THE JOURNAL OF Organic Chemistry®

VOLUME 40, NUMBER 23

NOVEMBER 14, 1975

Photochemical Formation of 12-Methylene-*cis*-bicyclo[8.2.0]dodecan-1-ol from 2-Methylenecyclododecanone. Restricted Rotation in a Biradical Intermediate

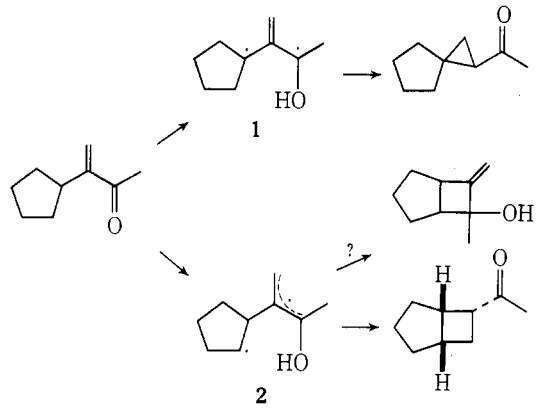
John J. Hemperly, Steven Wolff,* and William C. Agosta*

Laboratories of The Rockefeller University, New York, New York 10021

Received July 2, 1975

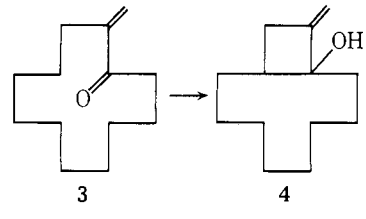
Irradiation of 2-methylenecyclododecanone (**3**) leads to 12-methylene-*cis*-bicyclo[8.2.0]dodecan-1-ol (**11**) in 87% yield, unaccompanied by the cyclobutyl or cyclopropyl ketones usually formed photochemically from α-methylene ketones. Pyrolysis of **11** leads to enone **15** and bicyclic ketone **14**, which is the cyclobutyl ketone anomalously absent from irradiation of **3**. The structures of **11**, **14**, and **15** are supported by spectroscopic and chemical data. Restricted rotation about the C(α)–C(β) bond in biradical intermediate **13** is advanced as an explanation for the exceptional behavior of **3**. These results suggest the importance of conformational mobility of a short-lived biradical in determining the products formed on photolysis of α-methylene ketones.

Photochemical isomerization of a variety of α-methylene ketones leads to cyclobutyl ketones, accompanied in some cases by related cyclopropyl ketones and methylenecyclobutanols.[1] Equation 1 gives a typical example in which all three types of products are found. There is good evidence



(1)

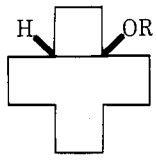
that the cyclopropyl and cyclobutyl ketones arise by way of biradical intermediates in which β hydrogen (**1**, for cyclopropyl ketones) or γ hydrogen (**2**, for cyclobutyl ketones) has been abstracted by the carbonyl oxygen.[2] It is quite likely that the methylenecyclobutanols also arise by way of biradical intermediates (as **2**),[1] although there is no direct evidence for this, and the possibility remains open that these alcohols represent a concerted $[_\sigma 2 + _\pi 2]$ cycloaddition[3] of the γ carbon–hydrogen bond with the carbonyl group. The major photoproduct is cyclobutyl ketone in most cases, and frequently no methylenecyclobutanol is found at all. An exception to this generalization is the photolysis of 2-methylenecyclododecanone (**3**), which furnishes solely a single isomer of the related methylenecyclobutanol **4** in high yield (eq 2).[1] Ketone **3** is the only medium- or large-ring compound investigated, and its exceptional photochemical behavior presumably is related to this structural feature. Our purpose in the present study was to investigate this isomerization of **3** in more detail; in this connection we have determined the stereochemistry of **4** and carried out sensitization and quenching experiments on its formation from **3**. In addition we have studied the thermolysis of **4** and succeeded thereby in preparing the cyclobutyl ketone which is anomalously absent in photolysis of **3**. The results are discussed in detail below; they permit us to offer a reasonable explanation for the behavior of **3** in terms of restricted rotation in a biradical intermediate, thus providing an instructive example of conformational control over the fate of a short-lived intermediate.



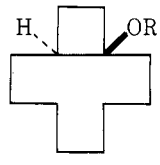
(2)

The convenient availability of both isomers of bicyclo[8.2.0]dodecan-1-ol, **5** and **6**, from photolysis of cyclododecanone[4] suggested that a simple proof of the stereochemistry of **4** would involve its correlation with one of these known alcohols. This approach was successful in demonstrating a cis ring fusion in **4**, and the structural formulas showing the degradation incorporate this result for convenience. Before removing the exo methylene group of **4** we first protected the hydroxyl function as the methyl ether. Reaction[5] of **4** with sodium hydride in tetrahydrofuran containing methyl sulfate yielded methyl ether **7** as the only product. As we discuss in a later paragraph, use of a different solvent here can lead to molecular rearrangement

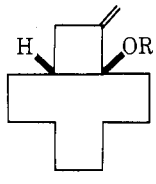
rather than simple etherification. Oxidation of **7**, first with osmium tetroxide in pyridine[6] and then directly with aqueous sodium periodate, furnished the α-methoxy ketone **8**. Attempts to combine these two steps through use of a catalytic amount of osmium tetroxide in the presence of periodate[7] were unsuccessful and apparently led to overoxidation. Wolff–Kishner reduction of **8** then gave the desired simple methyl ether **9**.[8] This degradation product was identical with an authentic sample of **9** prepared from the cis alcohol **5**, and it was readily distinguishable from the trans ether **10** prepared from **6**. The methylenecyclobutanol from irradiation of **3** accordingly is 12-methylene-*cis*-bicyclo[8.2.0]dodecan-1-ol (**11**).



