for 1 h. The reaction mixture was quenched with ca. 5 mL of cold water, and the solvent was removed by rotary evaporation. The residue was dissolved in EtOAc (50 mL), washed with water (3 × 50 mL) and brine (50 mL), dried over $MgSO_4$, filtered, and evaporated to afford 0.80 g (96%) of **12b** as a brown oil, which solidified upon evacuation: ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.65 (s, 1 H), 8.11 (dd, J = 1.6, 8.7 Hz, 1 H), 7.99 (d, J = 8.9 Hz, 1 H), 7.86 (d, J = 8.6 Hz, 1 H), 7.62 (d, J = 1.6 Hz, 1 H), 7.32 (dd, J = 2.2, 8.9 Hz, 1 H), 5.56 (s, 2 H), 3.60 (s, 3 H), 2.38 (s, 3 H).

Methoxymethyl 6-Hydroxy-2-naphthoate (12c). A solution of acetoxy ester **12b** (0.65 g, 2.37 mmol) in a mixture of 40 mL of MeOH, 7 mL of saturated aqueous $NaHCO_3$, and 7 mL of H_2O was stirred at room temperature for 6 h. The reaction mixture was quenched with 1 N HCl (ca. 10 mL) to afford a tan precipitate. MeOH was removed by rotary evaporation, and the solid was isolated by rapid filtration. The solid was dissolved in EtOAc (50 mL), and the solution was washed with brine, dried over $MgSO_4$, filtered, and concentrated to afford 0.57 g (97%) of **12c** as a tan solid: mp 130-132 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.58 (s, 1 H), 8.05 (dd, J = 1.6, 8.6 Hz, 1 H), 7.80 (d, J = 8.6 Hz, 1 H), 7.72 (d, J = 8.6 Hz, 1 H), 7.17 (m, 2 H), 5.55 (s, 2 H), 5.49 (s, 1 H), 3.60 (s, 3 H); HRMS m/z [$(M - H)^+$] calcd 231.0657, obsd 231.0658.

Kinetics Studies. The reaction of imide esters **10d** and **10h** with amine **9** in the presence and absence of templates **11a** and **11b** was performed in $CHCl_3$ solution containing ca. 4 equiv of Et_3N. A Waters 600 HPLC equipped with a UV detector (254 nm) was used for the analysis of reaction mixtures. Analyses were performed with a mixture of water-methanol-Et_3N (30:70:0.1) as the mobile phase and a reverse-phase column (Beckman C_{18} column, Ultrasphere ODS dp, 5 μm, 4.6 mm i.d. × 25 cm, flow rate = 1.5 mL/min). The integrations and concentrations of all the peaks were calculated on an NEC computer with Waters 820 Baseline software. In case of prolonged reactions (>100 min), a methanol flush was performed between injections to ensure complete elution of esters **10d** and **10h**. $CHCl_3$ was dried over molecular sieves or by passage through Al_2O_3 before use. All experiments were performed at ambient temperature (21.5-23.0 °C). Each run was performed 2-4 times to obtain average values for the data.

Calibration of HPLC. The HPLC was calibrated by the injection of solutions of amine **9** and template **11a** of varying concentration. A linear relationship between concentration and peak area was observed. Reaction mixtures were analyzed on the basis of either the area of the template peak or the *ratio* of the amine and template peaks.

Reaction Procedures. During initial studies (data presented in Figures 1 and 5), reactions were performed in 100 μL of solvent in 1-mL. Wheaton serum vials equipped with aluminum caps and Teflon-coated silicone septa (procedure A). During subsequent studies (data presented in Figures 2-4), 1-mL Wheaton screw-cap vials equipped with Mininert valves were used to minimize evaporative losses of solvent, and 500 μL of solvent was used to reduce changes in concentration arising from solvent evaporation (procedure B).

Typical Reaction Procedure A. Reaction of Imide Ester 10d and Amine 9. A 1-mL Wheaton serum vial equipped with a aluminum cap and a silicone rubber septum coated with Teflon was charged with 20 μL of $CHCl_3$, ca. 1 μL of Et_3N, 40 μL of amine **9** stock solution (2.05×10^{-2} M), and 40 μL of pentafluoro ester stock solution **10d** (2.05×10^{-2} M). The reaction mixture was shaken gently with a mechanical shaker. Aliquots (1.0 μL) were withdrawn periodically and analyzed by HPLC.

Typical Reaction Procedure B. Reaction of Imide Ester 10d and Amine 9 in the Presence of Template 11a. A 1-mL Wheaton reaction vial equipped with a Mininert valve and a stir vane was charged with 260 μL of $CHCl_3$ and 4.6 μL of Et_3N. Stock solutions of amine **9** (100 μL, 8.2×10^{-2} M), template **11a** (40 μL, 4.1×10^{-2} M), and pentafluoro ester **10d** (100 μL, 8.2×10^{-2} M) were added by a microliter syringe. Aliquots (10 μL) were withdrawn from the reaction solution periodically, diluted with 90 μL of $CHCl_3$, and analyzed by HPLC (10 μL injected).

Acknowledgment. We are grateful to the National Science Foundation for support of this research. J.S.N. thanks the NSF for a postdoctoral fellowship.

Inside-Outside Stereoisomerism. 5. Synthesis and Reactivity of *trans*-Bicyclo[*n*.3.1]alkanones Prepared via the Intramolecular Photocycloaddition of Dioxenones[†,‡]

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Abstract: The stereoselectivity of the intramolecular photocycloaddition of a series of bicyclic dioxenones has been examined. The selective formation of trans-fused photoadducts is observed in almost all cases, which upon fragmentation lead to the synthesis of bicycloalkanones with an "inside-outside" or trans intrabridgehead stereochemical relationship. This methodology has been applied to the synthesis of several "inside-outside" bicycloalkanones that cannot otherwise be prepared. The unusual reactivity of both the dioxanone photoadducts and the bicycloalkanone fragmentation products is described.

Introduction

The de Mayo reaction has served as an important example of the utility of enone photocycloaddition chemistry in organic synthesis for almost 30 years. Cycloaddition of the enol of a β-diketone with an alkene leads to the formation of a cyclobutane, which on fragmentation gives a product containing a 1,5-dicarbonyl moiety.[4,5] Since the pioneering studies of Oppolzer[6] and Pattenden,[7] the intramolecular version of this reaction has attracted considerable attention as a powerful method for the construction of structurally complex polycyclic ring systems beginning with readily available starting materials. However, the application of this reaction to the construction of bridged bicyclic

† Dedicated to Professor Ronald C. D. Breslow on the occasion of his 60th birthday.

‡ For the previous paper in this series, see: Winkler, J.; Sridar, V.; Rubo, L.; Hey, J.; Haddad, N. *J. Org. Chem.* **1989**, *54*, 3004.

(1) Address correspondence to this author at the University of Pennsylvania. Recipient of the American Cyanamid Young Faculty Award (1989-1992) and a National Institutes of Health Research Career Development Award (1988-1993). Fellow of the Alfred P. Sloan Foundation (1987-1989).

(2) University of Chicago.

(3) Address correspondence to this author at Brown University regarding the X-ray structural data for **6** and **17**.

(4) de Mayo, P. *Pure Appl. Chem.* **1964**, *9*, 597. de Mayo, P. *Acc. Chem. Res.* **1971**, *4*, 41.

(5) For an excellent recent review of the application of the intramolecular [2 + 2] photocycloaddition reaction in organic synthesis, see: Crimmins, M. *Chem. Rev.* **1988**, *88*, 1453 and references cited therein.

(6) Oppolzer, W. *Acc. Chem. Res.* **1982**, *15*, 135.

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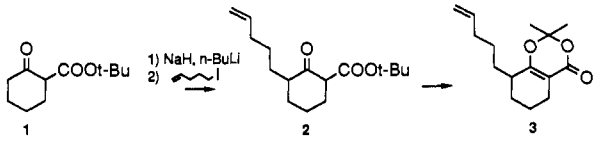
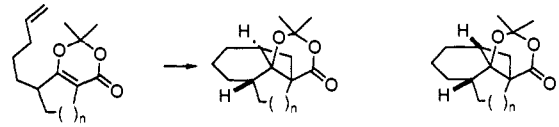
Scheme I



1 2 3

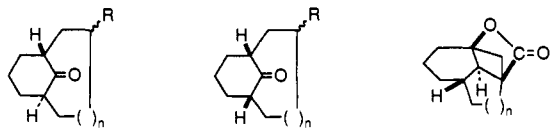
Scheme II



3 n=2
12 n=1
21 n=3
22 n=4
23 n=6

4 n=2
13 n=1
24 n=3
31 n=4
37 n=6

14 n=1
25 n=3



5 n=2; R=COOMe
6 n=2; R=COOH
10 n=2; R=H

15 n=1; R=COOMe
17 n=1; R=COOH
19 n=1; R=H

26 n=3; R=COOH
28 n=3; R=COOMe

35 n=4; R=CHO
36 n=4; R=COOH

11 n=2; R=H

16 n=1; R=COOMe
18 n=1; R=COOH
20 n=1; R=H

27 n=3; R=COOH
30 n=3; R=COOMe

32 n=4; R=COOH
33 n=4; R=H

38 n=6; R=COOH
39 n=6; R=H

29 n=3
34 n=4
40 n=6

ring systems has met with limited success.[7] In addition, regiochemical complications surrounding the selective alkylation and enolization of the starting β-diketones have somewhat limited the generality of this methodology in synthesis.

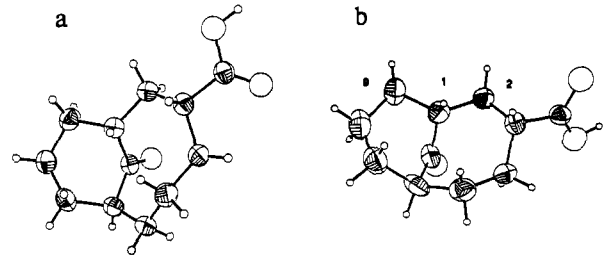
The analogous reaction of β-keto esters would address both of these regiochemical ambiguities as both the selective enolization and alkylation of β-keto esters is well-known.[8] However, the photochemical reactivity of β-keto esters is not the same as that of the corresponding β-diketones. Irradiation of a β-keto ester in the presence of an alkene leads not to cyclobutane formation from the enol of the keto ester, but instead to oxetane formation via the keto ester carbonyl.[9] Baldwin has reported a solution to this problem using dioxenone heterocycles as covalently locked enol tautomers of β-keto esters.[10] Intermolecular cycloaddition occurs in good yield using stoichiometric quantities of a variety of different alkenes. However, the regiochemical outcome of the cycloaddition with unsymmetrical alkenes proved to be difficult to predict on the basis of existing models for enone photocycloaddition. We reasoned that the intramolecular version of the dioxenone photocycloaddition reaction could provide greater regiochemical control and that the intramolecular dioxenone photocycloaddition might also be useful for the construction of bridged ring systems that are not accessible using standard de Mayo methodology.[11,12]

Results and Discussion

To examine the preparation of bridged bicyclic ring systems using this methodology, the requisite photosubstrate **3** was prepared as outlined below (Scheme I).[13] Dianion alkylation of *tert*-butyl 2-oxocyclohexanecarboxylate (**1**) (Scheme I) with 4-pentenyl iodide gave the alkylated keto ester **2** in 89% yield, which on reaction with trifluoroacetic anhydride and trifluoroacetic acid in acetone gave the dioxenone photosubstrate **3** in 59% yield.

