Synthesis of Fused-Ring Cyclobutenones via a Tandem [2 + 2] Cycloaddition–β-Elimination Sequence

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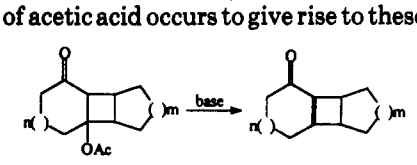
The usual course of the de Mayo reaction involves a base-catalyzed retro-aldol ring fragmentation of initially formed photoadduct **3** to produce medium-sized ring compound **4**. It is known that this sequence of events can be altered if the cyclobutane carbon adjacent to the resultant ketone carbonyl of the photoadduct is substituted with a hydrogen atom. Under the basic conditions of the second step, an elimination of the elements of acetic acid to produce cyclobutene derivatives **17** and **18** occurs. The detailed stereochemistry of photoadduct **12**, resistant to this elimination, was determined by X-ray crystallography, and further examples of the elimination chemistry are presented to ascertain the scope and limitations of this reaction. The tandem [2 + 2] cycloaddition–β-elimination sequence provides a straightforward and facile synthesis of cyclobutenone derivatives.

From its inception, the de Mayo reaction[1] (see Scheme I) has found great utility in the synthesis of natural products.[2] This utility stems from the ease with which a variety of medium-sized ring systems can be assembled. An example of this power is found in several approaches to the synthesis of taxol that have been published.[3]

The normal course of events in a de Mayo reaction is depicted in Scheme I. A photochemical [2 + 2] cycloaddition of a β-acetoxy-α,β-unsaturated ketone **1** with an olefin **2** gives rise to a cyclobutanol derivative **3**. Exposure of **3**, in a subsequent step, to base produces the ring-expanded product **4**. This occurs via saponification of the acetate ester. The resultant alkoxide **5** undergoes a retro-aldol reaction to afford enolate **6** which upon workup gives the observed product **4**.

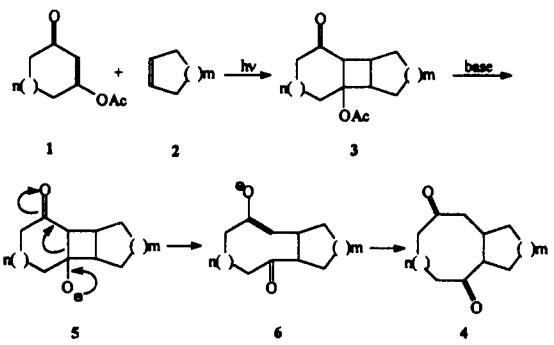
During the course of our investigations of the de Mayo reaction, we observed that the second step of this sequence can, in specific instances, be diverted. Instead of the usual saponification–retro-aldol sequence upon treatment with base, we isolated cyclobutene derivatives, such as **7**, from these reactions. Presumably, a β-elimination of the elements of acetic acid occurs to give rise to these products.



3 7 = 56q

A review of the literature revealed a limited number of examples of this reaction manifold. Despite all the chemistry published on the de Mayo reaction,[1] we are aware of only five reports describing this transformation.[4] Initial studies were independently published by de Mayo[4a] and Cantrell[4b] in 1969. Later, Eaton[4c] used this elimination in the synthesis of propellanes, while more recently[4d,e] this reaction has been observed in attmpted de Mayo reactions to afford medium-sized rings. In an effort to see if this elimination reaction is a general phenomenon, we decided to investigate this process further. In addition, this reaction could provide a viable alternative for the synthesis of cyclobutenones.[5] The following describes our preliminary findings on this chemistry.

Scheme I



1 2 3 5 6 4

Results and Discussion

While in the initial stages of our efforts in the development of new methodology, we became interested in the de Mayo reaction of enone **8** with olefin **9**. The products from this reaction were not the expected cyclooctane

(1) (a) de Mayo, P.; takeshita, H.; Satter, A. B. M. A. *Proc. Chem. Soc. London* **1962**, 119. (b) de Mayo, P.; Takeshita, H. *Can. J. Chem.* **1963**, *41*, 440. (c) de Mayo, P. *Acc. Chem. Res.* **1971**, *4*, 41.

(2) For reviews and leading references see: (a) Bauslaugh, P. G. *Synthesis* **1970**, 287. (b) Oppolzer, W. *Acc. Chem. Res.* **1982**, *15*, 135. (c) Becker, D.; Haddad, N. *Org. Photochem.* **1989**, *10*, 1.

(3) (a) Neh, H.; Blechert, S.; Schnick, W.; Jansen, M. *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 905. (b) Swindell, C. S.; de Solms, S. J.; Springer, J. P. *Tetrahedron Lett.* **1984**, *25*, 3797, 3801; **1985**, *26*, 289. (c) Kojima, T.; Inouye, Y.; Kakisawa, H. *Chem. Lett.* **1985**, 323. (d) Berkowitz, W. F.; Perumattam, J.; Amarasekara, A. S. *Tetrahedron Lett.* **1985**, *26*, 3665. (e) Berkowitz, W. F.; Amarasekara, A. S. *Tetrahedron Lett.* **1985**, *26*, 3663. (f) Cervantes, H.; Khac, D. D.; Fetizon, M.; Guir, F.; Deloeil, J.-C.; Lallemand, J.-Y.; Prange, T. *Tetrahedron* **1986**, *42*, 3491. (g) Swindell, C. S.; Britscher, S. F. *J. Org. Chem.* **1986**, *51*, 793. (h) Berkowitz, W. F.; Amarasekara, A. S. Perumattam, J. J. *J. Org. Chem.* **1987**, *52*, 1119. (i) Benchick-le-Hocine, H.; Khac, D. D.; Fetizon, M. *Synth. Commun.* **1987**, *17*, 913.

