}H_{22}$: C, 87.56; H, 12.44. Found: C, 87.39; H, 12.38.

Diones 7a, 7b, 7c. Dione 7b. Batches of 6 g of alkene **6b** (total 44 g, 0.27 mol) in 35 ml of methylene chloride containing 1 ml of freshly distilled pyridine[18] was ozonized at −78 °C for 3 h. The mixture was allowed to come to room temperature, and the successive batches were added dropwise to a stirred mixture of 750 ml of water, 6.6 g of zinc dust, and 23 ml of glacial acetic acid. The stirring was continued for 1 h after the last addition. The solution was filtered, extracted with chloroform, the chloroform extracts washed with $NaHCO_3$ and water, and dried over anhydrous $MgSO_4$. The residue was distilled to yield 48 g (91%) of 2-(4-oxohexyl)cyclohexanone (**7b**), bp 107–110 °C (0.05 mm). A small sample was purified by preparative GLC on a 15 ft Carbowax column at 185 °C: ir 1700 cm^{-1}; NMR 1.00 (t, J = 7 Hz, methyl H), 2.32 ppm (complex signal due of protons on C's α to carbonyls); MS m/e 196 (16, M^+), 149 (63, M − 57), 121 (62, M − 75), 98 (100, M − 98).

Anal. Calcd for $C_{12}H_{20}O_2$: C, 73.43; H, 10.27. Found: C, 73.22; H, 10.10.

Dione 7a. Alkene **6a** was ozonized as above to give 2-(4-oxohexyl)-cyclopentanone (**7a**): ir 1745 and 1720 cm^{-1}; NMR 1.00 (t, J = 7 Hz, methyl H), 2.2–2.5 ppm (complex signal due to protons on C's α to carbonyls); MS m/e 182 (30, M^+), 153 (10, M − 29), 138 (47, M − 44), 135 (43, M −47), 110 (100, M − 72), 107 (67, M − 75).

Anal. Calcd for $C_{11}H_{18}O_2$: C, 72.49; H, 9.95. Found: C, 72.35; H, 9.96.

Dione 7c. Alkene **6c** was ozonized as above to give ca. 50% yield of 2-(4-oxohexyl)cycloheptanone (**7c**), which was purified by filtration through a silica column in CCl_4/ether. Spectral and analytical samples were again purified by preparative GLC: ir 1710 cm^{-1}, with some evidence of splitting; NMR 1.00 (t, J = 8 Hz, methyl H), 2.2–2.6 ppm (complex signal due to protons on C's α to carbonyls); MS m/e 210 (6, M^+), 167 (16, M − 43), 163 (20, M − 47), 135 (26, M − 75), 126 (32, M − 84), 112 (100, M − 98).

Anal. Calcd for $C_{13}H_{22}O_2$: C, 74.24; H, 10.54. Found: C, 74.32: H, 10.68.

All diones slowly turned yellow in light, and were stored under N_2, in the dark at 0 °C or below.

After samples of the pure diones and intermediates were available, losses in the syntheses, resulting mainly from purification problems, were greatly reduced by carrying all steps from the ketones **2** to the diones **7** without intermediate purification. The major impurities were compounds with molecular weight (by MS) 28 amu higher than those of the desired compounds. These doubtless arise from dialkylation of the starting ketones, a not unexpected side reaction.[6]

Cyclization of Diones. Dione 7b. Dione **7b** (0.20 g, 1.02 mmol) in 15 ml of anhydrous methanol was refluxed overnight under nitrogen with 0.11 g (2.04 mmol) of sodium methoxide. Water was added, and the mixture extracted with ether. The ether extract was washed three times with water, dried over $MgSO_4$, and evaporated to give 0.19 g of a crude mixture of two products. Samples of the products were obtained by preparative GLC on a 15 ft Carbowax column at 160 °C. The major component was 8-propionyl-$\Delta^{1(9)}$-bicyclo[4.3.0]nonane (**8b**): uv max (EtOH) 255 nm (ϵ 4356);[19] ir 1675, 1610 cm^{-1}; NMR 1.00 ppm (t, J = 7 Hz methyl H), no vinyl signals; MS m/e 178 (73, M^+), 149 (100, M − 29), 121 (33, M − 57).

Anal. Calcd for $C_{12}H_{18}O$: C, 80.85; H, 10.18. Found: C, 80.62; H, 10.08.