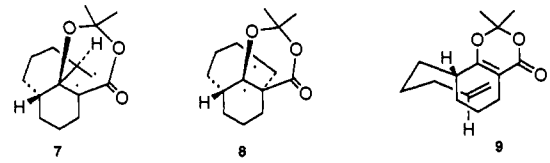
Irradiation of **3** (0.02 M in 1:9 acetone/acetonitrile, Pyrex immersion well, 0 °C) for 4 h produced photoadduct **4** (Scheme II), which was directly submitted to the fragmentation conditions (0.1 equiv of *p*-TsOH, methanol, reflux, 18 h)[13] to provide **5** in 80% overall yield. X-ray analysis on the derived keto acid (3 equiv of 1 M aqueous lithium hydroxide/methanol–tetrahydrofuran, 25 °C) **6** (recrystallized as a monohydrate from methanol, mp 104–109 °C for the liberation of H_2O, then 137–139 °C) confirmed the trans intrabridgehead stereochemical relationship (Scheme III).[14]

Scheme III[a]



[a] ORTEP plots for X-ray crystal structures of (a) *trans*-bicyclo[5.3.1]undecan-11-one **6** and (b) *trans*-bicyclo[4.3.1]decan-10-one **17**.

Scheme IV



7 8 9

The exclusive formation of the trans-fused photoadduct **4** is consistent with initial formation of the β bond to the dioxenone to give an intermediate cyclohexane diyl **7** (Scheme IV). Formation of the isomeric eight-membered ring diyl **8** (α bond formation) would ultimately produce the less strained cis-ring-fusion stereochemistry in the cycloaddition, since the rate of intersystem crossing for the triplet diyl is slower than ring flipping.[15] Chairlike folding of the nascent six-membered ring as shown in **9** would lead to the requisite trans orientation of the indicated hydrogens and

(7) Begley, M.; Mellor, M.; Pattenden, G. *J. Chem. Soc., Perkin Trans. 1* **1983**, 1905.
(8) Huckin, S.; Weiler, L. *J. Am. Chem. Soc.* **1974**, *96*, 1082.
(9) Tada, M.; Kokubo, T.; Sato, T. *Bull. Chem. Soc. Jpn.* **1970**, *43*, 2162.
(10) Baldwin, S.; Wilkinson, J. *J. Am. Chem. Soc.* **1980**, *102*, 3634.
(11) For the application of this methodology to the synthesis of monocyclic cycloalkanone propionates, see: Winkler, J.; Hey, J.; Hannon, F.; Williard, P. *Heterocycles* **1987**, *25*, 55.
(12) For an unsuccessful effort to prepare the bicyclo[5.3.1]undecane moiety using standard de Mayo conditions, see ref 7.

(13) For a preliminary account of the synthesis of *trans*-bicyclo[5.3.1]-undecan-11-one, see: Winkler, J.; Hey, J.; Williard, P. *J. Am. Chem. Soc.* **1986**, *108*, 6425.
(14) The bicyclo[5.3.1] carboxylic acid crystallized in the centrosymmetric, monoclinic space group $P2_1/n$. The unit cell parameters were determined to be a = 6.454 (2) Å, b = 16.047 (6) Å, c = 11.752 (4) Å, and β = 99.62 (2)° by least-squares fitting of 25 independent reflections in the range 24° ≤ 2θ ≤ 26°. The unit cell contained two asymmetric units of molecular formula $C_{12}H_{18}O_3$ in a volume of 11 199.95 (8) Å^3, which produces a calculated density of 1.24 g/cm^3. A total of 2252 reflections were recorded in the range 3.5° ≤ 2θ ≤ 48° with a Nicolet R3m/E crystallographic system using the θ–2θ scan routine and graphite monochromated Mo Kα radiation (λ = 0.71069 Å). A total of 1566 unique reflections were observed using the criterion [$F_o > 2.5\sigma(F_o)$]. After Lorentz and polarization corrections, the structure was solved by the SHELTXTL 5.1 programs. All non-hydrogen atoms were refined anisotropically. The approximate locations of all hydrogen atoms were determined by Fourier difference syntheses. In the final stages of refinement, the hydrogen atoms were placed in calculated positions and allowed to ride with the atom to which they were attached. The final agreement factors are R = 0.067 and R_w = 0.088 for 145 independent variables, where $R_w = [\sum wD^2/S(wF_o^2)]^{1/2}$; $D = |F_o - F_c|$ and the weighting scheme is $w = 1/[\sigma^2(F_o) + 0.0002F_o^2]$. Tables of atomic coordinates, bond lengths and angles, and anisotropic thermal parameters are included in the supplementary material.
(15) (a) For a discussion of intersystem crossing, see: Caldwell, R.; Carlacci, L.; Doubleday, C.; Furlani, T.; King, H.; McIver, J. *J. Am. Chem. Soc.* **1988**, *110*, 6907. (b) For the relative energies of cyclooctane conformations, see: Hendrickson, J. *J. Am. Chem. Soc.* **1967**, *89*, 7036.

is consistent with the exclusive formation of **4** (Scheme II) in the photocycloaddition.

Barton decarboxylation of keto acid **6** provided *trans*-bicyclo[5.3.1]undecan-11-one (**10**) (Scheme II),[16,17] which was easily distinguished spectroscopically from the known *cis*-bicyclo[5.3.1]undecan-11-one (**11**). While the ^{13}C spectrum of *cis*-**11** shows the seven lines that one would expect from a compound with a plane of symmetry, the 11-line ^{13}C spectrum of trans-bridged **10** reveals neither a plane nor an axis of symmetry, indicating that the *trans*-bicyclo[5.3.1]undecane is quite rigid. Even at 150 °C (dimethyl-d_6 sulfoxide), there was no coalescence of the 11 resonances in the ^{13}C NMR spectrum of **10**. All attempts to interconvert **10** and **11** under either acidic or basic conditions were unsuccessful. The bridgehead carbon–hydrogen bonds are nearly parallel to the carbonyl group, with dihedral angles determined in the X-ray analysis to be 19° and 156°, so that the kinetic acidity of each is quite low.

Molecular mechanics calculations reveal that *trans*-**10** is ca. 10 kcal/mol more strained that the corresponding *cis*-**11** and that the strain energy difference jumps to 20 kcal/mol in the case of the bicyclo[4.3.1]decan-10-one and 40 kcal/mol for the bicyclo[3.3.1]nonan-9-one. Intrigued by the high level of stereoselectivity in the formation of **4** and the access to the highly unusual trans-bridged bicyclic ring system that it afforded, we decided to examine (1) the scope of this trans-selective photocycloaddition, (2) the applicability of this methodology to the construction of other possibly more highly strained trans-bridged bicyclic ring systems, and (3) the physical properties of homologous trans-bridged cycloalkanones, i.e., the determination of the [*n*.3.1] ring size at which trans–cis equilibration becomes possible, establishing the minimal orientation of the C_α—H and C=O bonds that is required for deprotonation and equilibration to occur in these ring systems.

Preparation of *trans*-Bicyclo[4.3.1]decan-10-one. A Remarkably Distorted C–C–C Bond Angle.[18] We next examined the photocycloaddition of **12**, the synthesis of which followed directly from the preparation of **3**. In striking contrast to the irradiation of **3**, which resulted in the exclusive formation of a trans-fused photoadduct, i.e., **4**, irradiation of **12** (0.02 M in 1:9 acetone/acetonitrile, Pyrex immersion well, 0 °C) for 4 h resulted in the formation of two diastereomeric photoadducts, **13** and **14**, which upon fragmentation (0.1 equiv *p*-TsOH, methanol, reflux, 72 h) led to a 1:5 mixture of keto esters **15** and **16** in 65% overall yield. To determine the intrabridgehead stereochemical relationships in the photoaddition/fragmentation sequence, the separated keto esters were submitted to ester hydrolysis, acid chloride formation, and Barton decarboxylation to provide the *trans*- and *cis*-bicyclo[4.3.1]decan-10-ones, **19** and **20**, respectively. Inspection of the ^{13}C NMR spectra of these compounds led to the assignment of the major product, **20** [IR ($CHCl_3$) 1692 cm^{-1}; ^{13}C NMR ($CDCl_3$) δ 19.6, 27.6, 31.7, 33.1, 48.7, 218.0], as the outside-outside cis-bridged compound and the minor product **19** [IR ($CHCl_3$) 1748 cm^{-1}; ^{13}C NMR ($CDCl_3$) δ 21.0, 25.5, 28.1, 29.3, 31.9, 34.9, 35.3, 49.5, 49.6, 219.1], as the trans-bridged isomer, which contains neither a plane nor an axis of symmetry. Unambiguous proof for the inside–outside stereochemical relationship followed from the single-crystal X-ray analysis of **17** (Scheme III), the most striking feature of which is that, to accommodate the inside–outside stereochemical relationship, the C_9–C_1–C_2 bond angle in **17** is 130°, the most obtuse bond angle recorded to date for an sp^3 carbon.[19]

The striking difference in the stereoselectivity of the photocycloadditions of **3** and **12** can be attributed to the dramatic increase in the strain energy difference between the *cis*- and *trans*-bicyclo[5.3.1]undecanones (ca. 10 kcal/mol) and *cis*- and *trans*-bicyclo[4.3.1]decanones (ca. 20 kcal/mol). In the photocyclization of **3**, the exclusive formation of the inside–outside photoadduct **4** was explained via a chairlike six-membered ring in the photocycloaddition. It was not expected that the chairlike orientation of the nascent six-membered ring as shown in **9** (Scheme IV) should be particularly sensitive to the keto ester ring size, i.e., **12** instead of **3**. However, photocycloaddition of **12** results in the predominant formation of the "outside–outside" or cis-bridged bicyclic products. A later transition state for the photocycloaddition of **12** than that for **3**, reflecting the increased energy difference between the cis- and trans-bridged products, would account for the predominant formation of the more stable cis-bridged photoadduct **14** in the irradiation of **12**.

Synthesis and Reactivity of Homologous *trans*-Bicyclo[*n*.3.1]alkanones. A series of homologous dioxenone photosubstrates **21–23**, prepared from cycloheptanone, cyclooctanone, and cyclodecanone, was next examined. Irradiation of **21** (Scheme II) (9 mM in degassed $CH_3CN/(CH_3)_2CO$ (9:1), 450-W medium-pressure Hg lamp, Pyrex immersion well, 0 °C, 2 h) led to the formation of a 4.5:1 mixture of diastereomeric photoadducts **24** and **25** in 82% combined yield, which were readily separated by flash chromatography. Fragmentation of the separated photoadducts under basic conditions (2 N KOH, MeOH, 25 °C, 18 h, 87% yield) gave the trans- and cis-bridged oxobicyclododecanecarboxylic acids, **26** and **27**, respectively.[20] No isomerization of **26** to **27** was observed when the separated diastereomers were resubmitted to the basic conditions of the fragmentation reaction, even at elevated temperatures (2 N KOH, MeOH, reflux, 18 h), or upon reaction of **28**, the methyl ester derived from **26**, with lithium diisopropylamide in THF, in accord with the results reported for bicyclo[5.3.1]- and bicyclo[4.3.1]-

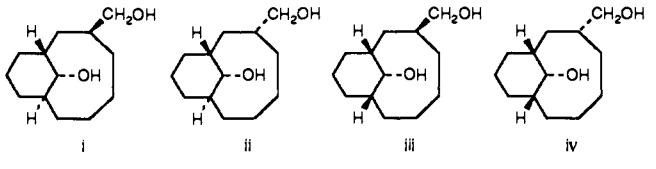
(16) For a recent review describing inside–outside stereoisomerism, see: Alder, R. *Acc. Chem. Res.* **1983**, *16*, 321. For previous syntheses of inside–outside bicycloalkanes, see: (a) Gassman, P.; Korn, S.; Bailey, T.; Johnson, T.; Finder, J.; Clardy, J. *Tetrahedron Lett.* **1979**, 3401. (b) Haines, A.: Karntiang, P. *J. Chem. Soc., Perkin Trans. 1* **1979**, 2577. (c) Gassman, P.; Thummel, R. *J. Am. Chem. Soc.* **1972**, *94*, 7183. (d) Park, C.; Simmons, H. *J. Am. Chem. Soc.* **1972**, *94*, 7184. (e) McMurry, J.; Hodge, C. *J. Am. Chem. Soc.* **1984**, *106*, 6450. (f) Gassman, P.; Hoye, R. *J. Am. Chem. Soc.* **1981**, *103*, 2498.