(4) (a) Challand, B. D.; Hikino, H.; Kornis, G.; Lange, G.; de Mayo, P. *J. Org. Chem.* **1969**, *34*, 794. (b) Cantrell, T. S.; Haller, W. S.; Williams, J. C. *J. Org. Chem.* **1969**, *34*, 509. (c) Eaton, P. E.; Nyi, N. *J. Am. Chem. Soc.* **1971**, *93*, 2786. (d) Umehara, M.; Oda, T.; Ikebee, Y.; Hishida, S. *Bull. Chem. Soc. Jpn.* **1976**, *49*, 1075. (e) Benchikh-le-Hocine, M.; Khac, D. D.; Cervantes, H.; Fetizon, M. *New J. Chem.* **1986**, *10*, 715.

(5) For representative preparation and use of cyclobutenones see: (a) Manicagli, R.; Malanga, C.; Lardicci, L. *J. Org. Chem.* **1982**, *47*, 2288. (b) Danheiser, R. L.; Gee, S. K.; Sard, H. *J. Am. Chem. Soc.* **1982**, *104*, 7670. (c) Danheiser, R. L.; Gee; S. K. *J. Org. Chem.* **1984**, *49*, 1672. (d) Schmit, C.; Sahroui-Taleb, S.; Dirrerding, E.; Dehasse-De Lombaert, C. G.; Ghosez, L. *Tetrahedron Lett.* **1984**, *25*, 5043. (e) Danheiser, R. L.; Gee, S. K.; Perez, J. J. *J. Am. Chem. Soc.* **1986**, *108*, 806. (f) Danheiser, R. L.; Savariar, S. *Tetrahedron Lett.* **1987**, *28*, 3299.

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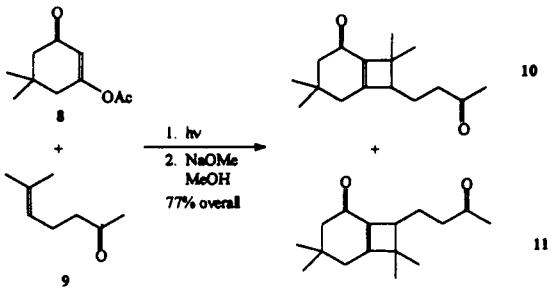
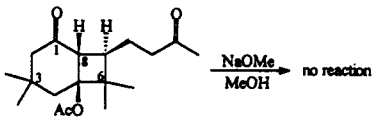
derivatives but cyclobutene compounds 10 and 11. The



photochemical step had proceeded as expected; however, the basic conditions had not effected the saponification–retro–aldol reaction sequence. Instead, an elimination of acetic acid was the preferred reaction pathway which had occurred in good overall yield (77%). In fact, the yield of the elimination step was excellent. The mixture of **10** and **11** (1:1.2, respectively) reflects the rgiochemical outcome of the photochemical step. It is interesting to note that one of the intermediate photoadducts, **12**, was resistant



12

to the reaction with base and was recovered unchanged. Recrystallization of this compound afforded crystals suitable for X-ray analysis, and an ORTEP plot for the structure of **12** is shown in Figure 1. The molecular dimensions for **12** are in accord with anticipated values and serve to establish the structure and its stereochemistry unequivocally. The six-membered ring has a distorted chair conformation (with C1 −0.375(3) Å and C4 0.555(3) Å from the best plane through atoms C2, C3, C5, C8); the cyclobutane ring is puckered (with a fold angle about the C5···C7 axis of 33.2(2)° and ring torsion angles −23.6, −23.7, 23.3, and 23.6°). The substituents on the cyclobutane ring (H, acetoxy, and the oxobutyl side chain) are all syn to each other. In this isomer the torsion angle O(1)–C(1)–C(8)–H for the cyclohexylcarbonyl and the adjacent hydrogen on C8 of the cyclobutane ring is 21.6(11)°. This is clearly far from the ideal 90° value required for deprotonation based on stereoelectronic effects. Furthermore, the two sets of geminal-dimethyl groups (at C6 and C3) flank the acetate moiety providing steric hinderance toward nucleophilic attack of the ester carbonyl. Therefore, this isomer remains untouched by the base as a result of these effects acting in synergy.

Since the observed elimination reaction proceeded readily, we decided to investigate the scope and limitations of this chemistry. Our goal was to determine if this elimination reaction was a general phenomenon which could be used as a preparative method for the generation of fused-ring cyclobutenones.

A systematic study was begun by using the enol acetates of 1,3-cyclohexadione **13** and dimedone **8** with a series of cyclic olefins **14**. Irradiation of a solution of **13** or **8** with **14** produced the corresponding photoadducts **15** and **16** as a mixture of isomers. Where possible, this mixture was separated by chromatography and the stereochemistries of the resultant photoadducts were determined.

The photocycloaddition of **8** and **14a** to produce **16a** has previously been carried out,[4d] and our stereochemical

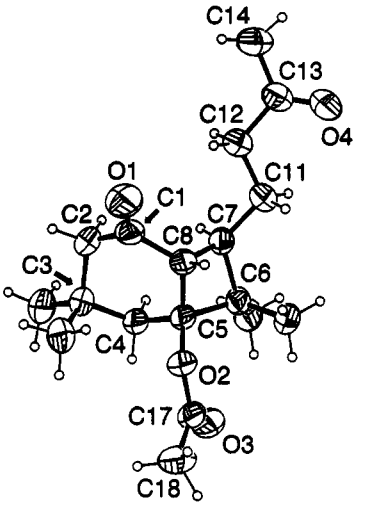
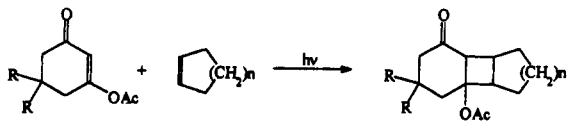


Figure 1. ORTEP plot of compound **12** as determined by X-ray crystallography. The atom numbering is arbitrary.

assignments began with this compound. Comparison of our high-field (400-MHz) ^{1}H NMR spectra with those published for **16a** reconfirm the original assignments of



