General Photoisomerization Approach to *trans*-Benzobicyclo[5.1.0]octenes: Synthetic and Mechanistic Studies†

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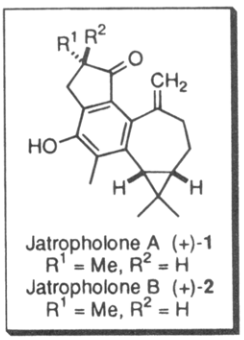
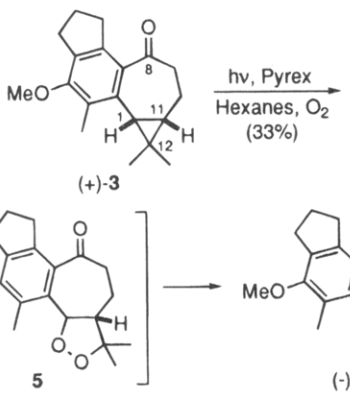
Received July 27, 1994®

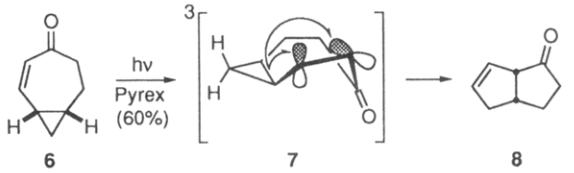
The preparation and photoisomerization of *cis*-bicyclo[5.1.0]octenes (+)-**3**, **16**, and **21**–**23** are described. For the benzannulated substrates, the primary photochemical events established photostationary states between the cis isomers and the trans-fused cyclopropanes (+)-**9**, **32**, **37**, and **44**. Studies employing enantioenriched **21**, **32**, and **44** demonstrated that the reactions occurred primarily but not exclusively via cleavage of the peripheral benzylic cyclopropane bonds. Utilization of the triplet quencher piperylene revealed a predominance of triplet diradical intermediates in the trans-to-cis conversions and afforded an improved protocol for preparative isomerizations.

In studies leading to the total synthesis of jatrophalones A and B (**1** and **2**),[1] we discovered that the benzannulated cyclopropyl ketone (+)-**3** furnished diketone (−)-**4** upon irradiation in hexanes saturated with oxygen. The





apparent predominance of peripheral cyclopropane bond cleavage, which presumably led to **4** via endoperoxide **5**, was particularly striking; photolysis of the parent bicyclo[5.1.0]oct-2-en-4-one (**6**) reportedly involves scission of the central cyclopropane bond, furnishing **8** via the electronically favored "transoid" triplet diradical **7**.[2] In this full account, we describe further studies of **3** as well as the



preparation and photoisomerization of several other benzannulated bicyclo[5.1.0]octenones. Key findings include the following: (1) the establishment of photostationary states between the cis- and trans-fused cyclopropanes; (2) the generation of triplet diradical intermediates in the trans-to-cis conversions; and (3) determination of lower limits for the contributions of central bond cleavage in the cis–trans interconversions of **21** and **23**. In addition, these experiments served to define a general and efficient photochemical route to *trans*-benzobicyclo[5.1.0]octenes, enhanced by the triplet quencher piperylene.[3]

Photooxidation and Photoisomerization of Cyclopropyl Ketone (+)-3. To establish that peripheral bond cleavage in the photolysis of (+)-**3** was independent of oxygen, we repeated the reaction under anaerobic conditions. Irradiation of (+)-**3** through Pyrex in degassed hexanes (0.07 M) for 30 min furnished a new crystalline solid in 68% yield (85% based on recovered **3**). The trans-fused cyclopropane structure (+)-**9** was initially deduced from spectroscopic data, including a 200-MHz ^{1}H COSY experiment, and later confirmed through the aegis of single-crystal X-ray analysis.[4–7]

Prolonged irradiation of either (+)-**3** or (+)-**9** (0.06 M, hexanes, 6 h) established a photostationary state (ca. 4:1 trans/cis) and in turn furnished ketone (+)-**10** (30% yield)

† This paper is dedicated to the memory of Professor Paul G. Gassman whose untimely death on April 21, 1993, deprived the international chemical community of one of its most productive and respected colleagues.

® Abstract published in *Advance ACS Abstracts,* October 1, 1994.

(1) Smith, A. B., III; Liverton, N. J.; Hrib, N. J.; Sivaramakrishnan, H.; Winzenberg, K. N. *J. Org. Chem.* **1985**, *50*, 3239.

(2) Paquette, L. A.; Meehan, G. V.; Henzel, R. P.; Eizember, R. F. *J. Org. Chem.* **1973**, *38*, 3250.

(3) For a preliminary communication, see: Wood, J. L.; Liverton, N. J.; Visnick, M.; Smith, A. B., III. *J. Am. Chem. Soc.* **1989**, *111*, 4530.

(4) Carroll, P. J.; Liverton, N. J.; Smith, A. B., III. *Acta Crystallogr.* **1986**, *C42*, 1594.

(5) For a related photochemical transformation, see: Pirkle, W. H.; Lunsford, W. B. *J. Am. Chem. Soc.* **1972**, *94*, 7201.

(6) For a review of cis–trans photoisomerization of aryl and vinyl cyclopropanes, see: Hixson, S. S. In *Organic Photochemistry*; Padwa, A., Ed.; Marcel Dekker: New York, 1979; Vol. 4, pp 191–260.

(7) For other preparations of trans [*n*.1.0] bicyclic systems, see: (a) Wiberg, K. B.; de Meijere, A. *Tetrahedron Lett.* **1969**, 519. (b) Gassman, P. G.; Williams, F. J.; Seter, J. *J. Am. Chem. Soc.* **1968**, *90*, 6893. (c) Gassman, P. G.; Seter, J.; Williams, F. J. *J. Am. Chem. Soc.* **1971**, *93*, 1673. (d) Ashe, A. J., III. *Tetrahedron Lett.* **1969**, 523. (e) Gassman, P. G.; Bonser, S. M. *J. Am. Chem. Soc.* **1983**, *105*, 667. (f) Gassman, P. G.; Mlinaric-Majerski, K. *J. Org. Chem.* **1986**, *51*, 2397. (g) Masamune, S.; Baker, P. M.; Hojo, K. *J. Chem. Soc., Chem. Commun.* **1969**, 1203.

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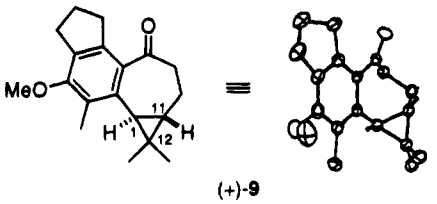
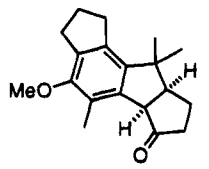
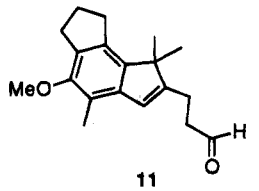


(+)-9

and aldehyde **11** (6%) via marked skeletal rearrangement. The formulation of **11** was determined by X-ray analysis of the derived acid **12**, whereas the structure of (+)-**10** was inferred from spectral data in conjunction with the photoisomerization of (+)-**10** to **11**.



(+)-10



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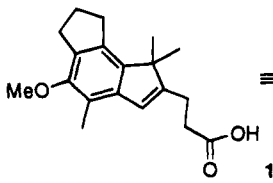

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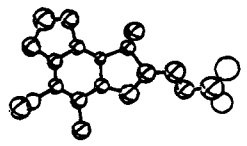
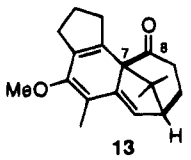
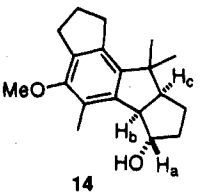


A self-consistent mechanistic picture for the formation of **4**, **9**, **10**, and **11** involves initial generation of the photostationary state via rupture of the C(1,12) peripheral bond in **3** and **9**, affording the corresponding 1,3-diradical. In the presence of oxygen, diradical capture affords the putative endoperoxide **5**, whereupon homolysis of the O–O σ-bond and hydrogen atom transfer would lead to **4**. Heterolytic conversion of **5** to **4** may also be feasible. In the absence of oxygen the diradical can rearrange to **13** (not observed), which in turn would undergo C(7,8) Norrish type I α-cleavage followed by irreversible hydrogen abstraction or reversible radical recombination, furnishing **11** or **10**, respectively.[8] Formation of **11** via irradiation of **10** is consistent with the reversibility of the latter process.



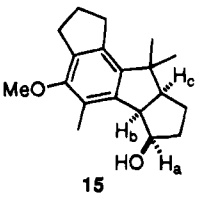
13

This mechanistic scenario requires retention of the absolute stereochemistry at the C(11) center. To probe for possible C(11) racemization, we determined the enantiomeric purity of the product ketone (+)-**10**. Reduction of (+)-**10** with $NaBH_4$ provided a mixture of diastereomeric alcohols **14** and **15** (ca. 1:1); the configurational assignments were based on TLC mobilities and NOE studies. Proton NMR analysis of the Mosher esters prepared from **14**[9] revealed an enantiomeric purity of 66% ee, compared with 88% ee for (+)-**3**.[10] Accordingly, scission of the peripheral cyclopropane bond cannot be the sole pathway for establishment of the photostationary state; loss of stereochemical integrity at C(11) can occur only via rupture of the central cyclopropane bond.



14

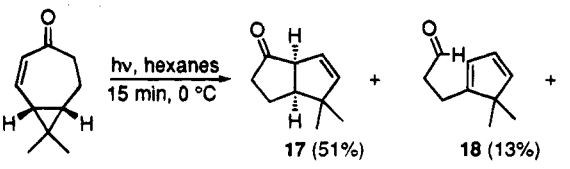
NOE: $H_a \rightarrow H_b$ = 2%
$H_b \rightarrow H_c$ = 6%



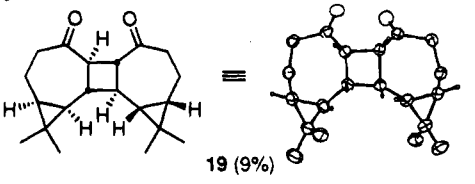
15

NOE: $H_a \rightarrow H_b$ = 4%
$H_b \rightarrow H_c$ = 6%

The Influence of Benzannulation: Photochemistry of Bicycle 16. In the context of Paquette's studies of the parent cyclopropane **6** (*vide supra*),[2] the preference for peripheral bond cleavage in the photolysis of (+)-**3** presumably reflects the inability of a benzannulated triplet intermediate to adopt a "transoid" conformation, diminishing the stereoelectronic effects favoring central bond cleavage. In addition, the geminal methyl groups would promote peripheral bond cleavage by stabilizing the incipient radical.[11] To explore the effect of geminal methyl substitution in a system compatible with a "transoid" triplet conformation, we briefly investigated the photochemistry of 8,8-dimethyl-*cis*-bicyclo[5.1.0]oct-2-en-4-one (**16**).[12] Irradiation of **16** for 15 min in degassed hexanes (0.07 M) rapidly furnished ketone **17** (51% yield), aldehyde **18** (13%), and trans,trans head-to-head dimer **19** (9%). The structures of **17** and **18** were assigned via spectral analysis, whereas the formulation of **19** derived from X-ray analysis.[43]



16 17 (51%) 18 (13%)



19 (9%)

Photolysis of the substrate lacking an aromatic ring thus led to central bond cleavage, the cyclopropane methyl groups notwithstanding. However, adiabatic conversion of a transoid triplet to products, as in Paquette's system,[2] does not account for the formation of photodimer **19**. A more satisfactory mechanism involves conversion of the triplet to both **17** and the ground-state *trans*-cycloheptenone **20**.[13] The highly strained enone **20** could then undergo a thermally allowed

(8) Chapman, O. L.; Weiss, D. S. In *Organic Photochemistry*; Chapman, O., Ed.; Marcel Dekker: New York, 1973; Vol. 3, pp 241–250.

(9) Dale, J. A.; Dull, D. L.; Mosher, H. S. *J. Org. Chem.* **1969**, *34*, 2543.

(10) The enantiomeric purity of (+)-**3** was determined via HPLC with a Daicel Industries Chiralpak OT-(+) column.

(11) Kerr, J. A. *Chem. Rev.* **1966**, *66*, 465.

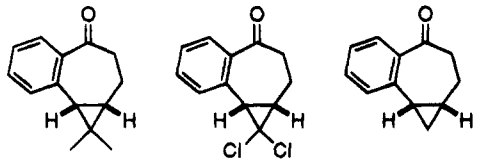
(12) For the preparation of **16**, see: Taylor, M. D.; Smith, A. B., III. *Tetrahedron Lett.* **1983**, *24*, 1867. Also see: Taylor, M. D.; Minaskanian, G.; Winzenberg, K. N.; Santone, P.; Smith, A. B., III. *J. Org. Chem.* **1982**, *47*, 3960.

(13) The photochemical generation and spectroscopic observation of *trans*-cycloheptenone was reported simultaneously by Corey and Eaton: (a) Corey, E. J.; Tada, M.; LaMahieu, R.; Libit, L. *J. Am. Chem. Soc.* **1965**, *87*, 2051. (b) Eaton, P. E.; Lin, K. *J. Am. Chem. Soc.* **1965**, *87*, 2052.

20

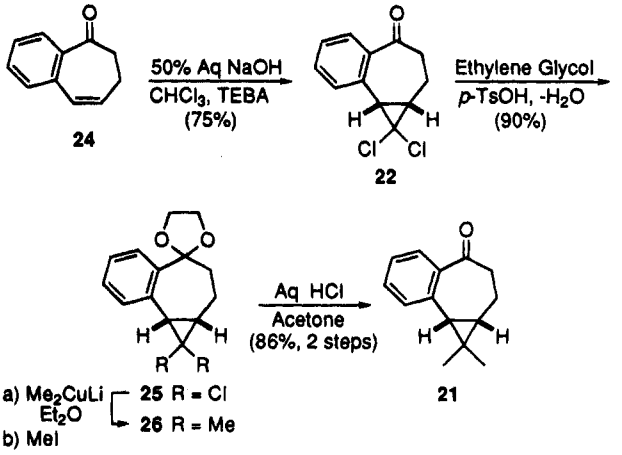
$[_\pi 2_s + _\pi 2_a]$ cycloaddition[14] with **16** (**20**$_s$ + **16**$_s$) to afford **19**. Alternatively, the thermal $[_\pi 2_a + _\sigma 2_s]$ 1,3-sigmatropic (i.e., vinylcyclopropane) rearrangement of **20** constitutes a second pathway leading to **17**.[15] The latter processes would diminish the concentration of **20**, accounting for the absence of products derived from its dimerization. Finally, aldehyde **18** could arise via secondary photochemistry involving Norrish type I α-cleavage of ketone **17** followed by hydrogen abstraction; the formation of **18** by photolysis of **17** established the viability of this pathway.[16]

Preparation of Cis-Fused, Benzannulated Cyclopropyl Ketones 21–23. Having established the critical role of the aromatic ring in the interconversion of cis- and trans-fused bicyclo[5.1.0]octenones, we next explored the effects of the cyclopropyl substituents. To this end we prepared **21**–**23** from the known and readily available



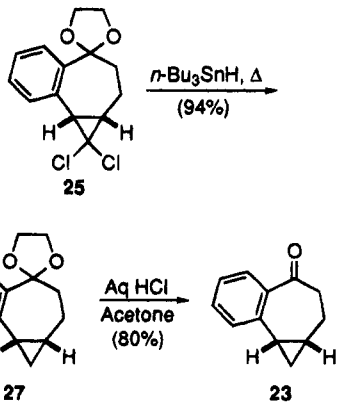
21 22 23

intermediate benzosuberenone (**24**).[17] Treatment of **24** with dichlorocarbene, generated by decomposition of chloroform under phase-transfer conditions, furnished cyclopropane **22** in 75% yield.[18] After protection as the ethylene ketal **25**, the geminal methyl groups were introduced via the protocol of Corey and Posner:[19] reaction of **25** with 2 equiv of lithium dimethylcuprate at −20 °C for 2.5 days followed by addition of excess methyl iodide[20] afforded **26**. Deketalization then gave **21** in 86% yield for the two steps (58% overall from benzosuberenone).



24 22 21

The parent cyclopropane **23** likewise derived from dichloride **25** in two steps. Reduction of **25** with 2 equiv of tri-*n*-butyltin hydride at 160 °C for 3 h generated **27** in 94% yield;[21] acidic hydrolysis then afforded **23** (80%; four steps, 51% overall from benzosuberenone).



25 27 23

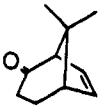
In an effort to expedite the synthesis of **23**, we attempted the direct methylenation of **24** via a procedure described by Simmons.[22] Exposure of **24** to diiodomethane and diethylzinc at reflux gave the α-methyl ketone **28** as the sole product (37% yield). We speculated that **28** arose via cyclopropanation of a zinc enolate followed by ring-opening.[22] Accordingly, we prepared the hydroxy substrate **29** in 99% yield via $NaBH_4$ reduction of **24**. The methylenation conditions employed earlier efficiently and stereoselectively transformed **29** to the syn hydroxy cyclopropane **30** (86%). Titration with Jones reagent[23] then furnished **23** in 96% yield (73% overall from benzosuberenone).

To unambiguously established the generation of a single isomer in the cyclopropanation of **29**, we prepared

(14) Hart, H.; Dunkelblum, E. *J. Org. Chem.* **1979**, *44*, 4752.

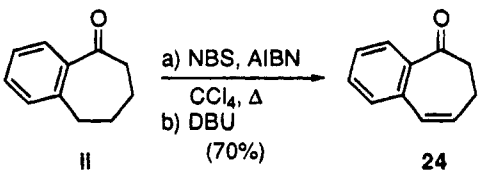
(15) Woodward, R. B.; Hoffmann, R. *The Conservation of Orbital Symmetry*; Verlag Chemie International: Deerfield Beach, FL, 1981; Chapter 7, pp 114–140.