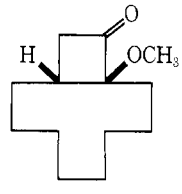
5, R = H
9, R = CH_3



6, R = H
10, R = CH_3



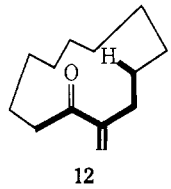
7, R = CH_3
11, R = H



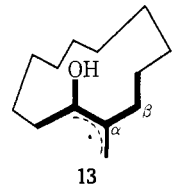
8

We next turned attention to investigation of the reactive excited state in the photoisomerization of **3** through sensitization and quenching experiments. In connection with understanding the unusual photochemical behavior of **3** it was important to determine whether this was due to some unexpected change in behavior of its excited states. We found that rearrangement of **3**, like that of the previously examined α-methylene ketones,[2] could be neither quenched nor sensitized. Isomerization of **11** proceeded equally well in benzene and in benzene containing 4 *M* 2,3-dimethyl-1,3-butadiene, and irradiation of a benzene solution of **3** and sufficient propiophenone to absorb 90% of the incident radiation gave no evidence for sensitized formation of **11**. Previous experiments have shown that the simple α-methylene ketone chromophore can indeed accept triplet energy from propiophenone.[2] Thus, **3** is in no apparent way different from other α-methylene ketones[2] which yield cyclobutyl ketones, cyclopropyl ketones, and little or no methylenecyclobutanol; there is no indication that the unique photochemical behavior of **3** is the consequence of a change in the multiplicity of the reactive excited state.[9]

There are two features of this photoisomerization requiring explanation, the formation of only the cis isomer of the methylenecyclobutanol (that is, **11**) and the total lack of any ketonic product. The unique steric situation in **3** provides an attractive explanation for both points. The unstrained geometry necessary for hydrogen transfer from the γ carbon to oxygen in **3** is shown in **12**.[10] We assume that biradical **13** is formed, just as has been demonstrated to be



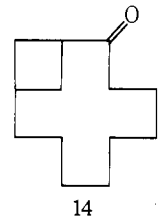
12



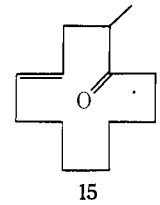
13

the case for α-methylene ketones which isomerize to cyclobutyl ketones.[2] In **13**, however, rotation about the C(α)–C(β) bond is severely impeded by the methylene chain constituting the remainder of the molecule, and the probability of bringing the α-methylene group into position for closure to cyclobutyl ketone enol is greatly reduced. Now, as noted above, the observed product **11** very probably arises by way of the alternative collapse of biradical **13** at the carbon bearing oxygen, a cyclization that can take place without prior C(α)–C(β) bond rotation. Not only are such delocalized biradicals already clearly implicated[2] in the photochemistry of other α-methylene ketones, but also there is evidence that singlet hydrogen transfer reactions of saturated alkanones involve analogous biradical intermediates.[11] Whatever the path to **11**, however, the reduced probability of C(α)–C(β) bond rotation in **13** can enhance formation of **11**. If **13** is an intermediate leading to **11**, competition for its collapse to the observed product is decreased; on the other hand, if **11** originates only in a concerted cycloaddition, the obvious path available to **13** is reverse transfer of hydrogen with regeneration of starting ketone **12** in its ground state.[12] It also follows from the geometry of **12** and **13** that the cis isomer of the product will be favored on steric grounds. Cyclization to form a trans-fused bicyclo[8.2.0]dodecane would require that the hydroxyl group be thrust into the methylene chain as the new carbon–carbon bond is formed. This unfavorable interaction does not occur during closure to the cis isomer **11**. The same effect is apparent in the photolysis of cyclododecanone; there the cis alcohol **5** predominates, but a minor amount of trans isomer **6** is also found.[4]

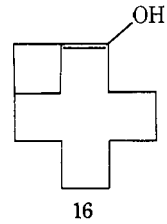
In this investigation we have also studied the thermolysis of **11** and succeeded in preparing by this route cyclobutyl ketone **14**, the "normal" photochemical product not observed on photolysis of **3**. Liquid-phase pyrolysis of **11** at 250° for 4 hr led to essentially complete destruction of starting material with formation of ketones **14** and **15**. The