The minor component was 8-propionyl-$\Delta^{1(6)}$-bicyclo[4.3.0]nonane (**9b**): uv (EtOH) end absorption 207 nm (ϵ 3570); ir 1705 cm^{-1}; NMR 0.98 (t, J = 7 Hz, methyl H), 2.37 (q, J = 7 Hz, CH_2CH_3), 2.1 ppm (signal due to allylic H); MS m/e 178 (15, M^+), 149 (13, M − 29), 121 (100, M − 57).

Anal. Calcd for $C_{12}H_{18}O$: C, 80.85; H, 10.18. Found: C, 80.94; H, 9.98.

Dione 7a. Treatment of dione **7a** in the same manner yielded, as major component, 2-propionyl-$\Delta^{1(2)}$-bicyclo[3.3.0]octene (**8a**): uv max (EtOH) 253 nm (ϵ 4230); ir 165 cm^{-1}, with shoulder at 1640 cm^{-1}; NMR 1.09 (t, J = 7 Hz, methyl H), 2.60 ppm (q, J = 7 Hz, $COCH_2CH_3$), no vinyl signals; MS m/e 164 (55, M^+), 135 (100, M − 29), 107 (38, M − 57).

Anal. Calcd for $C_{11}H_{16}O$: C, 80.44; H, 9.82. Found: C, 80.23; H, 9.82.

The minor component was 2-propionyl-$\Delta^{1(5)}$-bicyclo[3.3.0]octene (**9a**): uv end absorption; ir 1705 cm^{-1}; NMR 1.03 ppm (t, J = 7 Hz, methyl H), no vinyl signal; MS m/e 164 (18, M^+), 135 (12, M − 29), 107 (100, M − 57).

Anal. Calcd for $C_{11}H_{16}O$: C, 80.44; H, 9.82. Found: C, 81.56; H, 9.96.

Dione 7c. Treatment of dione **7c** in the same manner yielded, as major component, 10-propionyl-$\Delta^{1(10)}$-bicyclo[5.3.0]decene (**8c**): uv max (EtOH) 257 nm (ϵ 4163); ir 1660, 1600 cm^{-1}; NMR 1.00 ppm (t, J = 7 Hz, methyl H), no vinyl signal; MS m/e 192 (26, M^+), 163 (100, M − 29), 135 (16, M − 57).

Anal. Calcd for $C_{13}H_{20}O$: C, 81.20; H, 10.48. Found: C, 80.89; H, 10.66.

The minor component was 10-propionyl-$\Delta^{1(7)}$-bicyclo[5.3.0]decene (**9c**): uv (EtOH) end absorption 209 nm (ϵ 3676); ir 1705 cm^{-1}; NMR 1.08 ppm (t, J = 7 Hz, methyl H), no vinyl signal; MS m/e 192 (10, M^+), 163 (10, M − 29), 135 (100, M − 57).

Anal. Calcd for $C_{13}H_{20}O$: C, 81.20; H, 10.48. Found: C, 81.37; H, 10.25.

Other Cyclization Conditions. Dione **5a** was cyclized to the same product mixture as above under each of the following conditions: potassium *tert*-butoxide in *tert*-butyl alcohol, reflux 24 h; potassium *tert*-butoxide in Me_2SO, reflux 24 h; KOH in EtOH/water, reflux 48 h; K_2CO_3 in EtOH/water, reflux 48 h.

Dione **5b** was also cyclized to the same mixture as above using potassium *tert*-butoxide in *tert*-butyl alcohol.

Acknowledgments. We acknowledge the generous financial support of the Robert A. Welch Foundation. We thank Robert S. Brown, Purvis Harper, and Mary B. Neal for assistance with the syntheses.