13 R=H
8 R=Me

14 a n=1
b n=2
c n=4

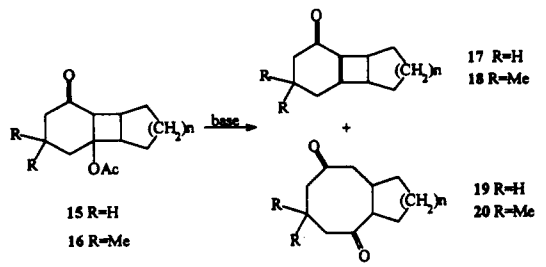
15 R=H
16 R=Me

the cis and trans isomers of the 6–4 ring fusion. Furthermore, ^{13}C NMR spectroscopy provided a simple method for determining this stereochemistry. For the compound with a cis 6–4 ring fusion, the chemical shift for the acetate carbinol carbon was observed to be approximately 80 ppm, while in the trans isomer this resonance shifted downfield to approximately 90 ppm. A similar observation was made in the case of compound **12**. Here, the crystal structure unequivocally indicates cis ring fusion, and the ^{13}C chemical shift for this carbon was 83.70 ppm. Presumably, this shift is due to the additional ring strain found in the trans isomer compared to the cis isomer. A mixture of cis and trans isomers for the 6–4 ring fusion was also observed from compounds **15a**, **15b**, and **16b** (this compound was originally synthesized by de Mayo,[4a] however, no mention of stereochemistry was reported). In addition, ^{13}C NMR could be used to quickly distinguish between these two isomers. The 4–5 and 4–6 ring fusions for these compounds were determined to be cis by NMR and chemical transformations (vide infra); thus, the photochemistry produced two diastereomers: cis-anti-cis and trans-anti-cis.

In compounds **15c** and **16c**, the 6–4 ring fusion also exhibited this same mixture of cis and trans as determined by ^{13}C NMR; however, the 4–8 ring fusion was now also a mixture of cis and trans (vide infra). Here, the greater flexibility inherent in the 8-membered ring must be allowing the diradical intermediate in the photochemistry to close in both orientations, thus producing the cis and trans ring fusions.

With the photoadducts in hand, we proceeded to investigate the elimination reaction. Treatment of **15** or **16** with base resulted in elimination of acetic acid to afford the cyclobutene derivatives **17** or **18** and not the ring-

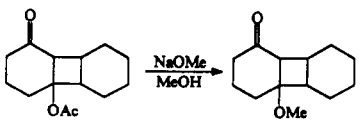
expanded compounds **19** or **20** (with one exception).



Although **18b** was the major product from the reaction of **16b**, **20b** could also be isolated as a minor product in some reactions. These results indicate that, in the presence of base, the preferred reaction pathway is to generate the more strained cyclobutene derivative rather than produce the cyclooctadione derivative and release ring strain. The acetate of the photoadducts is an ester of a tertiary alcohol; therefore, the carbonyl is sterically hindered toward nucleophilic attack. Since a saponification reaction is required for the de Mayo reaction to proceed, this step is retarded. The only other option afforded the base by the molecule is an elimination reaction which produces a more strained system. A quick survey of the literature[2] shows that a majority of the published cases of the de Mayo reaction have been designed so that the carbon atom of the cyclobutyl ring adjacent to the carbonyl of the ketone is quaternary in nature. This would prevent the elimination reaction from occurring, thereby allowing for only the retro-aldol reaction to proceed.

From the reactions that generated compounds **17a**, **17b**, **18a** and **18b**, only one product was isolated, the cis ring-fused isomer. However for **15c** and **16c**, the formation of **17c** and **18c** afforded an inseprable mixture of two products, the cis and trans ring-fused compounds as detected by NMR. Furthermore, it was found that **20b**, upon prolonged exposure to base, epimerized to the trans fused isomer reconfirming the initial cis assignment. Since both isomers, cis and trans, of the acetate produced the olefin, an E_1cb mechanism for the elimination is presumably in operation. This is in agreement with the observations in the reaction to form **10** and **11**.

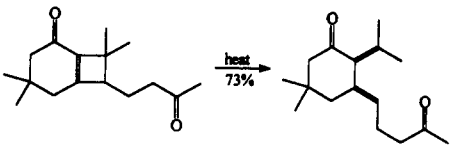
The nature of the base plays an important role in this elimination reaction. Using such bases as LiOH, NaOH, KOH, or K_2CO_3 in MeOH or EtOH and LDA resulted only in recovery or destruction of starting material. Shifting to stronger alkoxide bases afforded the desired cyclobutene compounds; however, an interesting side reaction now became obvious. While the elimination reaction for the dimedone series of compounds could be carried out with NaOMe–MeOH at 0 °C, these conditions for the series of compounds derived from **13** did not produce, for example, enone **17b** but methyl ether **21**, which



15b **21**

also had been observed by de Mayo.[4a] Apparently enone **17b** is labile under these conditions and in the presence of either methanol or methoxide undergoes a Michael addition. This Michael addition presumably is less of a problem in the dimedone series since the axial methyl of the *gem*-dimethyl moiety provides steric hinderance toward nucleophilic attack at the β-carbon. We have found that the use of NaH–tBuOH in THF circumvents this problem; however, we are still searching for a better base that balances basicity with nucleophilicity or steric hinderance.

Since compound **10** is a cyclobutene derivative, we thought it would be able to undergo an electrocyclic ring opening to a butadiene derivative. This would not only reconfirm the structure of these products but would point out one attribute of their synthetic versatility. To this

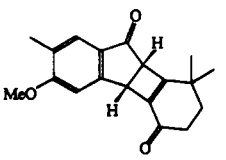


10 **22**

end, compound **10** was subjected to thermolytic conditions. Refluxing in isooctane for 24h effected cycloreversion to diene **22**. The depicted olefin geometry is assumed based on steric arguments. The ease with which this reaction took place should make these compounds very useful in synthetic strategies.

Conclusions

We have shown that the elimination of acetic acid from the photoadducts of β-acetoxy enones with a variety of olefins is a general reaction. Treatment with relatively strong base does not lead to the retro-aldol ring opening but to fused-ring cyclobutenones in a facile and efficient manner. The cyclobutene compounds thus produced have the ability to be used as synthetic intermediates. For example, compound **10** underwent a ring-opening reaction to butadiene derivative **22** upon thermolysis, which could be used in a Diels–Alder reaction. We are presently examining other thermal and photochemical methods for carrying out this transformation and will report those results in due course. Also, the synthesis of cyclobutene containing natural products such as neofavelanone[6] **23** is being pursued using this methodology.