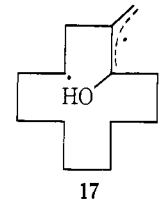
14



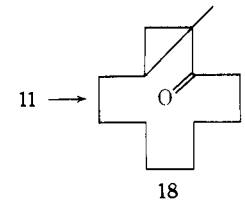
15



16



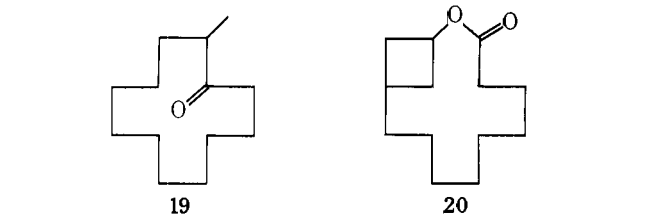
17



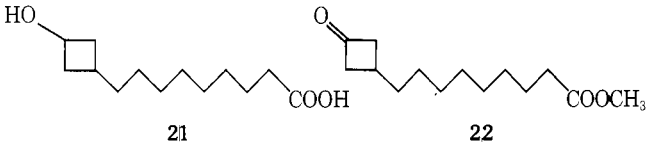
18 (3)

isomerization leading to **14** undoubtedly involves a [1,3] shift in the methylenecyclobutane to give initially enol **16** which then ketonizes. This type of rearrangement was not observed in an earlier study of thermal reactions of 2-methylenecyclobutanols,[13] although it has good analogy in the degenerate rearrangement of simple methylenecyclobutanes.[14] It could involve the same 1,4 biradical **17** (≡ **13**) expected on irradiation of 2-methylenecyclododecanone (**3**). If so, the fact that **17** leads to ketone **14** when formed

thermally but not when generated photochemically from **3** can be attributed to the higher temperature involved, which permits in the thermal process the very rotation discussed above as being restricted in the photochemical reaction. This attractive similarity of the two processes may be only a formal one, however, since a labeling study has shown that at least a portion of the methylenecyclobutane automerization follows a symmetry allowed course which is antarafacial in the allylic component.[14] Formation of **15**, on the other hand, can be rationalized by the intermediacy of **18**; that is to say, **11** undergoes ring contraction followed by opening of the cyclopropane, as shown in eq 3. The first step is a known thermal reaction of 2-methylenecyclobutanols,[13] while the pyrolytic ring opening is familiar in other 2-alkylcyclopropyl ketones.[1,15] The structure of **15**, including the trans geometry of the double bond, is based on spectroscopic properties, mechanistic considerations, and its mild catalytic hydrogenation to yield 2-methylcyclododecanone (**19**), an authentic sample of which was available from hydrogenation of **3**. The structure of **14** is defined by the following chemical evidence. Baeyer–Villiger oxidation of **14** furnished lactone **20**, which was hydrolyzed to hydroxy acid **21**. Esterification and oxidation then gave keto ester **22**, which was fully characterized. The ir and NMR



19 **20**



21 **22**

$PhCH_2CH{=}CH_2$ $PhCH{=}CHCH_3$

23 **24**

spectra of **22** show that it contains a 3-alkylcyclobutanone, a carbomethoxy group, and an unbranched aliphatic chain, thus requiring the structure assigned. If **14** indeed arises by way of its enol **16**, ketonization probably should yield a mixture of cis and trans isomers. Comparison of the 220-MHz NMR spectrum of **14** with the spectra of several simple cis and trans 3-substituted cyclobutyl methyl ketones[1] suggested that this was the case.[16]

It is interesting that when the etherification of **11** was carried out using sodium hydride in hexamethylphosphoramide rather than in tetrahydrofuran, rearrangement of **11** to **15** occurred. Further experiments showed that the presence of the methylating agent (methyl iodide or sulfate) was unnecessary, but that the yield of **15** was capricious and varied between 0 and 30%, apparently depending on the history of the solvent. The same cyclopropyl ketone intermediate (**18**) can be invoked in this case as was discussed above in the thermal conversion of **11** to **15**. In simple cases, however, it has been noted previously that the ring contraction of 2-methylenecyclobutanols (as **11** → **18**) does not occur in base.[13] It is possible that the transformation here is related to the curious rearrangement of 3-phenylpropene (**23**) to 1-phenylpropene (**24**) which occurs without evolution of hydrogen in hexamethylphosphoramide containing sodium hydride.[17]

A variety of factors undoubtedly influences the course of the photochemical rearrangement of α-methylene ketones. This investigation of the anomalous photochemical behavior of **3** provides evidence that the relative amounts of cyclobutyl ketone and methylenecyclobutanol formed can be controlled by conformational mobility. In most examples of these transformations rotation about the C(α)–C(β) bond is relatively free, and the delocalized biradical (corresponding to **2** or **13**) couples preferentially at the α-methylene group, furnishing cyclobutyl ketone enol.[1,2] This preference for coupling after rotation exists despite the simpler alternative possibility of direct collapse, without rotation about the C(α)–C(β) bond, to form methylenecyclobutanol. Selective formation of ketone from the biradical can be attributed most simply to a steric effect, with more rapid closure on the unsubstituted α-methylene carbon than on the disubstituted carbonyl carbon. This suggestion finds support in the recent demonstration that the rate of intramolecular radical addition to a double bond is strongly influenced by the degree of substitution at the site of reaction.[18] Only in a substrate such as **3**, with restricted rotation about the C(α)–C(β) bond, does formation of a methylenecyclobutanol become the predominant mode of photochemical rearrangement.