(16) (a) Another plausible pathway involves the intermediacy of bicyclic ketone **i**. We could not detect **i** via spectroscopic analysis of the crude photolysate.[16b] In contrast, the benzannulated analog **33** was readily isolated after irradiation of **21** for 3 h. (b) Hua, D. H.; Gung, W. Y.; Ostrander, R. A.; Takusagawa, F. *J. Org. Chem.* **1987**, *52*, 2509.



i

(17) (a) For the preparation of benzosuberenone (**24**) from benzosuberone (**ii**), we modified the original published[17b] sequence by employing 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) in place of collidine to effect dehydrobromination. We also used the radical initiator AIBN instead of benzoyl peroxide, an alternative reported previously.[17c] These changes improved the isolated yield of **24** from 30 to 70% for the two steps. (b) Buchanan, G. L.; Lockhart, D. R. *J. Chem. Soc.* **1959**, 3586. (c) Burdett, K. A.; Shenton, F. L.; Yates, D. H.; Swenton, J. S. *Tetrahedron* **1974**, *30*, 2057.



ii 24

(18) (a) Perchonock, C. D.; Lantos, I.; Finkelstein, J. A.; Holden, K. G. *J. Org. Chem.* **1980**, *45*, 1950. (b) Makosza, M.; Kacprowicz, A.; Fedorynski, M. *Tetrahedron Lett.* **1975**, 2119. (c) Makosza, M.; Wawrzyniewicz, M. *Tetrahedron Lett.* **1969**, 4659.

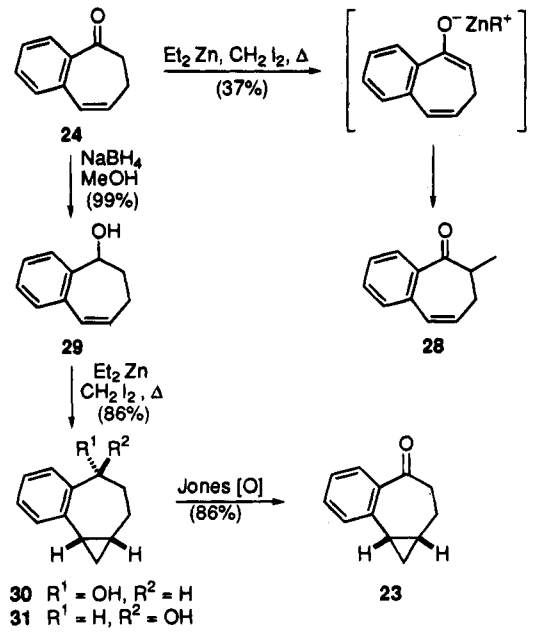
(19) Corey, E. J.; Posner, G. H. *J. Am. Chem. Soc.* **1968**, *90*, 5615.

(20) Kitatani, K.; Hiyama, T.; Nozaki, H. *J. Am. Chem. Soc.* **1976**, *98*, 2362.

(21) Seyferth, D.; Yamazaki, H.; Alleston, D. L. *J. Org. Chem.* **1963**, *28*, 703.

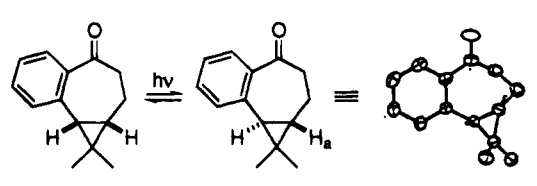
(22) Simmons, H. E.; Cairns, T. L.; Vladuchick, S. A.; Hoiness, C. M. *Org. React.* **1973**, *20*, 1.

(23) Bowden, K.; Heilbron, I. M.; Jones, E. R. H.; Weedon, B. C. L. *J. Chem. Soc.* **1946**, 39.

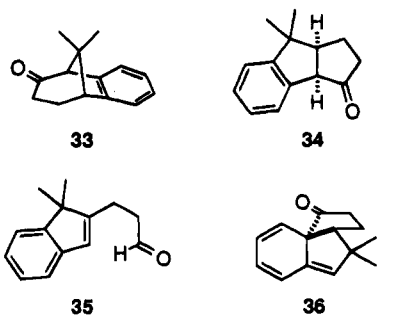


a sample containing both diastereomers via sodium borohydride reduction of **23**, which provided a 6:1 (GC) mixture of alcohols **30** and **31** in 83% yield. The minor isomer, readily resolved by capillary GC, could not be detected in the cyclopropanation mixture. Importantly, the 500-MHz ^{1}H NMR spectrum of the mixture of **30** and **31** clearly indicated that the cyclopropane derived from **29** was identical with the major product of the $NaBH_4$ reaction. The latter observation is in complete accord with both the steric requirements for reduction of **23** (i.e., hydride delivery from the convex face) and the known haptophilic nature of the Simmons–Smith reagent.[22]

Photochemistry of Cis-Fused Cyclopropanes 21–23. The behavior of jatropholone intermediate **3** led us to employ short reaction times for initial photochemical studies of ketone **21**. After irradiation of **21** in degassed hexanes (0.09 M) for 35 min, TLC analysis indicated the presence of starting material and a single product, the latter isolable in 37% yield (93% based on recovered **21**). The assignment of the trans structure **32** was initially based upon the diagnostic ^{1}H NMR upfield shift of the homobenzylic cyclopropyl proton (H_a, δ 0.54) and eventually confirmed by single-crystal X-ray analysis.[24,43]



As in the isomerization of (+)-**3**, a photostationary state (1:1, trans/cis) was established upon irradiation of either **21** or **32**. In addition, prolonged irradiation (3 h) of **21** inefficiently furnished ketones **33** and **34** (9 and 5% yields) and aldehyde **35** (2%). The structures of **34** and **35** were deduced via spectroscopic comparison with the analogous secondary photoproducts derived from (+)-**3** (i.e., **10** and **11**, respectively). Ketone **33** was characterized by spectroscopic analysis, including complete homonuclear decoupling of the 500-MHz ^{1}H NMR spectrum, in conjunction with high-resolution mass spectrometry.



Mechanistically, the photolyses of ketones **21** and (+)-**3** appear to be very similar, and the formation of **34** and **35** can be rationalized in terms of the analysis presented above for **3**. The secondary photoproduct **33** presumably arises via scission of the central cyclopropane bond and the intermediacy of **36**. The isolation of **33** finds no precedent in the earlier experiments but is compatible with the evidence for some central bond cleavage in the isomerization of (+)-**3**.

Next we explored the photochemistry of dichloro ketone **22**. Upon irradiation of **22** (0.5 M) in degassed hexanes and benzene (2.5:1) for 1 h, TLC analysis revealed the presence of starting material, a significant amount of a new product, and a few minor components. Purification by HPLC afforded ketone **37** in 28% yield (77% based on recovered **22**). In contrast with the ^{1}H NMR spectra of trans-fused cyclopropanes (+)-**9** and **32**, the homobenzylic proton of **37** (δ 1.53) was not shifted significantly upfield via-à-vis the corresponding resonance for **22**; nonetheless, homonuclear decoupling experiments supported the trans ring-fusion geometry. To establish the structure unambiguously, we again turned to X-ray analysis;[25] surprisingly, the ring-fusion cyclopropane bond in **37** is shorter than the average of the corresponding bond lengths for 79 1,1-dichlorocyclopropanes in the Cambridge Crystallographic Data Base (1.508 vs 1.524 Å), even though all of the latter structures appear to be less strained than **37**. Verification of the trans geometry confirmed that the geminal chlorine atoms did not alter the primary photochemical event.

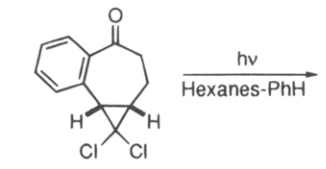
As in the previous examples, ketone **22** was then subjected to prolonged irradiation (6 h), furnishing trans cyclooctene **38** (16% yield) and an inseparable mixture of **37** and *cis*-cyclooctene **39** (21%). The generation of **38** and **39** reflects the propensity of *gem*-dichloro cyclopropanes to undergo photochemical electrocyclic ring opening.[26] Structural assignments for the cyclooctenes also derived from single-crystal X-ray analyses.[25,43]

As foreshadowed by the systems studied earlier, irradiation of the trans-fused cyclopropane **37** produced the cis isomer **22** as well as **38** and **39**. Although the behavior of **37** and **22** was suggestive of a photostationary state, efforts to establish this rigorously were hampered by the facile formation of the ring-opened isomers. Not surprisingly, **38** and **39** readily interconverted photochemically but neither reverted to a cyclopropyl progenitor. The isolation of **38** via standard silica-gel flash

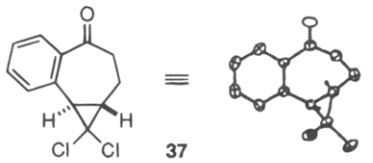
(24) Suitable crystals were obtained by slow sublimation of **32** (72 h, 40 °C, 30 mmHg). For X-ray analysis the crystal was mounted in a sealed capillary to circumvent sublimation in the diffractometer.

(25) Wood, J. L.; Carroll, P. J.; Smith, A. B., III. *J. Chem. Soc., Chem. Commun.* **1992**, 1433.

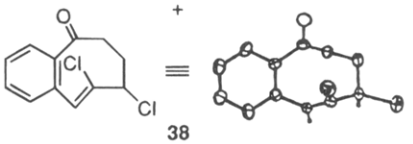
(26) See, for example: Hart, H.; Weiner, M. *Tetrahedron Lett.* **1981**, *22*, 3115. For an example of thermal ring opening, see: Ioffe, A. I.; Nefedov, O. M. *Izv. Akad. Nauk, Ser. Khim.* **1974**, 1536 (English translation, p 1455).



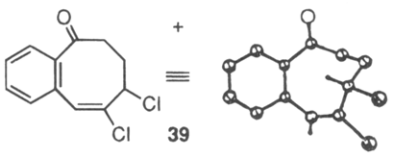
22



37

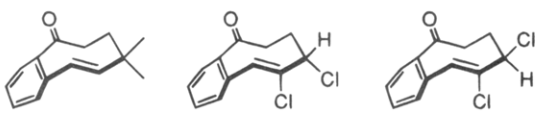


38



39

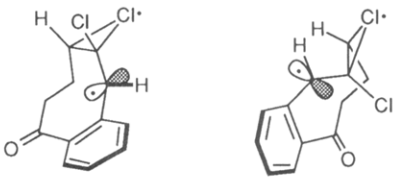
chromatography was striking, given the reported instability of the dimethyl congener **40**.[27]



40 38 41

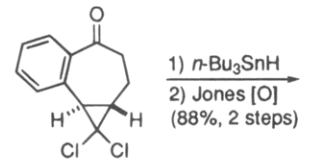
Another unexpected result was the absence of the diastereomeric *trans*-cyclooctene **41**. The configurational stability of medium-ring trans olefins has been recognized for many years. In a classic study employing a platinum complex with an optically active amine, Cope resolved *trans*-cyclooctene and determined the 35.6 kcal/mol activation energy for its racemization.[28,29] We attempted to rationalize the selective formation of **38** from both **22** and **37** by performing MM2 calculations on **38** and **41**. Each diastereomer was subjected to a multiconformer analysis of the eight-membered ring, employing C(1,2), C(3,4), and C(5,6) torsion angle rotations of 20° with a C(7,8) closure bond distance of 1−2 Å.[30] However, after generation and minimization of ca. 80 conformers for each isomer, the minimum energy conformations of **38** and **41** differed by only 0.6 kcal/mol; this value would correspond to an ca. 2.7:1 mixture of **38** and **41** at equilibrium. The MM2 global minimum conformation of **38** proved to be nearly identical with the X-ray structure.

We then sought to generate **41** via thermolysis of trans olefin **38**; indeed, upon warming to 150 °C in 1,2-dichlorobenzene, isomerization proceeded readily to furnish a 3:1:1 mixture of **38**, **39**, and the elusive isomer **41**. The resultant ratio of trans-olefin diastereomers nearly matched the equilibrium value predicted by MM2. With purified **41** in hand, we reviewed the 500-MHz ^{1}H NMR spectrum of the crude photolysate derived from **22** and discovered that **41** had in fact been formed, albeit in less than 1% yield. Although we cannot present a complete rationale for the predominant formation of **38**, one speculative possibility involves the intervention of chlorine-bridged diradical intermediates **42** and **43**.[31] In this mechanistic scenario, the initial interconversion of **22** and **37** could occur via either peripheral [i.e., C(1,12)] or central [C(1,11)] cyclopropane bond cleavage. Participation of the exo and endo chlorine atoms in the scission of the central bond of **22** would give rise to the cis- and trans-bridged intermediates **42** and **43**, respectively, which in turn could selectively furnish the observed products.[32]



42 43

The third substrate in this series, ketone **23**, was initially photolyzed for brief periods in the usual fashion, but irradiation for 30 min (0.05 M) in degassed hexanes resulted in little or no product formation, as determined by 500-MHz ^{1}H NMR analysis. To explore further the apparent inertness of **23**, we prepared an authentic sample of the trans isomer **44** via reduction of **37** with tri-*n*-butylin hydride,[21] followed by Jones oxidation of the resultant secondary alcohol.[23] The structure of **44** was confirmed by single-crystal X-ray analysis.[43]



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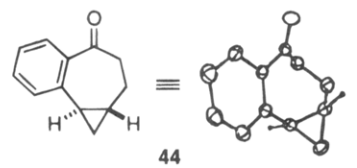


44

Reinvestigation of the photolysis of **23**, employing capillary GC to monitor the reaction, then revealed that **44** was generated in ca. 8% yield. In contrast with the isomerizations of **3**, **21**, and **22**, prolonged irradiation of **23** did not lead to significant secondary photochemistry. However, irradiations of pure **23** and **44** did furnish

(27) Hart, H.; Suzuki, M. *Tetrahedron Lett.* **1975**, 3447. Suzuki, M.; Hart, H.; Dunkelblum, E.; Li, W. *J. Am. Chem. Soc.* **1977**, *99*, 5083. For discussion of the contrasting behavior of **38** and **40**, see ref 25.

(28) Cope, A. C.; Ganellin, C. R.; Johnson, H. W., Jr.; VanAuken, T. V.; Winkler, H. J. S. *J. Am. Chem. Soc.* **1963**, *85*, 3276.

(29) Cope, A. C.; Pawson, B. A. *J. Am. Chem. Soc.* **1965**, *87*, 3649.

(30) Lipton, M.; Still, W. C. *J. Comput. Chem.* **1988**, *9*, 343.

(31) (a) Cristol, S. J.; Ilenda, C. S. *Tetrahedron Lett.* **1976**, 3681. (b) Cristol, S. J.; Tenud, L.; Daughenbaugh, R. J. *Tetrahedron Lett.* **1977**, 1099.

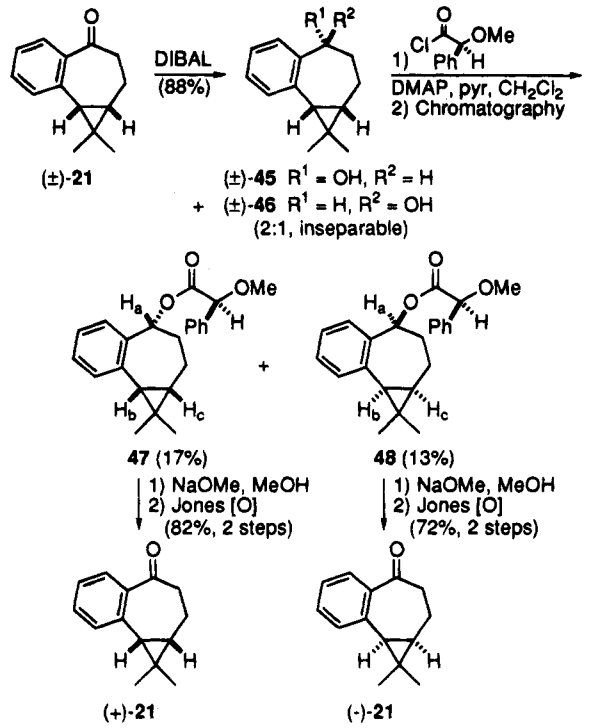
(32) (a) A less likely mechanism involves concerted ring-opening and chlorine migration. Because chlorine can migrate with either *s* or *p* orbitals,[32b] both photochemical and thermal pathways for generation of the ring-opened products are symmetry allowed. Predominant formation of **38** could be rationalized by invoking a thermal or photochemical antidisrotatory[32c] concerted process. The stabilization derived from S_N2-like participation of the cyclopropane σ-bond would have to compensate for developing ring strain. (b) For a complete analysis of the thermal opening of geminal dichloro cyclopropanes, see: Ioffe, A. I.; Nefedov, O. M. *Izv. Akad. Nauk, Ser. Khim.* **1974**, 1536 (English translation, p 1455). (c) For discussion of antidisrotatory opening of cyclopropanes, see: DePuy, C. H. *Acc. Chem. Res.* **1968**, *1*, 33.

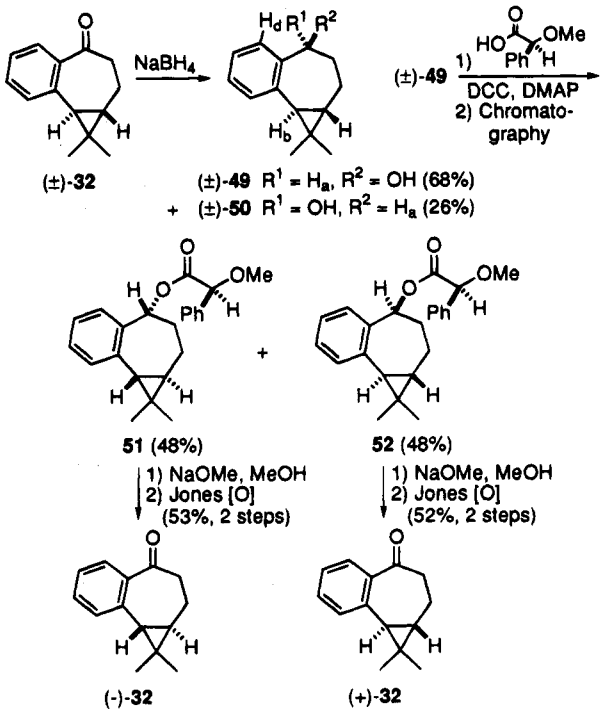
identical isomer ratios (ca. 1:11, trans/cis), indicative of a photostationary state.