(17) For the stereoselective synthesis of the *trans*-bicyclo[4.4.1]undecane moiety of the ingenane diterpenes, see: (a) Winkler, J.; Henegar, K.; Williard, P. *J. Am. Chem. Soc.* **1987**, *109*, 2850. (b) Funk, R.; Olmstead, T.; Parvez, M. *J. Am. Chem. Soc.* **1988**, *110*, 3298.

(18) For a preliminary account of the synthesis of *trans*-bicyclo[4.3.1]-decan-10-one, see: Winkler, J.; Hey, J.; Williard, P. *Tetrahedron Lett.* **1988**, 4691.

(19) The bicyclo[4.3.1] carboxylic acid crystallized in the monoclinic space group $P2_1/a$. The unit cell parameters were determined to be a = 7.077 (2) Å, b = 6.361 (2) Å, c = 23.050 (7) Å, and β = 97.17 (2)° by least-squares fitting to the positions of 25 independent reflections in the range 24° ≤ 2θ ≤ 34°. The unit cell contained four asymmetric units of molecular formula $C_{11}H_{16}O_3$ in a volume of 1029.69 (1.0) Å^3, which produces a calculated density of 1.27 g/cm^3. A total of 1636 reflections were recorded in the range 3.5° ≤ 2θ ≤ 45° with a Nicolet R3m/E crystallographic system using the θ–2θ scan routine and graphite monochromated Mo Kα radiation (λ = 0.71069 Å). A total of 1197 unique reflections were observed using the criterion [F_o > 2.5σ(F_o)]. After Lorentz and polarization corrections, the structure was solved by the SHELTXTL 4.1 programs. All non-hydrogen atoms were refined anisotropically. The approximate locations of all hydrogen atoms were determined by Fourier difference syntheses. In the final stages of refinement the hydrogen atoms were placed in calculated positions and allowed to ride with the atom to which they were attached. The final agreement factors are R = 0.0615 and weighted R_w = 0.0873 for 128 independent parameters. Tables of atomic coordinates, bond lengths and angles, and anisotropic thermal parameters are included in the supplementary material.

(20) The cis and trans intrabridgehead relative stereochemistries can be assigned by examination of the ^1H NMR of the alcohols i–iv, which are obtained on reduction of **28** and **30** (Scheme II) (LAH, THF, 12 h, 25 °C), respectively. The coupling constants for the carbinol methine to the two bridgehead protons were J = 5.9, 11.0 Hz and J = 2.4, 10.4 Hz for the trans bridged isomers i and ii, and J = 3.4, 3.4 Hz and J = 3.9, 3.9 Hz for the cis bridged isomers iii and iv. These values are consistent with two equatorial–axial coupling constants in each of the cis isomers, and one equatorial–axial and one axial–axial coupling constant in the trans bridged isomers. Empirically, it was found that in all of the bicyclic compounds examined, the two ring-junction methines in the trans-fused products, i.e., **28**, are different by ca. 0.8 ppm in the ^1H NMR and ca. 10 ppm in the ^{13}C NMR, while the differences in the cis isomers, i.e., **30**, are much smaller, <0.1 ppm in ^1H NMR and 1–2 ppm in the ^{13}C NMR.



alkanones.[13,18] When the fragmentation of the photoadducts **24**/**25** was performed under acidic conditions (cat. *p*-TsOH, methanol, reflux, 18 h), the trans isomer **24** gave a 9:1 mixture of the expected **28** and a rearrangement product, lactone **29**, in 79% combined yield, while the cis isomer **25** provided exclusively the expected keto ester **30** (82% yield). The formation of the rearranged product **29** could result from hydrolysis of **24**, followed by hydride transfer and lactonization to give **29**. To establish the generality of these results both with respect to the stereoselectivity of the photocycloaddition and the unusual acid fragmentation product, the irradiation of dioxenone photosubstrates **22** and **23**, derived from cyclooctanone and cyclodecanone, respectively, was next examined.

Irradiation of **22** (9 mM in degassed $CH_3CN/(CH_3)_2CO$, 450-W medium-pressure Hg lamp, Pyrex immersion well, 0 °C, 2 h) led to the formation of a single photoadduct **31** in 82% yield, which on basic fragmentation as described above gave *exclusively* the cis-bridged keto acid **32** in 80% yield. Barton decarboxylation then led to the formation of the cis-bridged bicyclo[7.3.1]tridecan-13-one **33** (60% yield). In an effort to determine whether the cis stereochemistry was established in the photocycloaddition or was a consequence of epimerization under the basic fragmentation conditions, the acid fragmentation of **31** was examined. However, treatment of **31** with catalytic *p*-toluenesulfonic acid in methanol (reflux, 18 h, 76% yield) led to the exclusive formation of the rearranged lactone, **34** (IR (film) 1770 cm^{-1}). Recourse to reductive fragmentation of **31** using DIBAL-H[10] led to the formation of the keto aldehyde, **35**, which was submitted without purification to reduction ($LiAlH_4$, THF, 10 h, 25 °C)[21] and oxidation (PDC, DMF, 25 °C, 16 h), to give the trans-bridged keto acid, **36** (48% overall yield from **31**). Exposure of **36** to the basic fragmentation conditions (2 N KOH, MeOH, 25 °C, 18 h, 90% yield) led to the formation of material that was identical with **32**, the product of fragmentation of photoadduct **31** under basic conditions, *demonstrating that bicyclo[7.3.1]tridecan-13-one is the smallest [n.3.1]bicyclic ring system in which epimerization of trans to cis intrabridgehead stereochemistry can be observed.*

Similar results were observed in the ten-membered ring series. Irradiation of **23** (10 mM in degassed $CH_3CN/(CH_3)_2CO$ (9:1), 450-W medium-pressure Hg lamp, Pyrex immersion well, 0 °C, 3 h) produced photoadduct **37** in 80% yield, which was directly submitted to the basic fragmentation conditions (2 N KOH, MeOH, 25 °C, 18 h) to provide the cis keto acid **38** in 83% yield. Barton decarboxylation of **38** gave *cis*-bicyclo[9.3.1]pentadecan-15-one **39** (63% overall yield). The nine-line ^{13}C NMR spectrum of **39** is consistent with the assignment of cis intrabridgehead stereochemistry, as is the C_{15}–H singlet that is observed in the 500-MHz ^1H NMR spectrum for the carbinol obtained from **39** on LAH reduction. Acid hydrolysis of photoadduct **37** led once again to the exclusive formation of the rearranged lactone **40**[22] in 72% yield.

Another significant difference between the results of this study and our earlier work[23] is the behavior of the photoadducts on acidic fragmentation, which can be attributed to the inherent difference in the stabilities of A and B (Scheme V). As a consequence of the trans-fusion of the bicyclo[4.2.0]octane moiety, the R group in A is pseudoaxial, while it is pseudoequatorial in B. When the starting ring size is small, i.e., a six-membered ring in the case of bicyclo[5.3.1]undecan-11-one, the tether between R and R′ is too short for the hydride shift, which would lead to the formation of two trans-fused bicyclo[4.2.0]octane moieties. However, when the size of the tether between R and R′ increases, the rearrangement becomes a competing pathway in the case of **24** and the exclusive pathway in the case of **31** and **37**.

Scheme V

A B

Conclusion

With the exception of the preparation of *cis*-bicyclo[4.3.1]decan-10-one, the intramolecular dioxenone photocycloaddition leads to the selective formation of the trans-fused photoadducts, which can be fragmented to bicyclic bicyclo[*n*.3.1]alkanes with a trans or "inside–outside" intrabridgehead stereochemical relationship. In contrast to our earlier results with bicyclo[4.3.1]- and bicyclo[5.3.1]alkanones and the lack of equilibration reported herein for the bicyclo[6.3.1]dodecane ring system, i.e., **26** and **27**, the isomerization of **36** to **32** does occur and establishes that *trans*-bicyclo[7.3.1]tridecan-13-one is the smallest [*n*.3.1] "inside–outside" bicyclic ring system in which equilibration via ketone enolization is possible. Further structural studies on *trans*-bicyclo[6.3.1]dodecan-12-one and bicyclo[7.3.1]tridecan-13-one are underway and will be reported in due course.

Experimental Section

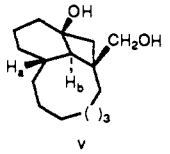
All solvents were reagent grade. Anhydrous tetrahydrofuran (THF) was distilled from sodium. Organolithium reagents were obtained from Aldrich and standardized by titration with diphenylacetic acid. Merck precoated silica gel plates (250 μm) with fluorescent indicator were used for analytical TLC. Merck silica gel 60 (particle size 0.04–0.063 mm) was employed for flash chromatography. Melting points were obtained on a Thomas-Hoover capillary melting point apparatus and are uncorrected. Infrared spectra were recorded on either an FT Nicolet SX-20 or a Perkin-Elmer Model 281B spectrophotometer. NMR spectra were measured with either Bruker AM-500 (500 MHz) or GE OMEGA-300 (300 MHz) spectrometers. ^{13}C chemical shifts are reported in δ values (parts per million) relative to chloroform (δ $CDCl_3$ = 77.0). Most of the ^{13}C spectra have been studied by APT (attached proton test) to determine the number of protons attached to each carbon. High-resolution mass spectra were obtained with a VG Micromass 7070H high-resolution chemical ionization spectrometer connected to a Kratos DS-50-S data system.

***tert*-Butyl 3-(4′-Pentenyl)-2-oxocyclohexanecarboxylate (2).** A solution of 2.968 g of *tert*-butyl 2-oxocyclohexanecarboxylate in 5 mL of dry THF was added dropwise to a slurry of 0.812 g of NaH (50% in oil, 1.1 equiv) in 30 mL of THF at 0 °C under a nitrogen atmosphere. The resulting mixture was stirred for 10 min at 0 °C and then treated with 2.43 M *n*-BuLi (1.05 equiv), added dropwise. After 10 min of additional stirring at 0 °C, the pale yellow reaction mixture was treated with 2.87 mL of HMPA (1.1 equiv). After another 10 min of additional stirring at 0 °C, the mixture was treated with a solution of 3.242 g of 4-pentenyl iodide in THF (1.1 equiv). The reaction mixture was warmed to 25 °C with stirring for 3 h. The resulting solution was poured into a pH 7 aqueous phosphate buffer and extracted with diethyl ether. The combined organic layers were washed with water, dried over $MgSO_4$, concentrated, and purified by chromatography to give 3.562 g of keto ester **2** (89%). IR (neat) 2978, 2935, 2862, 1738, 1714, 1641, 1393, 1368, 1314, 1255. 1237, 1160 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.50 (s, 9 H), 4.99 (m, 2 H), 5.82 (m, 1 H); MS 267, 253, 225, 211, 193, 165, 155, 142, 117.

5,6,7,8-Tetrahydro-2,2-dimethyl-8-(4′-pentenyl)-4*H*-1,3-benzodioxin-4-one (3). A solution of 857 mg of keto ester **2**, 11.8 mL of acetone (50 equiv), 0.91 mL of trifluoroacetic anhydride (2 equiv), and 6.20 mL of trifluoroacetic acid (25 equiv) was stirred at 25 °C under a nitrogen

(21) The trans intrabridgehead stereochemistry could be established by analysis of the ^1H NMR spectrum of the diol, as the C-13 carbinol methine showed 2.4- and 10.9-Hz coupling constants to the two bridgehead methines (see ref 20).