Experimental Section

Materials and Equipment. All VPC was carried out using a Varian Aerograph Model A-90-P3 with one of the following columns: A, 30% Carbowax 20M, 10 ft × 0.375 in.; B, 15% XF-1150, 5 ft × 0.25 in.; C, 20% DEGS, 5 ft × 0.25 in.; D, 25% DEGS, 20 ft × 0.25 in.; E, 10% Carbowax 20M, 5 ft × 0.25 in.; F, 25% QF-1, 15 ft × 0.375 in.; G, 25% QF-1, 10 ft × 0.25 in.; H, 25% QF-1, 50 ft × 0.25 in. Column B was prepared using 60–80 Chromosorb W in stainless steel tubing; all other columns employed 45–60 Chromosorb W in aluminum tubing. The column oven was operated at 68–205°, and the helium carrier gas flow rate was 100–200 ml/min. Tetrahydrofuran (THF) and dioxane were distilled from $LiAlH_4$; hexamethylphosphoramide (HMPA) was distilled from CaH_2. These solvents and reagent grade pyridine were stored over molecular sieves. Unless otherwise noted, ir and NMR spectra were obtained for CCl_4 solutions, the former on a Perkin-Elmer Model 237B spectrophotometer and the latter on a Varian T-60A (60 MHz) or HR-220 (220 MHz) spectrometer. Solutions were dried over anhydrous $MgSO_4$; melting points are corrected. Unless otherwise noted, all solvents were removed in vacuo with a rotary evaporator. Unless otherwise noted, all products were obtained as colorless oils.

Photolysis of Cyclododecanone. A solution of cyclododecanone (3 g) in cyclohexane (65 ml) in a toroidal vessel was irradiated with a Hanovia 450-W medium-pressure mercury lamp in a quartz immersion well using a Pyrex filter for 5 days. The solution was flushed with dry nitrogen for 20 min prior to irradiation and kept under nitrogen during photolysis. The solvent was removed, and the resulting oil was analyzed by VPC on column A to yield two major products in a ratio of 1:5, as previously reported.[4] The first and minor of these was an oil, *trans*-bicyclo[8.2.0]dodecan-1-ol (**6**): ir 3590 (m), 3450 (w), 2920 (s), 2845 (m), 1475 (m), 1440 (m), and 910 cm^{-1} (m); NMR (220 MHz) δ 2.55–2.29 (m, 1 H), 1.97–1.04 (m, 21 H).

Anal. Calcd for $C_{12}H_{22}O$: C, 78.83; H, 12.19. Found: C, 79.06; H, 12.16.

The second major peak was a solid, mp 45.8–47.8° (lit.[4] 47–49°), *cis*-bicyclo[8.2.0]dodecan-1-ol (**5**), and had ir and NMR (60 MHz) spectra that compared favorably with the published data.

A similar photolysis of a 0.1 *M* solution of cyclododecanone in benzene quenched with 2.0 *M* 1,3-pentadiene afforded only the cis isomer **5**, as shown by VPC on column A.

1-Methoxy-*cis*-bicyclo[8.2.0]dodecane (9). This compound was prepared by treatment of cis alcohol **5** (264 mg, 1.45 mmol) with sodium hydride (75 mg of a 53% mineral oil dispersion, 1.66 mmol) and methyl iodide (237 mg, 1.67 mmol) in dimethyl sulfoxide. Work-up followed by bulb-to-bulb distillation afforded 192 mg of a clear oil, approximately 40% of which was the desired ether. Further purification was accomplished by VPC on column A, and the major peak was collected to yield **9**: ir 3005 (m), 2950 (s), 2875 (s), 2845 (m), 1470 (m), 1435 (m), 1265 (w), 1180 (w), 1090 (m), and 1070 cm^{-1} (m); NMR (220 MHz) δ 3.02 (s, 3 H), 2.39–2.22 (br, 1 H), 1.95–1.15 (m, 20 H).

Anal. Calcd for $C_{13}H_{24}O$: C, 79.53; H, 12.32. Found: C, 79.55; H, 12.41.

1-Methoxy-*trans*-bicyclo[8.2.0]dodecane (10). This ether was

prepared according to the method of Brown et al.[5] using trans alcohol **6** (157 mg, 0.86 mmol) with dimethyl sulfate as the methylating agent.

The crude reaction product (162 mg) after work-up was purified on column A to yield **10:** ir 2960 (m), 2920 (s), 2850 (m), 2805 (m), 1470 (m), 1440 (m), and 1065 cm^{-1} (m); NMR (220 MHz) δ 3.07 (s, 3 H), 2.51–2.32 (m, 1 H), 2.12–1.78 (m, 5 H), 1.67–1.21 (m, 14 H), 1.21–1.02 (m, 1 H).