Preparation of Enantioenriched Cyclopropane Substrates. The cyclopropane isomerizations described above proceeded via competing peripheral and central bond homolyses. To quantitate the discrimination between these pathways in the parent and dimethyl cyclopropane series, we investigated the loss in product optical activity upon photolysis of scalemic **21**, **23**, **32**, and **44**. Whereas isomerization via C(1,12) peripheral bond scission must occur with retention of configuration at C(11), C(1,11) central bond cleavage would afford racemic product if the intermediate diradical retained no memory of the configuration of its progenitor. The loss of product optical activity would then correspond to the fraction of isomerization involving central bond cleavage. Alternatively, if central bond isomerization could occur with partial retention at C(11), the loss of product optical activity at low conversion would provide an experimental lower limit for the contribution of central bond cleavage.[33,34]

The investigation of course entailed the preparation of enantiomerically enriched substrates. To this end, DIBAL reduction of (±)-**21** at −5 °C afforded an inseparable 2:1 (GC) mixture of diastereomeric alcohols (±)-**45** and (±)-**46** in 88% yield.[35] The assignments of relative stereochemistry reflect the expected preference for hydride delivery from the convex face, as observed in the reduction of **23** *(vide supra)*. Derivatization with *(S)*-(+)-*O*-methylmandelic acid chloride (98% ee) then afforded four diastereomeric esters;[36] **47** and **48** were cleanly separated via flash chromatography (17 and 13% yields, respectively). The observation of strong NOE enhancements of H_b upon irradiation of H_a in **47** and **48** (14 and 10%) suggested that both esters derived from the syn alcohol [i.e., (±)-**45**]; as anticipated, removal of the chiral auxiliaries in **47** and **48** with NaOMe in methanol provided (+)- and (−)-**45** in 98 and 91% yields. The absolute configurations of the alcohol moieties were assigned by NMR analysis of the respective *O*-methylmandelates (**47** and **48**),[37] and esterification of (−)-**45** with Mosher's acid[9] followed by ^1H NMR analysis revealed an enantiomeric purity of 90% ee. Finally, titration of (+)- and (−)-**45** with Jones reagent[23] efficiently furnished enantiomerically enriched (+)- and (−)-**21**, respectively.

An analogous sequence was employed for resolution of (±)-**32**. In this series, initial reduction with $NaBH_4$ gave pure (±)-**49** and (±)-**50** in 68 and 26% yields after chromatography. The relative configurations again were deduced via NOE studies: irradiation of H_a in **49** induced an 8% enhancement of H_b, whereas the analogous experiment with **50** resulted only in 10% enhancement of H_d. Derivatization of (±)-**49** with *(S)*-(+)-*O*-methylmandelic acid (DCC, DMAP) afforded esters **51** and **52**, each in 48% yield, after separation by HPLC. Assignment of the carbinol absolute stereochemistry[37] and removal of the chiral auxiliaries (NaOMe, methanol) then furnished alcohols (−)- and (+)-**49** (ca. 75−90% yields), which upon Jones oxidation gave ketones (−)- and (+)-**32**, respectively (60−70%). Mosher analysis of (+)-**49** established an enantiomeric purity of 93% ee.





The stereoselective formation of alcohol **30** en route to (±)-**23** facilitated the implementation of our resolution

(33) This scenario would not necessarily apply to the isomerization of geminal dichlorocyclopropanones **22** and **37**. Here, the intermediacy of chlorine-bridged diradicals **42** and **43** may preclude racemization.

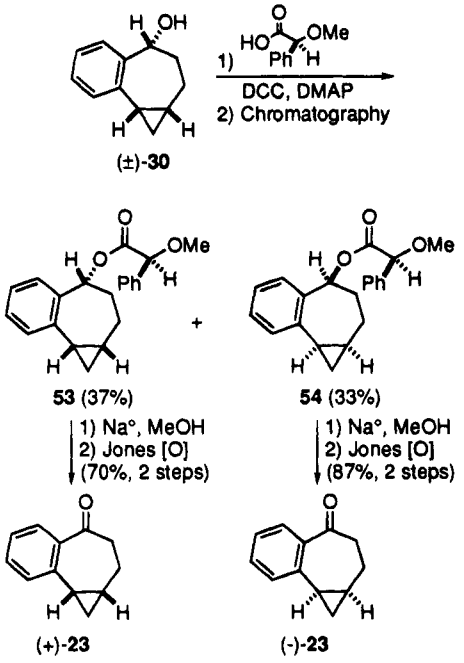
(34) We did not determine the enantiomeric purities of the recovered reactants in these experiments. Such measurements could provide additional information about the propensities for racemization in central bond homolyses.

(35) Wilson, K. E.; Seidner, R. T.; Masamune, S. *J. Chem. Soc., Chem. Commun.* **1970**, 213.

(36) (a) Hassner, A.; Alexanian, V. *Tetrahedron Lett.* **1978**, 4475. (b) Neises, B.; Steglich, W. *Angew. Chem., Int. Ed. Engl.* **1978**, *17*, 522.

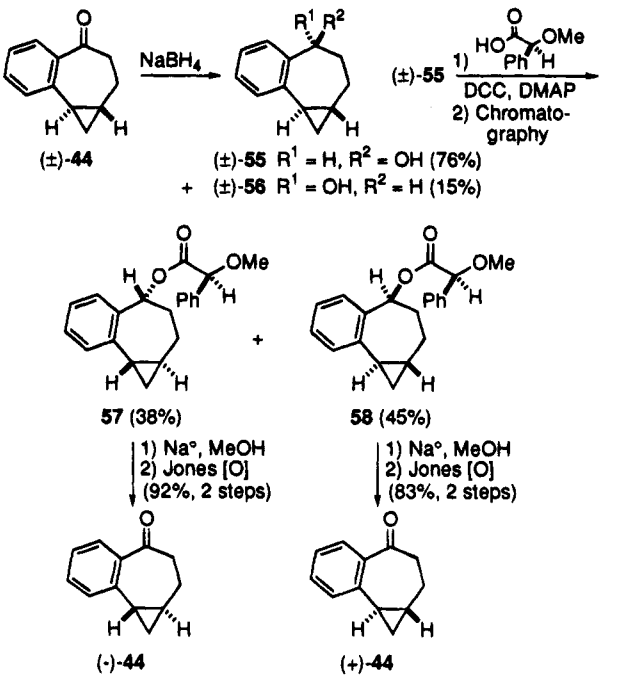
(37) Trost, B. M.; Belletire, J. L.; Godleski, S.; McDougal, P. G.; Balkovec, J. M.; Baldwin, J. J.; Christy, M. E.; Ponticello, G. S.; Varga, S. L.; Springer, J. P. *J. Org. Chem.* **1986**, *51*, 2370. Ohtani, I.; Kusumi, T.; Ishitsuka, M. O.; Kakisawa, H. *Tetrahedron Lett.* **1989**, *30*, 3147. Ohtani, I.; Kusumi, T.; Kashman, Y.; Kakisawa, H. *J. Org. Chem.* **1991**, *56*, 1296. Ohtani, I.; Kusumi, T.; Kashman, Y.; Kakisawa, H. *J. Am. Chem. Soc.* **1991**, *113*, 4092.

protocol for the latter substrate. Esterification of (±)-**30** with *(S)*-(+)-*O*-methylmandelic acid (DCC, DMAP) provided diastereomeric esters **53** and **54** in 37 and 33% yields after flash chromatography. The absolute configurations of the cyclopropyl carbinols again derived from analysis of the mandelate ^{1}H NMR spectra.[37] Removal of the chiral auxiliary (NaOMe, methanol) provided (+)- and (−)-**30** (83 and 88% yields), and oxidation with Jones reagent then afforded (+)-**23** (84%) and (−)-**23** (99%), respectively. Mosher analysis revealed enantiomeric purities of 93% ee for both (+)- and (−)-**30**.



The last resolution entailed reduction of (±)-**44** with $NaBH_4$ as before, furnishing alcohols (±)-**55** and (±)-**56** in 76 and 15% yields after chromatography. The relative configurations, deduced via NOE studies, reflected the same stereochemical preference as observed in the reduction of ketone **32**. Derivatization of the major isomer [(±)-**55**] with *(S)*-(+)-*O*-methylmandelic acid (DCC, DMAP) then afforded the readily separable esters **57** and **58** (38 and 45% yields). Following the determination of absolute stereochemistry,[37] removal of the chiral auxiliary by methanolysis afforded (−)-**55** and (+)-**55** in 97 and 89% yields from **57** and **58**. Finally, Jones oxidation provided ketones (−)-**44** and (+)-**44** (93−95% yields). The enantiomeric purities of (−)-**55** and (+)-**55** proved to be >98 and 88% ee, as determined by Mosher analysis.

Mechanistic Studies: Central vs Peripheral Bond Cleavage. With the requisite enantiomerically enriched substrates in hand, we turned to the mechanistic investigations. As noted above, the potential for direct racemization of the reactants and products necessitated measurement of losses in optical activity at low conversions. This constraint in turn precluded the use of optical rotation or techniques involving derivatization, as such methods would require unrealistically large quantities of enantimerically enriched materials. Fortunately, a number of HPLC columns containing scalemic stationary phases are now commercially available, although at considerable expense. Moreover, the presence of aromatic chromophores in our substrates and the extreme sensitivity of UV detection rendered the determination of enantiomeric purities by HPLC particularly attractive.



To this end, we discovered that Daicel Industries Chiralcel OC column would separate the cis-fused cyclopropanes (+)- and (−)-**21**, whereas the Daicel Chiralpak OT-(+) column resolved the corresponding trans enantiomers (+)- and (−)-**32**.[38]

At low conversion (ca. 2%), irradiation of (−)-**21** (90% ee) produced (−)-**32** of 78% ee. The observed decrease in enantiomeric purity corresponds to a minimum of 13% central bond cleavage. Similarly, photolysis of (+)-**32** (93% ee) furnished (+)-**21** of 72% ee, requiring at least 23% central bond cleavage.

Although the Chiralcel OC and Chiralpak OT-(+) columns were ineffective, the Daicel Chiralcel OD column did give satisfactory separation of (+)- and (−)-**23**. Unfortunately, the HPLC resolution of (+)- and (−)-**44** was never achieved. We nonetheless explored the photolysis of (−)-**44** (98% ee) at low conversion; the formation of (−)-**23** with an enantiomeric purity of 70% ee indicated that this conversion involved at least 28% central bond cleavage.

The observed partitioning between peripheral and central bond cleavage in the photoisomerizations of enriched **21** and **32** was not unexpected, in view of the formation of secondary photoproducts **33** and **34** in earlier experiments. The modest increase in central bond homolysis for the trans-fused isomer **32** may reflect weakening of this bond or improved central bond overlap with the π-system, vis-à-vis **21**.[39] On the other hand, the apparent predominance of peripheral bond cleavage in the photolysis of the enriched parent **44** was quite surprising. Here we had anticipated that the influence of radical stabilities, the "twist-bent" central bond,[40] and favorable π-system overlap would lead to a preference for central bond cleavage.

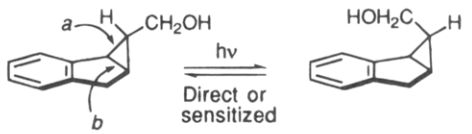
These results suggest that other factors control the sense of bond cleavage in **44**. A possible rationale for the observed selectivity derives from studies reported by

(38) Daicel Chemical Industries, Ltd., New York, NY.
(39) Hixson, S. S.; Borovsky, J. *J. Am. Chem. Soc.* **1976**, *98*, 2840 and references cited therein.
(40) (a) Gassman, P. G. *J. Chem. Soc., Chem. Commun.* **1967**, 793. (b) Dixon, D. A.; Gassman, P. G. *J. Am. Chem. Soc.* **1988**, *110*, 2309.

Table 1. Influence of the Triplet Quencher Piperylene on the Photoisomerizations of 3, 21, 22, and 23

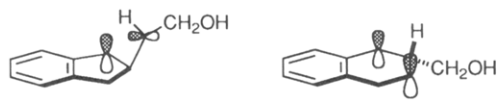
substrate	0.0 M piperylene cis/trans (6 h) (% secondary products)	0.05 M piperylene cis/trans (6 h) (% secondary products)	0.5 M piperylene cis/trans (6 h) (% secondary products)
3	1:4 (36)	1:9 (<5)	1:50 (0)
21	1:1 (17)	1:4 (3)	1:8 (2)
22	1:1 (70)	1:4 (60)	1:23 (26)
23	13:1 (0)	4:1 (0)	2:1 (0)

Hixson, who investigated the competition between peripheral and central bond scission in the photochemical interconversion of exo and endo cyclopropyl indenes **59** and **60**.[39] The ee's of the products produced by photolysis



59 **60**

of enantiomerically enriched **59** or **60** depended upon the conditions employed. At low conversion, direct irradiation reportedly proceeded via 19% central *(b)* and 81% peripheral *(a)* bond cleavage. In contrast, acetone sensitization furnished products arising solely via cleavage of bond *a*. The difference in reactivity was attributed to the stereoelectronic preferences of intermediate singlet and triplet diradicals. Specifically, diradical **62** can be viewed as a cyclic orbital array analogous to benzocyclobutadiene. By providing excited-state electron delocalization, the latter geometry would favor a singlet process.[39] In contrast, diradical **61** can readily adopt an orthogonal orientation between the two *p*-orbitals, better suited to triplet states which prefer configurations with maximal separation of the unpaired electrons.



61 **62**

The Influence of Piperylene: Evidence for Photoisomerization via Triplet Diradicals. The above argument could likewise explain the observed preference for peripheral rather than central bond cleavage in our isomerizations if they also occurred via triplet mechanisms. To explore this possibility, we briefly investigated the effects of the triplet quencher piperylene (mixture of isomers) on the reactions of **3** and **21**–**23**. For each substrate, a 0.05 M solution in hexanes (C_6D_6 for **22**) was divided into three portions. One third was used as a control, and the others were adjusted to 0.05 and 0.5 M in piperylene. Each set of three samples was then irradiated in a merry-go-round apparatus. The reactions were monitored by HPLC (for **3**), GC (**21** and **23**), and ^{1}H NMR (**22**).

Piperylene profoundly altered the photochemical behavior of (+)-**3** (Table 1). A quencher concentration of only 0.05 M increased the photostationary **9:3** (trans:cis) ratio from 4:1 to greater than 9:1 and significantly inhibited the formation of secondary photoproducts **10** and **11**. Upon increasing the piperylene concentration to 0.5 M, the reaction produced the trans cyclopropane **9** almost exclusively, and the secondary photochemistry was completely suppressed!

The effects of piperylene on the photoisomerization of **21** were almost as dramatic. The inclusion of 0.05 M piperylene again shifted the photostationary state toward the trans isomer (**32**) and diminished the formation of secondary products **33** and **34**. Moreover, in the presence of 0.5 M piperylene, the photostationary state ratio of **21** to **32** increased further to ca. 1:8, and the combined yield of **33** and **34** was reduced to less than 2%.

Qualitatively, piperylene influenced the photochemistry of **22** in similar fashion, but the suppression of secondary photoproducts was less effective, as evidenced by the formation of **38** and **39** in 26% yield after 6 h at a quencher concentration of 0.5 M. This anomalous behavior could reflect either the facile formation of a chlorine-bridged diradical or the intervention of symmetry-allowed singlet processes *(vide supra)*. It is also noteworthy that piperylene altered the proportions of the ring-opened isomers. Specifically, the **38:39** ratio increased from ca. 1:2 in the control to ca. 3:1 in the presence of 0.5 M quencher.

For the parent cyclopropane **23**, piperylene again shifted the photostationary state, although the trans isomer (**44**) did not predominate even at a quencher concentration of 0.5 M.

These observations indicate that the photoisomerizations of the trans cyclopropanes **9**, **32**, **37**, and **44** proceed primarily via the triplet manifold. The initial cis-to-trans conversions of **3**, **21**, **22**, and **23** must occur either via triplets at rates faster than diffusion or via singlet excited states; the predominance of peripheral bond cleavage suggests the former alternative.

By increasing the trans/cis ratios and inhibiting secondary photochemistry, piperylene quenching also led to an improved protocol for preparative isomerizations. We have employed this tactic to enhance the most problematic conversion encountered in this study; in the presence of 0.13 M piperylene, irradiation of 7 g of **23** routinely afforded over 1 g of **44**. The more dramatic effects of piperylene in other analytical experiments suggest that this approach will be general, furnishing a variety of *trans*-benzobicyclo[5.1.0]octenes in multigram quantities.

Summary. We have discovered a remarkably efficient photochemical route to the strained *trans*-benzobicyclo[5.1.0]octene ring system. In each case, formation of the primary and secondary photoproducts is best rationalized by invoking a stationary state between the cis- and trans-fused cyclopropanes, established via predominant but not exclusive cleavage of peripheral cyclopropane bonds. The latter preference, demonstrated in isomerizations of enantiomerically enriched **21**, **32**, and **44**, is in accord with expectations for the generation of triplet diradicals; piperylene quenching studies in turn confirmed the intermediacy of triplets in the trans-to-cis conversions. By increasing the trans:cis ratios and reducing the extent of secondary photochemistry, the triplet quenching experiments also led to improved protocols for preparative isomerizations.

Experimental Section[41,43]

Diketone (−)-4. A solution of ketone (+)-**3** (105 mg, 0.037 mmol) in distilled hexane (240 mL) was continuously saturated

with oxygen and irradiated for 5 h at 0 °C. Flash chromatography (silica, 25% EtOAc/hexanes) afforded (+)-**3** (39 mg, 33% recovery) and (−)-**4**, the latter as a colorless oil: $[\alpha]^{25}_D$ −35.8° (*c* 0.69, $CHCl_3$); IR ($CHCl_3$) 3500 (w), 3020 (m), 2980 (m), 2940 (m), 2885 (m), 1760 (w), 1680 (s), 1555 (m), 1450 (m), 1395 (m), 1385 (m), 1345 (m), 1320 (w), 1290 (s), 1450 (s), 1200 (m), 1125 (m), 1150 (m), 980 (w), 950 (w), 910 (w) cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 3.81 (s, 3 H), 3.42 (dt, *J* = 7.5, 17.5 Hz, 1 H), 3.01−2.87 (m, 4 H), 2.81−2.72 (m, 2 H), 2.32 (s, 3 H), 2.35−2.12 (m, 2 H), 2.92−2.17 (m, 2 H), 1.30 (s, 3 H), 1.13 (s, 3 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 211.0, 201.0, 157.9, 146.8, 141.3, 139.0, 129.0, 127.2, 71.7, 59.8, 59.6, 41.5, 33.8, 30.2, 29.9, 26.9, 25.2, 20.3, 12.3; high-resolution mass spectrum (CI, NH_3) *m/z* 316.1679 (M^+; calcd for $C_{19}H_{24}O_4$ 316.1675).