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Experimental Section

General Procedures and Materials. Melting points were taken on a Fischer-Johns melting point apparatus and are uncorrected. ^1H and ^{13}C NMR spectra were recorded in $CDCl_3$ at 400 and 100 MHz, respectively, unless specified otherwise.

All solvents used for chromatography were distilled prior to use. Reactions were monitored by TLC using E. Merck precoated silica gel 60 F-250 (0.25-mm thickness) aluminum-backed plates. The plates were visualized by immersion in *p*-anisaldehyde solution and warming on a hotplate. E. Merck silica gel 60 (70–230 mesh) was used for column chromatography, and radial chromatography was performed on a Chromatotron Model 8924. All solvents were reagent grade, and anhydrous solvents were dried prior to use as follows: CH_2Cl_2 was distilled from CaH_2; ether, THF, and benzene were distilled from benzophenone ketyl.

(6) Endo, Y.; Ohta, T.; Nozoe, S. *Tetrahedron Lett.* **1992**, *33*, 353.

Compounds obtained from commercial sources were used directly as received. Although compounds **16a**,[4d] **16b**,[4a] **18a**,[4d] and **18b**[4a] are known compounds, we are reporting alternate experimental procedures that have improved yields, as well as high-field ^1H and ^{13}C NMR spectral data.

Representative Procedure for Photocycloaddition Reactions. A solution of enol acetate **8** (11.0 mmol) or **13** (13.0 mmol) and olefin **14** (110 mmol or 130 mmol, respectively) in 20 mL of CH_2Cl_2 was degassed with argon for 5 min. The mixture was irradiated with a Hanovia 450-W medium-pressure mercury arc lamp through pyrex at 0 °C until the reaction was judged complete by TLC. The solvent and excess olefin were removed in vacuo, and the crude product purified by column chromatography (300 g of silica gel; ethyl acetate:hexanes = 1:9). Analytical samples were obtained by recrystallization from the indicated solvents.

Representative Procedures for Base-Induced Elimination Reactions. Method A (*tert*-Butoxide). To a solution of acetate **15** (0.3 to 0.8 mmol) in 5 mL of THF at 0 °C was added *tert*-butyl alcohol (0.45–1.2 mmol) and NaH (0.36–0.96 mmol). The reaction mixture was warmed to rt and stirred for 24 h before being poured into water and extracted with CH_2Cl_2 (5×), and the combined extracts (Na_2SO_4) were dried. After filtration and removal of the solvent in vacuo, the crude product was purified by radial chromatography (1-mm plate, ethyl acetate:hexanes=1:9).

Method B (Methoxide). To a solution of the photoadducts (4.0 mmol) in 25 mL of MeOH was added sodium methoxide (20 mmol). The solution was stirred at 0 °C for 2 h before being poured into water and extracted with CH_2Cl_2 (4×), and the combined extracts (Na_2SO_4) were dried. After filtration and removal of the solvent in vacuo, the crude products were purified by chromatography (160g silical gel, ethyl acetate:hexanes = 1:9).

Attempted de Mayo Reaction of 8 and 9. Irradiation of **8** (2.0 g, 11.0 mmol) and **9** (13.8 g, 110 mmol) in 36 mL of CH_2Cl_2 according to the general procedure for 32 h provided, after chromatography, recovered **8** (0.53 g) and the photoadducts (2.11 g) in 85% yield (based on recovered **8**). The photoadducts were inseparable by chromatography (IR(CCl_3) 2951, 2926, 2873, 1732, 1720, 1708 cm^{-1}), and the mixture was carried on to the next step.

Reaction of the photoadducts (1.13 g, 3.7 mmol) with sodium methoxide (0.99 g, 18.5 mmol) according to method B afforded recovered **12** (0.30 g), **10** (0.27 g) in 40% yield (based on recovered **12**), and **11** (0.34 g) in 51% yield (based on recovered **12**).

4,4,8,8-Tetramethyl-7-(3-oxobutyl)bicyclo[4.2.0]oct-$\Delta^{1,6}$-en-2-one (10): IR (CCl_4) 1719, 1675, 1235, 1162, 1037 cm^{-1}; ^1H NMR δ 2.48 (m, 3 H), 2.17 (m, 2 H), 2.16 (s 3 H), 2.10 (ABq, 2 H, J_{AB} = 18.4, $\Delta\nu_{AB}$ = 29.9 Hz), 1.76 (m, 2 H), 1.28 (s, 3 H), 1.19 (s, 3 H), 1.04 (s, 3 H), 1.03 (s, 3 H); ^{13}C NMR δ 207.85, 194.05, 168.68, 146.12, 55.43, 52.25, 45.59, 42.28, 38.52, 36.48, 29.85, 28.88, 28.53, 26.11, 21.93, 20.77; HRMS calcd for $C_{16}H_{24}O_2$ 248.1776, found 248.1776.

4,4,7,7-Tetramethyl-8-(3-oxobutyl)bicyclo[4.2.0]oct-$\Delta^{1,6}$-en-2-one (11): IR (CCl_4) 1717, 1674, 1365, 1242, 1181, 1153, 985 cm^{-1}; ^1H NMR δ 2.81 (ddd, 1 H, J = 18.0, 9.2, 4.8 Hz), 2.63 (m, 2 H), 2.20 (ABq, 2 H, J_{AB} = 16.0, $\Delta\nu_{AB}$ = 23.5 Hz), 2.16 (s, 3 H), 2.04 (AB portion of ABX, 2 H, J_{AB} = 18.4, J_{AX} = 2.0, J_{BX} = 2.4, $\Delta\nu_{AB}$ = 20.6 Hz), 1.82 (m, 1 H), 1.51 (m, 1 H), 1.19 (s, 3 H), 1.12 (s, 3 H), 1.06 (s, 3 H), 1.03 (s, 3 H); ^{13}C NMR δ 209.35, 195.07, 177.75, 139.41, 52.64, 51.66, 47.26, 42.61, 36.53, 35.78, 30.19, 29.02, 28.56, 24.64, 23.41, 19.56; HRMS calcd for $C_{16}H_{24}O_2$ 248.1776, found 248.1778.