Anal. Calcd for $C_{13}H_{24}O$: C, 79.53; H, 12.32. Found: C, 79.38; H, 12.38.

2-Methylenecyclododecanone (3). A mixture of cyclododecanone (18.2 g, 0.10 mol), diethylamine hydrochloride (10.96 g, 0.10 mol), paraformaldehyde (3.0 g, 0.10 mmol), and absolute ethanol (4 ml) was heated to reflux on a steam bath. After 1 hr, an additional 3.0 g (0.10 mol) of paraformaldehyde was added, and the resulting mixture was similarly heated overnight. The solution was then acidified with 10% HCl and diluted with water. The mixture was extracted with ether, and the organic phase was washed with brine. After drying, the ether was removed to yield a yellow oil. This oil was distilled under high vacuum to yield 4.46 g (23% yield) of clear oil. In general, this material was pure enough for preparative photolyses. For the quenching and sensitization experiments, the oil was purified by VPC on column A to give crystalline 2-methylenecyclododecanone (**3**) identical with material from an alternative synthesis.[10]

Hydrogenation of 2-Methylenecyclododecanone (3). A solution of **3** (188 mg) in methanol containing ~10 mg of 5% Pd/C was hydrogenated at atmospheric pressure for 2 hr. The catalyst was removed by suction filtration, and the solvent was removed. The resulting oil was purified by VPC on column B to yield 97 mg of 2-methylcyclododecanone (**19**):[19] ir 2920 (s), 2855 (m), 1710 (s), 1460 (m), 1440 (m), 1375 (w), and 1110 cm^{-1} (m); NMR (220 MHz) δ 2.70–2.50 (m, 2 H), 2.22 (ddd, J = 16, 8, 4 Hz, 1 H), 1.75–1.42 (m, 5 H), 1.40–1.04 (br s, 13 H), 1.01 (d, J = 7 Hz, 3 H).

12-Methylene-*cis*-bicyclo[8.2.0]dodecan-1-ol (11). This compound was prepared photochemically from **3** using a Rayonet RPR-100 reactor equipped with 16 RPR-3000 Å lamps. Work-up gave **11** (87%) identical with that previously reported.[1]

1-Methoxy-12-methylene-*cis*-bicyclo[8.2.0]dodecane (7). This ether was prepared from **11** (1.24 g, 6.4 mmol) as described above for **10.** The crude reaction product after work-up was purified by column chromatography on neutral alumina (activity III); pentane was used to elute the desired product and minor contaminents (177 mg, 13% yield). Elution with increasing concentrations of diethyl ether afforded the starting material, which could be recycled. Further purification was accomplished by VPC on column D, and the major peak was collected to yield **7:** ir 3105 (w), 2955 (s), 2880 (m), 2845 (w), 1665 (w), 1470 (m), 1435 (w), 1080 (m), and 875 cm^{-1} (m); NMR (220 MHz) δ 4.85–4.79 (m, 2 H), 3.14 (s, 3 H), 2.69–2.54 (m, 1 H), 2.50–2.35 (m, 1 H), 2.02–1.87 (m, 1 H), 1.78–1.14 (m, 16 H).

Anal. Calcd for $C_{14}H_{24}O$: C, 80.71; H, 11.61. Found: C, 80.84; H, 11.79.

10-Methoxy-*cis*-bicyclo[8.2.0]dodecan-11-one (8). A solution of **7** (135 mg, 0.65 mmol) in pyridine (10 ml) was added to a cooled solution of osmium tetroxide (177 mg, 0.70 mmol) in pyridine (1.5 ml) and washed in with an additional 2 × 0.5 ml of pyridine. The reaction mixture was stirred at room temperature for 7 hr. A solution of $NaHSO_4$ (306 mg) in water (3.65 ml) and pyridine (1.7 ml) was added and the reaction mixture was stirred for 1 hr. The mixture was extracted with chloroform; the extract was washed with dilute HCl to remove pyridine, saturated $NaHCO_3$, water, and brine. After removal of solvent, 188.5 mg of yellow oil was obtained: ir 3485 (br, w); transparent at 875 cm^{-1}.

Solid sodium metaperiodate (167 mg, 0.78 mmol) was added to a suspension of the crude diol in dioxane (6 ml) and water (2 ml) and was stirred at room temperature overnight. The mixture was poured into water and extracted with ether. The ether extracts were washed with saturated $NaHCO_3$, water, and brine. Removal of the solvent gave 124 mg of a yellow oil which was purified by VPC on column E to yield **8:** ir 2920 (s), 2845 (m), 1775 (s), 1475 (m), 1445 (m), 1385 (w), 1110 (m), and 1045 (m) cm^{-1}; NMR (220 MHz) δ 3.29 (s, 3 H), 3.07–2.88 (m, 1 H), 2.51–2.30 (m, 2 H), 1.92–0.72 (m, 16 H).

Anal. Calcd for $C_{13}H_{22}O_2$: C, 74.24; H, 10.54. Found: C, 74.28; H, 10.76.