Anaerobic Photolysis of Ketone (+)-3. A solution of ketone (+)-**3** (8 mg, 0.03 mmol) in benzene (1 mL) was degassed via five freeze−pump−thaw cycles and irradiated for 6 h at room temperature. Flash chromatography (silica, 10% EtOAc/hexanes) gave (+)-**3** (0.7 mg, 8% recovery), (+)-**9** (2.6 mg, 33%), (+)-**10** (2.4 mg, 30%), and **11** (0.5 mg, 6%).

(+)-**9**: colorless solid; mp 124−125 °C; $[\alpha]^{19}_D$ +175° (*c* 0.40, $CHCl_3$); UV (EtOH) λ_{max} 311 (ε 1,559, sh), 270 (4,587), 222 (12,055), 204 (11,587) nm; IR ($CHCl_3$) 3040 (s), 2980 (s), 2860 (w), 1680 (s), 1580 (m), 1460 (w), 1370 (w), 1300 (m), 1240 (m), 1215 (m), 1160 (w), 1140 (s), 1160 (w), 920 (m), 900 (m), 820 (m), 770 (m) cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 3.81 (s, 3 H), 3.26 (dt, *J* = 9.5, 17.5 Hz, 1 H), 3.09 (dt, *J* = 10.0, 17.5 Hz, 1 H), 2.98−2.70 (m, 4 H), 2.41−2.28 (m, 1 H), 2.24 (s, 3 H), 2.25−2.02 (m, 1 H), 2.01−1.81 (m, 1 H), 1.72−1.51 (m, 1 H), 1.30 (s, 3 H), 1.29 (d, *J* = 7.2 Hz, 1 H), 1.10 (s, 3 H), 0.71−0.55 (m, 1 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 206.4, 156.1, 145.6, 142.1, 137.9, 134.2, 127.1, 59.2, 47.4, 35.3, 33.5, 33.4, 31.3, 30.0, 25.4, 24.3, 23.0, 21.4, 13.1; high-resolution mass spectrum (CI, NH_3) *m/z* 284.1780 (M^+; calcd for $C_{19}H_{24}O_2$ 284.1777).

(+)-**10**: colorless oil; $[\alpha]^{24}_D$ +50.9° (*c* 0.22, $CHCl_3$); IR ($CHCl_3$) 3000 (m), 2960 (s), 2860 (m), 1740 (s), 1470 (m), 1455 (m), 1405 (m), 1360 (w), 1315 (w), 1290 (m), 1230 (m), 1200 (w), 1150 (m), 1080 (m), 980 (w) cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 3.78 (d, *J* = 7.9 Hz, 1 H), 3.70 (s, 3 H), 2.99−2.65 (m, 5 H), 2.30 (s, 3 H), 2.29 (m, 1 H), 2.19−1.92 (m, 3 H), 1.95−1.68 (m, 2 H), 1.28 (s, 3 H), 1.21 (s, 3 H); high-resolution mass spectrum (CI, NH_3) *m/z* 284.1770 (M^+; calcd for $C_{19}H_{24}O_2$ 284.1777).

11: colorless oil; IR (CCl_4) 3080 (w), 2960 (m), 2940 (s), 2880 (m), 2840 (m), 2720 (w), 1730 (s), 1620 (w), 1590 (w), 1470 (m), 1460 (m), 1430 (m), 1410 (m), 1380 (m), 1360 (m), 1330 (w), 1300 (m), 1250 (w), 1200 (m), 1170 (m), 1100 (m), 1070 (w), 1000 (m), 800 (m) cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 9.95 (apparent t, *J* = 1.0 Hz, 1 H), 6.35 (apparent t, *J* = 1.2 Hz, 1 H), 3.78 (s, 3 H), 3.05−2.80 (m, 6 H), 2.58 (apparent t, *J* = 7.0 Hz, 2 H), 2.29 (s, 3 H), 2.11 (dt, *J* = 7.0, 15.0 Hz, 2 H), 1.29 (s, 6 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 201.8 (−), 155.9 (+), 153.7 (+), 143.4 (+), 141.2 (+), 136.8 (+), 132.4 (+), 121.3 (−), 119.9 (+), 59.7 (−), 50.7 (+), 41.8 (+), 30.3 (+), 29.2 (+), 25.8 (+), 21.8 (−), 18.9 (+), 11.7 (−); high-resolution mass spectrum (CI, NH_3) *m/z* 284.1767 (M^+; calcd for $C_{19}H_{24}O_2$ 284.1777).

Acid 12. A solution of aldehyde **11** (30.0 mg, 0.105 mmol) in acetone (2 mL) was cooled to 0 °C and treated with Jones reagent (2.19 M, ca. 2 mL) until a red color persisted for 2 min. The reaction was quenched with 2-propanol (1 mL), H_2O (3 mL), and EtOAc (10 mL). The aqueous layer was extracted with EtOAc (3 × 10 mL), and the combined organic phases were dried ($MgSO_4$), filtered, and concentrated *in vacuo*. Flash chromatography (silica, gradient elution: 25 → 35% EtOAc/hexanes) afforded **12** (22.5 mg, 71% yield) as a colorless solid: mp 131−132 °C; IR ($CHCl_3$) 3000 (m), 2960 (s), 1710 (s), 1610 (w), 1460 (m), 1420 (m), 1400 (m), 1370 (w), 1310 (w), 1290 (m), 1260 (s), 1220 (m), 1200 (m), 1190 (m), 1160 (m), 1090 (s), 1020 (m), 850 (w) cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 6.39 (s, 1 H), 3.78 (s, 3 H), 3.00 (apparent t, *J* = 7.1 Hz, 2 H), 2.92 (apparent t, *J* = 7.1 Hz, 2 H), 2.79 (apparent t, *J* = 9.0 Hz, 2 H), 2.51 (apparent t, *J* = 9.0 Hz, 2 H), 2.29 (s, 3 H), 2.10 (apparent t, *J* = 7.0 Hz, 2 H), 1.25 (s, 6 H); high-resolution mass spectrum (CI, NH_3) *m/z* 300.1734 (M^+; calcd for $C_{19}H_{24}O_3$ 300.1726).

Alcohols 14 and 15. A solution of (+)-**10** (16.0 mg, 0.056 mmol) in methanol (1 mL) was cooled to 0 °C, and $NaBH_4$ (10.6 mg, 0.281 mmol) was added in one portion. The mixture was stirred for 1 h, allowed to warm to room temperature, and quenched with H_2O (50 μL). The resultant mixture was adsorbed onto silica gel *in vacuo*; flash chromatography (silica, 10% EtOAc/hexanes) afforded a slower eluting alcohol **14** (6.5 mg, 40% yield) and a faster eluting alcohol **15** (4.2 mg, 26% yield).

14: colorless oil; ^1H NMR (500 MHz, $CDCl_3$) δ 4.32 (br t, 1 H), 3.77 (s, 3 H), 3.49−3.46 (d, *J* = 12.0 Hz, 1 H), 2.97−2.82 (m, 4 H), 2.64 (dd, *J* = 16.0, 7.0 Hz, 1 H), 2.31 (s, 3 H), 2.13−1.95 (m, 4 H), 1.88−1.79 (m, 1 H), 1.66 (d, *J* = 3.0 Hz, 1 H), 1.60−1.44 (m, 1 H), 1.33 (s, 3 H), 1.15 (s, 3 H); high-resolution mass spectrum (CI, methane) *m/z* 286.1925 [M^+; calcd for $C_{19}H_{26}O_2$ 286.1926].

15: colorless oil; ^1H NMR (500 MHz, $CDCl_3$) δ 4.51 (br t, 1 H), 3.76 (s, 3 H), 3.75−3.69 (dd, *J* = 10.0, 6.0 Hz, 1 H), 3.49 (dd, *J* = 12.0, 8.0 Hz, 1 H), 2.94 (apparent t, 1 H), 2.92−2.86 (m, 2 H), 2.62 (dd, *J* = 18.0, 8.0 Hz, 1 H), 2.22 (s, 3 H), 2.12−2.04 (m, 3 H), 1.95 (dd, *J* = 12.0, 8.0 Hz, 1 H), 1.82−1.72 (m, 1 H), 1.70−1.62 (m, 1 H), 1.57 (br s, 1 H), 1.31 (s, 3 H), 1.28 (s, 3 H); high-resolution mass spectrum (CI, methane) *m/z* 286.1925 [M^+; calcd for $C_{19}H_{26}O_2$ 286.1926].

Photolysis of Ketone 16. A solution of ketone **16** (55 mg, 0.36 mmol) in hexanes (4.8 mL) was irradiated for 15 min at room temperature. Flash chromatography (silica, gradient elution: 10 → 30% EtOAc/hexanes) furnished **17** (28 mg, 51% yield), **18** (7 mg, 13%), and **19** (10 mg, 18%).

17: colorless oil; UV (EtOH) λ_{max} 210 (ε 1,496), 293 (78) nm; IR ($CHCl_3$) 3020 (m) 2960 (s), 2920 (m), 1740 (s), 1470 (w), 1460 (w), 1410 (w), 1570 (w), 1230 (m), 1670 (m) cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 5.58 (dd, *J* = 4.0, 8.0 Hz, 1 H), 5.45 (dd, *J* = 2.5, 8.0 Hz, 1 H), 3.42 (m, 1 H), 2.53 (m, 1 H), 2.24 (m, 2 H), 1.96 (m, 1 H), 1.73 (m, 1 H), 1.12 (s, 3 H), 1.09 (s, 3 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 217.9 (+), 142.9 (−), 124.4 (−), 59.4

(41) **Materials and Methods.** Reactions were carried out under an argon atmosphere in glassware flame-dried under vacuum, unless othewise stated. Diethyl ether, tetrahydrofuran (THF), and 1,2-dimethoxyethane (DME) were freshly distilled under nitrogen from sodium/benzophenone. Benzene, dichloromethane, and diisopropylamine were freshly distilled under nitrogen from calcium hydride. *n*-Butyllithium was purchased from Aldrich and standardized by titration with diphenylacetic acid or menthol/triphenylmethane. LDA was generated immediately prior to use by reaction of diisopropylamine with *n*-butyllithium in the indicated solvent at 0 °C for 30 min. DIBAL was purchased from Aldrich as a 1.0 M solution in hexanes. Ethanol-free chloroform was prepared by washing successively with H_2SO_4, H_2O, and K_2CO_3 followed by distillation from P_2O_5. Copper(I) iodide was purified via a published procedure: Kauffman, G. B.; Teter, L. A. *Inorg. Synth.* **1963**, *7*, 9. Unless stated otherwise, all reactions were magnetically stirred and monitored by thin-layer chromatography (TLC) using 0.25-mm, precoated silica gel plates from E. Merck. Silica gel 60 (particle size 0.040−0.063 mm) supplied by E. Merck was used for flash chromatography. Alumina chromatography was performed using "alumina adsorption" (nonactivated) purchased from Fisher Scientific. Melting points were measured with a Bristoline heated-stage microscope and are corrected. Ultraviolet spectra were recorded on an IBM Model 9420 UV−vis spectrophotometer. Infrared spectra were recorded on a Perkin-Elmer Model 283B spectrophotometer using polystyrene as an external standard. Carbon and proton NMR spectra were measured on Bruker AM-500, AM-250, or WM-200 spectrometers. Chemical shifts are reported relative to internal tetramethylsilane (^1H and ^{13}C, δ 0.00) or chloroform (^1H, δ 7.24; ^{13}C, δ 77.0). For ^{13}C spin-echo and broad-band decoupling experiments, chemical shifts identified as (+) designate singlets or triplets, whereas the (−) resonances denote doublets or quartets. NOE experiments were performed with the Bruker NOEDIFF microprogram; samples were degassed with argon in the NMR tubes for no less than 20 min. Mass spectra were obtained with a VG Micromass 70/70H or VG ZAB-E spectrometer. Microanalyses were performed by Robertson Labs, Madison, NJ. Single-crystal X-ray data were collected with an Enraf-Nonius CAD-4 automated diffractometer. Gas chromatography was performed with a Hewlett-Packard Model 5790A capillary GC and a 25-m × 0.2-mm column packed with crosslinked methyl silicone gum. High-performance liquid chromatography (HPLC) was performed with a Waters analytical/semipreparative system. All photochemical experiments were carried out with a 450-W Hanovia medium-pressure mercury lamp (part no. 679A0360) suspended in a Pyrex well cooled with tap water. The determination of enantiomeric excess by the Mosher method involved esterification of the substrate alcohol with (*R*)-(+)-MTPA and 1,3-dicyclohexylcarbodiimide (DCC) in CH_2Cl_2, followed by purification and ^1H NMR integration of the resultant esters. Where possible, the racemic alcohol was also subjected to the analysis protocol as a control.

(−), 50.4 (−), 47.8 (+), 39.4 (+), 29.7 (−), 23.4 (+), 21.6 (−); high resolution mass spectrum (CI, NH_3) *m/z* 150.1044 (M^+; calcd for $C_{10}H_{14}O$ 150.1041).

18: colorless oil; IR ($CHCl_3$) 3020 (m), 2985 (s), 2920 (m), 2900 (m), 2860 (m), 2820 (w), 2730 (w), 1730 (s), 1605 (w), 1460 (m), 1435 (w), 1410 (w), 1390 (w), 1360 (w), 1220 (m) cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 9.82 (apparent t, J = 2.0 Hz, 1 H), 6.24 (d, J = 6.0 Hz, 1 H), 6.19 (dd, J = 3.0, 6.0 Hz, 1 H), 5.85 (m, 1 H), 2.75 (m, 2 H), 2.48 (m, 2 H), 1.59 (s, 3 H), 1.08 (s, 3 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 201.9 (+), 156.0 (+), 145.7 (−), 127.1 (−), 122.3 (−), 52.6 (+), 41.5 (+), 21.7 (−), 18.8 (+); high-resolution mass spectrum (CI, NH_3) *m/z* 150.1043 (M^+; calcd for $C_{10}H_{14}O$ 150.1041).

19: colorless solid; mp 174−176 °C; IR ($CHCl_3$) 3010 (m), 2980 (m), 2940 (m), 2920 (m), 1700 (s), 1450 (w), 1430 (w), 1380 (w), 1330 (m), 1220 (m), 1205 (m), 1170 (m) cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 2.91 (m, 1 H), 2.42 (m, 2 H), 2.05 (m, 1 H), 1.47 (m, 1 H), 1.04 (s, 3 H), 0.98 (s, 3 H), 0.87 (m, 2 H), 0.65 (m, 1 H); high-resolution mass spectrum (CI, NH_3) *m/z* 300.2079 (M^+; calcd for $C_{20}H_{28}O_2$ 300.2082).

***cis*-Dichlorocyclopropane 22.** A solution of benzosuberenone[17] (**24**) (19.4 g, 122 mmol) in chloroform (ethanol free, 39 mL) was treated with triethyl(benzyl)ammonium chloride (TEBA) (0.279 g, 1.22 mmol) and 50% aqueous NaOH (24 mL). The resulting dark-red solution was stirred vigorously and warmed to 50 °C for 15 h. The solution was then cooled and poured into a separatory funnel containing H_2O and CH_2Cl_2 (1:1, 75 mL). The aqueous phase was extracted with CH_2Cl_2 (3 × 75 mL) and the combined organic phases were washed with brine (50 mL), dried (Na_2SO_4), filtered, and concentrated *in vacuo*. Flash chromatography (silica, 15% EtOAc/hexanes) afforded **22** (22.0 g, 75% yield) as a colorless solid. A small sample was rechromatographed (silica, 5% EtOAc/hexanes), providing analytically pure **22** as a colorless solid: mp 84−85 °C; UV (MeOH) λ_{max} 283 (ϵ 980), 242 (5882), 211 (14 705) nm; IR ($CHCl_3$) 3040 (w), 3000 (m), 2930 (w), 2880 (w), 2860 (w), 1680 (s), 1600 (s), 1480 (m), 1440 (m), 1400 (w), 1390 (w), 1320 (s), 1305 (w), 1280 (s), 1240 (s), 1220 (m), 1170 (w), 1100 (w), 1070 (w), 1020 (w), 990 (w), 970 (w), 920 (s), 890 (m), 860 (w), 825 (s), 815 (s), 690 (m), 560 (m) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.52 (apparent t, J = 6.8 Hz, 2 H), 7.41−7.35 (comp m, 2 H), 2.90−2.85 (comp m, 2 H), 2.77 (m, 1 H), 2.31−2.23 (comp m, 2 H), 1.63 (m, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 205.1, 139.3, 132.4, 131.7, 131.2, 129.1, 128.1, 64.3, 40.7, 34.4, 34.1, 20.9; high-resolution mass spectrum (CI, NH_3) *m/z* 240.0077 (M^+; calcd for $C_{12}H_{10}Cl_2O$ 240.0102).

Anal. Calcd for $C_{12}H_{10}Cl_2O$: C, 59.78; H, 4.18. Found: C, 59.54; H, 4.17.