Crystals of **12**, suitable for single-crystal X-ray analysis, were obtained by recrystallization from isooctane. Details of the crystal structure analysis (cell data, data collection, processing, and refinement) are concisely summarised in Table I (supplementary material). Full details are available from the authors or from the Cambridge Crystallographic Data Centre.[7]

1β-Acetoxy-3,3,8,8-tetramethyl-7β-(3-oxobutyl)bicyclo[4.2.0]octan-5-one (12): mp (isooctane) = 64–65 °C; IR (CCl_4) 1736, 1718, 1700, 1246, 1214, 1167, 1026, 965 cm^{-1}; ^1H NMR δ 2.61 (d, 1 H, J = 10.1 Hz), 2.45 (ddd, 1 H, J = 14.1, 8.6, 5.8 Hz), 2.30 (ddd, 1 H, J = 17.7, 8.4, 1.9 Hz), 2.19 (ABq, 2 H, J_{AB} = 15.0, $\Delta\nu_{AB}$ = 39.6 Hz), 2.14 (ABq, 2 H, J_{AB} = 15.6, $\Delta\nu_{AB}$ = 181.7 Hz), 2.08 (s, 3 H), 1.97 (s, 3 H), 1.76 (ddd, 1 H, J = 15.2, 9.6, 5.5 Hz), 1.70 (m, 1 H), 1.61 (m, 1 H), 1.20 (s, 3 H), 1.04 (s, 3 H), 0.98 (s, 3 H), 0.89 (s, 3 H); ^{13}C NMR δ 210.93, 208.18, 169.96, 83.70, 54.11, 52.00, 45.28, 42.58, 40.54, 38.11, 34.12, 31.72, 29.93, 26.52, 23.59, 23.17, 21.39, 17.49.

2-Acetoxytricyclo[6.3.0.0^{2,7}]undecan-6-one (15a). Irradiation of **13** (2.0 g) and **14a** (8.8 g) for 40 h provided, after chromatography, 1.22 g (42%) of **15a** as a mixture of isomers; cis:trans = 1.2:1. **Cis isomer**: mp (hexanes) = 47–48 °C; IR ($CHCl_3$) 1737, 1707, 1320, 1268, 1244, 1222, 1189, 1059, 1022 cm^{-1}; ^1H NMR δ 2.81 (t, 1 H, J = 7.2 Hz), 2.54 (t, 1 H, J = 7.2 Hz), 2.50 (t, 1 H, J = 6.0 Hz), 2.46 (m, 1 H), 2.34 (dt, 1 H, J = 18.0, 8.0 Hz), 2.11 (m, 1 H), 2.02 (s, 3 H), 1.97 (m, 3 H), 1.90–1.63 (m, 4 H), 1.62–1.51 (m, 2 H); ^{13}C NMR δ 210.51, 169.87, 78.53, 55.72, 47.74, 39.09, 38.11, 32.68, 32.60, 27.00, 25.41, 21.56, 18.79. Anal. Calcd for $C_{13}H_{18}O_3$: C, 70.23; H, 8.17. Found: C, 70.59; H, 8.46. **Trans isomer**: mp (hexanes) = 78–79 °C; IR ($CHCl_3$) 1733, 1369, 1258, 1211, 1181, 1131, 1013, 940 cm^{-1}; ^1H NMR δ 3.32 (m 1 H), 2.92 (m, 1 H), 2.77 (d, 1 H, J = 8.4 Hz), 2.24 (m, 3 H), 2.01 (s, 3 H), 1.97–1.78 (m, 7 H), 1.57 (m, 2 H); ^{13}C NMR δ 206.57, 170.01, 90.71, 55.88, 50.02, 41.86, 39.04, 30.38, 27.46, 26.93, 25.32, 22.56, 21.86. Anal. Calcd for $C_{13}H_{18}O_3$: C, 70.23; H, 8.17. Found: C, 70.04; H, 8.29.

2-Acetoxytricyclo[6.4.0.0^{2,7}]dodecan-6-one (15b). Irradiation of **13** (2.0 g) and **14b** (10.6 g) for 32 h provided, after chromatography, 2.35 g (77%) of **15b** as a mixture of isomers; cis:trans = 4.9:1. **Cis isomer**: mp (hexanes) = 84–85 °C; IR ($CHCl_3$) 1739, 1704, 1317, 1252, 1221, 1198, 1172, 1141, 1095, 1020 cm^{-1}; ^1H NMR δ 2.93 (d, 1 H, J = 10.4 Hz), 2.52 (m, 2 H), 2.45–2.25 (m, 3 H), 2.01 (s, 3 H), 1.92–1.72 (m, 4 H), 1.69–1.55 (m, 3 H), 1.51–1.26 (m, 3 H), 0.99 (m, 1 H); ^{13}C NMR δ 210.17, 169.92, 79.89, 52.02, 42.08, 38.34, 32.11, 31.03, 24.73, 22.24, 21.86, 21.36, 21.19, 20.41. **Trans isomer**: mp (hexanes) = 82–83 °C; IR ($CHCl_3$) 1738, 1711, 1315, 1242, 1211, 1168, 1128, 1028 cm^{-1}; ^1H NMR δ 3.15 (d, 1 H, J = 8.8 Hz), 2.36 (m, 1 H), 2.30 (dd, 1 H, J = 12.8, 8.0 Hz), 2.23 (m, 1 H), 2.15–1.84 (m, 4 H), 2.07 (s, 3 H), 1.78–1.62 (m, 5 H), 1.50–1.14 (m, 4 H); ^{13}C NMR δ 210.55, 170.70, 90.50, 56.64, 49.22, 42.76, 40.80, 29.18, 29.06, 27.55, 26.40, 25.98, 21.76, 21.18. Anal. Calcd for $C_{14}H_{20}O_3$: C, 71.14; H, 8.54. Found: C, 71.00; H, 8.97.