(22) The assigned structures of lactones **29**, **34**, and **40** were consistent with ^1H and ^{13}C NMR, including APT and HETCOR experiments. The relative stereochemistries were assigned on the basis of v, the reduction product of **40** ($LiAlH_4$, THF, 12 h, 25 °C), which showed a 17% NOE difference for one of the methylenes of the CH_2OH on irradiation of H_a and the absence of any effect on irradiation of H_b. In addition, the appearance of H_b as a clean doublet (J = 10 Hz) is also consistent with the trans,trans stereochemistry indicated in the lactone structures.



v

(23) For another dioxanone photoadduct fragmentation pathway, see: Winkler, J.; Hey, J.; Darling, S. *Tetrahedron Lett.* **1986**, 5959.

atmosphere for 24 h. The solution was concentrated to provide 924 mg of crude material, which was purified by chromatography with 10% ethyl acetate in petroleum ether (R_f = 0.30) to give 473 mg of dioxenone **3** (59% yield): IR (neat) 2939, 2862, 1727, 1644, 1398, 1389, 1370, 1303, 1268, 1206, 1152 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.80–1.80 (m, 9 H), 1.66 (s, 3 H), 1.67 (s, 3 H), 1.90–2.30 (m, 4 H), 4.90–5.00 (m, 2 H), 5.70–5.82 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ 19.56 (CH_2), 21.72 (CH_2), 24.83 (CH_3), 25.55 (CH_3), 26.46 (CH_2), 26.91 (CH_2), 30.79 (CH_2), 33.70 (CH_2), 36.95 (CH), 102.42 (C), 105.93 (C), 114.51 (CH_2), 138.34 (CH), 162.00 (C), 167.25 (C); MS (*m/z*, relative intensity) 250 (M^+, 4), 234 (2), 192 (87), 151 (13), 137 (83), 124 (100), 111 (20); exact mass calcd for $C_{15}H_{22}O_3$ 250.1569, found 250.1574.

The same procedure was followed for the synthesis of dioxenone **12**, which was prepared in 48% overall yield from *tert*-butyl 2-oxocyclopentanecarboxylate: IR (neat) 2960, 2880, 1738, 1645, 1418, 1201, 1389, 1377, 1147 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.15–1.60 (m, 4 H), 1.55 (s, 3 H), 1.56 (s, 3 H), 1.88–2.08 (m, 4 H), 2.30–2.42 (m, 2 H), 2.60–2.68 (m, 1 H), 4.78–4.92 (m, 2 H), 5.58–5.68 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ 24.11 (CH_2), 24.56 (CH_3), 25.21 (CH_3), 25.90 (CH_2), 26.18 (CH_2), 31.12 (CH_2), 33.31 (CH_2), 43.26 (CH), 102.28 (C), 107.88 (C), 114.48 (CH_2), 137.93 (CH), 160.04 (C), 173.37 (C); MS (*m/z*, relative intensity) 236 (M^+, 0.5), 178 (51), 150 (11), 123 (34), 110 (100); exact mass calcd for $C_{14}H_{20}O_3$ 236.1412, found 236.1434.

(1*S,2*S**,6*S*,10*R**)-13,13-Dimethyl-12,14-dioxatetracyclo[8.4.0.1^{2,10}.0^{1,6}]pentadecan-11-one (4).** A solution of 360 mg of dioxenone **3** (1.44 mmol) in 300 mL of 9:1 acetonitrile/acetone was degassed with nitrogen, cooled to 0 °C, and irradiated through a Pyrex filter for 2 h. The solution was concentrated and purified by flash chromatography using 10% ethyl acetate/petroleum ether to provide 325 mg of photoadduct **4** (90% yield): IR (neat) 2940, 2860, 1736, 1261 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.10–1.75 (m, 7 H), 1.68 (s, 6 H), 1.80–1.95 (m, 3 H), 2.00–2.05 (m, 2 H), 2.08–2.15 (m, 1 H), 2.52 (dd, J = 4, 5 Hz, 1 H), 2.58–2.65 (m, 1 H), 2.85–2.92 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ 22.32 (CH_2), 22.47 (CH_2), 24.24 (CH_2), 26.04 (CH_2), 27.97 (CH_2), 29.86 (CH_2), 30.38 (CH_3), 30.60 (CH_3), 35.21 (CH), 35.25 (CH), 37.00 (CH_2), 44.03 (C), 80.49 (C), 106.41 (C), 173.50 (C); MS (CI, *m/z*, relative intensity) 250 (M^+, 0.2), 192 (27), 164 (4), 137 (36), 124 (100), 105 (5); exact mass calcd for $C_{15}H_{22}O_3$ 250.1569, found 250.1563.

(1*R,3*R**,7*R**)-Methyl 11-Oxobicyclo[5.3.1]undecane-3-carboxylate (5).** A solution of 1.308 g of photoadduct **4** (5.23 mmol) and 36 mg of *p*-TsOH (0.04 equiv) in 40 mL of methanol was heated at reflux for 18 h. The solution was concentrated and purified by flash column chromatography with 20% ethyl acetate in petroleum ether to provide 813 mg of keto ester **5** (80% yield): IR (neat) 2960, 2880, 1725, 1430, 1180 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.35–2.10 (m, 14 H), 2.35–2.44 (m, 1 H), 2.50–2.58 (m, 1 H), 3.34–3.42 (m, 1 H), 3.65 (s, 3 H); MS (*m/z*, relative intensity) 224 (M^+, 30), 192 (36), 164 (100), 156 (31), 136 (30), 122 (22), 109 (20); exact mass calcd for $C_{13}H_{20}O_3$ 224.1412, found 224.1414.

(1*R,3*R**,7*R**)-3-Carboxybicyclo[5.3.1]undecan-11-one (6).** A solution of 982 mg of keto ester **5** (4.38 mmol) and 480 mg of LiOH in 50 mL of methanol was stirred at 25 °C for 10 h. The solution was diluted with diethyl ether, acidified with HCl, extracted with methylene chloride, dried over magnesium sulfate, and purified by flash column chromatography to give 737 mg of keto acid **6** (80% yield). The keto acid **6** was also obtained in 90% yield on exposure of photoadduct **4** to 2 N KOH in methanol at 25 °C for 18 h followed by acidification and extractive isolation: IR (neat) 3000–3400, 2960, 2880, 1705, 1725, 1460, 1420 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.30–2.20 (m, 13 H), 2.30–2.42 (m 1 H), 2.50–2.60 (m, 2 H), 3.30–3.40 (m, 1 H); MS (*m/z*, relative intensity) 210 (M^+, 100), 192 (54), 164 (72), 149 (30), 136 (36), 122 (34), 109 (52). A crystal of **6** suitable for x-ray crystallographic analysis was obtained by slow evaporation of a methanol solution of **6**.

***trans*-Bicyclo[5.3.1]undecan-11-one (10).** To a solution of 219 mg of keto acid **6** (1.04 mmol) in 25 mL of benzene was added 1 mL of oxalyl chloride. The reaction flask was then charged with nitrogen, and 50 μL of dimethylformamide was added. The resulting solution was stirred for 1 h at 25 °C and then evaporated under reduced pressure. The crude acid chloride was dissolved in 10 mL of toluene and added dropwise to a refluxing slurry of 185 mg of the sodium salt of 2-mercaptopyridine *N*-oxide (1.2 equiv), 14 mg of DMAP (1 equiv), and 2 mL of *tert*-butyl mercaptan in 10 mL of toluene. After refluxing for 1.5 h, the solution was cooled and extracted with aqueous sodium bicarbonate, 1 N aqueous HCl, and water. The organic layers were evaporated and purified by flash column chromatography with 5% THF in petroleum ether to give 110 mg of ketone **10** (64% yield): IR (neat) 2930, 2860, 1728, 1457, 1441 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.00–2.10 (m, 16 H), 2.35–2.42 (m, 1 H), 3.20–3.30 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ 23.8, 24.2, 28.5, 28.8, 29.1, 33.4, 34.6, 34.7, 46.9, 51.2, 222.4; MS (*m/z*, relative intensity) 166 (M^+, 51), 123 (19), 111 (70), 98 (100); exact mass calcd for $C_{11}H_{18}O$ 166.1358, found 166.1354.

12,12-Dimethyl-11,13-dioxatetracyclo[7.4.0.1^{2,9}.0^{1,6}]tetradecan-10-one (13 and 14). A solution of 501 mg of dioxenone **12** (2.12 mmol) in 300 mL of 9:1 acetonitrile/acetone was degassed for 20 min and photolyzed at 0 °C in a small, Pyrex immersion well with a 450-W Hanovia mercury vapor lamp for 1.5 h. The solution was concentrated and purified by flash chromatography (R_f = 0.32, 0.26 in 10% ethyl acetate/hexane) to give 61 mg of trans photoadduct **13** and 115 mg of cis photoadduct **14** (12% and 23%, respectively). These yields varied from run to run because **14** appeared to be unstable to silica gel. The yields and relative ratios of photoadducts **13** and **14** are more accurately reflected in the results of the following fragmentation reaction. A mixture of 322 mg of crude photoadducts (**13** and **14**) and 15 mg of *p*-TsOH in 15 mL of methanol was heated at reflux for 24 h. The solution was concentrated and purified by chromatography to give 235 mg of a mixture of the trans and cis keto esters (**15** and **16**) in a ratio of 1:5 by NMR integration of the methyl esters (65% overall yield for the two steps). Thus, the ratio of trans to cis photoadducts was actually 1:5. This ratio was also confirmed by ^{1}H NMR analysis of the crude photoadduct. *trans*-**13** (1*S**,2*S**,6*S**,9*R**): IR (neat) 2950, 2880, 1750, 1375, 1330, 1290 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.20–1.82 (m, 10 H), 1.49 (s, 3 H), 1.58 (s, 3 H), 2.15–2.50 (m, 4 H); ^{13}C NMR ($CDCl_3$) δ 19.55 (CH_2), 20.90 (CH_2), 26.98 (CH_2), 28.85 (CH_3), 29.38 (CH_3), 30.88 (CH_2), 32.66 (CH_2), 33.66 (CH), 40.06 (CH), 40.73 (CH_2), 45.64 (C), 87.22 (C), 106.78 (C), 173.17 (C). *cis*-**14** (1*S**,2*R**,6*S**,9*R**): IR (neat) 2950, 2880, 1750, 1375, 1330, 1290 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.40–1.76 (m, 7 H), 1.62 (s, 3 H), 1.64 (s, 3 H), 1.95–2.18 (m, 4 H), 2.28–2.38 (m, 1 H), 2.45–2.62 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 13.50 (CH_2), 23.56 (CH_2), 23.67 (CH_2), 26.38 (CH_2), 27.15 (CH_2), 27.97 (CH_3), 29.78 (CH_3), 34.47 (CH_2), 35.82 (CH), 42.44 (CH), 45.64 (C), 81.03 (C), 106.62 (C), 173.47 (C); MS (*m/z*, relative intensity) 236 (M^+, 0.3), 178 (41), 150 (7), 134 (5), 123 (31), 110 (100).

(1*R,3*R**,6*R**)-Methyl 10-Oxobicyclo[4.3.1]decane-3-carboxylate (15).** A solution of 144 mg of trans photoadduct **13** (0.61 mmol) and 15 mg of *p*-TsOH (0.08 mmol, 0.13 equiv) in 15 mL of methanol was heated at reflux for 24 h. The solution was concentrated and purified by flash column chromatography with 10% ethyl acetate in petroleum ether (R_f = 0.90 in 30% ethyl acetate/petroleum ether) to give 107 mg of keto ester **15** (84% yield): IR (neat) 2960, 2870, 1711, 1398, 1312, 1243, 1220, 1189 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.40–1.60 (m, 3 H), 1.70–1.85 (m, 4 H), 2.10–2.20 (m, 4 H), 2.30–2.40 (m, 2 H), 2.65 (dd, J = 10, 12 Hz, 1 H), 2.75 (br s, 1 H), 3.71 (s, 3 H); MS (*m/z* relative intensity) 210 (M^+, 5), 192 (3), 178 (25), 155 (36), 142 (53), 133 (15), 123 (58), 110 (100).