Dimethylcyclopropane Ketal 26. A slurry of CuI (12.8 g, 67.4 mmol) in Et_2O (134 mL) was cooled to 0 °C, and MeLi (1.4 M in Et_2O, 96.3 mL, 134.8 mmol) was added. The milky white suspension first turned bright yellow and then became clear and colorless. The flask was cooled to −15 °C, and dichloride **25** (3.84 g, 13.5 mmol) was added as an ethereal solution (5 mL). A small amount of yellow precipitate formed around the rim but the solution remained colorless. The flask was fitted with a new additional septum and placed in a freezer at −20 °C. After 60 h, the reaction was warmed to 0 °C and MeI (16.7 mL, 269 mmol) was added. The suspension turned yellow instantly. The resultant mixture was stirred for 30 min while being warmed to ambient temperature and then poured into saturated aqueous NH_4Cl (45 mL) and concentrated NH_4OH solution (5 mL). The biphasic mixture was extracted with EtOAc (3 × 75 mL), and the combined organic phases were washed with brine, dried (Na_2SO_4), filtered, and concentrated *in vacuo*. This material was typically used without purification in the next step. An analytical sample was isolated via flash chromatography (silica, 5% EtOAc/hexanes) as a colorless solid: mp 44−45 °C (MeOH); IR ($CHCl_3$) 3000 (s), 2950 (s), 2890 (s), 1600 (w), 1490 (m), 1450 (m), 1380 (m), 1350 (m), 1340 (m), 1320 (m), 1270 (m), 1260 (s), 1230 (m), 1190 (m), 1160 (s), 1150 (s), 1010 (s), 1000 (s), 950 (m), 920 (m), 895 (m), 855 (m), 810 (m), 580 (m) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.44 (dd, J = 0.6, 7.4 Hz, 1 H), 7.23 (m, 1 H), 7.16 (comp m, 2 H), 4.00 (comp m, 2 H), 3.84 (m, 1 H), 3.62 (m, 1 H), 2.16 (td, J = 5.4, 13.9 Hz, 1 H), 2.04 (ddd, J = 1.2, 5.9, 14.1 Hz, 1 H), 1.95 (d, J = 9.2 Hz, 1 H), 1.77 (m, 1 H), 1.22 (s, 3 H), 1.02 (ddd, J = 4.4, 8.6, 12.4 Hz, 1 H), 0.87 (s, 3 H), 0.77 (ddd, J = 6.1, 12.7, 26.0 Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 140.1, 136.7, 132.8, 127.9, 125.6, 125.3, 64.3, 63.8, 36.5, 29.9, 28.6, 25.5, 21.4, 20.6, 17.1, 17.0; high-resolution mass spectrum (CI, NH_3) *m/z* 245.1533 [$(M + H)^+$; calcd for $C_{16}H_{21}O_2$ 245.1541].

Anal. Calcd for $C_{16}H_{20}O_2$: C, 78.65; H, 8.25. Found: C, 78.47; H, 7.97.

Cyclopropyl Ketone (±)-21. A solution of crude acetal **26** in acetone (20 mL) was treated with concd HCl (12 M, 0.2 mL). After 3 h at room temperature the reaction was quenched with excess $NaHCO_3$. Following concentration *in vacuo*, the residue was diluted with H_2O (20 mL) and the resultant mixture extracted with Et_2O (3 × 30 mL). The combined organic phases were dried (Na_2SO_4), filtered, and concentrated *in vacuo*. Flash chromatography (silica, 5% EtOAc/hexanes) afforded (±)-**21** (2.33 g, 86% yield, two steps) as a colorless oil: UV (MeOH) λ_{max} 212 (ϵ 13 588), 243.2 (5116), 290 (782) nm; IR ($CHCl_3$) 3080 (w), 3000 (m), 2980 (m), 2940 (m), 2860 (m), 1670 (s), 1590 (m), 1480 (w), 1450 (m), 1440 (w), 1400 (w), 1370 (w), 1320 (m), 1280 (s), 1220 (m), 1120 (w), 1020 (w), 1000 (w), 925 (w), 880 (w) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.48 (dd, J = = 1.4, 7.7 Hz, 1 H), 7.39 (td, J = 1.5, 7.5 Hz, 1 H), 7.25 (td, J = 1.0, 7.5 Hz, 1 H), 7.15 (d, J = 7.7 Hz, 1 H), 2.84 (ddd, J = 3.2, 13.4, 18.6 Hz, 1 H), 2.70 (dt, J = 3.7, 18.7 Hz, 1 H), 2.04−2.00 (m, 1 H), 1.83 (d, J = 8.8 Hz, 1 H), 1.41−1.32 (m, 1 H), 1.24 (s, 3 H), 1.18 (ddd, J = 5.0, 7.7, 13.9 Hz, 1 H), 0.96 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 208.1 (+), 140.3 (+), 136.9 (+), 132.6 (−), 131.4 (−), 128.9 (−), 126.6 (−), 42.4 (+), 29.4 (−), 28.7 (−), 28.4 (−), 21.5 (+), 20.1 (+), 17.0 (−); high-resolution mass spectrum (CI, NH_3) *m/z* 200.1137 (M^+; calcd for $C_{14}H_{16}O$ 200.1201).

Cyclopropyl Ketone (−)-21. A solution of **48** (0.100 g, 0.285 mmol) in MeOH (10.0 mL) was treated with NaOMe (50.0 mg, 0.925 mmol) and stirred at ambient temperature for 2 h. Following addition of silica gel (ca. 0.5 g) and concentration *in vacuo*, flash chromatography (silica, 20% EtOAc/hexanes) afforded alcohol (−)-**45**. The latter was dissolved in acetone (5.0 mL) and treated with Jones reagent (2.61 M) at ambient temperature until a red color persisted. After 15 min the excess oxidant was destroyed by adding 2-propanol until a green color persisted. The acid was then neutralized with solid $NaHCO_3$ until gas evolution ceased. The mixture was filtered through Celite and the filtrate adsorbed onto silica gel (ca. 0.5 g) *in vacuo*. Flash chromatography (silica, 5% EtOAc/hexanes) then afforded (−)-**21** (40.8 mg, 72% yield for two steps) as a colorless oil: $[\alpha]^{26}_D$ −128.6° (*c* 4.0, $CHCl_3$); 90% ee [determined via ^1H NMR analysis of the Mosher esters derived from alcohol (−)-**45**].

Cyclopropyl Ketone (+)-21. Following the procedure described above for (−)-**21**, methanolysis of ester **47** (0.259 g, 0.739 mmol) followed by Jones oxidation and flash chromatography furnished (+)-**21** (0.121 g, 82% yield, two steps) as a colorless oil: $[\alpha]^{26}_D$ +127.5° (*c* 4.1, $CHCl_3$).

Ketone (±)-23. Method A. A solution of acetal **27** (0.201 g, 0.929 mmol) in acetone (5.0 mL) was treated with concentrated HCl (12 M, 0.10 mL) and the resultant mixture stirred at room temperature for 2 h. Adsorbtion onto silica (ca. 1.0 g) *in vacuo* and flash chromatography (silica, 5% EtOAc/hexanes) gave (±)-**23** (0.128 g, 80% yield). **Method B.** At ambient temperature a solution of alcohol **30** (95.1 mg, 0.545 mmol) in acetone (1.5 mL) was treated with Jones reagent (2.19 M, 0.30 mL, 0.657 mmol). After 5 min excess oxidant was destroyed by adding 2-propanol (ca. 1.0 mL) and the mixture partitioned between H_2O (1 mL) and EtOAc (2 mL). The aqueous phase was extracted with EtOAc (3 × 3 mL) and the combined extracts were dried (Na_2SO_4), filtered, and adsorbed onto silica (ca. 1.0 g) *in vacuo*. Flash chromatography (silica, 10% EtOAc/hexanes) afforded (±)-**23** (91.2 mg, 96% yield) as a colorless oil: UV (MeOH) λ_{max} 285 (ϵ 511), 244 (4,591), 213 (10,103) nm; IR ($CHCl_3$) 3070 (m), 3010 (m), 2940 (m), 2870 (w), 1670 (s), 1600 (m), 1490 (m), 1450 (m), 1400 (w), 1330 (m), 1320 (m), 1280 (s), 1250 (m), 1210 (s), 1100 (m), 1020 (m), 940 (m), 910 (w), 880 (m), 840 (m) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.34−7.31 (comp m, 3 H), 7.20−7.17 (m, 1 H), 2.76 (ddd, J = 3.5, 12.5, 18.8 Hz, 1 H), 2.59 (dt, J = 3.9, 19.9 Hz, 1 H), 2.20 (ddd,

J = 3.0, 7.4, 13.9 Hz, 1 H), 1.99 (td, J = 5.2, 8.5 Hz, 1 H), 1.48–1.44 (comp m, 2 H), 1.08 (td, J = 4.6, 8.5 Hz, 1 H), 0.52 (dd, J = 4.9, 9.8 Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 208.5 (+), 139.5 (+), 138.9 (+), 132.2 (−), 131.5 (−), 128.1 (−), 126.8 (−), 42.4 (+), 25.2 (+), 17.8 (−), 17.1 (−), 14.7 (+); high resolution mass spectrum (CI, NH_3) m/z 173.0972 [$(M + H)^+$; calcd for $C_{12}H_{13}O$ 173.0966].

Ketone (+)-23. A solution of (+)-**30** (323 mg, 1.85 mmol) in acetone (2 mL) was titrated with Jones reagent (2.19 M) until a red color persisted for 2 min. The reaction mixture was then quenched with 2-propanol (ca. 1 mL) and diluted with H_2O (3 mL) and EtOAc (10 mL). The aqueous layer was extracted with EtOAc (3 × 10 mL), and the combined extracts were dried ($MgSO_4$), filtered, and concentrated *in vacuo*. Flash chromatography (silica, 30% EtOAc/hexanes) gave (+)-**23** (268 mg, 84% yield) as a colorless oil: $[\alpha]^{24}_D$ +188° (*c* 2.2, $CHCl_3$).

Ketone (−)-23. Following the procedure described above for (+)-**23**, Jones oxidation of (−)-**30** (367 mg, 2.11 mmol) and flash chromatography afforded (−)-**23** (360 mg, 99% yield) as a colorless oil: $[\alpha]^{24}_D$ −185° (*c* 2.0, $CHCl_3$).

Dichloro Ethylene Ketal 25. A solution of ketone **22** (13.2 g, 54.7 mmol), ethylene glycol (4.6 mL, 83.2 mmol), and PTSA (1.0 g, 5.47 mmol) in benzene (60 mL) was heated to reflux for 8 h with azeotropic water removal via a Dean-Stark trap. The mixture was then allowed to cool and the acid neutralized with solid $NaHCO_3$ (ca. 5 g). The resultant solution was washed with H_2O (50 mL) and the aqueous phase extracted with hexanes (3 × 50 mL). The combined organic layers were washed with brine (30 mL), dried (Na_2SO_4), filtered, and concentrated *in vacuo*. Flash chromatography (silica, 5% EtOAc/hexanes) provided **25** (14.0 g, 90% yield) as a yellow solid: mp 80.5–91.5 °C; IR ($CHCl_3$) 3010 (m), 2960 (m), 2890 (m), 1485 (m), 1450 (m), 1350 (m), 1310 (w), 1280 (m), 1250 (m), 1160 (s), 1120 (m), 1060 (s), 1000 (m), 960 (w), 950 (m), 940 (m), 915 (m), 820 (w), 810 (s), 590 (m) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.46 (dd, J = 1.3, 7.7 Hz, 1 H0, 7.41 (d, J = 7.6 Hz, 1 H), 7.34 (m, 1 H), 7.26 (m, 1 H), 4.04–3.96 (comp m, 2 H), 3.83 (td, J = 5.8, 7.3 Hz, 1 H), 3.62 (td, J = 5.4, 6.9 Hz, 1 H), 2.96 (d, J = 10.6 Hz, 1 H), 2.18 (m, 1 H), 2.12–2.02 (comp m, 3 H), 0.95 (m, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 139.7, 132.5, 131.3, 128.3, 127.1, 125.2, 109.7, 66.4, 64.3, 64.1, 35.5, 35.3, 31.8, 21.6; high-resolution mass spectrum (CI, NH_3) m/z 285.0433 [$(M+H)^+$; calcd for $C_{14}H_{15}{}^{35}Cl_2O_2$ 285.0449].

Dihydro Ketal 27. A solution of dichloride **25** (0.501 g, 1.75 mmol) in tri-*n*-butyltin hydride (4.0 mL, 14.9 mmol) was treated with AIBN (30.0 mg, 0.182 mmol) and heated at 160 °C for 3 h. The reaction mixture was then cooled to room temperature and, without workup, subjected to flash chromatography (silica, 5% EtOAc/hexanes), affording **27** (0.358 g, 94% yield) as a colorless oil: IR ($CHCl_3$) 3080 (m), 3020 (s), 2960 (m), 2930 (m), 2900 (m), 1740 (w), 1600 (w), 1480 (m), 1450 (m), 1360 (w), 1340 (w), 1320 (w), 1280 (m), 1260 (m), 1210 (m), 1160 (s), 1110 (w), 1060 (s), 1030 (m), 1000 (m), 980 (m), 950 (m), 940 (m), 900 (w), 840 (m) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40 (dd, J = 1.2, 7.6 Hz, 1 H), 7.36 (d, J = 7.5 Hz, 1 H), 7.24 (td, J = 1.4, 7.4 Hz, 1 H), 7.17 (apparent t, J = 7.5 Hz, 1 H), 4.04–3.99 (comp m, 2 H), 3.88–3.85 (m, 1 H), 3.68–3.64 (m, 1 H), 2.18–2.11 (comp m, 2 H), 2.04 (br dt, J = 5.2, 14.5 Hz, 1 H), 1.96 (ddd, J = 1.6, 5.8, 14.2 Hz, 1 H), 1.20–1.12 (m, 1 H), 1.05 (td, J = 4.4, 8.2 Hz, 1 H), 0.47 (ddd, J = 5.8, 12.4, 14.2 Hz, 1 H), 0.30 (dd, J = 4.7, 9.7 Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 139.3 (+), 139.1 (+), 132.3 (−), 128.3 (−), 125.8 (−), 124.5 (−), 110.8 (+), 64.3 (+), 63.8 (+), 36.4 (+), 26.4 (+), 19.0 (−), 14.9 (+), 13.2 (−); high-resolution mass spectrum (CI, NH_3) m/z 217.1250 [$(M + H)^+$; calcd for $C_{14}H_{17}O_2$ 217.1229].

Ketone 28. Treatment of a solution of benzosuberenone (**24**) (0.100 g, 0.632 mmol) in DME (3.0 mL) with CH_2I_2 (51 μL, 0.63 mmol) and then Et_2Zn (1.0 M in hexanes, 0.63 mL, 0.63 mmol) led to a slight exotherm and discoloration to light yellow. The mixture was heated at reflux for 3 h, cooled to room temperature, and poured into a mixture of 1 M aqueous HCl (15 mL) and EtOAc (10 mL). The aqueous phase was extracted with EtOAc (3 × 10 mL), and the combined organic solutions were dried over $MgSO_4$. Upon drying the organic phase became orange, presumably indicative of I_2 formation, and the solution was then washed with 10% aqueous sodium thiosulfate. The resultant light yellow organic phase was concentrated *in vacuo*. Flash chromatography (silica, 5% EtOAc/hexanes) afforded **24** (33.3 mg, 33% recovery) and **28** (35.1 mg, 32% yield), the latter a colorless oil: IR ($CHCl_3$) 3020 (m), 2980 (m), 2940 (m), 1685 (s), 1600 (m), 1490 (w), 1465 (m), 1450 (m), 1430 (w), 1385 (m), 1310 (w), 1300 (w), 1285 (w), 1250 (m), 1010 (w), 970 (m) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.77 (dd, J = 0.9, 7.7 Hz, 1 H), 7.43 (td, J = 1.4, 7.5 Hz, 1 H), 7.27 (td, J = 1.1, 7.5 Hz, 1 H), 7.20 (d, J = 7.7 Hz, 1 H), 6.43 (dd, J = 1.9, 11.8 Hz, 1 H), 6.03 (ddd, J = 4.2, 6.6, 11.7 Hz, 1 H), 3.23–3.16 (m, 1 H), 2.52–2.46 (m, 1 H), 2.41–2.34 (m, 1 H), 1.22 (d, J = 6.8 Hz, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 205.0 (+), 137.1 (+), 135.0 (+), 131.9 (−), 131.4 (−), 131.2 (−), 130.7 (−), 129.3 (−), 127.2 (−), 44.2 (−), 33.1 (+), 16.2 (−); high-resolution mass spectrum (CI, NH_3) m/z 173.0960 [$(M + H)^+$; calcd for $C_{12}H_{13}O$ 173.0966].

Alcohol 29.[42] A solution of benzosuberenone (**24**) (1.75 g, 11.0 mmol) in methanol (4.0 mL) was cooled to 0 °C, and solid $NaBH_4$ (0.400 g, 10.6 mmol) was added. The mixture was stirred for 30 min, warmed to room temperature, and cautiously quenched with 1 M aqueous HCl (ca. 2 mL). After dilution with H_2O and extraction with EtOAc (3 × 10 mL), the organic extracts were dried (Na_2SO_4), filtered, and concentrated *in vacuo*. Flash chromatography (silica, 20% EtOAc/hexanes) afforded **29** (1.76 g, 99% yield) as a colorless oil: IR ($CHCl_3$) 3610 (m), 3430 (br, m), 3080 (w), 3020 (s), 2940 (s), 2840 (w), 1490 (m), 1460 (s), 1430 (m), 1400 (m), 1300 (m), 1250 (br, m), 1115 (m), 1050 (s), 995 (m), 950 (m), 925 (m), 835 (w) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.42 (d, J = 7.2 Hz, 1 H), 7.25–7.18 (comp m, 3 H), 6.40 (dd, J = 1.5, 12.1 Hz, 1 H), 5.94 (dt, J = 4.1, 12.1 Hz, 1 H), 4.88 (dd, J = 6.2, 7.7 Hz, 1 H), 2.59–2.46 (comp m, 2 H), 2.23–2.08 (comp m, 2 H), 1.92 (d, J = 5.7 Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 142.6 (+), 134.1 (+), 132.4 (−), 131.4 (−), 129.4 (−), 127.4 (−), 126.8 (−), 126.6 (−), 73.3 (−), 34.0 (+), 26.8 (+); high-resolution mass spectrum (CI, NH_3) m/z 160.0860 (M^+; calcd for $C_{11}H_{12}O$ 160.0888).