Wolff–Kishner Reduction of 8. A mixture of **8** (100 mg, 0.475 mmol), hydrazine (1.6 ml of a 97% solution, 47.5 mmol), and a solution of ethylene glycolate derived from 3 ml of dry ethylene glycol and sodium hydride (109 mg, 4.75 mmol) was heated in an evacuated sealed tube overnight. The reaction product was poured into water and extracted with pentane. The organic extracts were washed with water and brine. After drying, the solvent was removed through a Vigreux column to yield a clear oil. VPC on column D yielded 11.9 mg of clear oil whose 220-MHz NMR and ir spectra and VPC retention time were identical with those of the authentic material **9.**

Quenching and Sensitization Experiments. Solutions of 0.013 M 2-methylenecyclododecanone in benzene containing 0.1–4.0 M of a mixture of *cis*- and *trans*-1,3-pentadiene were irradiated in Pyrex tubes in a Rayonet RPR-100 reactor equipped with 3500 Å lamps for 24 hr. The solutions were degassed with nitrogen for 10 min prior to irradiation. The extent of conversion of **3** to **11**, as assessed by VPC on column G, was 47%; the same value was obtained for a simultaneously irradiated ("merry-go-round" apparatus) sample containing no 1,3-pentadiene.

Attempts to form **11** in the presence of a triplet sensitizer were unsuccessful. Solutions of **3** (0.019 M) in benzene containing 3.7 or 8.9 molar equiv of propiophenone were irradiated as above in a RPR-204 reactor for 21 hr. The final ratios of **11** to **3**, as assessed by VPC on column G, were 0.097:1 and 0.072:1, respectively, as compared to 0.23:1 for a simultaneously irradiated control solution.

Irradiation of a 0.019 M solution of **3** in cyclohexane containing 0.051 M *cis*-1,3-pentadiene as above for 3 hr produced as much *trans*-1,3-pentadiene (<5%) as a simultaneously irradiated 0.051 M *cis*-1,3-pentadiene solution (assessed by VPC on column H). Formation of **11** was not suppressed (~3.5% yield), as observed with the mixture of *cis*- and *trans*-pentadienes. A similar experiment containing 0.05 M ketone **3** and 0.91 M *cis*-1,3-pentadiene gave equivalent results.

***trans*-2-Methylcyclododec-4-enone (15).** In a dry flask under nitrogen, THF (2 ml) and HMPA (2 ml) were added to sodium hydride (9 mg, 0.375 mmol). To this was added a solution of **11** (30 mg, 0.155 mmol) in THF (0.5 ml). The reaction mixture was heated overnight at 45–50°. The excess NaH was carefully destroyed with methanol and water. This solution was extracted with ether. The organic extracts were washed with 1% HCl, water, and brine. After drying, the solvent was removed to yield 12 mg of yellow oil. Purification by VPC on column D yielded *trans*-2-methylcyclododec-4-enone (**15**): ir 3015 (w), 2920 (s), 2850 (m), 1715 (s), 1455 (m), 1430 (m), 1410 (w), 970 (m), and 710 cm^{-1} (w); NMR (220 MHz) δ 5.42–5.32 (m, 2 H), 2.68–2.50 (m, 1 H), 2.50–2.30 (m, 1 H), 2.30–1.53 (m, 6 H), 1.53–0.91 (m, 9 H), 0.97 (d, J = 7 Hz, 3 H); mass spectrum m/e 194.1663 (M^+, calcd for $C_{13}H_{22}O$, 194.1670).

Similar results were obtained when *tert*-butyl alcohol or dimethyl sulfate was present in the reaction mixture. In the latter case, there was also evidence by VPC for the presence of **7.**

Hydrogenation of **15** (53 mg) as described above for **3** yielded, after VPC on column B, a material whose 220-MHz NMR and ir spectra were identical with those of 2-methylcyclododecanone (**19**) as prepared above.

Pyrolysis of 12-Methylene-*cis*-bicyclo[8.2.0]dodecan-1-ol (11). A 606-mg sample of **11** was heated in a sealed evacuated tube in a Wood's metal bath at 245° for 4 hr. Bulb-to-bulb distillation of the resulting semisolid under high vacuum yielded 255 mg of clear oil. Analysis by VPC on column F indicated the presence of two significant products. The first-eluted product was collected and was found to have ir and 220-MHz NMR spectra identical with those of **15.**

The second eluted major product was similarly purified and collected to yield bicyclo[9.1.1]tridecan-2-one (**14**): ir 2920 (s), 2850 (m), 1700 (s), 1465 (m), 1440 (m), and 1350 cm^{-1} (m); NMR (220 MHz) δ 2.94–2.69 (m, 1 H), 2.50–2.26 (m, 3 H), 2.26–2.05 (m, 3 H), 1.86–1.69 (m, 3 H), 1.48–1.14 (m, 12 H); mass spectrum m/e 194.1668 (M^+, calcd for $C_{13}H_{22}O$, 194.1670).