(1*R,3*R**,6*R**)-3-Carboxybicyclo[4.3.1]decan-10-one (17).** A solution of 900 mg of keto ester **15** (4.3 mmol) and 300 mg of LiOH in 50 mL of methanol was stirred at 25 °C for 24 h. The solution was acidified with 1 N HCl, extracted with diethyl ether, washed with water, dried over magnesium sulfate, and purified by flash chromatography to yield 773 mg of keto acid **17** (92%). The keto acid **17** could also be obtained directly in 90% yield by the reaction of trans photoadduct **13** with 2 N KOH in methanol at 25 °C for 18 h, followed by acidification and extractive isolation: IR (neat) 3000–3500, 2960, 2880, 1742, 1705, 1460, 1420, 1280, 1270, 1190 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.35–2.10 (m, 9 H), 2.12–2.22 (m, 1 H), 2.28–2.35 (m, 1 H), 2.38–2.48 (m, 2 H), 2.50–2.54 (m, 1 H), 2.88–2.98 (m, 1 H); MS (*m/z*, relative intensity) 196 (M^+, 43), 150 (40), 133 (31), 123 (65), 108 (52), 95 (100). A crystal of **17** suitable for x-ray crystallographic analysis was obtained by slow evaporation of a methanol solution of **17** at 25 °C.

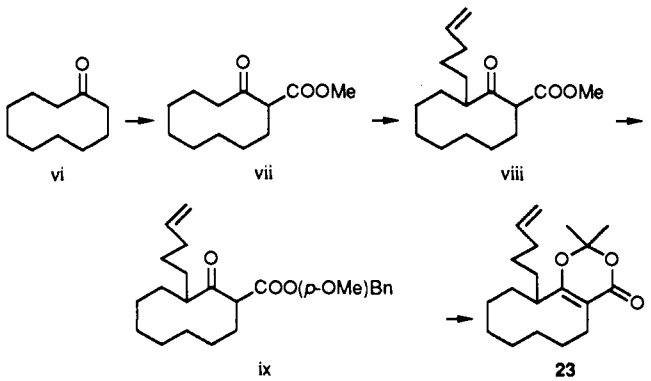
***trans*-Bicyclo[4.3.1]decan-10-one (19).** To 650 mg of keto acid **17** (3.32 mmol) in 10 mL of benzene was added 2 mL of oxalyl chloride at 25 °C with stirring. The reaction flask was charged under nitrogen and treated with 10 μL of DMF. The reaction was stirred at 25 °C for 1 h and then evaporated under reduced pressure to remove excess reagents. The resulting crude acid chloride was taken up directly in 10 mL of toluene and added dropwise to a refluxing slurry of 951 mg of the sodium salt of 2-mercaptopyridine *N*-oxide (6.38 mmol, 1.9 equiv), 31 mg of DMAP (0.08 equiv), and 1.40 mL of *tert*-butyl mercaptan in 10 mL of toluene. After refluxing for 1.5 h, the solution was cooled and extracted with aqueous sodium bicarbonate, 1 N aqueous HCl, and water. The solution was evaporated and purified by chromatography with 20% diethyl ether in pentane to give 297 mg of ketone **17** (59% yield): IR (neat) 2935, 2865, 1748, 1461, 1446, 1376 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.15–2.00 (m, 12 H), 2.20–2.30 (m, 2 H), 2.45–2.52 (m, 1 H), 2.92–3.02 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ 21.0, 25.5, 28.1, 29.3, 31.9, 35.0, 35.3, 49.5, 49.7, 219.1; MS (*m/z*, relative intensity) 152 (M^+, 87), 124 (13), 109 (27), 96 (100); exact mass calcd for $C_{10}H_{16}O$ 152.1201, found 152.1201.

(1*R,3*R**,6*S**)- and (1*R**,3*S**,6*S**)-Methyl 10-Oxobicyclo[4.3.1]decane-3-carboxylate (16a,b).** A solution of 115 mg of the cis photoadduct **14** (0.49 mmol) and 10 mg of *p*-TsOH (0.1 equiv) in 15 mL of methanol was heated at reflux for 24 h. The crude solution of epimeric keto esters was concentrated and purified by chromatography with 10%

ethyl acetate in petroleum ether to give 38 mg of high-R_f keto ester **16a** and 40 mg of low-R_f keto ester **16b** (76% yield). High-R_f keto ester **16a**: IR (neat) 2960, 2880, 1731, 1700, 1430, 1178, 1155 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.52–2.20 (m, 11 H), 2.22–2.35 (m, 2 H), 2.65–2.85 (m, 2 H), 3.78 (s, 3 H). Low-R_f keto ester **16b**: ^1H NMR ($CDCl_3$) δ 1.35–2.30 (m, 13 H), 2.70–2.85 (m, 2 H), 3.79 (s, 3 H); MS (*m/z*, relative intensity) 210 (M^+, 78), 178 (59), 150 (100), 133 (77), 124 (67), 111 (52); exact mass calcd for $C_{12}H_{18}O_3$ 210.1256, found 210.1272.

(1*R,3*R**,6*S**)-3-Carboxybicyclo[4.3.1]decan-10-one (18).** A solution of 320 mg of keto esters **16a,b** (1.52 mmol) and 200 mg of LiOH in 50 mL of methanol was stirred at 25 °C for 24 h. The solution was acidified with 1 N HCl, extracted with diethyl ether, washed with water, dried over magnesium sulfate, and purified by chromatography to yield 269 mg of keto acid **18** (90%). The keto acid **18** was also obtained directly from **14** in 91% yield by reaction with 2 N KOH in methanol at 25 °C for 18 h, followed by acidification and extractive workup. **18**: IR (neat) 3000–3500, 2960, 2880, 1706, 1430, 1178, 1155 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.40–1.85 (m, 10 H), 2.10–2.40 (m, 2 H), 2.75–2.80 (m, 3 H); MS (*m/z*, relative intensity) 196 (M^+, 45), 178 (10), 150 (41), 133 (34), 123 (62), 111 (100).

***cis*-Bicyclo[4.3.1]decan-10-one (20).** To 245 mg of keto acid **18** in 10 mL of benzene was added 2 mL of oxalyl chloride at 25 °C with stirring. The reaction flask was charged under nitrogen and treated with 10 μL of DMF. The reaction was stirred at 25 °C for 1 h and then evaporated under reduced pressure. The resulting crude acid chloride was taken up directly in 10 mL of toluene and added dropwise to a refluxing slurry of 358 mg of the sodium salt of 2-mercaptopyridine *N*-oxide (1.9 equiv), 12 mg of DMAP (0.1 equiv), and 0.5 mL of *tert*-butyl mercaptan in 10 mL of toluene. After refluxing for 1.5 h, the solution was cooled and extracted with aqueous sodium bicarbonate, 1 N aqueous HCl, and water. The solution was evaporated and purified by chromatography with 20% diethyl ether in pentane to give 100 mg of ketone **20** (53% yield): IR (neat) 2929, 1692, 1456, 1450 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.45–2.00 (m, 14 H), 2.70–2.76 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 19.2, 27.6, 31.4, 33.0, 48.7, 218.0 MS (*m/z*, relative intensity) 152 (M^+, 98), 124 (18), 110 (41), 98 (100); exact mass calcd for $C_{10}H_{16}O$ 152.1201, found 152.1182.



Methyl 2-Oxocyclodecanecarboxylate (vii). To a solution of 1.7 mL of diisopropylamine (10.8 mmol) in 45 mL of dry THF at −78 °C was added 4.3 mL of 2.5 M *n*-BuLi/hexane (10.8 mmol). The solution was stirred for 0.5 h at −78 °C and then treated with a solution of 1.6 g of cyclodecanone (10.4 mmol) in 30 mL of dry THF. After 30 min at −78 °C, 935 mg of methyl cyanoformate (11 mmol) was added to the reaction mixture. The solution was stirred for 3 h and warmed to 25 °C. The reaction mixture was quenched with 1 mL of H_2O, washed with saturated aqueous NaCl, dried over $MgSO_4$, and purified by flash chromatography with 2% EtOAc/hexane to give 1.77 g of keto ester vii (80% yield): IR (neat) 2928, 2857, 1750, 1709, 1643, 1608, 1475, 1439, 1372, 1325 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.21–1.50 (m, 11 H), 1.60–1.75 (m, 2 H), 2.25–2.50 (m, 3 H), 3.67 (s, 3 H), 12.82 (s, 1 H); MS (*m/z*, relative intensity) 212 (M^+, 25), 181 (54), 180 (30), 152 (100), 135 (31), 129 (39), 124 (54), 115 (43), 112 (71), 111 (61).

Methyl 2-Oxo-3-(4′-pentenyl)cyclodecanecarboxylate (viii). To a suspension of 122 mg of NaH (1.1 equiv, 60% in oil) in 50 mL of THF was added, dropwise, 590 mg of the keto ester vii (2.8 mmol) in 15 mL of THF at 0 °C under nitrogen. The solution was allowed to stir for 30 min and was then treated with 1.16 mL of 2.5 M *n*-BuLi and 0.5 mL of HMPA (added dropwise). After 45 min, 0.7 mL of 1-iodo-4-pentene in 10 mL of THF was added dropwise to the reaction mixture. The solution was stirred at 0 °C for 18 h and then warmed to 25 °C. The reaction was quenched with water, extracted with ethyl acetate, washed with brine, dried over $MgSO_4$, and purified by flash chromatography with 1% EtOAc/hexane to give 547 mg of keto ester viii (70% yield): IR (neat) 2928, 2857, 1646, 1605, 1439, 1369, 1325, 1229, 1198 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.75–2.00 (m, 18 H), 2.25–3.00 (m, 3 H), 3.64 (s, 3 H), 4.77–5.00 (m, 2 H), 5.59–5.79 (m, 1 H), 12.82 (s, 1 H); MS (*m/z*, relative intensity) 280 (M^+, 29), 212 (100), 180 (27), 169 (29), 166 (27), 152 (60), 135 (30), 111 (49), 109 (57).

***p*-Methoxybenzyl 2-Oxo-3-(4′-pentenyl)cyclodecanecarboxylate (ix).** A solution of 537 mg of viii (1.9 mmol) and 0.75 mL of *p*-methoxybenzyl alcohol (6 mmol) in 100 mL of toluene was heated at reflux under a Dean–Stark trap for 18 h. The resulting solution was evaporated under reduced pressure and purified by flash column chromatography with 3% ethyl acetate/hexane to give 646 mg of keto ester ix (87% yield): IR (neat) 2930, 2858, 1748, 1706, 1642, 1607, 1516, 1472, 1443, 1367, 1324, 1228 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.50–2.90 (m, 20 H), 3.35–3.45 (m, 1 H), 4.21 (s, 3 H), 5.27–5.48 (m, 2 H), 5.50–5.60 (m, 2 H), 6.08–6.25 (m, 1 H), 7.20–7.30 (m, 2 H), 7.60–7.75 (m, 2 H), 13.35 (s, 1 H); MS (*m/z*, relative intensity) 386 (M^+, 37), 358 (6), 339 (2), 318 (5), 265 (4), 249 (5), 222 (100), 137 (83).