2-Acetoxytricyclo[6.6.0.0^{2,7}]tetradecan-6-one (15c). Irradiation of **13** (2.0 g) and **14c** (14.3 g) for 47 h provided, after chromatography, 3.07 g (90%) of **15c** as a mixture of isomers; cis:trans = 1.4:1. **Cis isomer**: IR (CCl_4) 1730, 1698, 1680, 1368, 1240, 1180, 1027 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 2.60 (d, 1 H, J = 9.2 Hz), 2.50 (d, 1 H, J = 9.2 Hz), 2.38 (m, 6 H), 2.23 (m, 4 H), 1.99 (s, 3 H), 1.98 (s, 3 H), 1.96–1.54 (m, 18 H), 1.54–0.96 (m, 12 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 209.56, 209.49, 170.36, 169.86, 81.11, 80.29, 57.20, 56.78, 51.22, 49.11, 40.12, 38.52, 38.29, 38.05, 36.95, 31.99, 30.27, 28.59, 28.42, 28.38, 27.55, 27.34, 27.10, 26.58, 25.69, 26.25, 25.29, 22.66, 21.71, 21.50, 20.01, 19.39; HRMS calcd for $C_{16}H_{24}O_3$: 264.1725, found 264.1735. **Trans isomer**: IR (CCl_4) 1735, 1368, 1235, 1211, 1017, 945 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 2.92 (m, 2 H), 2.52 (m, 4 H), 2.24 (m, 6 H), 2.04 (s, 6 H), 2.02–1.52 (m, 18 H), 1.49–1.04 (m, 12 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 207.53, 206.31, 170.70, 170.10, 92.88, 92.54, 60.35, 57.83, 54.20, 51.04, 41.49, 39.40, 37.46, 35.68, 31.84, 30.54, 29.62, 28.06, 27.67, 27.51, 27.30, 26.75, 26.42, 25.39, 24.76, 24.66, 23.84, 23.08, 21.84, 21.59; HRMS calcd for $C_{16}H_{24}O_3$ 264.1725, found 264.1727.

2-Acetoxy-4,4-dimethyltricyclo[6.3.0.0^{2,7}]undecan-6-one (16a).[4d] Irradiation of **8** (2.0 g) and **14a** (7.5 g) for 24 h provided, after chromatography, 1.97 g (72%) of **16a** as a mixture of isomers; cis:trans = 1.9:1. **Trans isomer**: mp (hexanes) = 113–114 °C (lit.[4d] mp = 117–118 °C); ^1H NMR δ 3.27 (ddd, 1 H, J = 8.4, 6.4, 2.0 Hz); 2.86 (m, 1 H), 2.74 (d, 1 H, J = 8.8 Hz), 2.18 (ABq, 2 H, J_{AB} = 16.8, $\Delta\nu_{AB}$ = 32.7 Hz), 2.02 (ABq, 2 H, J_{AB} = 14.8, $\Delta\nu_{AB}$ = 154.9 Hz), 2.01 (s, 3 H), 1.82 (m, 4 H), 1.59 (m, 2 H), 1.15 (s, 3 H), 1.04 (s, 3 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 206.45, 170.12, 89.26, 53.74, 53.39, 49.98, 41.49, 40.63, 35.34, 34.59, 32.84, 30.30, 26.84, 25.43, 22.14. **Cis isomer**: mp (hexanes) = 126–126.5 °C (lit.[4d] mp = 126–127 °C); ^1H NMR δ 2.86 (ddd, 1 H, J = 8.4, 5.2, 2.8 Hz), 2.55 (m, 1 H), 2.54 (brs, 1 H), 2.21 (ABq, 2 H, J_{AB} = 15.6,

(7) The authors have deposited atomic coordinates for this structure with the Cambridge Crystallographic Data Centre. The coordinates can be obtained, on request, from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, UK.

$\Delta\nu_{AB}$ = 29.2 Hz), 2.15 (ABq, 2 H, J_{AB} = 15.6, $\Delta\nu_{AB}$ = 224.3 Hz), 1.99 (s, 3 H), 1.80–1.48 (m, 6 H), 1.01 (s, 3 H), 0.88 (s, 3 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 210.80, 169.53, 79.56, 53.35, 52.05, 50.31, 45.00, 39.68, 33.67, 32.09, 31.01, 26.93, 26.63, 25.92, 21.49.

2-Acetoxy-4,4-dimethyltricyclo[6.4.0.0^{2,7}]dodecan-6-one (16b).[4a] Irradiation of 8 (2.0 g) and **14b** (9.0 g) for 17 h provided, after chromatography, 2.46 g (85%) of **16b** as a mixture of isomers; cis:trans = 4.3:1. **Cis isomer**: mp (hexanes) = 92.5–93.5 °C; IR (CCl_4) 1738, 1702, 1369, 1343, 1238, 1189, 1154, 1060, 1049, 1027 cm^{-1}; ^{1}H NMR δ 2.83 (d, 1 H, J = 10.8 Hz), 2.49 (dd, 1 H, J = 18.4, 7.6 Hz), 2.27 (m, 1 H), 2.20 (AB portion of ABXX′, 2 H, J_{AB} = 15.2, J_{AX} = 0.0, J_{BX} = 1.6, $J_{BX'}$ = 2.4, $\Delta\nu_{AB}$ = 105.9 Hz), 2.13 (AB portion of ABX_2, 2 H, J_{AB} = 15.6, J_{AX} = 2.0, J_{BX} = 0.0, $\Delta\nu_{AB}$ = 227.5 Hz), 1.95 (s, 3 H), 1.71 (m, 1 H), 1.58 (m, 3 H), 1.45–1.22 (m, 3 H), 1.00 (s, 3 H), 0.94 (m, 1 H), 0.87 (s, 3 H); ^{13}C NMR δ 210.14, 169.72, 79.85, 51.56, 51.30, 43.39, 43.06, 34.40, 32.00, 31.38, 26.43, 24.73, 22.20, 21.79, 21.38, 21.17. Anal. Calcd for $C_{16}H_{24}O_3$: C, 72.73; H, 9.09. Found: C, 72.69; H, 8.97. **Trans isomer**: mp (hexanes) = 125–126 °C; IR (CCl_4) 1742, 1726, 1368, 1265, 1248, 1228, 1199, 1166, 1017 cm^{-1}; ^{1}H NMR δ 2.75 (d, 1 H, J = 10.6 Hz), 2.19 (ABq, 2 H, J_{AB} = 14.4, $\Delta\nu_{AB}$ = 297.6 Hz), 2.18 (m, 1 H), 2.16 (ABq, 2 H, J_{AB} = 15.2, $\Delta\nu_{AB}$ = 26.8 Hz), 2.02 (s, 3 H), 1.93 (m, 1 H), 1.71 (m, 4 H), 1.22 (m, 3 H), 1.12 (s, 3 H), 1.07 (m, 1 H), 1.02 (s, 3 H); ^{13}C NMR δ 205.57, 170.35, 93.28, 58.83, 54.80, 53.93, 45.27, 40.96, 37.78, 34.28, 31.52, 31.19, 29.04, 26.04, 25.74, 21.59. Anal. Calcd for $C_{16}H_{24}O_3$: C, 72.73; H, 9.09. Found: C, 72.75; H, 9.01.