A sample of **14** was equilibrated in 0.5 ml of 2 M methanolic KOH at room temperature for 3 hr. Extractive work-up with pentane yielded a yellow residue whose 220-MHz NMR spectrum was identical with that of the VPC-collected material above.

Conversion of 14 to Methyl 9-(3-oxocyclobutane)nonanoate (22). A pertrifluoroacetic acid solution was prepared[20] using trifluoroacetic anhydride (0.2 ml, 1.44 mmol) and 75% H_2O_2 (27 μl, 0.788 mmol) in methylene chloride (1.0 ml). The peracid solution was added to an ice-cooled, magnetically stirred suspension of bicyclo[9.1.1]tridecan-2-one (**14,** 100 mg, 0.52 mmol) and sodium dihydrogen phosphate (292 mg) in methylene chloride (1.5 ml) with the aid of an additional 0.5 ml of methylene chloride. The reaction mixture was heated to gentle reflux (50°C) for 3.5 hr. At the end of this time, more CH_2Cl_2 was added and the reaction mixture was

washed with water, 10% Na_2CO_3, water, and brine. After drying, the solvent was removed to yield 107 mg of a pale yellow oil (**20**) whose ir spectrum indicated the absence of starting material: ir 2940 (s), 2865 (s), 1780 (m), 1730 (s), 1455 (m), 1250 (s), 1220 (s), 1165 (s), 1140 (s), and 1015 cm^{-1} (m).

Without further purification, the crude lactone mixture **20** was hydrolyzed with 5% methanolic KOH (10 ml) and water (1 ml) for 1 day. The reaction mixture was diluted with water and extracted with ether to remove neutral materials. The aqueous phase was acidified and extracted with ether. The organic extracts were dried, and solvent was removed to yield 104 mg of a white solid, mp 80–82.5°, **21**: ir (KBr) 3470 (m), 1690 cm^{-1} (s). A portion of the crude **21** (86 mg, 0.38 mmol) was esterified with diazomethane to yield 106 mg of an oil which was used without further purification: ir 3585 (m), 3410 (br), 1740 cm^{-1} (s). This hydroxy ester was oxidized with CrO_3–pyridine according to the procedure of Ratcliff and Rodehorst[21] to yield 62 mg of oil, which was purified by VPC on column C to yield **22**: ir 2920 (s), 2845 (s), 1785 (s), 1745 (s), 1460 (m), 1435 (m), 1385 (m), 1360 (m), 1245 (m), 1195 (m), 1170 (m), 1110 (m), and 1085 cm^{-1} (m); NMR (220 MHz) δ 3.61 (s, 3 H), 3.15–2.97 (m, 2 H), 2.67–2.49 (m, 2 H), 2.36–2.21 (m, 1 H), 2.22 (t, J = 6 Hz, 2 H), 1.69–1.47 (m, 4 H), 1.39–1.21 (s, 10 H).

Anal. Calcd for $C_{14}H_{24}O_3$: C, 69.96; H, 10.07. Found: C, 69.94; H, 9.89.

Registry No.—**3**, 3045-76-9; **5**, 35522-56-6; **6**, 35522-60-2; **7**, 56468-02-1; **8**, 56468-03-2; **9**, 56468-04-3; **10**, 56498-05-6; **11**, 56498-06-7; **14**, 56468-05-4; **15**, 16837-94-8; **19**, 56468-06-5; **20**, 56468-07-6; **22**, 56468-08-7; cyclododecanone, 830-13-7.