Alcohol (±)-30. A solution of alcohol **29** (3.53 g, 22.0 mmol) in DME (44 mL) was treated with CH_2I_2 (3.5 mL, 44.0 mmol) and Et_2Zn (1.0 M in hexanes, 44.0 mL, 44.0 mmol) and heated at reflux for 6 h. After being cooled to room temperature the reaction was quenched by slow addition of sodium EDTA (50 mL, saturated aqueous solution). The resultant mixture was diluted with H_2O (25 mL), stirred vigorously for 30 min, and then extracted with EtOAc (3 × 100 mL). The combined extracts were washed with brine (50 mL) and adsorbed onto silica (ca. 20 g) *in vacuo*. Flash chromatography (silica, 20% EtOAc/hexanes) gave (±)-**30** (3.32 g, 86% yield) as a colorless solid which sublimed at 80 °C (atmospheric pressure): mp 104 °C; IR ($CHCl_3$) 3620 (m), 3450 (br, m), 3080 (m), 3020 (s), 2940 (s), 2880 (m), 1490 (m), 1455 (m), 1350 (m), 1330 (w), 1275 (m), 1250 (m), 1190 (m), 1100 (m), 1040 (s), 965 (w), 950 (w), 940 (w), 920 (w), 840 (m), 625 (m) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.43 (d, J = 7.6 Hz, 1 H), 7.29–7.24 (comp m, 2 H), 7.20 (td, J = 1.3, 7.4 Hz, 1 H), 5.55 (td, J = 2.7, 8.5 Hz, 1 H), 2.35–2.27 (m, 1 H), 2.06 (dt, J = 4.8, 13.4 Hz, 1 H), 1.98–1.94 (m, 1 H), 1.91 (br s, 1 H), 1.38–132 (m, 1 H), 1.05–0.97 (comp m, 2 H), 0.46–0.38 (m, 1 H), 0.37–0.28 (m, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 142.5 (+), 136.5 (+), 130.7 (−), 127.0 (−), 126.8 (−), 122.3 (−), 70.3 (−), 33.7 (+), 26.4 (+), 16.7 (−), 13.3 (+), 12.6 (−); high-resolution mass spectrum (CI, NH_3) m/z 174.1070 (M^+; calcd for $C_{12}H_{14}O$ 174.1045).

Anal. Calcd for $C_{12}H_{14}O$: C, 82.72; H, 8.09. Found: C, 82.42; H, 8.37.

(42) Alcohol **29** has been previously prepared in scalemic form by microbial oxidation and by enzymatic hydrolysis of the corresponding racemic acetate: (a) Boyd, D. R.; Dorrity, M. R. J.; Malone, J. F.; McMordie, R. A. S.; Sharma, N. D.; Dalton, H.; Williams, P. *J. Chem. Soc., Perkin Trans. 1* **1990**, 489. (b) Ito, S.; Kasai, M.; Ziffer, H.; Silverton, J. V. *Can. J. Chem.* **1987**, *65*, 574.

(43) The author has deposited atomic coordinates for (+)-**9**, **12**, **19**, **32**, **37–39**, and **44** 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.

Alcohol (+)-30. A solution of **53** (735 mg, 2.28 mmol) in MeOH (25 mL) was treated with sodium metal (0.53 mg, 2.28 mmol) at ambient temperature. After 1 h, the reaction mixture was quenched with 1 M HCl (2.5 mL) and concentrated *in vacuo*. Flash chromatography (silica, 20% EtOAc/hexanes) afforded (+)-**30** (330 mg, 83% yield) as a colorless oil: $[\alpha]^{24}_D$ +78.4° (*c* 2.09, $CHCl_3$).

Alcohol (−)-30. Via the procedure described above for (+)-**30**, methanolysis of **54** (780 mg, 2.42 mmol) furnished (−)-**30** (370 mg, 88% yield) as a colorless oil: $[\alpha]^{24}_D$ −78.0° (*c* 2.18, $CHCl_3$).

Alcohols 30 and 31. A solution of (±)-**23** (90.1 mg, 0.523 mmol) in methanol (2 mL) was cooled to 0 °C, and solid $NaBH_4$ (20.0 mg, 0.529 mmol) was added. After 30 min the reaction was warmed to room temperature and stirred for 1.5 h. The reaction mixture was then adsorbed onto silica (ca. 0.50 g) *in vacuo*. Flash chromatography (silica, 20% EtOAc/hexanes) provided a 5.7:1 (GC) mixture of **30** and **31** (75.2 mg, 83% yield) as a colorless solid. The diastereomers were inseparable by HPLC. However, where distinguishable, the data reported below reflect that derived from the minor isomer **31**.

31: IR ($CHCl_3$) 3620 (m), 3450 (br, m), 3080 (m), 3020 (m), 2950 (m), 2880 (m), 1490 (s), 1460 (s), 1400 (m), 1350 (m), 1330 (m), 1280 (m), 1240 (m), 1200 (m), 1110 (m), 1040 (s), 990 (m), 965 (m), 950 (m), 920 (m), 840 (m), 630 (m) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.42 (d, J = 7.5 Hz, 1 H), 7.29−7.18 (comp m, 5 H), 7.15 (apparent t, J = 7.5 Hz, 1 H), 7.02 (d, J = 7.4 Hz, 1 H), 5.54 (dd, J = 7.2, 10.0 Hz, 1 H), 4.85 (d, J = 6.0 Hz, 1 H), 2.34−2.26 (comp m, 2 H), 2.14−1.87 (comp m, 6 H), 1.37−1.31 (m, 1 H), 1.25−1.19 (m, 1 H), 1.13−1.06 (m, 1 H), 1.04−0.96 (comp m, 3 H), 0.59−0.54 (m, 1 H), 0.46−0.37 (comp m, 2 H), 0.31−0.27 (m, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 142.6 (+), 140.6 (+), 139.6 (+), 136.5 (+), 132.5 (−), 130.7 (−), 128.1 (−), 128.0 (−), 127.0 (−), 126.8 (−), 126.4 (−), 122.3 (−), 75.9 (−), 70.2 (−), 33.6 (+), 32.9 (+), 26.8 (+), 26.4 (+), 17.7 (−), 16.7 (−), 15.5 (+), 13.9 (−), 13.3 (+), 12.6 (−); high resolution mass spectrum (CI, NH_3) *m/z* 174.1040 (M^+; calcd for $C_{12}H_{14}O$ 174.1045).

***trans*-Dimethylcyclopropyl Ketone (±)-32.** A solution of (±)-**21** (74.1 mg, 0.370 mmol) in hexanes (4 mL) was degassed with argon for 15 min and then irradiated for 35 min. Following concentration *in vacuo*, HPLC (silica, 5% EtOAc/hexanes) afforded (±)-**32** (27.6 mg, 37% yield) and (±)-**21** (44.3 mg, 60% recovery). Photolyses on a 2.0-g scale worked equally well and after flash chromatography (silica, 5% EtOAc in hexanes) furnished (±)-**32** as a colorless solid: mp 55 °C (sublimed, 72 h, 40 °C, 30 mmHg); UV (MeOH) λ_{max} 212 (ϵ 15.521), 248 (5,452), 293 (1,374) nm; IR ($CHCl_3$) 3060 (w), 3000 (m), 2960 (s), 2860 (m), 1660 (s), 1590 (s), 1480 (w), 1450 (m), 1430 (w), 1380 (w), 1350 (w), 1310 (m), 1280 (m), 1250 (m), 1170 (m), 1150 (w), 1130 (w), 1090 (w), 1020 (m), 1000 (w), 960 (w), 930 (w), 915 (w), 870 (w) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.73 (d, J = 0.9, 7.5 Hz, 1 H), 7.33 (td, J = 1.3, 7.3 Hz, 1 H), 7.23 (comp m, 2 H), 3.13 (td, J = 8.9, 10.2 Hz, 1 H), 2.92 (ddd, J = 1.7, 5.9, 11.4 Hz, 1 H), 2.34 (m, 1 H), 1.66 (dddd, J = 8.3, 9.0, 7.5, 7.4 Hz, 1 H), 1.42 (d, J = 7.4 Hz, 1 H), 1.29 (s, 3 H), 1.17 (s, 3 H), 0.54 (ddd, J = 5.7, 7.4, 12.3 Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 205.5, 145.4, 143.4, 130.8, 129.2, 127.2, 126.2, 47.3, 37.3, 32.9, 31.6, 24.1, 22.8, 21.4; high-resolution mass spectrum (CI, NH_3) *m/z* 200.1194 (M^+; calcd for $C_{14}H_{16}O$ 200.1201).

Anal. Calcd for $C_{14}H_{16}O$: C, 83.96; H, 8.06. Found: C, 83.67; H, 8.12.

***trans*-Dimethylcyclopropyl Ketone (+)-32.** A solution of alcohol (+)-**49** (10.8 mg, 0.053 mmol) in acetone (0.5 mL) was treated with Jones reagent (2.61 M) at ambient temperature until a red color persisted. The reaction was stirred 15 min further, and the excess oxidant was quenched with 2-propanol. The green chromium salts were removed by filtration through Celite, and the filtrate was adsorbed onto silica (0.05 g) *in vacuo*. Flash chromatography (silica, 5% EtOAc/hexanes) then gave (+)-**32** (7.3 mg, 68% yield) as a colorless oil: $[\alpha]^{24}_D$ +102° (*c* 0.73, $CHCl_3$); 93% ee [determined via ^1H NMR analysis of the Mosher esters derived from alcohol (+)-**49**].

***trans*-Dimethylcyclopropyl Ketone (−)-32.** Following the procedure described above for (+)-**32**, Jones oxidation of alcohol (−)-**49** (11.0 mg, 0.054 mmol) followed by flash chromatography afforded (−)-**32** (6.5 mg, 60% yield) as a colorless oil: $[\alpha]^{24}_D$ −97° (*c* 0.65, $CHCl_3$).

Tricyclic Ketones 33 and 34 and Aldehyde 35. A solution of (±)-**21** (94.1 mg, 0.427 mmol) in hexanes (5 mL) was degassed with a slow stream of argon for 20 min and then irradiated for 3 h. Concentration *in vacuo* and HPLC (silica, 10% EtOAc/hexanes) furnished **32** (36.7 mg, 39% yield), **33** (8.6 mg, 9%), **34** (4.4 mg, 5%), **35** (2.3 mg, 2%), and **21** (37.2 mg, 40% recovery).

33: colorless oil; IR ($CHCl_3$) 3010 (m), 2960 (s), 2880 (m), 1710 (s), 1465 (m), 1415 (m), 1395 (m), 1375 (m), 1350 (w), 1300 (m), 1220 (br, m), 1150 (m), 1125 (m), 1040 (w), 1010 (w), 950 (w), 930 (w) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.37 (apparent t, J = 7.3 Hz, 1 H), 7.32 (td, J = 1.9, 6.9 Hz, 1 H), 7.27−7.22 (comp m, 2 H), 3.28 (s, 1 H), 2.93 (apparent t, J = 2.9 Hz, 1 H), 2.28−2.23 (m, 1 H), 2.16 (dd, J = 7.4, 17.1 Hz, 1 H), 2.08−2.01 (m, 1 H), 1.89 (ddd, J = 2.8, 9.6, 12.9 Hz, 1 H), 1.23 (s, 3 H), 1.07 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 210.6, 146.9, 142.1, 127.8, 126.8, 124.2, 124.1, 67.9, 50.0, 49.7, 33.3, 26.7, 25.5, 21.5; high-resolution mass spectrum (CI, NH_3) *m/z* 200.1180 (M^+; calcd for $C_{14}H_{16}O$ 200.1201).

34: colorless oil; IR ($CHCl_3$) 3080 (w), 3000 (m), 2960 (s), 2860 (m), 1745 (s), 1680 (m), 1600 (w), 1480 (m), 1460 (m), 1410 (m), 1390 (m), 1370 (m), 1300 (m), 1280 (m), 1250 (m), 1210 (m), 1160 (m), 1150 (m), 1020 (w), 960 (w), 940 (w), 910 (w), 890 (w), 830 (w) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.48 (d, J = 7.3 Hz, 1 H), 7.34 (dd, J = 1.0, 6.1 Hz, 1 H), 7.33−7.24 (comp m, 2 H), 3.89 (d, J = 7.0 Hz, 1 H), 2.85 (dt, J = 7.0, 10.7 Hz, 1 H), 2.39−2.32 (comp m, 2 H), 2.15−2.11 (m, 1 H), 1.60 (dt, J = 1.6, 10.7 Hz, 1 H), 1.46 (s, 3 H), 1.28 (s, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 217.4, 151.0, 136.9, 127.8, 126.9, 124.8, 122.8, 55.9, 53.3, 46.1, 39.6, 31.5, 23.9, 21.6; high-resolution mass spectrum (CI, NH_3) *m/z* 200.1175 (M^+; calcd for $C_{14}H_{16}O$ 200.1201).

35: colorless oil; IR ($CHCl_3$) 3060 (w), 3010 (w), 2960 (m), 2920 (m), 2860 (w), 2720 (w), 1730 (s), 1670 (m), 1610 (m), 1470 (s), 1450 (m), 1430 (w), 1410 (m), 1380 (m), 1360 (m), 1300 (w), 1280 (w), 1260 (m), 1210 (w), 1100 (m), 1010 (m) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 9.87 (apparent t, J = 1.3 Hz, 1 H), 7.29 (d, J = 7.3 Hz, 1 H), 7.24 (d, J = 7.2 Hz, 1 H), 7.19 (td, J = 1.0, 7.2 Hz, 1 H), 7.14 (td, J = 1.2, 7.3 Hz, 1 H), 6.31 (apparent t, J = 1.6 Hz, 1 H), 2.84 (ddd, J = 1.3, 7.2, 8.1 Hz, 2 H), 2.60 (td, J = 1.7, 7.8 Hz, 2 H), 1.25 (s, 6 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 201.8, 157.0, 153.5, 142.0, 126.5, 124.4, 122.7, 121.1, 120.3, 50.4, 48.1, 41.6, 24.1, 19.0; high-resolution mass spectrum (CI, NH_3) *m/z* 200.1182 (M^+; calcd for $C_{14}H_{16}O$ 200.1201).

***trans*-Dichlorocyclopropane 37.** A solution of ketone **22** (0.508 g, 2.11 mmol) in benzene (4 mL) and hexanes (10 mL) was degassed with argon for 10 min and then irradiated for 1 h; benzene was employed to enhance solubility. Concentration *in vacuo* and flash chromatography (silica, 5% EtOAc/hexanes) afforded **22** (0.321 g, 63% recovery) and **37** (0.145 g, 28% yield), the latter a colorless solid: mp 74−75 °C; UV (MeOH) λ_{max} 288 (ϵ 1,136), 248 (6,097), 210 (15,004) nm; IR ($CHCl_3$) 3080 (w), 3020 (m), 2980 (m), 2950 (m), 2880 (m), 1670 (s), 1600 (s), 1480 (m), 1460 (m), 1450 (m), 1440 (m), 1320 (m), 1290 (m), 1250 (s), 1215 (s), 1190 (s), 1175 (m), 1165 (m), 1120 (m), 1105 (m), 1060 (m), 1045 (m), 1030 (s), 990 (m), 920 (m), 890 (m), 850 (m) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.82 (d, J = 8.1 Hz, 1 H), 7.49−7.44 (comp m, 2 H), 7.36 (td, J = 1.6, 7.4 Hz, 1 H), 3.01 (td, J = 11.9, 9.2 Hz, 1 H), 2.98 (ddd, J = 1.6, 6.1, 11.9 Hz, 1 H), 2.59−2.52 (m, 1 H), 2.42 (d, J = 10.3 Hz, 1 H), 1.94−1.87 (m, 1 H), 1.53 (td, J = 4.6, 10.6 Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 202.7 (+), 143.5 (+), 138.4 (+), 131.5 (−), 130.0 (−), 127.8 (−), 126.8 (−), 68.6 (+), 45.9 (+), 41.9 (−), 37.0 (−), 25.5 (+); high-resolution mass spectrum (CI, NH_3) *m/z* 258.0460 [$(M + NH_4)^+$; calcd for $C_{12}H_{14}Cl_2NO$ 258.0452].

Anal. Calcd for $C_{12}H_{10}Cl_2O$: C, 59.78; H, 4.18. Found: C, 59.98; H, 4.27.

***trans*-Dichlorobenzocyclooctene 38.** A solution of cyclopropane **22** (17.1 mg, 0.071 mmol) in hexanes (1.0 mL) was degassed with a slow stream of argon for 5 min and then

irradiated for 6 h. Concentration *in vacuo* and flash chromatography (silica, 10% EtOAc/hexanes) gave **38** (2.8 mg, 16% yield), **22** (3.6 mg, 21% recovery), and an inseparable mixture of **37** and **39** (3.6 mg, 21%).

38: colorless solid; mp 186 °C; IR ($CHCl_3$) 3070 (w), 3010 (w), 2960 (w), 1680 (s), 1615 (m), 1595 (m), 1480 (w), 1450 (m), 1435 (m), 1330 (m), 1280 (m), 1250 (m), 1210 (m), 1190 (m), 1145 (m), 1125 (m), 1090 (w), 1030 (w), 980 (w), 910 (s), 870 (m), 820 (m), 620 (m) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.59 (d, J = 7.8 Hz, 1 H), 7.51 (apparent t, J = 7.5 Hz, 1 H), 7.41 (apparent t, J = 7.6 Hz, 1 H), 7.30 (d, J = 7.6 Hz, 1 H), 7.25 (s, 1 H), 4.87 (dd, J = 6.1, 10.4 Hz, 1 H), 2.89 (td, J = 1.5, 12.2 Hz, 1 H), 2.84–2.75 (m, 1 H), 2.66 (apparent t, J = 12.5 Hz, 1 H), 2.45 (dd, J = 6.5, 12.5 Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 204.6 (+), 145.5 (+), 145.1 (+), 135.7 (+), 131.8 (−), 129.6 (−), 128.9 (−), 127.3 (−), 127.1 (−), 61.9 (−), 44.4 (+), 18.7 (+); high resolution mass spectrum (CI, NH_3) m/z 240.0086 (M^+; calcd for $C_{12}H_{10}{}^{35}Cl_2O$ 240.0109).

Anal. Calcd for $C_{12}H_{10}Cl_2O$: C, 59.78; H, 4.18. Found: C, 59.48; H, 4.18.