Registry No.—**2a,** 1489-28-7; **2b,** 1196-55-0; **2c,** 19198-29-9; **3a,** 14661-63-3; **3b,** 13837-12-2; **3c,** 59562-88-8; **4a,** 59562-89-9; **4b,** 59562-90-2; **4c,** 59562-91-3; **5a,** 59562-92-4; **5b,** 59562-93-5; **6a,** 59563-01-8; **6b,** 59563-02-9; **6c,** 59563-03-0; **7a,** 59574-51-5; **7b,** 59574-52-6; **7c,** 59574-53-7; **8a,** 59562-95-7; **8b,** 59562-96-8; **8c,** 59562-97-9; **9a,** 59562-98-0; **9b,** 59562-99-1; **9c,** 59563-00-7; 1-(1-morpholino)cyclohexene, 670-80-4; methyl vinyl ketone, 78-94-4; 1-(1-morpholino)cyclopentene, 936-52-7; 1-(1-morpholino)cycloheptene, 7182-08-3; 2-ethyl-$\Delta^{1(2)}$-bicyclo[4.4.0]decenol-3, 59574-54-8; 2-ethyl-3-acetoxy-$\Delta^{1(2)}$-bicyclo[4.4.0]decene, 59574-55-9; 2-ethyl-$\Delta^{1(2)}$-bicyclo[4.3.0]nonenol-3, 59574-56-0; 2-ethyl-3-acetoxy-$\Delta^{1(2)}$-bicyclo[4.3.0]nonene, 59574-57-1; *cis*-11-ethyl-$\Delta^{1(11)}$-bicyclo[5.4.0]undecenol-10, 59574-58-2; *trans*-11-ethyl-$\Delta^{1(10)}$-bicyclo[5.4.0]undecenol-10, 59574-59-3; *cis*-11-ethyl-10-acetoxy-$\Delta^{1(10)}$-bicyclo[5.4.0]undecene, 59574-60-6; *trans*-11-ethyl-10-acetoxy-$\Delta^{1(10)}$-bicyclo[5.4.0]undecene, 59574-61-7; 2-(oxobutyl)cycloheptanone, 26871-79-4.

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Equilibria between α,β- and β,γ-Unsaturated Ketones in Six-Membered Rings Fused β,γ to Five-, Six-, and Seven-Membered Rings

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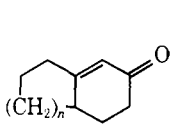
Received March 15, 1976

The equilibria between α,β- and β,γ-unsaturated ketones have been determined for a series of bicyclic ketones **2**, **4**, and **8** and **3**, **5**, and **9**. Alkylation on the α position increases the percentage of β,γ-unsaturated isomer at equilibrium. Steric and hyperconjugation effects in these and other acyclic and cyclic unsaturated ketones, esters, carboxylic acid salts, and nitriles are discussed.

In the course of the synthetic work described in the preceeding paper,[1] we encountered several α,β-unsaturated ketones in which the percentage of β,γ-unsaturated isomer present, even after equilibration, seemed significantly high. Accordingly, we undertook a systematic study of the available unsaturated ketones.

It has long been recognized that α,β-unsaturated carbonyl compounds, when treated with acid or base, tautomerize to a mixture of α,β- and β,γ-unsaturated isomers. The earliest work was that of Kon and Linstead, who investigated alkali catalyzed equilibria in series of acyclic unsaturated carboxylic acids[2-8] **17a/18a**, cyanides[9-10] **17b/18b**, and ethyl esters[5,11] **17c/18c**. This work has been summarized with the assistance of Linstead.[12] Unsubstituted carboxylic acid salts and esters equilibrate to give almost exclusively the α,β isomer. One γ-alkyl substituent will shift the equilibrium toward the β,γ isomer, while two γ substituents will suffice to make the β,γ isomer predominate. Substitution on the β carbon seems, from limited evidence in the acid series, to favor the β,γ isomer, but not to the same degree as a γ substituent. α-Substitution in the carboxylic acid series moderately favors the α,β isomer.



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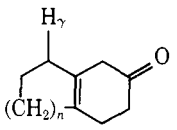
b, $n = 2$
c, $n = 3$



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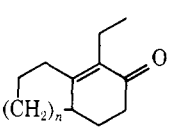

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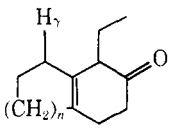

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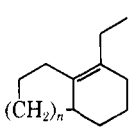

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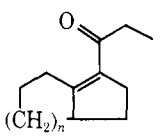

8a, $n = 1$
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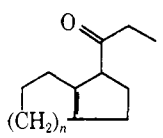

9a, $n = 1$
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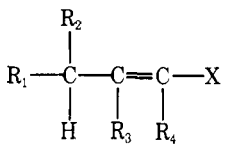
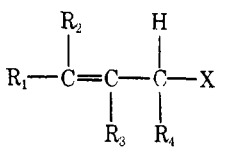


17a, $X = CO_2^-$
b, $X = CN$
c, $X = CO_2Et$
d, $R_1 = R_3 = R_4 = H$; $R_2 = Et$; $X = COCH_3$
e, $R_1 = Et$; $R_3 = H$; $R_4 = Me$; $X = CO_2Et$



18a, $X = CO_2^-$
b, $X = CN$
c, $X = CO_2Et$
d, $R_1 = R_3 = R_4 = H$; $R_2 = Et$; $X = COCH_3$
e, $R_1 = Et$; $R_3 = H$; $R_4 = Me$; $X = CO_2Et$