13,13-Dimethyl-12,14-dioxa-2-(4′-pentenyl)bicyclo[8.4.0]tetradec-1-(10)-en-11-one (23). A solution of 600 mg of keto ester ix (1.55 mmol) in 10 mL of acetone was cooled to −78 °C under N_2 pressure and treated with 10 mL of trifluoroacetic anhydride and 10 mL of trifluoroacetic acid (added dropwise). The reaction mixture was warmed to 25 °C over 18 h. The resulting mixture was added dropwise to a cold solution of saturated aqueous $NaHCO_3$. The aqueous solution was determined to be basic by pH paper and was then extracted with ethyl acetate and purified by flash column chromatography with 4% ethyl acetate/hexane (R_f = 0.44 in 10% EtOAc/hexane) to yield 238 mg of dioxenone **23** (50% yield): IR (neat) 2928, 2857, 1724, 1626, 1383, 1336, 1265, 1205, 1130 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.20–1.55 (m, 13 H), 1.60–1.75 (m, 2 H), 1.62 (s, 3 H), 1.68 (s, 3 H), 1.80–2.10 (m, 3 H), 2.25–2.40 (m, 1 H), 2.50–2.60 (m, 1 H), 2.90–3.05 (m, 1 H), 4.90–5.05 (m, 2 H), 5.65–5.80 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ 20.83 (CH_2), 21.42 (CH_2), 22.61 (CH_2), 25.00 (CH_2), 25.25 (CH_2 and CH_3), 25.83 (CH_3), 26.70 (CH_2), 27.64 (CH_2), 33.02 (CH_2), 33.08 (CH_2), 33.68 (CH_2), 39.24 (CH), 104.32 (C), 104.60 (C), 114.77 (CH_2), 138.32 (CH), 161.81 (C), 168.18; MS (*m/z*, relative intensity) 306 (M^+, 0.8), 248 (50), 220 (21), 180 (35), 135 (100), 123 (56); exact mass calcd for $C_{19}H_{30}O_3$ 306.2195, found 306.2173.

The same procedure was followed for the syntheses of dioxenones **21** and **22**. **21**: IR (neat) 2960, 2880, 1740, 1650, 1450, 1400, 1385, 1320, 1280, 1215, 1155 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.10–1.78 (m, 10 H), 1.58 (s, 3 H), 1.60 (s, 3 H), 1.96–2.04 (m, 2 H), 2.30–2.40 (m, 2 H), 2.45–2.50 (m, 1 H), 4.88–4.98 (m, 2 H), 5.68–5.80 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ 22.30 (CH_2), 24.29 (CH_3), 25.40 (CH_3), 26.37 (CH_2), 26.50 (CH_2), 26.69 (CH_2), 28.54 (CH_2), 29.08 (CH_2), 33.49 (CH_2), 43.07 (CH), 104.44 (C), 105.39 (C), 114.65 (CH_2), 138.20 (CH), 162.88 (C), 171.18; MS (*m/z*, relative intensity) 265 (M^+ + H, 95), 206 (65), 138 (100); exact mass calcd for $C_{16}H_{24}O_3$ 264.1725, found 264.1703. **22**: IR (neat) 2960, 2880, 1735, 1645, 1455, 1400, 1380, 1340, 1270, 1110 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.70–1.70 (m, 14 H), 1.64 (s, 6 H), 1.95–2.05 (m, 2 H), 2.72–2.80 (m, 1 H), 4.90–5.00 (m, 2 H), 5.70–5.82 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ 24.30 (CH_2), 24.65 (CH_3), 25.67 (CH_2), 25.98 (CH_3), 27.09 (CH_2), 27.35 (CH_2), 30.41 (CH_2), 30.67 (CH_2), 33.71 (CH_2), 35.10 (CH_2), 38.53 (CH), 104.76 (C), 105.45 (C), 114.71 (CH_2), 138.42 (CH), 162.00 (C), 168.06; MS (*m/z*, relative intensity) 278 (100, M^+), 219 (17), 186 (10), 162 (20); exact mass calcd for $C_{17}H_{26}O_3$ 278.1882, found 278.1883.

14,14-Dimethyl-13,15-dioxatetracyclo[9.4.0.0^{1,11}.0^{1,6}]hexadecan-12-one (24 and 25). A solution of 600 mg of dioxenone **21** (2.27 mmol) in 250 mL of acetonitrile/acetone (7:3) was degassed for 0.5 h, and the resulting solution was irradiated through a Pyrex filter at 0 °C for 2 h. The solution was concentrated and purified by flash column chromatography with 5% EtOAc/hexane (**24**; R_f = 0.77; **25**; R_f = 0.72 in 30% EtOAc/hexane) to give 490 mg of **24** and **25** (82% yield, ratio of **24** to **25** is ca. 4.5 to 1 based on ^1H NMR). ***trans*-24 (1*S**,2*S**,6*R**,11*R**)**: IR (neat) 2960, 2880, 1750, 1465, 1395, 1380, 1320, 1285, 1260 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.00–1.98 (m, 13 H), 1.52 (s, 3 H), 1.63 (s, 3 H), 2.05–2.18 (m, 2 H), 2.30–2.52 (m, 2 H), 2.68–2.82 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ 20.73 (CH_2), 23.89 (CH_2), 25.21 (CH_2), 26.85 (CH_2), 29.52 (CH_3), 30.25 (CH_2), 31.05 (CH_2), 32.02 (CH_3), 34.01 (CH_2), 37.46 (CH), 37.55 (CH), 37.71 (CH_2), 50.52 (C), 79.27 (C), 106.78 (C), 176.11; MS (*m/z*, relative intensity) 265 (M^+ + H, 2), 224 (50), 207 (100), 178 (10), 138 (32); exact mass calcd for $C_{16}H_{24}O_3$ 264.1725, found 264.1742. ***cis*-25 (1*S**,2*R**,6*R**,11*R**)**: ^1H NMR ($CDCl_3$) δ 1.10–2.00 (m, 13 H), 1.58 (s, 3 H), 1.66 (s, 3 H), 2.30–2.42 (m, 3 H), 2.46–2.55 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 23.46 (CH_2), 26.10 (CH_2), 27.39 (CH_2), 27.94 (CH_2), 30.09 (CH_2), 30.20 (CH_2), 30.47 (CH_2), 30.60 (CH_3), 30.59 (CH_3), 38.26 (CH_2), 43.54 (CH), 47.71 (C), 50.99 (CH), 82.78 (C), 104.91 (C), 171.94.

(1*R,3*R**,8*S**)- and (1*R**,3*S**,8*S**)-3-Carboxybicyclo[6.3.1]dodecan-12-one (26).** A solution of 95 mg of photoadduct **24** (0.36 mmol) in 10 mL of 2 N KOH/MeOH was stirred at 25 °C for 18 h. The

reaction was diluted with water and extracted with 40 mL of ethyl acetate. The organic layers were washed with 2 N aqueous HCl, dried over $MgSO_4$, and purified by flash column chromatography with 50% ethyl acetate/hexane (R_f = 0.09 in 30% ethyl acetate/hexane) to give 70 mg of keto acid **26** (87% yield): IR (neat) 3000–3500, 2960, 2900, 1720, 1470 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.95–2.15 (m, 12 H), 2.18–2.32 (m, 2 H), 2.52–2.64 (m, 3 H), 2.95–3.02 (m, 1 H), 3.16–3.22 (m, 1 H); ^{13}C NMR ($CDCl_3$) (revealed the presence of two isomers in an ca. 1:1 ratio) δ 20.51 (CH_2), 22.47 (CH_2), 22.99 (CH_2), 24.83 (2C of CH_2), 25.16 (CH_2), 27.12 (CH_2), 28.19 (CH_2), 30.78 (CH_2), 32.66 (CH_2), 32.80 (CH_2), 33.81 (CH_2), 34.06 (CH_2), 34.32 (CH_2), 35.04 (CH_2), 38.07 (CH_2), 43.27 (CH), 43.96 (CH), 44.68 (CH), 45.66 (CH), 48.82 (CH), 51.82 (CH), 181.75 (OC=O), 181.93 (OC=O), 220.59, 220.81; MS (m/z, relative intensity) 242 ($M^+ + NH_4$, 100), 225 (82), 207 (85), 178 (16), 161 (21); exact mass calcd for $C_{13}H_{20}O_3$ 224.1412, found 224.1440.

(1*R,3*R**,8*R**)- and (1*R**,3*S**,8*R**)-3-Carboxybicyclo[6.3.1]dodecan-12-one (27).** A solution of 50 mg of photoadduct **25** (0.19 mmol) in 10 mL of 2 N KOH/MeOH was stirred at 25 °C for 18 h. The reaction mixture was then diluted with water and extracted with 40 mL of ethyl acetate. The organic solution was washed with 2 N aqueous HCl, dried over $MgSO_4$, and purified by flash column chromatography with 50% EtOAc/hexane (R_f = 0.18 in 50% EtOAc/hexane) to give 37 mg of keto acid (87% yield): IR (neat) 3000–3500, 2960, 2880, 1720, 1705, 1470 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.05–2.25 (m, 16 H), 2.45–2.75 (m, 3 H); ^{13}C NMR ($CDCl_3$) (revealed the presence of two isomers in an ca. 1:1 ratio) δ 16.67 (CH_2), 17.24 (CH_2), 24.03 (CH_2), 26.29 (CH_2). 26.40 (CH_2). 27.07 (CH_2), 27.43 (CH_2), 28.75 (CH_2), 31.82 (CH_2), 32.84 (CH_2), 33.57 (CH_2), 33.82 (CH_2), 34.07 (CH_2), 34.57 (CH_2), 35.24 (CH_2), 35.70 (CH_2), 43.54 (CH), 43.90 (CH), 48.19 (CH), 52.01 (CH), 52.40 (CH), 53.01 (CH), 180.86 (OC=O), 182.09 (OC=O). 221.35 (2 C of C=O).

(1*R,3*R**,8*S**)-Methyl 12-Oxobicyclo[6.3.1]dodecane-3-carboxylate (28) and (1*S**,5*R**,10*R**,13*R**)-12-Oxatetracyclo[8.2.1.1.0^{5,13}]tetradecan-11-one (29).** A solution of 83 mg of photoadduct **24** (0.31 mmol) and 5 mg of *p*-TsOH in 30 mL of methanol was heated at reflux for 18 h. The methanol was evaporated and the residue was purified by flash column chromatography with 15% EtOAc/hexane (**28**; R_f = 0.05; **29**; R_f = 0.18 in 10% EtOAc/hexane) to give of 53 mg of **28** (71%) and 5 mg of **29** (8%). **28**: IR (neat) 2950, 2880, 1745, 1720, 1455, 1200 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.02–1.30 (m, 3 H), 1.35–1.54 (m, 3 H), 1.60–2.20 (m, 10 H), 2.58–2.65 (m, 2 H), 3.00–3.08 (m, 1 H), 3.64 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 20.57 (CH_2), 25.11 (CH_2), 25.67 (CH_2), 27.36 (CH_2), 30.68 (CH_2), 32.58 (CH_2), 33.12 (CH_2), 34.35 (CH_2), 43.53 (CH), 44.03 (CH), 49.07 (CH_3), 51.84 (CH), 176.50, 220.18; MS (m/z, relative intensity) 256 ($M^+ + NH_4$), 239 ($M^+ + H$), 207 (40), 160 (15); exact mass calcd for $C_{14}H_{22}O_3$ 238.1569, found 238.1583. **29**: IR (neat) 2960, 2880, 1770, 1460 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.20–2.18 (m, 15 H), 2.20–2.32 (m, 1 H), 2.32–2.40 (m, 1 H), 2.67 (d, J = 8.9 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ 18.82 (CH_2). 22.39 (CH_2), 23.50 (CH_2), 25.26 (CH_2), 26.43 (CH_2), 27.27 (CH), 32.27 (CH_2), 37.04 (CH_2), 40.53 (CH_2), 42.43 (CH), 50.74 (C), 86.14 (C), 185.47 (C); MS (relative intensity) 206 (M^+, 45), 188 (29), 161 (21), 151 (76), 138 (44), 133 (53), 109 (100); exact mass calcd for $C_{13}H_{18}O_2$ 206.1307, found 206.1324.