***cis*-Dichlorobenzocyclooctene 39.** A solution of *trans*-benzocyclooctene **38** (20.1 mg, 0.083 mmol) in a mixture of benzene (2.5 mL) and hexanes (2.5 mL) was degassed for 15 min with a slow stream of argon and then irradiated for 2 h. Concentration *in vacuo* followed by preparative TLC (silica, 10% EtOAc/hexanes) afforded **39** (6.2 mg, 30% yield) as a colorless solid: mp 119–120 °C; IR ($CHCl_3$) 3070 (w), 3020 (w), 2940 (m), 2860 (w), 1680 (s), 1635 (m), 1600 (m), 1485 (m), 1450 (m), 1340 (m), 1320 (m), 1270 (m), 1250 (m), 1190 (m), 1165 (m), 1100 (m), 1030 (m), 990 (m), 935 (m), 895 (m), 870 (m), 850 (m), 820 (m), 655 (w), 610 (w), 580 (m) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.10 (d, J = 7.9 Hz, 1 H), 7.55 (td, J = 0.7, 7.3 Hz, 1 H), 7.44 (apparent t, J = 7.4 Hz, 1 H), 7.27 (d, J = 8.1 Hz, 1 H), 7.16 (s, 1 H), 4.88 (dd, J = 4.5, 13.1 Hz, 1 H), 2.24 (td, J = 3.9, 12.4 Hz, 1 H), 2.62–2.55 (comp m, 2 H), 2.47–2.40 (m, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 201.4, 136.0, 135.3, 133.7, 132.8, 131.4, 130.4, 129.9, 128.9, 55.5, 38.6, 38.3; high-resolution mass spectrum (CI, NH_3) m/z 240.0100 (M^+; calcd for $C_{12}H_{10}{}^{35}Cl_2O$ 240.0108).

***trans*-Dichlorobenzocyclooctene 41.** A solution of ketone **38** (34 mg, 0.14 mmol) in 1,2-dichlorobenzene (2 mL) was heated at 150 °C for 3 h. The solution was then subjected to flash chromatography (silica, 10% EtOAc/hexanes), affording **38** (15 mg, 44% recovery) and a 53:47 mixture (NMR) of **39** and **41** (10 mg, 29% yield). Further purification by HPLC (silica, 5% EtOAc/hexanes) provided pure **41** as a colorless oil: IR ($CHCl_3$) 2460 (w), 2420 (w), 1665 (s), 1590 (w), 1430 (w), 1320 (w), 910 (m) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.86 (s, 1 H), 7.60 (dd, J = 1.2, 7.7 Hz, 1 H), 7.52 (td, J = 1.3, 7.5 Hz, 1 H), 7.41 (apparent t, J = 7.5 Hz, 1 H), 7.33 (d, J = 7.5 Hz, 1 H), 4.72 (d, J = 4.3 Hz, 1 H), 3.25–3.18 (m, 1 H), 2.95 (td, J = 1.0, 12.3 Hz, 1 H), 2.60 (dd, J = 6.6, 14.9 Hz, 1 H), 2.35 (ddd, J = 1.1, 6.5, 12.5 Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 205.6, 144.5, 142.7, 136.8, 132.0, 129.7, 128.8, 127.7, 127.0, 60.5, 44.2, 39.1; high-resolution mass spectrum (CI, NH_3) m/z 258.0427 [$(M + NH_4)^+$; calcd for $C_{12}H_{14}Cl_2NO$ 258.0453].

Ketone (±)-44. Method A. A solution of ketone **37** (0.161 g, 0.669 mmol) and AIBN (10.1 mg, 0.060 mmol) in tri-*n*-butyltin hydride (2.0 mL, 7.43 mmol) was heated at 140 °C for 3 h. After being cooled to room temperature, the reaction mixture was poured into a 50 mL beaker and Jones reagent (2.19 M) was added until a red color persisted. Excess oxidant and acid were neutralized with 2-propanol and solid $NaHCO_3$, respectively. The mixture was then diluted with water (75 mL) and extracted with EtOAc (3 × 75 mL), and the combined organic solutions were dried (Na_2SO_4), filtered, and concentrated *in vacuo*. Flash chromatography (silica, 10% EtOAc/hexanes) afforded (±)-**44** (0.102 g, 88% yield). **Method B.** A solution of (±)-**23** (6.61 g, 38.4 mmol) and piperylene (13.0 g, 192 mmol) in hexanes (1.4 L) was passed through a Millipore membrane filter and then irradiated for 6 h. After concentration of the resulting milky white solution *in vacuo*, flash chromatography (silica, 2% EtOAc/hexanes) gave (±)-**44** (1.23 g, 19% yield) and (±)-**23** (5.11 g, 77% recovery).

(±)-**44**: colorless solid; mp 75–76 °C; UV (MeOH) λ_{max} 291 (ϵ 976), 248 (5,010), 210 (13,572) nm; IR ($CHCl_3$) 3070 (m), 3010 (m), 2980 (m), 2940 (m), 2880 (m), 1670 (s), 1605 (s), 1470 (m), 1460 (m), 1440 (m), 1350 (w), 1320 (s), 1290 (s), 1250 (s), 1180 (s), 1160 (m), 1130 (m), 1105 (m), 1080 (m), 1050 (m), 1030 (m), 1000 (w), 960 (m), 945 (m), 930 (m), 910 (m), 890 (m), 840 (m), 590 (m), 580 (m) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.63 (d, J = 7.5 Hz, 1 H), 7.27 (td, J = 1.2, 7.4 Hz, 1 H), 7.18 (dd, J = 5.1, 7.1 Hz, 2 H), 3.09 (dt, J = 8.4, 11.8 Hz, 1 H), 2.90–2.86 (m, 1 H), 2.42–2.35 (m, 1 H), 1.58–1.32 (comp m, 4 H), 0.55–0.47 (m, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 205.6 (+), 145.5 (+), 143.7 (+), 131.0 (−), 128.9 (−), 126.3 (−), 47.9 (+), 27.3 (+), 23.4 (−), 20.6 (−), 18.1 (+); high-resolution mass spectrum (CI, NH_3) m/z 173.0970 [$(M + H)^+$; calcd for $C_{12}H_{13}O$ 173.0966].

Ketone (+)-44. A solution of (+)-**55** (253 mg, 1.45 mmol) in acetone (2 mL) was titrated with Jones reagent (2.19 M) until a red color persisted for 2 min. The reaction mixture was then quenched with 2-propanol (ca. 1 mL) and diluted with H_2O (3 mL) and EtOAc (10 mL). The aqueous layer was extracted with EtOAc (3 × 10 mL) and the combined organic phases were dried ($MgSO_4$), filtered, and concentrated *in vacuo*. Flash chromatography (silica, 30% EtOAc/hexanes) furnished (+)-**44** (233 mg, 93% yield) as a colorless solid: $[\alpha]^{24}_D$ +375° (*c* 1.95, $CHCl_3$).

Ketone (−)-44. Following the procedure described above for (+)-**44**, Jones oxidation of (−)-**55** (226 mg, 1.30 mmol) and flash chromatography afforded (−)-**44** (212 mg, 95% yield) as a colorless solid: $[\alpha]^{24}_D$ −419° (*c* 2.19, $CHCl_3$).

Alcohols (±)-45 and (±)-46. A solution of (±)-**21** (0.208 g, 1.04 mmol) in benzene (5 mL) was cooled in an ice bath until the solvent began to freeze. The bath was then removed and DIBAL (1.0 M in hexanes, 1.55 mL) was added in one portion. After 5 min a 10% aqueous solution of Rochelle's salt (5 mL) was added and the resulting biphasic mixture stirred vigorously for 90 min. The aqueous layer was separated and extracted with Et_2O (3 × 10 mL), and the combined organic phases were dried (Na_2SO_4), filtered, and concentrated *in vacuo*. Flash chromatography (silica, 20% EtOAc/hexanes) gave an inseparable mixture (ca. 2:1 by GC) of diastereomers (±)-**45** and (±)-**46** (0.182 g, 88% yield) as a colorless solid: mp 93–96 °C; IR ($CHCl_3$) 3600 (m), 3420 (br, w), 3060 (w), 2990 (s), 2920 (s), 2830 (s), 1600 (w), 1480 (m), 1450 (s), 1380 (m), 1340 (w), 1270 (w), 1205 (m), 1130 (w), 1100 (m), 1030 (s), 1000 (m), 975 (m), 950 (m), 905 (s) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.42 (d, J = 7.4 Hz, 1 H), 7.20 (dd, J = 7.0, 14.3 Hz, 2 H), 7.13 (comp m, 3 H), 7.04 (d, J = 7.2 Hz, 1 H), 7.00 (d, J = 7.1 Hz, 1 H), 5.34 (br apparent t, J = 8.7 Hz, 1 H), 4.72 (d, J = 5.3 Hz, 1 H), 2.76 (br s, 2 H), 2.27–2.19 (m, 1 H), 2.03–1.91 (comp m, 2 H), 1.82 (d, J = 8.5 Hz, 1 H), 1.78–1.70 (comp m, 2 H), 1.65 (d, J = 8.6 Hz, 1 H), 1.39–1.34 (m, 1 H), 1.20 (s, 3 H), 1.18 (s, 3 H), 1.05–1.00 (m, 1 H), 0.92 (s, 3 H), 0.90 (s, 3 H), 0.82–0.64 (comp m, 2 H), 0.64–0.57 (m, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.4 (+), 141.4 (+), 137.1 (+), 134.1 (+), 132.8 (−), 130.8 (−), 128.6 (−), 127.5 (−), 126.4 (−), 126.3 (−), 126.0 (−), 123.0 (−), 75.8 (−), 69.8 (−), 33.2 (+), 32.7 (+), 28.7 (−), 28.6 (−), 28.5 (−), 27.8 (−), 25.9 (−), 25.0 (−), 21.6 (+), 20.7 (+), 20.5 (+), 19.7 (+), 16.8 (+); high-resolution mass spectrum (CI, NH_3) m/z 202.1331 (M^+; calcd for $C_{14}H_{18}O$ 202.1358).

Alcohol (−)-45. Ester **48** (38.2 mg, 0.109 mmol) was dissolved in MeOH (6 mL), solid NaOMe (60.0 mg, 1.11 mmol) was added, and the reaction was stirred at room temperature for 12 h. Silica gel (ca. 0.25 g) was then added and the mixture concentrated *in vacuo*. Flash chromatography of the resultant powder (silica, 20% EtOAc/hexanes) provided (−)-**45** (20.2 mg, 91% yield) as a colorless oil: $[\alpha]^{25}_D$ −34° (*c* 2.0, $CHCl_3$); ^1H NMR (250 MHz, $CDCl_3$) δ 7.45 (d, J = 7.4 Hz, 1 H), 7.27 (apparent t, J = 7.3 Hz, 1 H), 7.19 (apparent t, J = 7.3 Hz, 1 H), 7.08 (d, J = 7.3 Hz, 1 H), 5.45 (br apparent t, J = 8.5 Hz, 1 H), 2.36–2.26 (m, 1 H), 1.92 (br s, 1 H), 1.83–1.75 (m, 1 H), 1.72 (d, J = 8.6 Hz, 1 H), 1.48–1.36 (m, 1 H), 1.20 (s, 3 H), 0.92 (s, 3 H), 0.89–0.81 (m, 1 H), 0.63 (ddd, J = 6.6, 12.3, 26.1 Hz, 1 H); ^{13}C NMR (62.8 MHz, $CDCl_3$) δ 143.4, 134.3, 131.1, 126.6, 122.9, 70.1, 33.4, 28.8, 27.8, 25.1, 20.6, 19.9, 16.9.

Alcohol (+)-45. Following the procedure described above for (−)-**45**, methanolysis of ester **47** (51.7 mg, 0.147 mmol)

followed by flash chromatography afforded (+)-**45** (29.3 mg, 98% yield) as a colorless oil: $[\alpha]^{24}_D$ +35° (*c* 2.2, $CHCl_3$).

Esters 47 and 48. A solution of (*S*)-(+)-*O*-methylmandelic acid (0.367 g, 2.21 mmol) in neat thionyl chloride (6 mL) was heated at reflux for 45 min, cooled, and concentrated *in vacuo*. The resultant oil was added to a solution of (±)-**45** and (±)-**46** (0.172 g, 0.849 mmol), pyridine (2.0 mL), and DMAP (ca. 1.0 mg) in CH_2Cl_2 (4 mL). The mixture was stirred at room temperature for 12 h and then diluted with cold 1 M HCl (5 mL). The biphasic mixture was separated and the organic phase washed with 10% aqueous $NaHCO_3$ (5 mL). The latter aqueous layer was extracted with CH_2Cl_2 (3 × 10 mL), and the combined organic solutions were dried (Na_2SO_4), filtered, and concentrated *in vacuo*. Two purifications by flash chromatography (silica, 5% EtOAc/hexanes, then 2% EtOAc/hexanes) were required to obtain analytically pure **47** (51.7 mg, 17% yield) and **48** (38.2 mg, 13%).

47: colorless oil; IR ($CHCl_3$) 3060 (m), 2990 (m), 2920 (s), 2860 (m), 2815 (w), 1750 (s), 1600 (w), 1490 (w), 1460 (m), 1380 (m), 1350 (m), 1330 (m), 1320 (m), 1300 (m), 1260 (m), 1180 (s), 1110 (s), 1070 (w), 1000 (s), 970 (w), 710 (m), 690 (m) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.52 (d, J = 7.0 Hz, 2 H), 7.39–7.32 (comp m, 3 H), 7.18 (d, J = 4.4 Hz, 3 H), 7.09 (m, 1 H), 6.47 (dd, J = 7.3, 10.1 Hz, 1 H), 4.9 (s, 1 H), 3.47 (s, 3 H), 2.19–2.12 (m, 1 H), 1.80 (d, J = 8.7 Hz, 1 H), 1.72 (dt, J = 4.9, 14.3 Hz, 1 H), 1.37–1.32 (m, 1 H), 1.19 (s, 3 H), 0.92–0.85 (m, 1 H), 0.89 (s, 3 H), 0.61 (ddd, J = 6.6, 12.4, 26.6 Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.7 (+), 138.8 (+), 136.4 (+), 134.3 (+), 131.4 (−), 128.6 (−), 128.5 (−), 127.0 (−), 126.5 (−), 122.9 (−), 82.7 (−), 73.2 (−), 57.5 (−), 29.7 (+), 28.7 (−), 27.8 (−), 24.7 (−), 20.1 (+), 20.0 (+), 16.8 (−); high-resolution mass spectrum (CI, isobutane) *m/z* 351.1928 [(M + H)$^+$; calcd for $C_{23}H_{27}O_3$ 351.1960].

48: colorless oil; IR ($CHCl_3$) 3060 (w), 2990 (s), 2930 (s), 2860 (m), 2830 (m), 1740 (s), 1600 (w), 1490 (m), 1460 (s), 1380 (s), 1350 (m), 1330 (m), 1300 (m), 1250 (s), 1200 (s), 1100 (s), 1070 (m), 1010 (s), 970 (m), 720 (m), 690 (m) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.49 (dd, J = 1.8, 7.8 Hz, 2 H), 7.40–7.33 (comp m, 3 H), 7.10 (td, J = 0.9, 7.4 Hz, 1 H), 7.03 (d, J = 7.5 Hz, 1 H), 6.94 (apparent t, J = 7.5 Hz, 1 H), 6.64 (d, J = 7.7 Hz, 1 H), 6.48 (dd, J = 7.3, 10.2 Hz, 1 H), 4.88 (s, 1 H), 3.45 (s, 3 H), 2.31–2.23 (m, 1 H), 1.79 (d, J = 9.0 Hz, 1 H), 1.79–1.75 (m, 1 H), 1.54–1.49 (m, 1 H), 1.18 (s, 3 H), 0.93–0.88 (m, 1 H), 0.89 (s, 3 H), 0.67–0.58 (m, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.5 (+), 138.8 (+), 136.4 (+), 134.2 (+), 131.2 (−), 128.8 (−), 128.6 (−), 127.5 (−), 126.8 (−), 124.4 (−), 122.8 (−), 82.9 (−), 72.9 (−), 57.3 (−), 30.2 (+), 28.7 (−), 27.8 (−), 24.7 (−), 20.2 (+), 20.0 (+), 16.9 (−); high-resolution mass spectrum (CI, isobutane) *m/z* 351.1948 [(M + H)$^+$; calcd for $C_{23}H_{27}O_3$ 351.1960].

NOE studies: irradiation of H_a in **47** resulted in a 14.3% enhancement of H_b, whereas irradiation of H_a in **48** gave a 10% enhancement of H_b.

Alcohols (±)-49 and (±)-50. A solution of (±)-**32** (0.145 g, 0.729 mmol) in methanol (6 mL) was cooled to 0 °C, and $NaBH_4$ (28.2 mg, 0.745 mmol) was added in one portion. The reaction was stirred for 20 min, allowed to warm to room temperature, and quenched with H_2O (50 μL). The resultant mixture was adsorbed onto silica gel (ca. 0.60 g) *in vacuo*, and flash chromatography (silica, 7.5% EtOAc/hexanes) afforded (±)-**49** (0.101 g, 68% yield) and (±)-**50** (37.9 mg, 26%).

(±)-**49**: colorless solid; sublimes 120 °C (atmospheric pressure); IR (KBr) 3280 (br, s), 2980 (m), 2940 (s), 2880 (m), 1600 (w), 1460 (m), 1450 (m), 1340 (w), 1160 (w), 1100 (w), 1040 (s), 1000 (w), 890 (w), 750 (s), 730 (m) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.54 (d, J = 7.6 Hz, 1 H), 7.16 (td, J = 1.2, 7.4 Hz, 1 H), 7.07 (comp m, 2 H), 5.14 (d, J = 10.5 Hz, 1 H), 2.28 (comp m, 2 H), 1.92 (br s, 1 H), 1.86–1.79 (m, 1 H), 1.62–1.53 (m, 1 H), 1.32 (s, 3 H), 1.22 (s, 3 H), 1.07 (d, J = 7.4 Hz, 1 H), 0.0–(−0.04) (m, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 148.7 (+), 141.8 (+), 126.1 (−), 125.0 (−), 124.4 (−), 122.9 (−), 73.5 (−), 37.5 (+), 36.3 (−), 34.0 (−), 30.3 (+), 28.2 (+), 23.6 (−), 22.1 (−); high-resolution mass spectrum (CI, NH_3) *m/z* 202.1370 (M$^+$; calcd for $C_{14}H_{18}O$ 202.1358).