2-Acetoxy-4,4-dimethyltricyclo[6.6.0.0^{2,7}]tetradecan-6-one (16c). Irradiation of 8 (2.0 g) and **14c** (12.1 g) for 62 h provided, after chromatography, 2.95 g (92%) of **16c** as a mixture of isomers; cis:trans = 4.1:1. **Cis isomer**: mp (hexanes) = 114–114.5 °C; IR (CCl_4) 1736, 1703, 1368, 1239, 1191, 1028 cm^{-1}; ^{1}H NMR δ 2.28 (AB portion of ABX, 2 H, J_{AB} = 15.8, J_{AX} = 2.0, J_{BX} = 0, $\Delta\nu_{AB}$ = 331.6 Hz), 2.57 (d, 1 H, J = 10.0 Hz), 2.44 (dd, 1 H, J = 8.0, 2.6 Hz), 2.36 (d, 1 H, J = 15.6 Hz), 2.13 (m, 2 H), 1.99 (s, 3 H), 1.81 (m, 1 H), 1.74–1.10 (m, 11 H), 1.04 (s, 3 H), 0.89 (s, 3 H); ^{13}C NMR δ 209.67, 170.02, 81.17, 55.80, 51.59, 50.49, 43.32, 37.58, 34.21, 31.35, 30.37, 27.98, 26.51, 26.40, 25.63, 25.08, 23.14, 21.65. **Trans isomer**: mp (hexanes) = 103–104 °C; IR (CCl_4) 2931, 2854, 1732, 1456, 1368, 1248, 1229, 1148, 1020, 937 cm^{-1}; ^{1}H NMR δ 2.91 (d, 1 H, J = 14.8 Hz), 2.57 (ddd, 1 H, J = 14.0, 10.4, 4.0 Hz), 2.48 (d, 1 H, J = 10.4 Hz), 2.16 (ABq, 2 H, J_{AB} = 16.4, $\Delta\nu_{AB}$ = 27.4 Hz), 2.14 (m, 1 H), 2.02 (s, 3 H), 1.95 (m, 2 H), 1.90–1.62 (m, 7 H), 1.41–1.06 (m, 4 H), 1.14 (s, 3 H), 1.00 (s, 3 H); ^{13}C NMR δ 206.15, 171.19, 90.94, 58.49, 54.97, 53.79, 44.83, 41.06, 36.92, 35.62, 34.74, 31.76, 29.88, 28.18, 27.19, 26.69, 26.51, 22.17. Anal. Calcd for $C_{18}H_{28}O_3$: C, 73.93; H, 9.65. Found: C, 74.22; H, 9.51.

Tricyclo[6.3.0.0^{2,7}]-Δ^{2,7}-undecen-6-one (17a). Reaction of **15a** (0.20 g, 0.80 mmol) with *tert*-butyl alcohol (0.11 mL, 1.2 mmol) and NaH (38 mg, 0.96 mmol, 60% dispersion) according to method A afforded 94 mg (64%) of **17a**: IR (film) 2939, 2858, 1674, 1424, 1369, 1289, 1207 cm^{-1}; ^{1}H NMR δ 3.42 (m, 1 H), 3.29 (dd, 1 H, J = 8.0, 3.2 Hz), 2.30 (m, 2 H), 2.15 (m,2 H), 2.05 (m, 2 H), 1.74 (dd, 1 H, J = 13.2, 6.0 Hz), 1.70 (dd, 1 H, J = 12.8, 6.8 Hz), 1.64 (dd, 1 H, J = 12.8, 6.4 Hz), 1.47 (dddd, 1 H, J = 24.8, 18.8, 12.4, 6.0 Hz), 1.29 (m, 1 H), 1.20 (m, 1 H); ^{13}C NMR δ 194.35, 172.40, 140.86, 49.15, 45.71, 38.06, 25.55, 24.59, 24.28, 23.62, 23.50; HRMS calcd for $C_{11}H_{14}O$ 162.1045, found 162.1041.

Tricyclo[6.6.0.0^{2,7}]-Δ^{2,7}-dodecen-6-one (17b). Reaction of **15b** (0.20 g, 0.85 mmol) with *tert*-butyl alcohol (0.11 mL, 1.3 mmol) and NaH (36 mg, 1.0 mmol, 60% dispersion) according to method A afforded 32 mg (21%) of **17b**: IR (film) 2929, 2861, 1673, 1448, 1424, 1373 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 3.16 (m, 1 H), 3.02 (dd, 1 H, J = 10.6, 5.1 Hz), 2.32 (m, 2 H), 2.24 (m, 2 H), 2.12 (m, 2 H), 1.71 (m, 3 H), 1.55 (m, 1 H), 1.43 (m, 3 H), 1.21 (m, 1 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 194.54, 175.68, 143.86, 42.52, 39.08, 38.02, 24.22, 23.01, 22.64, 18.67, 18.20; HRMS calcd for $C_{12}H_{16}O$ 176.1201, found 176.1198.