(1*R,3*R**,8*R**)-Methyl 12-Oxobicyclo[6.3.1]dodecane-3-carboxylate (30).** A solution of 27 mg of **25** (0.10 mmol) and 5 mg of *p*-TsOH in 20 mL of methanol was heated at reflux for 18 h. The methanol was evaporated, and the residue was purified by flash column chromatography with 10% ethyl acetate/hexane (R_f = 0.15 in 10% EtOAc/hexane) to give 20 mg of **30** (82%): IR (neat) 2950, 2880, 1750, 1705, 1480, 1450 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.08–1.26 (m, 1 H), 1.32–1.64 (m, 4 H), 1.75–2.10 (m, 10 H), 2.45–2.65 (m, 4 H), 3.66 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 17.43 (CH_2), 26.28 (CH_2), 26.42 (CH_2), 27.44 (CH_2). 32.21 (CH_2), 33.76 (CH_2), 33.99 (CH_2), 34.46 (CH_2), 43.62 (CH), 48.38 (CH_3), 51.68 (CH), 52.42 (CH), 175.29, 220.83; MS (m/z, relative intensity) 238 (M^+, 20), 206 (75), 160 (100), 152 (93), 121 (73).

(1*S,2*S**,6*R**,12*R**)-15,15-Dimethyl-14,16-dioxatetracyclo[10.4.0.1^{2,12}.0^{1,6}]heptadecan-13-one (31).** A solution of 600 mg of dioxenone **22** (2.16 mmol) in 250 mL of acetonitrile/acetone (9:1) was degassed for 0.5 h and then irradiated through a Pyrex filter at 0 °C for 2 h. The solution was concentrated and purified by flash chromatography with 3% ethyl acetate/hexane (R_f = 0.30 in 10% EtOAc/hexane) to give 490 mg of photoadduct **31** (82% yield): IR (neat) 2940, 2860, 1742, 1455, 1385, 1330, 1290, 1245 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.70–1.80 (m, 14 H), 1.58 (s, 3 H), 1.69 (s, 3 H), 1.85–1.96 (m, 3 H), 2.15–2.24 (m, 1 H), 2.26–2.32 (m, 1 H), 2.51 (dd, J = 10.5, 11.4 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ 22.26 (CH_2), 24.97 (CH_2), 25.61 (CH_2), 26.04 (CH_2). 27.38 (CH_2), 28.46 (CH_2), 30.51 (CH_3). 30.72 (CH_2), 31.56 (CH_3), 31.91 (CH_2), 41.00 (CH_2), 41.74 (CH), 43.38 (CH), 47.17 (C), 82.61 (C), 106.10 (C), 169.09; MS (m/z, relative intensity) 279 ($M^+ + H$, 16), 221 (100), 175 (53).

(1*S,3*R**,9*R**)-3-Carboxybicyclo[7.3.1]tridecan-13-one (32).** A solution of 175 mg of photoadduct **31** (0.63 mmol) in 10 mL of 2 N KOH/MeOH was stirred at 25 °C for 18 h. The reaction was diluted with water and extracted with 40 mL of ethyl acetate. The organic layers were washed with 2 N aqueous HCl, dried over $MgSO_4$, and purified by flash column chromatography with 40% ethyl acetate/hexane (R_f = 0.41 in 50% EtOAc/hexane) to give 120 mg of keto acid **32** (80% yield): mp 190–191 °C; IR (neat) 3000–3500, 2960, 2880, 1720, 1705, 1300 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.70–2.10 (m, 18 H), 2.28–2.48 (m, 1 H), 2.72–2.88 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 25.00 (CH_2), 26.15 (CH_2), 27.55 (CH_2), 28.40 (CH_2), 28.44 (CH_2), 30.17 (CH_2), 31.37 (CH_2), 39.39 (CH_2), 39.47 (CH_2), 45.79 (CH), 54.95 (CH), 56.49 (CH), 182.16, 214.33; MS (m/z, relative intensity) 256 ($M^+ + NH_4$, 35), 239 ($M^+ + H$, 100), 221 (74). 192 (30), 175 (42), 152 (20), 135 (25); exact mass calcd for $C_{14}H_{22}O_3$ 238.1569, found 238.1587.

***cis*-Bicyclo[7.3.1]tridecan-13-one (33).** To 90 mg of keto acid **32** (0.38 mmol) in 10 mL of benzene under nitrogen atmosphere was added 0.38 mL of oxalyl chloride. The reaction flask was then charged with nitrogen and 50 μL of dimethylformamide was added. The resulting solution was stirred for 1 h at 25 °C and then evaporated under reduced pressure. The crude acid chloride was dissolved in 10 mL of toluene and added dropwise to a refluxing slurry of 166 mg of the sodium salt of 2-mercaptopyridine *N*-oxide, 5 mg of DMAP, and 0.8 mL of *tert*-butyl mercaptan in 10 mL of toluene. The reaction was cooled to 25 °C and extracted with sodium bicarbonate and water. The organic layer was evaporated under reduced pressure, and the residue was purified by flash column chromatography with 2% EtOAc/hexane (R_f = 0.65 in 10% EtOAc/hexane) to give 44 mg of bicyclic ketone **33** (60% yield): IR (neat) 2960, 2880, 1730, 1490, 1460, 1415, 1330, 1230, 1160, 1110, 1055 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.65–2.10 (m, 20 H), 2.68–2.85 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 26.24 (CH_2), 26.27 (CH_2), 27.77 (CH_2), 28.62 (CH_2), 28.82 (CH_2), 39.62 (CH_2), 56.57 (CH), 215.35; MS (m/z, relative intensity) 195 ($M^+ + H$, 100), 176 (25), 135 (12), 123 (8), 109 (15); exact mass calcd for $C_{13}H_{22}O$ 194.1670, found 194.1652.

(1*S,5*R**,11*R**,14*R**)-13-Oxatetracyclo[9.2.1.1.0^{5,14}]pentadecan-12-one (34).** A solution of 132 mg of photoadduct **31** (0.48 mmol) and 5 mg of *p*-TsOH in 40 mL of methanol was heated at reflux for 18 h. The methanol was evaporated and the residue was purified by flash column chromatography with 10% EtOAc/hexane (R_f = 0.32) to give 80 mg of lactone **34** (76%): IR (neat) 2960, 2880, 1770, 1460, 1340, 1170 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.15–1.52 (m, 8 H), 1.55–2.02 (m, 9 H), 2.18–2.24 (m, 1 H), 2.52–2.62 (m, 1 H), 2.69 (d, J = 9.7 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ 16.35 (CH_2), 24.70 (CH), 24.75 (CH_2), 25.27 (CH_2), 26.26 (CH_2), 29.08 (CH_2), 32.75 (CH_2), 33.71 (CH_2), 35.72 (CH_2), 42.37 (CH), 42.51 (CH_2), 47.65 (C), 84.35 (C), 182.17; MS (m/z, relative intensity) 221 ($M^+ + H$, 45), 176 (15), 147 (12), 121 (100); exact mass calcd for $C_{14}H_{20}O_2$ 220.1463, found 220.1486.

(1*R,3*R**,9*S**)-3-Carboxybicyclo[7.3.1]tridecan-13-one (36).** To a solution of 60 mg of photoadduct **31** (0.21 mmol) in 20 mL of hexane at −60 °C was added 0.43 mL of DIBAL-H (2 equiv) and the resulting solution stirred for 1.5 h. The reaction mixture was quenched by the addition of a large excess of methanol followed by warming of the reaction mixture to 25 °C. The reaction mixture was then diluted with ethyl acetate, washed with 1 N aqueous HCl, and dried over $MgSO_4$ to give the crude keto aldehyde **35** (R_f = 0.18 in 10% EtOAc/hexane), which was dissolved in THF and treated with $LiAlH_4$ to give 28 mg of bicyclic diol (R_f = 0.23 in 50% EtOAc/hexane) in 57% yield. Bicyclic diol: IR (neat) 3040, 2940, 2880, 1475, 1455 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.05–1.75 (m, 19 H), 1.90–2.05 (m, 1 H), 2.13–2.21 (m, 1 H), 2.22–2.28 (m, 1 H), 2.70–2.78 (m, 1 H), 3.35 (dd, J = 9.8, 8.2, Hz, 1 H), 3.49 (d, J = 5.9, 10.0 Hz, 1 H), 3.50 (dd, J = 10.9, 2.4 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ 21.76 (CH_2), 25.39 (CH_2), 27.08 (CH_2), 27.75 (CH_2), 29.73 (CH_2), 31.32 (CH_2), 31.45 (CH_2), 32.01 (CH_2), 33.62 (CH), 34.52 (CH), 35.01 (CH_2), 41.36 (CH), 69.96 (CH_2), 79.78 (CH); MS (m/z, relative intensity) 224 ($M^+ + NH_4$, 11), 226 (M^+, 63), 209 (100), 191 (96), 175 (25), 149 (45), 135 (58), exact mass calcd for $C_{14}H_{26}O_2$ 226.1933, found 226.1913.

A solution of 50 mg of the crude bicyclic diol in 3 mL of DMF was treated with 5 equiv of PDC. The reaction mixture was stirred for 16 h at 25 °C and then partitioned between H_2O and EtOAc. The organic layers were washed with water, dried over $MgSO_4$, and concentrated to give 44 mg of keto acid **36** (84% yield): mp 118–119 °C; IR (neat) 3000–3500, 2960, 2880, 1710, 1450, 1250 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.15–2.00 (m, 17 H), 2.42–2.50 (m, 1 H), 2.52–2.62 (m, 1 H), 2.64–2.70 (m, 1 H), 3.42–3.50 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ 20.85 (CH_2), 22.02 (CH_2), 22.40 (CH_2), 23.38 (CH_2), 26.55 (CH_2), 28.71 (CH_2), 29.50 (CH_2), 36.80 (CH_2), 39.69 (CH_2), 42.46 (CH), 45.57 (CH), 52.55 (CH), 180.04, 220.59; exact mass calcd for $C_{14}H_{22}O_3$ 238.1569, found 238.1553.

(1*S,2*S**,6*R**,14*R**)-17,17-Dimethyl-16,18-dioxatetracyclo[12.4.0.1^{2,14}.0^{1,6}]nonadecan-15-one (37).** A solution of 850 mg of di-

oxenone **23** (2.78 mmol) in 250 mL of acetonitrile/acetone (7:3) was degassed for 0.5 h and then irradiated through a Pyrex filter at 0 °C for 2 h. The solution was concentrated and purified by chromatography with 3% EtOAc/hexane (R_f = 0.53 in 10% EtOAc/hexane) to give 680 mg of photoadduct **37** (80% yield): mp 100–101 °C; IR (neat) 2934, 2854, 1738, 1458, 1446, 1384, 1328, 1295, 1254, 1219, 1138, 1094 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.00–2.35 (m, 24 H), 1.58 (s, 3 H), 1.63 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 22.13 (CH_2), 23.98 (CH_2), 24.44 (CH_2), 26.44 (CH_2), 27.58 (CH_2), 28.60 (CH_2), 29.29 (CH_2), 29.72 (CH_2), 29.79 (CH_2), 30.82 (CH_3), 31.50 (CH_3), 35.23 (CH_2), 39.76 (CH_2), 44.21 (CH), 45.76 (CH), 50.08 (C), 84.28 (C), 105.24 (C), 170.88; MS (*m/z*, relative intensity) 306 (M^+, 9), 248 (100), 219 (59), 203 (22), 179 (28), 151 (29), 135 (92); exact mass calcd for $C_{19}H_{30}O_3$ 306.2195, found 306.2203.