(±)-**50**: colorless solid; mp 80–82 °C; IR ($CHCl_3$) 3600 (m), 3410 (br, m), 3060 (w), 3020 (m), 2920 (s), 2860 (s), 1600 (m), 1490 (m), 1460 (m), 1430 (m), 1380 (m), 1350 (w), 1320 (m), 1270 (w), 1240 (m), 1210 (m), 1170 (m), 1140 (w), 1110 (m), 1060 (s), 1050 (m), 1030 (m), 1015 (m), 1000 (m), 990 (m), 940 (s), 850 (w) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.14 (d, J = 7.4 Hz, 1 H), 7.12–7.00 (comp m, 3 H), 4.94 (d, J = 5.1 Hz, 1 H), 2.37–2.33 (m, 1 H), 2.17–2.14 (m, 1 H), 1.88–1.80 (comp m, 4 H), 1.29 (s, 3 H), 1.24 (s, 3 H), 0.10–0.06 (m, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 146.2 (+), 144.8 (+), 129.9 (−), 127.7 (−), 124.7 (−), 124.3 (−), 78.1 (−), 36.8 (−), 33.7 (+), 33.0 (−), 29.3 (+), 26.4 (+), 23.5 (−), 22.1 (−); high-resolution mass spectrum (CI, NH_3) *m/z* 202.1380 (M$^+$; calcd for $C_{14}H_{18}O$ 202.1358).

NOE studies: irradiation of H_a in **49** resulted in an 8% enhancement of H_b, and irradiation of H_b gave in an 8% enhancement of H_a. In contrast, the only effect of irradiation of H_a in **50** was a 10% enhancement of H_d.

Alcohol (−)-49. Ester **51** (28.5 mg, 0.081 mmol) was dissolved in methanol (1.5 mL) and solid NaOMe (20.1 mg, 0.370 mmol) was added. The resultant solution was stirred at room temperature for 4 h and then adsorbed onto silica gel (ca. 0.150 g) *in vacuo*. Flash chromatography (silica, 10% EtOAc/hexanes) afforded (−)-**49** (14.5 mg, 89% yield): $[\alpha]^{25}_D$ −89° (*c* 0.38, $CHCl_3$).

Alcohol (+)-49. Following the procedure described above for (−)-**49**, methanolysis of ester (−)-**52** (29.4 mg, 0.084 mmol) and flash chromatography gave (+)-**49** (12.8 mg, 76% yield): $[\alpha]^{25}_D$ +93° (*c* 0.67, $CHCl_3$).

Esters 51 and 52. A solution of (±)-**49** (44.1 mg, 0.218 mmol), (*S*)-(+)-*O*-methylmandelic acid (44.2 mg, 0.266 mmol), and DMAP (5.0 mg, 0.041 mmol) in CH_2Cl_2 (4.0 mL) was treated with DCC (54.1 mg, 0.262 mmol). A white precipitate formed almost immediately. The reaction mixture was stirred at room temperature for 1 h and then filtered through a pad of sand. The filtrate was adsorbed onto silica (ca. 0.20 g) *in vacuo* and subjected to flash chromatography (silica, 5% EtOAc/hexanes). Further purification via HPLC (silica, 5% EtOAc/hexanes) then afforded **51** (36.2 mg, 48% yield) and **52** (36.1 mg, 48%).

51: colorless oil; $[\alpha]^{25}_D$ −31° (*c* 0.78, $CHCl_3$); IR (CCl_4) 3080 (w), 3040 (w), 2980 (m), 2940 (s), 2870 (m), 2840 (w), 1750 (s), 1610 (w), 1495 (w), 1460 (m), 1370 (w), 1320 (w), 1280 (m), 1260 (m), 1200 (s), 1180 (s), 1120 (s), 1070 (w), 1000 (m), 920 (w) cm^{-1}; ^1H NMR (500 MHz, C_6D_6) δ 7.62 (d, J = 7.4 Hz, 2 H), 7.50 (d, J = 7.6 Hz, 1 H), 7.15 (apparent t, J = 7.8 Hz, 2 H), 7.09–7.03 (comp m, 2 H), 7.03–7.01 (comp m, 2 H), 6.43 (d, J = 10.6 Hz, 1 H), 4.83 (br s, 1 H), 3.25 (s, 3 H), 1.92–1.90 (m, 1 H), 1.80–1.71 (comp m, 2 H), 1.14 (s, 3 H), 1.17–1.08 (m, 1 H), 0.93 (s, 3 H), 0.89 (d, J = 7.5 Hz, 1 H), 0.14 (br s, 1 H); ^{13}C NMR (125 MHz, C_6D_6) δ 169.4, 145.0, 142.3, 137.5, 128.7, 128.6, 128.3, 127.5, 126.9, 125.5, 123.9, 83.3, 75.9, 57.3, 36.4, 34.6, 33.9, 30.5, 27.4, 23.5, 21.8; high-resolution mass spectrum (CI, NH_3) *m/z* 368.2250 [(M + NH_4)$^+$; calcd for $C_{23}H_{30}NO_3$ 368.2226].

52: colorless oil; $[\alpha]^{25}_D$ +107° (*c* 0.68, $CHCl_3$); IR (CCl_4) 3080 (w), 3040 (w), 2980 (m), 2940 (s), 2870 (m), 2830 (w), 1755 (s), 1740 (s), 1610 (w), 1490 (w), 1460 (m), 1370 (m), 1320 (m), 1280 (m), 1260 (m), 1200 (s), 1080 (s), 1020 (s), 1000 (s), 920 (w) cm^{-1}; ^1H NMR (500 MHz, C_6D_6) δ 7.59 (d, J = 7.7 Hz, 2 H), 7.28 (dd, J = 4.3, 4.9 Hz, 1 H), 7.15–7.12 (comp m, 2 H), 7.09–7.05 (m, 1 H), 7.00–6.95 (comp m, 3 H), 6.46 (dd, J = 1.8, 10.8 Hz, 1 H), 4.82 (s, 1 H), 3.23 (s, 3 H), 2.08–2.04 (m, 1 H), 1.93–1.89 (m, 1 H), 1.83–1.76 (m, 1 H), 1.27–1.15 (m, 1 H), 1.14 (s, 3 H), 0.94 (s, 3 H), 0.90 (d, J = 7.4 Hz, 1 H), 0.16 (br s, 1 H); ^{13}C NMR (125 MHz, C_6D_6) δ 169.3, 145.1, 142.1, 137.4, 128.8, 128.7, 128.3, 126.7, 125.4, 123.6, 83.7, 75.7, 57.1, 36.4, 34.9, 34.0, 30.5, 27.8, 23.6, 21.9; high-resolution mass spectrum (CI, NH_3) *m/z* 368.2220 [(M + NH_4)$^+$; calcd for $C_{23}H_{30}NO_3$ 368.2226].

Esters 53 and 54. A solution of alcohol (+)-**30** (1.00 g, 5.74 mmol) in CH_2Cl_2 (100 mL) was treated consecutively with DMAP (35 mg, 0.29 mmol), (*S*)-(+)-α-methoxyphenylacetic acid (1.15 g, 6.89 mmol), and 1,3-dicyclohexylcarbodiimide (DCC) (1.42 g, 6.89 mmol). The resultant mixture was stirred for 15 min and concentrated *in vacuo*. Flash chromatography (silica,

5% EtOAc/hexanes) followed by HPLC (silica, 10% EtOAc/hexanes) furnished **53** (680 mg, 37% yield) and **54** (605 mg, 33%).

53: colorless solid; mp 72–73 °C; IR ($CHCl_3$) 3010 (w), 2940 (w), 1745 (s), 1475 (w), 1450 (w), 1260 (m), 1180 (s), 1115 (s), 1005 (s) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.65 (d, J = 7.5 Hz, 2 H), 7.37 (d, J = 7.5 Hz, 1 H), 7.19–7.08 (m, 6 H), 6.67 (dd, J = 7.3, 10.1 Hz, 1 H), 4.88 (s, 1 H), 3.28 (s, 3 H), 2.10–2.02 (m, 1 H), 1.71–1.65 (m, 2 H), 1.30–1.24 (m, 1 H), 0.72–0.68 (m, 1 H), 0.59–0.52 (m, 1 H), 0.26–0.17 (m, 1 H), 0.07 (dd, J = 4.6, 9.2 Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.6, 137.9, 136.3, 130.8, 128.5, 128.4, 127.4, 126.9, 126.7, 122.2, 82.7, 73.1, 57.4, 29.8, 25.7, 16.6, 13.3, 12.2; high resolution mass spectrum (CI, NH_3) m/z 340.1885 [$(M + NH_4)^+$; calcd for $C_{21}H_{26}NO_3$ 340.1912].

54: colorless oil; IR ($CHCl_3$) 3010 (w), 2940 (w), 1750 (s), 1475 (w), 1450 (w), 1260 (m), 1180 (s), 1115 (s), 1005 (m) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.59 (d, J = 7.0 Hz, 2 H), 7.17–7.01 (m, 7 H), 6.72 (dd, J = 7.3, 10.2 Hz, 1 H), 4.84 (s, 1 H), 3.27 (s, 3 H), 2.11–2.19 (m, 1 H), 1.70–1.76 (m, 2 H), 1.43–1.37 (m, 1 H), 0.73–0.69 (m, 1 H), 0.63–0.58 (m, 1 H), 0.30–0.21 (m, 1 H), 0.08 (dd, J = 4.6, 9.2 Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.5, 137.8, 136.3, 136.2, 130.7, 128.7, 128.6, 127.4, 127.2, 126.5, 122.0, 82.7, 72.9, 57.2, 30.3, 25.7, 16.6, 13.3, 12.2; high-resolution mass spectrum (CI, NH_3) m/z 340.1903 [$(M + NH_4)^+$; calcd for $C_{21}H_{26}NO_3$ 340.1912].

Alcohols 55 and 56. A solution of ketone **44** (1.20 g, 6.97 mmol) in 2-propanol (25 mL) was treated with $NaBH_4$ (265 mg, 6.7 mmol). After 3 h, the reaction mixture was quenched with 1 M aqueous HCl (10 mL) and concentrated *in vacuo* to a volume of ca. 10 mL. The mixture was diluted with EtOAc (100 mL) and washed with H_2O (3 × 100 mL). The organic phase was dried ($MgSO_4$), filtered, and concentrated *in vacuo*, affording a white powder. Flash chromatography (silica, 15% EtOAc/hexanes) provided **55** (920 mg, 76% yield) and **56** (185 mg, 15%).

55: colorless solid; mp 127–128 °C; IR ($CHCl_3$) 3600 (m), 3020 (br, m), 3000 (m), 2930 (s), 2860 (m), 1600 (w), 1450 (m), 1105 (m), 1030 (s), 960 (w), 860 (w) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.55 (d, J = 7.0 Hz, 1 H), 7.18 (t, J = 7.6 Hz, 1 H), 7.11 (t, J = 7.1 Hz, 1 H), 6.97 (d, J = 7.1 Hz, 1 H), 5.27 (d, J = 10.7 Hz, 1 H), 2.37–2.41 (m, 1 H), 2.33–2.29 (m, 1 H), 1.87–1.84 (m, 1 H), 1.51 (ddd, J = 4.3, 12.1, 24.4 Hz, 1 H), 1.46 (dd, J = 1.6, 8.2 Hz, 1 H), 1.23 (apparent t, J = 7.6 Hz, 2 H), 0.10-(−0.14) (m, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 148.7, 142.2, 126.3, 125.1, 123.9, 121.7, 73.4, 38.2, 31.3, 22.8, 22.2, 15.2; high-resolution mass spectrum (CI, NH_3) m/z 174.1073 (M^+; calcd for $C_{12}H_{14}O$ 174.1045).

Anal. Calcd for $C_{12}H_{14}O$: C, 82.72; H, 8.10. Found, C, 82.45; H, 8.05.

56: colorless solid; mp 84–85 °C; IR ($CHCl_3$) 3600 (s), 3020 (br, m), 3000 (m), 2930 (s), 2860 (s), 1600 (w), 1450 (m), 1260 (m), 1030 (m), 975 (m), 920 (m) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.24–7.11 (m, 2 H), 7.0 (apparent t, J = 7.4 Hz, 2 H), 4.95 (dd, J = 1.7, 5.2 Hz, 1 H), 2.37–2.32 (m, 1 H), 2.27–2.23 (br s, 2 H), 2.04 (dd, J = 7.7, 15.3 Hz, 1 H), 1.87–1.81 (m, 1 H), 1.75 (td, J = 3.1, 11.4 Hz, 1 H), 1.37 (td, J = 5.3, 8.0 Hz, 1 H), 1.17 (td, J = 5.2, 7.7 Hz, 1 H), 0.05-(−0.03) (m, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 145.9, 145.5, 129.4, 128.0, 124.7, 122.8, 77.9, 34.1, 29.2, 23.0, 20.9, 14.3; high-resolution mass spectrum (CI, NH_3) m/z 192.1391 [$(M + NH_4)^+$; calcd for $C_{12}H_{18}NO$ 192.1388].

Anal. Calcd for $C_{12}H_{14}O$: C, 82.72; H, 8.10. Found: C, 82.47; H, 8.00.

Alcohol (−)-55. A solution of **57** (480 mg, 1.49 mmol) in MeOH (25 mL) was treated with sodium metal (34.3 mg, 1.49 mmol) at ambient temperature. After 1 h, the reaction mixture was quenched with 1 M HCl (2.5 mL) and concentrated *in vacuo*. Flash chromatography (silica, 20% EtOAc/hexanes) afforded (−)-**55** (252 mg, 97% yield) as a colorless solid: $[\alpha]^{24}_D$ −195° (*c* 2.00, $CHCl_3$).

Alcohol (+)-55. A solution of **58** (610 mg, 1.89 mmol) in MeOH (25 mL) was treated with sodium metal (43.5 mg, 1.89 mmol) at ambient temperature. After 1 h, the reaction mixture was quenched with 1 M HCl (2.5 mL) and concentrated *in vacuo*. Flash chromatography (silica, 20% EtOAc/hexanes) afforded (+)-**55** (293 mg, 89% yield) as a colorless solid: $[\alpha]^{24}_D$ +169° (*c* 2.02, $CHCl_3$).

Esters 57 and 58. A solution of alcohol (±)-**55** (750 mg, 4.31 mmol) in CH_2Cl_2 (25 mL) was treated consecutively with DMAP (27 mg, 0.22 mmol), (*S*)-(+)-α-methoxyphenylacetic acid (860 mg, 5.17 mmol), and 1,3-dicyclohexylcarbodiimide (1.07 g, 5.17 mmol). The mixture was stirred for 15 min and then concentrated *in vacuo*. Following initial flash chromatography (silica, 5% ether/petroleum ether), both esters were repurified by HPLC (silica, 10% EtOAc/hexanes) to provide **57** (530 mg, 38% yield) and **58** (615 mg, 45%).

57: colorless solid; mp 89–90 °C; IR ($CHCl_3$) 3000 (w), 2940 (m), 1745 (s), 1455 (w), 1360 (w), 1180 (s), 1110 (s) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.64 (d, J = 7.5 Hz, 2 H), 7.49 (d, J = 7.6 Hz, 1 H), 7.19–7.16 (m, 2 H), 7.11–7.06 (m, 2 H), 7.02 (t, J = 7.1 Hz, 1 H), 6.90 (d, J = 7.1 Hz, 1 H), 6.48 (d, J = 9.4 Hz, 1 H), 4.87 (s, 1 H), 3.28 (s, 3 H), 1.92–1.84 (m, 2 H), 1.67 (ddd, J = 4.1, 11.9, 24.3 Hz, 1 H), 1.22–1.18 (m, 1 H), 0.98 (ddd, J = 4.0, 11.7, 19.7 Hz, 1 H), 0.93 (dd, J = 7.1, 14.6 Hz, 1 H), 0.86 (td, J = 5.3, 7.8 Hz, 1 H), −0.35 (br s, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.3, 144.2, 142.2, 136.3, 128.6, 128.5, 126.9, 126.8, 125.1, 122.2, 82.6, 75.6, 57.4, 34.6, 30.4, 22.7, 21.9, 15.4; high-resolution mass spectrum (CI, NH_3) m/z 340.1941 [$(M + NH_4)^+$; calcd for $C_{21}H_{26}NO_3$ 340.1912].

58: colorless oil; IR ($CHCl_3$) 3000 (w), 2940 (w), 1745 (s), 1455 (w), 1180 (s), 1110 (s) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.60 (d, J = 7.1 Hz, 2 H), 7.21–7.09 (m, 4 H), 6.99–6.93 (m, 2 H), 6.87 (dd, J = 1.4, 6.6 Hz, 1 H), 6.50 (dd, J = 1.6, 11.0 Hz, 1 H), 4.84 (s, 1 H), 3.26 (s, 3 H), 2.07–2.04 (m, 1 H), 1.99–1.95 (m, 1 H), 1.76 (ddd, J = 4.2, 12.2, 24.6 Hz, 1 H), 1.23–1.19 (m, 1 H), 1.09 (ddd, J = 4.2, 12.1, 24.3 Hz, 1 H), 0.97–0.93 (m, 1 H), 0.90–0.84 (m, 1 H), −0.36 (br s, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.2, 144.4, 142.0, 136.3, 128.8, 128.7, 127.5, 126.6, 124.9, 123.9, 121.8, 82.9, 75.4, 57.3, 35.2, 30.9, 22.9, 22.1, 15.4; high-resolution mass spectrum (CI, NH_3) m/z 340.1889 [$(M + NH_4)^+$; calcd for $C_{21}H_{26}NO_3$ 340.1912].

Acknowledgment. We are pleased to acknowledge the support of this investigation by the National Institutes of Health (National Cancer Institute) through grant CA22807 to A.B.S. and a Postdoctoral Fellowship (CA08877) to T.P.K. The authors wish to thank Dr. Paul A. Sprengeler for helpful suggestions and critical comments. In addition, we thank Drs. George T. Furst and Patrick J. Carroll and Mr. John Dykins of the University of Pennsylvania Spectroscopic Service Centers for assistance in securing and interpreting high-field NMR spectra, X-ray crystal structures, and mass spectra.

Registry nos. provided by the author: (+)-**3**, 101836-56-0; (−)-**4**, 120666-82-2; (+)-**9**, 105990-58-7; (+)-**10**, 120666-83-3; **11**, 120666-84-4; **12**, 120666-85-5; (+)-**21**, 120666-81-1; (−)-**21**, 120710-33-0; (±)-**21**, 120710-31-8; (+)-**32**, 120710-35-2; (−)-**32**, 120710-34-1; (±)-**32**, 120710-32-9; **34**, 120666-86-6; **35**, 120666-87-7.