Tricyclo[6.6.0.0^{2,7}]-Δ^{2,7}-tetradecen-6-one (17c). Reaction of **15c** (0.10 g, 0.34 mmol) with *tert*-butyl alcohol (0.05 mL, 0.51 mmol) and NaH (16 mg, 0.41 mmol, 60% dispersion) according to method A afforded 42 mg (54%) of **17c**: IR (film) 2906, 2847, 1673, 1453, 1373, 1252 cm^{-1}; ^{1}H NMR δ 3.02 (m, 1 H), 2.87 (m, 1 H), 2.78 (m, 1 H), 2.68 (brd, 1 H, J = 11.6 Hz), 2.32 (m, 4 H), 2.19 (m, 4 H), 2.06 (m, 6 H), 1.96 (m, 3 H), 1.79 (m, 3 H), 1.62 (m, 2 H), 1.52–1.28 (m, 12 H), 1.18 (m, 2 H); ^{13}C NMR δ 194.89, 194.80, 173.95, 173.83, 142.50, 142.40, 52.96, 49.55, 49.24, 46.10, 38.27, 38.24, 32.42, 30.95, 30.21, 29.98, 29.48, 29.28, 28.12, 28.06, 25.96, 25.95, 25.79, 24.57, 24.29, 24.18, 23.44, 23.09; HRMS calcd for $C_{14}H_{20}O$ 204.1514, found 204.1500.

4,4-Dimethyltricyclo[6.3.0.0^{2,7}]-Δ^{2,7}-undecen-6-one (18a).[4d] Reaction of **16a** (0.30 g, 1.58 mmol) with sodium methoxide (0.43 g, 7.9 mmol) according to method B afforded 0.18 g (81%) of **18a**: ^{1}H NMR (200 MHz, $CDCl_3$) δ 3.39 (m, 1 H), 3.23 (m, 1 H), 2.13 (ABq, 2 H, J_{AB} = 18.0, $\Delta\nu_{AB}$ = 18.8 Hz), 2.03 (brs, 2 H), 1.81–1.06 (m, 6 H), 1.02 (s, 3 H), 0.97 (s, 3 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 194.20, 170.59, 139.50, 52.11, 48.89, 45.19, 37.86, 36.47, 29.52, 28.49, 25.62, 24.48, 23.98.

4,4-Dimethyltricyclo[6.4.0.0^{2,7}]-Δ^{2,7}-dodecen-6-one (18b).[4a] Reaction of **16b** (1.0 g, 4.9 mmol) with sodium methoxide (1.3 g, 24.5 mmol) according to method B afforded 0.73 g (94%) of **18b**: IR (CCl_4) 2934, 2864, 1677, 1558, 1458, 1371, 1244 cm^{-1}; ^{1}H NMR δ 3.14 (m, 1 H), 2.97 (m, 1 H), 2.20 (ABq, 2 H, J_{AB} = 16.0, $\Delta\nu_{AB}$ = 15.6 Hz), 2.19 (brs, 2 H), 1.76 (m, 3 H), 1.63 (m, 1 H), 1.45 (m, 4 H), 1.09 (s, 3 H), 1.07 (s, 3 H); ^{13}C NMR δ 194.33, 173.71, 142.59, 52.22, 42.29, 38.61, 36.61, 29.65, 29.57, 28.43, 23.35, 22.70, 18.80, 18.39; HRMS calcd for $C_{14}H_{20}O$ 204.1514, found 204.1509.

4,4-Dimethyltricyclo[6.6.0.0^{2,7}]-tetradecen-6-one (18c). Reaction of **16c** (1.0 g, 4.3 mmol) with sodium methoxide (1.2 g, 21.5 mmol) according to method B afforded 0.72 g (91%) of **18c**: IR (CCl_4) 2924, 2852, 1677, 1464, 1454, 1372, 1250, 1160, 1070, 972 cm^{-1}; ^{1}H NMR δ 2.98 (brd, 1 H, J = 11.6 Hz), 2.83 (brd, 1 H, J = 11.6 Hz), 2.74 (brd, 1 H, J = 12.0 Hz), 2.63 (brd, 1 H, J = 12.4 Hz), 2.24–2.00 (m, 9 H), 2.00–1.68 (m, 7 H), 1.68–1.24 (m, 13 H), 1.24–1.08 (m, 3 H), 103 (s, 3 H), 1.02 (s, 3 H); ^{13}C NMR δ 194.55, 194.43, 171.92, 171.89, 140.97, 140.92, 52.63, 52.33, 49.22, 48.51, 45.40, 37.73, 37.36, 36.61, 36.44, 32.34, 30.68, 30.12, 29.91, 29.36, 29.30, 29.21, 29.10, 28.56, 28.36, 28.01, 27.98, 25.88, 25.69, 24.29; HRMS calcd for $C_{16}H_{24}O$ 232.1827, found 232.1821.

2-Isopropylidene-3-(4-oxo-1-pentylidene)-5,5-dimethylcyclohexanone (22). A solution of **10** (0.055 g) in 10 mL of isooctane was refluxed under argon for 24 h. The solvent was removed in vacuo and the crude product chromatographed (20 g of silica gel, ethyl acetate:hexanes = 1:9) to afford 0.040 g (73% yield) of **22**: IR (CCl_4) 1719, 1690, 1613, 1446, 1365, 1265, 1214, 1159 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 5.17 (t, 1 H, J = 7.2 Hz), 2.49 (m, 2 H), 2.38 (m, 2 H), 2.28 (m, 4 H), 2.15 (s, 3 H), 1.93 (s, 3 H), 1.85 (s, 3 H), 0.98 (s, 6 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 207.99, 203.41, 139.32, 138.26, 134.71, 128.97, 56.48, 43.28, 41.43, 33.63, 29.94, 28.48, 22.97, 22.41, 21.83; HRMS calcd for $C_{16}H_{24}O_2$ 248.1776, found 248.1749.

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Supplementary Material Available: Table I (Summary of Data Collection, Structure Solution, and Refinement Details) and spectral data (^{1}H and ^{13}C NMR) for compounds **10**, **11**, **15c** (cis and trans), **17a–c**, **18b–c**, and **22** (21 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.