References and Notes

(1) R. A. Cormier, W. L. Schreiber, and W. C. Agosta, *J. Am. Chem. Soc.*, **95**, 4873 (1973).
(2) R. A. Cormier and W. C. Agosta, *J. Am. Chem. Soc.*, **96**, 618 (1974).
(3) R. B. Woodward and R. Hoffmann, *Angew. Chem.*, **81**, 797 (1969); *Angew. Chem., Int. Ed. Engl.*, **8**, 781 (1969).
(4) K. Matsui, T. Mori, and H. Nozaki, *Bull. Chem. Soc. Jpn.*, **44**, 3440 (1971), and references cited therein.
(5) C. A. Brown and D. Barton, *Synthesis*, 434 (1974).
(6) R. Criegee, B. Marchand, and H. Wannowius, *Justus Liebigs Ann. Chem.*, **550**, 99 (1942); J. S. Baran, *J. Org. Chem.*, **25**, 257 (1960).
(7) R. Pappo, D. S. Allen, Jr., R. U. Lemieux, and W. S. Johnson, *J. Org. Chem.*, **21**, 478 (1956).
(8) The conditions employed for this small-scale reaction were those described by R. A. Cormier and W. C. Agosta, *J. Am. Chem. Soc.*, **96**, 1867 (1974).
(9) An important point in this regard is that we find that on irradiation in benzene neither **3** nor the previously investigated[2] α-methylene ketones cause isomerization of 0.05 *M cis*-piperylene [see G. S. Hammond, P. A. Leermakers, and N. J. Turro, *J. Am. Chem. Soc.*, **83**, 2396 (1961)]. This result is contrary to our earlier report.[2] Thus, while there is no quenching of these rearrangements even by 4 *M* diene, there is no evidence that any triplets are being quenched at all. These observations have no effect on the present demonstration that **3** behaves like other α-methylene ketones, and the available data still support the earlier conclusion[2] that these are singlet reactions.
(10) Examination of ir and NMR spectra of various α-methylene ketones has led to the conclusion that **3** exists largely in an s-trans conformation, which is that required for γ-hydrogen abstraction as depicted in **12**: M. Mühlstädt, L. Zach, and H. Becwar-Reinhardt, *J. Prakt. Chem.*, **29**, 158 (1965); M. Mühlstädt, H. J. Köhler, D. Porzig, and M. Scholz, *ibid.*, **312**, 292 (1970).
(11) L. M. Stephenson, P. R. Cavigli, and J. L. Parlett, *J. Am. Chem. Soc.*, **93**, 1984 (1971); C. P. Casey and R. A. Boggs, *ibid.*, **94**, 6457 (1972).
(12) P. J. Wagner, *Acc. Chem. Res.*, **4**, 168 (1971), and references cited therein.
(13) J. P. Barnier, J. M. Denis, J. Salaun, and J. M. Conia, *Tetrahedron*, **30**, 1405 (1974), and references cited therein.
(14) J. E. Baldwin and R. H. Fleming, *J. Am. Chem. Soc.*, **95**, 5261 (1973), and references cited therein.
(15) R. M. Roberts, R. M. Landolt, R. N. Greene, and E. W. Heyer, *J. Am. Chem. Soc.*, **89**, 1404 (1967), and references cited therein.
(16) In both cis and trans model ketones the cyclobutyl proton α to the carbonyl group appears as a clean, symmetrical signal at δ ~3.0 ppm. The spectrum of **14** shows this signal as a broader, unsymmetrical multiplet, which is virtually unchanged on treatment with base.
(17) T. Cuvigny and H. Normant, *Bull. Soc. Chim. Fr.*, 1872 (1965).
(18) A. L. J. Beckwith, I. A. Blair, and G. Phillipou, *Tetrahedron Lett.*, 2251 (1974).
(19) Spectroscopic properties of **19** were in agreement with those previously reported by J. Casanova and B. Waegell, *Bull. Soc. Chim. Fr.*, 1289 (1971).
(20) W. D. Emmons and G. B. Lucas, *J. Am. Chem. Soc.*, **77**, 2287 (1955).
(21) R. Ratcliff and R. Rodehorst, *J. Org. Chem.*, **35**, 4000 (1970).

Bicyclo[4.2.1]non-3-en-2-one. A Convenient Synthesis and Evidence for a Boat Conformation in the Seven-Membered Ring[1,2]

Donald W. Boerth and Frederic A. Van-Catledge*

Department of Chemistry, University of Minnesota, Minneapolis, Minnesota 55455

Received May 20, 1975

The cycloaddition reaction of 2-(*N,N*-dimethylamino)bicyclo[2.2.1]heptene, prepared from bicyclo[2.2.1]heptan-2-one and dimethylamine with stannic chloride, with ethyl propynoate in refluxing toluene produced ethyl 2-(*N,N*-dimethylamino)bicyclo[4.2.1]nona-2,4-diene-3-carboxylate. Acid hydrolysis of the amino carboxylate derivative produced bicyclo[4.2.1]non-3-en-2-one in 41% overall yield, based on bicyclo[2.2.1]heptan-2-one. The NMR data for the title compound are best understood in terms of a boat conformation in the seven-membered ring, in contrast to the evidence available for the parent hydrocarbon.

Synthetic routes into the bicyclo[4.2.1]nonane ring system are relatively few in number.[3-9] Many of these involve low-yield reactions and/or multistep sequences which are synthetically unattractive. We were particularly interested in developing an efficient route to bicyclo[4.2.1]non-3-en-2-one (**1**), an important intermediate in some of our work. Also, the four-carbon bridge of this ring system seems to us a potentially interesting scaffolding for stereochemical and mechanistic studies. The best example of the methods we wished to improve upon is the reported synthesis of the 3-bromo derivative of **1**.[8] Although the bicyclo[2.2.1]heptane system would seem to be a logical starting point for such a synthesis, there is only one report of its use in the synthesis of the [4.2.1]bicyclic system.[5] We wish to report our successful scheme, based on the commercially available bicyclo[2.2.1]heptan-2-one (2-norbornanone) (**2**).

It is well known that cycloaddition reactions of ethyl propynoate with the enamines of cyclic ketones lead ultimately to bishomologated ketones.[10,11] Thus, we sought to prepare the enamine derivative of **2**. Enamine preparation was at first problematical owing, presumably, to the strain associated with introduction of a double bond into the bicycloheptyl system.[12] The classical method[13] (pyrrolidine and *p*-toluenesulfonic acid) was not at all fruitful. We chose dimethylamine as the base and investigated the various catalysts previously employed. Anhydrous calcium chloride[14] gave only trace amounts of the desired product **3**. Stannic chloride,[15] on the other hand, proved to be most