(1*R,3*R**,11*R**)-3-Carboxybicyclo[9.3.1]pentadecan-15-one (38).** A solution of 170 mg of photoadduct **37** (0.56 mmol) in 10 mL of 2 N KOH/MeOH was stirred at 25 °C for 18 h. The reaction was diluted with water and extracted with 40 mL of EtOAc. The combined organic layers were washed with 2 N aqueous HCl, dried over $MgSO_4$, and purified by chromatography with 40% EtOAc/hexane (R_f = 0.32 in 50% EtOAc/hexane) to give 122 mg of keto acid **38** (83% yield): mp 183–184 °C; IR (neat) 3000–3380, 2917, 2859, 1699, 1690, 907, 734 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.80–2.20 (m, 22 H), 2.30–3.00 (m, 3 H); major isomer ^{13}C NMR ($CDCl_3$) δ 20.79 (CH_2), 21.47 (CH_2), 24.72 (CH_2), 24.95 (CH_2), 25.33 (CH_2), 26.38 (CH_2), 28.30 (CH_2), 30.40 (CH_2), 31.12 (CH_2), 39.11 (CH_2), 40.34 (CH_2), 45.52 (CH), 50.47 (CH), 53.84 (CH), 182.19, 214.32; MS (*m/z*, relative intensity) 266 (M^+, 54), 248 (80), 220 (92), 203 (16), 163 (21), 150 (39), 138 (37), 121 (45), 110 (100), exact mass calcd for $C_{16}H_{26}O_3$ 266.1882, found 266.1859.

***cis*-Bicyclo[9.3.1]pentadecan-15-one (39).** To 120 mg of keto acid **38** (0.45 mmol) in 10 mL of benzene under nitrogen atmosphere was added 0.3 mL of oxalyl chloride. The reaction flask was then charged with nitrogen and 50 μL of dimethylformamide was added. The resulting solution was stirred for 1 h at 25 °C and then evaporated under reduced pressure. The crude acid chloride was dissolved in 10 mL of toluene and added dropwise to a refluxing slurry of 120 mg of the sodium salt of 2-mercaptopyridine *N*-oxide, 24 mg of DMAP, and 1.2 mL of *tert*-butyl mercaptan in 10 mL of THF. The reaction was cooled to 25 °C and extracted with saturated aqueous sodium bicarbonate and water. The organic layers were evaporated under reduced pressure, and the resulting residue was purified by chromatography with 3% EtOAc/hexane (R_f = 0.61 in 10% EtOAc/hexane) to give 84 mg of bicyclic ketone **39** as a white solid (63% yield): mp 58–59 °C; IR (neat) 2927, 2854, 1717, 1457, 1261 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.00–2.05 (m, 24 H), 2.60–2.80 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 22.76 (CH_2), 24.54 (CH_2), 24.78 (CH_2), 26.00 (CH_2), 26.44 (CH_2), 28.34 (CH_2), 39.72 (CH_2), 52.27 (CH), 216.10; MS (*m/z*, relative intensity) 222 (M^+, 100), 173 (8), 147 (8), 137 (15), 123 (27), 111 (49), 109 (37); exact mass calcd for $C_{15}H_{26}O$ 222.1984, found 222.2007.

Reduction of 39. A solution of 30 mg of bicyclic ketone **39** (0.14 mmol) and 40 mg of $LiAlH_4$ in 10 mL of dry THF was stirred at 25 °C for 12 h. The reaction was quenched with saturated aqueous NH_4Cl, extracted with ethyl acetate, dried over $MgSO_4$, and purified by chromatography with 5% EtOAc/hexane (R_f = 0.41 in 10% EtOAc/hexane) to give 28 mg of bicyclic alcohol (93% yield): mp 54–55 °C; IR (neat) 3520, 2950, 2880, 1480, 1450 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.20–1.75 (m, 27 H), 3.86 (s, 1 H); ^{13}C NMR ($CDCl_3$) δ 21.15 (CH_2), 23.35 (CH_2), 24.21 (CH_2), 26.15 (CH_2), 26.31 (CH_2), 26.58 (CH_2), 31.04 (CH_2), 39.59 (CH), 64.56 (CH); MS (*m/z*, relative intensity) 224 (M^+, 74), 206 (100), 188 (67), 117 (20); exact mass calcd for $C_{15}H_{28}O$ 224.2140, found 224.2114.

(1S*,5R*,13R*,16R*)-15-Oxatetracyclo[11.2.1.1.0^{5,16}]heptadecan-14-one (40). A solution of 230 mg of photoadduct **37** (0.75 mmol) and 5 mg of *p*-TsOH in 25 mL of methanol was heated at reflux for 18 h. The methanol was evaporated, and the residue was purified by flash column chromatography with 10% EtOAc/hexane (R_f = 0.33 in 10% EtOAc/hexane) to give 135 mg of lactone **40** (72% yield): IR (neat) 2960, 2900, 1770, 1470, 1455, 1325, 1190, 1170 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.10–2.25 (m, 22 H), 2.76–2.86 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 15.07 (CH_2), 19.05 (CH_2), 22.72 (CH_2), 23.16 (CH_2), 24.90 (CH_2), 25.94 (CH), 26.06 (CH_2), 27.25 (CH_2), 35.05 (CH_2), 37.27 (2 C of CH_2), 37.32 (CH), 41.97 (CH_2), 47.43 (C), 85.38 (C), 182.12; MS (*m/z*, relative intensity), 248 (M^+, 39), 220 (34), 191 (51), 163 (74), 149 (100), 135 (93), 121 (94), 107 (96); exact mass calcd for $C_{16}H_{24}O_2$ 248.1776, found 248.1800.

(1R*,3S*,8S*,12R*)- and (1R*,3R*,8S*,12R*)-12-Hydroxy-3-(hydroxymethyl)bicyclo[6.3.1]dodecane (Trans Diols i and ii). A solution of 35 mg of **28** (0.16 mmol) and 50 mg of $LiAlH_4$ in 25 mL of dry THF was stirred at 25 °C for 18 h. The reaction was quenched with saturated aqueous NH_4Cl, extracted with ethyl acetate, dried over $MgSO_4$, and purified by flash chromatography with 25% EtOAc/hexane as eluent (R_f = 0.45 and 0.29 in 50% EtOAc/hexane) to give 16 mg of diol i and 15 mg of diol ii (94% total yield). Low-R_f isomer: IR (neat) 3400, 2960, 2880, 1470, 1460 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.15–1.35 (m, 4 H), 1.38–1.78 (m, 13 H), 2.02–2.16 (m, 2 H), 2.22–2.28 (m, 1 H), 2.35–2.42 (m, 1 H), 3.22 (dd, *J* = 7.7, 10.1 Hz, 1 H), 3.29 (dd, *J* = 6.9, 10.1 Hz, 1H), 3.44 (dd, *J* = 10.4, 2.4 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ 22.30 (CH_2), 26.84 (CH_2), 28.88 (CH_2), 31.32 (CH_2), 32.14 (CH_2), 35.76 (CH_2), 35.83 (CH_2), 36.18 (CH), 38.80 (CH_2), 39..77 (CH), 41.70 (CH), 70.89 (CH_2), 79.97 (CH). High-R_f isomer: ^1H NMR ($CDCl_3$) δ 1.02–1.30 (m, 3 H), 1.34–2.14 (m, 17 H), 2.24–2.34 (m, 1 H), 3.25 (dd, *J* = 7.6, 10.1 Hz, 1 H), 3.37 (dd, *J* = 6.6, 10.1 Hz, 1 H), 3.77 (dd, *J* = 5.9, 11.0 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ 21.06 (CH_2), 28.01 (CH_2), 28.75 (CH_2), 30.19 (CH_2), 31.18 (CH_2), 32.68 (CH_2), 33.30 (CH), 34.36 (CH_2), 34.84 (CH_2), 38.82 (CH), 42.81 (CH), 70.69 (CH_2), 77.18 (CH); MS (*m/z*, relative intensity) 213 (M^+ + H, 13), 195 (100), 177 (90), 163 (58), 135 (42), 121 (53); exact mass calcd for $C_{13}H_{24}O_2$ 212.1776, found 212.1755.

(1R*,3S*,8R*,12R*)- and (1R*,3R*,8R*,12R*)-12-Hydroxy-3-(hydroxymethyl)bicyclo[6.3.1]dodecane (Cis Diols iii and iv). A solution of 18 mg of **30** (0.08 mmol) and 50 mg of $LiAlH_4$ in 25 mL of dry THF was stirred at 25 °C for 18 h. The reaction was quenched with saturated aqueous NH_4Cl, extracted with ethyl acetate, dried over $MgSO_4$, and purified by flash chromatography with 25% EtOAc/hexane as eluent (R_f = 0.39 and 0.25 in 50% EtOAc/hexane) to give 8 mg and 6 mg of diols iii and iv (82% total yield), respectively. Low-R_f isomer: ^1H NMR ($CDCl_3$) δ 1.20–1.70 (m, 14 H), 1.80–2.10 (m, 7 H), 3.31 (dd, *J* = 10.2, 7.2 Hz, 1 H), 3.37 (dd, *J* = 10.2, 6.9 Hz, 1 H), 3.96 (dd, *J* = 3.4, 3.4 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ 16.55 (CH_2), 26.38 (CH_2), 26.65 (CH_2), 30.61 (CH_2), 31.92 (CH_2), 33.97 (CH_2), 33.99 (CH_2), 35.72 (CH_2), 39.57 (CH), 40.56 (CH), 41.35 (CH), 70.16 (CH_2), 76.95 (CH). High-R_f isomer: ^1H NMR ($CDCl_3$) δ 1.20–2.40 (m, 21 H), 3.69 (dd, *J* = 10.2, 5.1 Hz, 1 H), 3.73 (dd, *J* = 10.2, 3.4 Hz, 1 H), 3.93 (dd, *J* = 3.9, 3.9 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ 16.50 (CH_2), 26.57 (CH_2), 28.36 (CH_2), 29.67 (CH_2), 30.21 (CH_2), 32.96 (CH_2), 33.68 (CH_2), 34.18 (CH_2), 36.88 (CH), 39.57 (CH), 39.99 (CH), 67.51 (CH_2), 75.97 (CH); MS (*m/z*, relative intensity) 212 (M^+, 28), 194 (34), 176 (45), 163 (100), 147 (44), 135 (90), 121 (75); exact mass calcd for $C_{13}H_{24}O_2$ 212.1776, found 212.1758.

(1S*,5R*,13S*,14R*)-1-Hydroxy-13-(hydroxymethyl)tricyclo-[11.1.1.0^{5,14}]pentadecane (v). A solution of 70 mg of lactone **40** (0.28 mmol) and 50 mg of $LiAlH_4$ in 25 mL of dry THF was stirred at 25 °C for 18 h. The reaction was quenched with saturated aqueous NH_4Cl, extracted with ethyl acetate, dried over $MgSO_4$, and purified by chromatography with 20% EtOAc/hexane as eluent (R_f = 0.63 in 50% EtOAc/hexane) to give 68 mg of diol v (96% yield): IR (neat) 3500, 2960, 2880, 1475 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.06 (dd, *J* = 11, 3 Hz, 1 H), 1.25–1.85 (m, 23 H), 2.12–2.22 (m, 1 H), 2.96 (d, *J* = 10 Hz, 1 H), 3.31 (d, *J* = 11 Hz, 1 H), 4.27 (d, *J* = 11 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ 19.39 (CH_2), 21.86 (CH_2), 22.74 (CH_2), 25.18 (CH_2), 26.17 (CH_2), 27.21 (CH_2), 28.98 (CH), 30.47 (CH_2), 32.13 (CH_2), 34.60 (CH_2), 38.64 (CH), 40.45 (CH_2), 41.41 (CH_2), 47.28 (C), 69.09 (CH_2), 72.95 (C); MS (*m/z*, relative intensity) 252 (M^+, 2), 234 (M^+ − 18, 9), 192 (4), 163 (55), 150 (100), 135 (39); exact mass calcd for $C_{16}H_{28}O_2$ 252.2089, found 252.2111.

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Supplementary Material Available: Tables of atomic coordinates, bond lengths and angles, and anisotropic thermal parameters for the X-ray crystal structures of *trans*-bicyclo[5.3.1]undecan-11-one **6** and *trans*-bicyclo[4.3.1]decan-10-one **17** (5 pages). Ordering information is given on any current masthead page.